

Clin-IQ Process Director/Mentor Handbook

A Guideline

by

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Supported by grant number NIGMS U54GM104938, NIGMS/NIH
OKLAHOMA SHARED CLINICAL & TRANSLATIONAL RESOURCES
OKLAHOMA CLINICAL and TRANSLATIONAL SCIENCES INSTITUTE

Clin-IQ Quick Start

1. **WHAT** is Clin-IQ?

A scholarly activity process that can be adapted and implemented with learners at many levels of clinical education training.

2. **WHY** do it?

- Meets all ACGME scholarly activity requirements, and those of many other clinical disciplines.
- Increases scholarly activities and productivity for faculty and trainees.
- No IRB.
- Creates a clinical learning community between disciplines and specialties, in academic and community settings across Oklahoma and beyond state borders.
- Involves all members of learning community in translating clinical research into clinical practice to improve overall health.

3. **WHO** participates in Clin-IQ? (pg 6)

- 1) academic faculty,
- 2) community-based faculty,
- 3) trainees at all levels of clinical education, and
- 4) practicing community clinicians of all disciplines and specialties.

4. **HOW** does it work? Steps to Implementing Clin-IQ (pg 6-13)

- 1) Identify a Clin-IQ Champion (pg 5)
- 2) START SMALL
- 3) Develop relationships with medical library reference staff (pg 5)
- 4) Begin with a well-built clinical PICO question (pg 11, 20).



CLIN-IQ PROCESS

DIRECTOR/MENTOR HANDBOOK



The purpose of the Oklahoma Shared Clinical & Translational Resource (OSCTR) is to facilitate the sharing of research resources statewide and beyond the borders of Oklahoma with the overall goal of improving health. Oklahoma Clinical and Translational Sciences Institute is the administrative arm of the OSCTR responsible for the day-to-day operations of the many components that make up the OSCTR.

The Clin-IQ Project is one of the OSCTR's translational research resources. As part of the Community Engagement Component of the OSCTR, Clin-IQ creates a learning community among private and academic clinicians, resident and other clinical trainees and academic faculty.

In brief, the Clin-IQ process can assist clinical training programs in:

- Meeting the many prescribed responsibilities for clinical training specified by certifying agencies.
- Increasing program and faculty scholarly output without placing untoward time constraints.

This handbook is directed toward those members of clinical training programs responsible for overseeing and/or enhancing scholarly activities within the program. The method described here has been tested over time and found to:

- Be acceptable to trainees and faculty.
- Encourage trainee involvement in scholarly activities and research.
- Increase faculty scholarly productivity.
- Be compatible with the structure of clinical training programs.
- Be adaptable to meet specific program needs.
- Facilitate connections between community –based clinicians and academia.

A detailed overview of the entire Clin-IQ Process followed by a flexible Clin-IQ Policy and Procedures Guide make up the main content of this Director/Mentor Handbook. This Handbook is intended to serve as a guide and can be tailored to fit each program's individual curricular structure and needs.

Attachments contain examples of materials, which can be also be adapted to meet your program needs including a step-by-step workbook for generating a Clin-IQ and materials to assist in preparation of the Clin-IQ from question to publication.

Our Clin-IQ program uses didactics as routine part of our Clin-IQ process to teach such skills as evaluating evidence from the medical literature and understanding statistics. Slides from those didactics are available upon request. Additionally, the OSCTR makes it possible for us to come to your program and help you however we can. Please contact us if there is any way we can assist you as you implement Clin-IQ. Thank you for the opportunity to share this scholarly research process with you.

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Acknowledgment

We owe a great debt to Cheryl B. Aspy, Ph.D., Professor Emeritus, Department of Family & Preventive Medicine, University of Oklahoma Health Sciences Center, for her assistance drafting this document.

WHAT CLIN-IQ OFFERS:



Clin-IQ Process Overview

CLIN-IQ (Clinical Inquiries) is a process that makes it both possible and beneficial for clinical trainees, faculty, and community clinicians to identify, ask and answer clinical questions through evidence-based assessment of the published research literature. Answers from Clin-IQ can change clinical practice.

PURPOSES. CLIN-IQ:

1. Contributes to compliance with Accreditation Council for Graduate Medical Education (ACGME) Residency Review Committee (RRC), Commission on Collegiate Nursing Education (CCNE) and other governing body scholarly activity requirements for trainee and faculty. As an example, the following statements are adapted from the RRC scholarly activity requirements for MD and DO post-graduate programs:

- clinical trainees should participate in scholarly activities;
- program faculty should encourage and support trainees in pursuit of scholarly activities;
- programs must have a curriculum that advances residents' knowledge of the basic principles of research, including how research is conducted, evaluated, explained to patients, and applied to patient care;
- program faculty must establish and maintain an environment of inquiry and scholarship with an active research component, and
- the sponsoring institution and program should allocate resources to facilitate involvement in scholarly activities.

Other disciplines (nursing, pharmacy, allied and public health, etc.) report to governing boards that may have similar requirements.

2. Enables a critically important link between academia and community practitioners that can inform both education and research, creating a learning community.

SPECIFIC CLIN-IQ GOALS, OBJECTIVES AND EVALUATION STRATEGIES

Specific goals of the Clin-IQ process are to:

1. Involve trainees in a clinically relevant, scholarly activity
2. Create a collaborative learning community between trainees, medical librarian consultants, faculty and community clinicians.
3. Create opportunities for presentation and publication of scholarly research.
4. Meet ACGME or other governing body requirements for trainee research.
5. Create a database of clinically relevant research questions.

Upon completion of the Clin-IQ Process, trainees will be able to:

1. Recognize and construct well-formulated, clinically relevant questions.
2. Access appropriate current literature to locate the highest level of evidence relevant to a clinical question.
3. Utilize Medical Reference Library consultants effectively.
4. Interpret the results from published literature.
5. Appraise the validity and strength of evidence of the literature selected.
6. Summarize the results for an audience of their peers, faculty mentors, and community clinicians.
7. Synthesize the literature in a written document.
8. Follow instructions for authors for scholarly writing.
9. Produce a publication ready document of their findings.

Evaluation of Clin-IQ projects

1. Faculty mentors review the document for accuracy, completeness, originality and readiness for publication; trainees revise as indicated.
2. Trainees review one another's projects and provide feedback.
3. A Clin-IQ Director reviews and designates the document for publication.
4. If submitted for publication, Clin-IQs undergo peer review.

MEASUREABLE OUTCOMES

1. Increased numbers of trainee and faculty scholarly publications, presentations and posters.
2. Closer ties between academic faculty and community clinicians across disciplines (e.g. more collaboration around professional meetings, development of practice-based research networks, etc.).

STEPS IN IMPLEMENTING THE CLIN-IQ PROCESS

STEP 1

Identify and Designate a Clin-IQ Champion/Director

This individual should possess a terminal degree in the clinical discipline of the training program. The Clin-IQ Director must have the authority to guide the process and the backing of the residency or other training program director. This gives the program credibility with the learners.

STEP 2

Develop a close and supportive relationship with medical librarian consultants.

Medical reference librarians are consulting partners with knowledge that benefits trainees and researchers at all levels by helping:

- a) Define the question. Forming well-built “PICO” questions facilitate locating current, relevant materials from the medical literature.
- b) Perform focused literature searches to save time.
- c) Find the highest level of evidence available to answer the question.

Meet with the medical library reference consultants before you initiate a Clin-IQ process. Provide them with all the materials your learners will be using.

Clin-IQ TIP:



- Your learners should take the Clin-IQ Toolkit, their question, and any other materials with them when they work with the Librarian Consultant. Attachment 2 is sample template workbook.

STEP 3

Define Requirements of Participation

A. Who.

There are many options for who can participate in the Clin-IQ process. The process is not limited to residents or trainees.

- Medical students or students in other colleges or department wishing to pursue a research project as part of an elective rotation
- All trainees or residents in each year
- Fellows or other post graduate learners
- Faculty members interested in adding to their CV for tenure and/or promotion or who simply wish to answer a clinical question they have encountered.
- Faculty members serving as mentors to younger faculty or trainees. Faculty mentors can play a major role in ensuring the success of Clin-IQ or any scholarly activity. Recruiting young faculty to serve as mentors gives them additional opportunities for publications and presentations.

B. How.

Required vs. Optional.

Program choice based on reason for initiating the Clin-IQ. For example:

- If more scholarly activity is needed to meet ACGME recommendations, Required might be best.
- If trainees, residents, fellows want more publications or the opportunity to present their work at scholarly meetings for career purposes, Optional may be appropriate.

Participation Structure: Clin-IQ participants can work independently or in teams. Both options come with positive and negatives aspects.

- Teams
 - may include learners at different stages (e.g., PGY-2 and PGY-3), such that the senior team member can help mentor the more junior member.
 - may choose partners or partners may be assigned.
 - ↑ may help keep the process moving by pushing each other or covering when team members are on busy rotations or vacation,
 - ↓ may have conflicts
- Individual projects
 - ↑ offers more flexibility
 - ↓ requires more responsibility
 - ↓ requires more questions than team approach
 - ↓ requires more mentor availability.

Clin-IQ TIP:



- If a team approach is elected, a signed contract with the division of work agreed upon in advance can prove useful if trainees work in teams.
- Attachment 1 is a sample contract.

Mentors: Faculty mentors may be assigned or chosen by trainees.

- Assigned.

Faculty mentors may be assigned based on:

- Interest in topic
- Need for publications and presentations
- Desire to work with process participants
- Department program requirement.

- Chosen.

Allowing trainees to choose their mentors comes with both positive and negative aspects. If the programs elects to let trainees choose their mentor, a list of available mentors and their interests should be provided.

↑ Trainees should choose a faculty mentor with whom they share an interest

↑ A compatible collaborative relationship is more likely as both trainee(s) and mentor are agreeable to the goals and outcomes

↓ Some faculty may receive multiple requests to serve as mentors. Rules may be needed to cover this contingency such as:

- ◆ First come, first chosen
- ◆ Faculty mentor choice based on question/interest.

Didactics. Didactics may accompany the process as part of an academic afternoon, journal club or other teaching opportunities. (Sample didactic slide sets are available upon request. Contact laine-mccarthy@ouhsc.edu)

C. When.

- Should balance time availability of participants and the need for concentrated effort.
- 6-9 months is a reasonable to complete a Clin-IQ; make adjustments as needed
- Set interim deadlines with some type of reward. Assigning points and honoring the individual or team with the most points is one possibility. Be creative. (See Sample Time Table beginning on page 16.)
- August or near the beginning of the academic year is good time to begin.
- January or February are reasonable completion deadlines; adjust as needed to the specific constraints and needs of each program.
- Have the learners prepare a poster for presentation. This gives them a sense of accomplishment and gives the process credibility.
- Final Clin-IQ should be in publishable format regardless of whether the manuscript will be accepted for publication.

Clin-IQ TIP:



- Presenting the poster to the department or at a local or national meeting should be considered.

STEP 4



Create a Question Bank

The **Question Bank** is a repository or database of clinical questions from which trainees or faculty may select study questions to answer for the Clin-IQ process.

A. Question Collection

- A process for collecting these questions must be identified and implemented by each program.
- Suggestions for collecting clinical questions:
 - 1) Clinicians may carry index cards when seeing patients to write questions that arise. A drop site/box may be placed in the clinic specifically for clinical questions.
 - 2) If the program/department participates in a practice-based research network, community clinicians should be encouraged to offer questions either via the index card method or e-mail to the Clin-IQ director/coordinator.
 - 3) A Clin-IQ question jar may be placed strategically at scientific or educational meetings for forums.
 - 4) Required in-house conferences or educational sessions may use submission of a Clinical Question to document attendance.
 - 5) Listservs and other online communication sources may solicit questions from clinicians.
 - 6) Medical Library Consultants field questions from individuals daily and may be a rich source of questions.
 - 7) Be creative. A backlog of questions makes prioritization and distribution easier.

Clin-IQ TIP:

- Clin-IQ questions can be entries in a raffle. Find a sponsor to offer a prize.

Clin-IQ TIP:

- Better too many questions than too few.
- Be creative about collecting and prioritizing questions.

B. Prioritization of questions.

- Assures that the questions are both interesting and clinically relevant.
- Here is an example of one method that has worked well:

			Relevance to Primary Care	Importance to you as a	Relevance to Primary Care	Importance to you as a	Relevance to Primary Care	Importance to you as a	Relevance to Primary Care	Importance to you as a
		Score 0-20 in each category: 0 = none, 5 = very little, 10 = somewhat, 15 = moderately, 20 = completely								
Ranking	Score	QUESTION	faculty		faculty		resident		community clinician	
1	33	In adults with coronary artery disease or at high risk of stroke, does taking 81 mg of aspirin daily result in improved outcomes compared to those taking 325 mg aspirin per day?	15	15	15	15	15	15	20	20
2	32	Are at home sleep studies as effective at diagnosing obstructive sleep apnea in adults as poly-	20	20	15	15	20	15	20	18
3	31	In adults with chronic pain does long term treatment with SSRI/SSNI (alone or in conjunction with other medications) control pain more effectively?	20	20	20	15	20	15	15	20

- Collect all questions in an anonymous spreadsheet or database.
- Distribute the database to a selected group of community and faculty clinicians and to residents/fellows or other potential participants.
- Tally the results and average to determine a rank. In the example, a total of 40 pts were possible.
- Determine a “cut line” below which questions were not deemed important or relevant enough to pursue. In the example, less than 20 pts was the cut line.

C. Question selection.

- Questions may be assigned or selected by trainees.
- Matched to interests (e.g., sports medicine, emergency medicine)
- Drawn from a hat or bowl
- Pick numbers and let trainees select in number order
- If trainee wrote a high priority question, allow them first pick.
- Be creative and adapt process to your particular program.

D. PICO format. PICO format. Authors are responsible for assuring questions are in PICO format. This process is included in the Preparation Toolkit or may be taught in a didactic session.

- Patient/Population
- Intervention/Indicator
- Comparison/Control
- Outcome

STEP 5

Review Process

Clin-IQ was designed to mimic the scholarly publications process in as many ways as possible. A formalized peer/mentor/faculty review process accomplishes an important part of this goal. A sample Reviewer Evaluation Form is attached (Attachment 6).

Reviewers look for

- Well-built PICO formatted question
- Appropriateness of search terms, inclusion and exclusion criteria
- Thoroughness of the search
- Currency of the articles selected (2008-present)
- Completeness of the document
- How well the authors followed the guidelines
- Potential incidences of plagiarism
- Rational and clinically relevant answer and conclusion
- Readiness for publication and potential external review.

Clin-IQ TIP:



- Schedule a time when all learners and mentors can come together and talk. This can validate the importance of Clin-IQ.

STEP 6

Presentation Process

Many post-graduate programs have opportunities for their trainees to present scholarly projects either through posters or podium presentations within the training setting. Clin-IQ projects are well suited for internal presentation as well as for external presentation at

Campus-wide settings,

- State and national professional meetings,
- Discipline-specific scientific and educational meetings.
- As many opportunities to share answers to clinically relevant questions should be explored, including PBRN annual convocations.

Clin-IQ TIP:



- These same venues can be rich sources for new clinical questions to add to your Question Bank.

STEP 7

Publication Process

- Identify as many potential publication sources as possible for Clin-IQ projects.
 - State medical and discipline-specific journals
 - The primary national journals in your discipline
 - A selection of published Clin-IQs can be found in Attachment 8
- Contact editors of these journals. You might be surprised at their willingness to help you.
- Sources of publication for brief reports such as Clin-IQs and case reports have become scarce over the past decade. However, more access to brief articles that answer clinical questions are catching the interest of editors.
- If possible, have someone designated as a Clin-IQ Editor to monitor the submission process.
- A formal process for revising Clin-IQs, especially those with inconclusive or low-level evidence answers will be helpful. Potential publishers may ask whether a system is in place to revisit and revise Clin-IQs as needed.

About Plagiarism.

Plagiarism and copyright infringement occur when an author extracts large portions of materials from a published document. Tables, figures, charts and graphs of any kind must be significantly altered or, preferably, created from data within a published study. Brief material (generally a sentence or two, less than a paragraph) may be quoted provided the material is placed in quotation marks (“ ”) and adequate citations to the sources are provided.

It is extremely important that your learners understand what constitutes plagiarism. Medical librarian consultants are well versed on this subject and may be able to assist you. In addition, there are software products, such as Turn-It-In, which can scan documents and identify potential plagiarized passages.

ROLES AND RESPONSIBILITIES OF DIRECTORS/MENTORS

Whether Program Director or Faculty Mentor, these individuals are ultimately responsible for success of Clin-IQ. These individuals also benefit from the roles they play in the process. They serve as


A. Teacher:

- is able to translate the goal into step by step tasks that are appropriate for the developmental level of the learner,
- serves as role model, by participating fully in the process,
- reinforces the importance of answering clinical questions to improve patient care by discussing and modeling how the answer to a question can change clinical outcomes.

B. Encourager:

- recognizes that each learner may need different types of encouragement, such as
 - inspiration
 - reassurance
 - a boost to meet the requirements of the project.
- understands the barriers experienced by the trainee and helps trainee be creative to overcome barriers.

Clin-IQ TIP:

Give Clin-IQ awards each year, e.g. 

- Best Clin-IQ and runners-up.
- Promptness, etc.
- Be creative!

C. Deadline Monitor:

- Deadlines with meaning can make the Clin-IQ process run more smoothly.
- Rewards for meeting deadlines can be as simple as
 - Assigning points for meeting deadlines.
 - Routine e-mail blasts with status reports (peer pressure).
 - Bulletin boards with point counts to encourage competition.
 - Electronic "Clin-IQ" newsletter.
 - Regular faculty mentor/learner meetings to review progress.
 - A regular deadline notification system.
 - A system that works within your educational setting. You may have to try different tactics to see what motivates your learners.
- Attachment 2 includes a sample Clin-IQ Academic Year Schedule with points assigned for completing assignments on time.

D. Reviewer:

The goal of the reviewer is to improve the quality of the document. The mentor

- Reads each component of the Clin-IQ.
- Makes clear and concise suggestions so authors can learn how and why edits should be made.
- Checks that each reference is current, relevant and appropriately discussed and cited in the paper.
- Combines encouragement with criticism (a Yes sandwich: This is great: this might be better if: I really like how you [fill in the blank]).
- A sample review form is provided in Attachment 6.

Clin-IQ TIP:



- Your feedback matters. The goal is creating the best Clin-IQ possible.

E. Co-Author:

- Assumes responsibility for the scientific integrity of the work and coaches trainee(s).
- Assures that plagiarism has not occurred. There are several plagiarism identification software programs available (e.g., Turn-It-In).
- Serves as corresponding author on papers submitted for publication.
- Once published, the mentor may be responsible for updating the answers.
- Depending on the involvement of the medical librarian consultant, this individual may serve as co-author as well. Many librarians in academic settings are faculty members with the same evaluation requirements as other faculty. They can assist the mentor with publication and should be considered for authorship.

REMEMBER: Mentors benefit from Clin-IQ. Take an active role in assuring the quality of each Clin-IQ produced.

Sample Clin-IQ Time Table

DATE	TASKS AND HOMEWORK
July -August	<ul style="list-style-type: none"> Pick teams Complete Clin-IQ Project Contract Agreement (see Attachment 1) Pick questions Mentors selected/assigned Ideas for search terms and limits Ideas for inclusion and exclusion criteria Summary of Issues. Work with a medical librarian consultant to find 1 or 2 <u>RECENT</u> review articles (2008-present) on which to base the Summary of Issues Read articles
September	<ul style="list-style-type: none"> Draft Summary of Issues. Edit Summary of Issues Summary of Evidence. Work with a medical librarian consultant to locate 2 <u>RECENT</u> (2008-present) evidence articles that represent the highest level for your question. Be sure to take your Clin-IQ workbook to the search session (see Attachment 2 for example). Read evidence articles. Draft Summary of Evidence and Conclusion Insert in-text citations Generate reference list
End of September	<p style="text-align: center;">Progress Report Presentation and Question Discussion</p> <ul style="list-style-type: none"> Bring 2 copies of the current version of your Clin-IQ. Be prepared to give a brief (~3 min) progress report and describe your approach to answering their question. Mentors, course coordinators and other trainees may offer suggestions.
October	<ul style="list-style-type: none"> Edit Summary of Issues Draft Summary of Evidence and Conclusion Insert in-text citations Create table, figure, graph Generate reference list to complete first draft E-mail 1st draft to mentor requesting review. Revise 1st draft of Clin-IQ paper based on colleague and mentor comments
November or December	<p style="text-align: center;">Colleague Clin-IQ Paper Review</p> <ul style="list-style-type: none"> Bring 2 copies of evidence articles and 2 copies of your Clin-IQ paper. Review and comment on another team's paper using peer review form (Attachment 6). That team will review your paper. Share comments with colleagues.
January	<ul style="list-style-type: none"> Team will have reviewed, revised and edited 1st draft and generated 2nd draft. E-mail mentor requesting review and copy Clin-IQ/Scholarly Activities Director.

February	<ul style="list-style-type: none"> • Incorporate mentor revisions and generate final draft. • A table, chart or graph to depict some aspect of your evidence should be included. • E-mail final draft, which includes a graphic, to Clin-IQ/Scholarly Activities Director for review. • Incorporate suggestions from Clin-IQ/Scholarly Activities Director
March	<ul style="list-style-type: none"> • Publication ready paper to Clin-IQ/Scholarly Activities Director incorporating changes their changes. • You now have a poster/publication ready document.
April	<ul style="list-style-type: none"> • As part of an academic afternoon or research day, present Clin-IQ findings to colleagues, mentors, faculty.
May	<ul style="list-style-type: none"> • As part of an academic afternoon or Clin-IQ required conference, participants, including faculty, must write a minimum of 2 new clinical questions for the question bank.

Attachments

- 1. Clin-IQ Example Project Contract Agreement**
- 2. Template for Completing a Clin-IQ**
- 3. Clin-IQ -Guidelines for Authors**
- 4. Glossary of Study Types**
- 5. Algorithm for determining level of evidence for an individual study**
- 6. Clin-IQ Review Form**
- 7. Sample of Completed Clin-IQ**

ATTACHMENT 1

Clin-IQ Example Project Contract Agreement

Each member of a Clin-IQ team (PGY2, PGY3) shall complete and sign this Clin-IQ project contract agreement. This agreement will serve to stipulate the tasks for each member of the Clin-IQ team and must be signed by your mentor. Return completed and signed agreement to the Clin-IQ Director.

Academic Year: _____

Resident Name: _____

Program Year ☐ PGY-2 ☐ PGY-3

Allocation of Responsibilities: INITIAL the Clin-IQ
Tasks for which you personally will be responsible

_____ Literature searching: 1-2 current review
articles and at least 2 current articles
relevant to your question that meet the
highest level of evidence available.

_____ Write Summary of Issues

_____ Write Summary of Evidence

_____ Table/Figure/Graph

_____ Conclusions

_____ Reference list and in-text citations

_____ Project presentation introduction and
Summary of Issues

_____ Project presentation Summary of Issues
and Conclusions

Resident Signature Date

Print Mentor Name

Mentor Signature Date

Resident Name: _____

Program Year ☐ PGY-2 ☐ 3

Allocation of Responsibilities: INITIAL the Clin-IQ
Tasks for which you personally will be responsible

_____ Literature searching: 1-2 current review
articles and at least 2 current articles
relevant to your question that meet the
highest level of evidence available.

_____ Write Summary of Issues

_____ Write Summary of Evidence

_____ Table/Figure/Graph

_____ Conclusions

_____ Reference list and in-text citations

_____ Project presentation introduction and
Summary of Issues

_____ Project presentation Summary of Issues
and Conclusions

Resident Signature Date

Print Mentor #2 Name (if applicable)

Mentor #2 Signature(if applicable) Date

ATTACHMENT 2. TEMPLATE FOR COMPLETING A CLIN-IQ

BUILD A CLIN-IQ

You may wish to refer to the [Guidelines for Authors](#) (Attachment 2) as you work through this template.

1: Choose a Question From the Database.

Write the question you have selected on the following lines.

2: Determine if the Question is in PICO Format; Rewrite it if it is Not.

PICO is an acronym for the components of a well-built clinical question.

P=patient, always your primary focus.

I=intervention, what are you proposing to do (not do, e.g., watchful waiting).

C=compared to what? Some questions (e.g., causation) won't have a comparison.

O=outcome, what do you want to happen.

Read the two questions below.

Before – Not Specific

Do myringotomy tubes help children with recurrent otitis media?

After – Very Specific, Well-Built

Patient	In infants and children to age 3 (or 4 or 5) with chronic otitis media,
Intervention	are myringotomy tubes better than
Comparison	episodic or prophylactic antibiotics
Outcome	for reducing the incidence and/or severity of disease with fewer side effects (diarrhea, others?)

Re-write the question you have selected on the following lines. Your mentor and/or your medical reference librarian consultant can help you formulate a PICO question.

P

I

C

O

3: Develop Search Terms, Limits and Inclusion/Exclusion Criteria Based on your PICO formatted question (above), select search terms for the literature search. Consult a medical librarian for help.

PICO Literature Search Strategy Example*

Patient(s)	Intervention	Comparison	Outcomes
Infant or preschool child ; chronic otitis media	AND myringotomy tubes	AND episodic or prophylactic antibiotics	AND Incidence or severity or side effects

*Adapted from Kerr J. Abdominal Imaging 33 (Sept): 31-33, 2008)

Search Terms:

Limits: (e.g., Human, English, Infants or Pre-School Children review, RCT)

ATTACHMENT 2. TEMPLATE FOR COMPLETING A CLIN-IQ

Inclusion and Exclusion Criteria: A brief discussion of which articles you chose to **include**, e.g., all clinical trials in humans that compared tubes with other treatments or with watchful waiting that were published in the past 5 years and included an *n* (number of subjects) of XX or greater) and articles you chose to **exclude** (children over age 5, adolescents, adults) (see Sample Clin-IQ, Attachment 6)

4: Search the Medical Literature

Consulting with a Medical Reference Librarian: Consulting with a medical reference librarian before you do a literature is most likely to yield the highest level of evidence with the least amount of irrelevant materials. You may work with a librarian to perform your search or you may perform the literature search yourself. If you choose to work with a librarian, here are some tips to make that interaction more productive.

- Conduct the interaction face-to-face. Medical librarians are trained to do “reference interviews” and will ask you questions about your topic that you may not have considered. Or, fill out the “Ask a Librarian” help request from the library webpage (page 7). You may have to do both to get the materials you need.
- Bring your project workbook with you to the consultation. The librarian will then understand the limited nature of your search and be better able to assist you.
- Medical librarians will be able to readily locate relevant review articles as well as evidence articles.
- Medical librarians are well-versed in evidence-based medicine, levels of evidence and study types. They can assist you in identifying which type of study (or studies) will best answer your question.
- You may also consider consulting with a medical librarian about
 - a) Inclusion and exclusion criteria
 - b) Search terms and limits

5: Locate 1 or 2 Review/Background Articles.

Based on search terms, locate 1 or 2 **current (2008 or newer)** review/background article available (you can do the search yourself but it is suggested that you work with a trained medical librarian). Your review article should include:

- **Clinical significance of the problem.**
- **Prevalence.**
- **Relevant issues.**

6: Write a draft of the summary of issues (word count = 200-300)

Should include how prevalence and clinical significance relate to your question. You have an example to work from (see sample Clin-IQ, Attachment 6).

7: Locate 2 Highest Level Evidence Articles. You can do this search yourself or work with a trained medical librarian (item 4 above). Be sure to identify which type of study qualifies as the highest level of evidence. See Figure 1 (Attachment 3) and Figure 2 (Attachment 4) for a discussion of levels of evidence.

- Find at least 2 **current (2008 or newer)** articles relevant to your question that meet the highest level of evidence available as shown on Figures 1 and 2 (Attachments 3 and 4).
- Read the articles
- Send the articles to your faculty mentor

ATTACHMENT 2. TEMPLATE FOR COMPLETING A CLIN-IQ

8: Write a draft of the summary of evidence (word count = 500-700)

- number of patients or papers, if meta-analysis or systematic review
- type of studies (include data on a table for clarity)
- statistical significance.¹
- intervention of interest
- outcome(s) of interest (morbidity, mortality, quality of life, etc.)
- weaknesses or conflicts
- cite references

9: Determine level of evidence of your body of literature (see Figures in Attachments 3 and 4)

Level of evidence for the answer (A, B, or C): _____

10: Answer the Question.

Answer: (Circle one): Yes No Inconclusive or 1-2 sentences if that is more responsive.

11: (Optional but recommended) Add a table, figure, chart or graph

- Tables, figures or charts can be added to elucidate data in the Summary of Evidence
- Tables, figures or charts must be original, created based on data available from the articles.
- Place an citation within the text indicating the context of the graphical material.(e.g., Figure 1, Table 2),

12: Write a Draft Conclusion (word count = 50-100)

- Conclusions (1-2 sentences), to include:
 - Summary of issue (relevance) linked to
 - Summary of evidence, linked to
 - The answer and how you would change your practice based on what you have learned.

13: Add Reference List: You must cite all the materials (books, journal articles, website, etc.) that you used to answer your question. You should only need 1-2 review articles and 2 evidence articles.

1. Review article #1
2. Review article #2 (optional)
3. Evidence article #1
4. Evidence article #2

¹An excellent Statistics tutorial can be found at <http://web.med.unsw.edu.au/QMP/QMPHome.htm>

ATTACHMENT 2. TEMPLATE FOR COMPLETING A CLIN-IQ

14: Complete Clin-IQ check list. Have you:

- ☐ Answered the question
- ☐ Prepared the reference list in proper format.
- ☐ Cited sources properly as shown in this Workbook in Guidelines for Clin-IQ Authors (Attachment 3) or Clin-IQ Example (Attachment 7).
- ☐ If you included a table, figure or graphic, is it original or adapted sufficiently from the source to avoid potential copyright violation or plagiarism (see A Word About Plagiarism below).
- ☐ If you included a table, figure or graphic, have to noted in the text where the table materials is discussed (Table 1, Figure 2, etc.).
- ☐ Shared your draft with your mentor and addressed all comments and suggestions.
- ☐ Requested a review from additional faculty or peers as suggested by your mentor (review form, Attachment 6)
- ☐ Revised draft until mentor feels it is publishable.

A WORD ABOUT PLAGIARISM: Plagiarism and copyright infringement occur when an author extracts large portions of materials from a published document. Tables, figures, charts and graphs of any kind must be significantly altered or, preferably, created from data within a published study. Brief material (generally a sentence or two, less than a paragraph) may be quoted provided the material is placed in quotation marks (“ ”) and adequate citations to the sources are provided.


A consult with a medical librarian can help you be re-assured that you have not exceeded copyright limitations or plagiarized material.

ATTACHMENT 3. GUIDELINES FOR AUTHORS

Clin-IQ -Guidelines for Authors

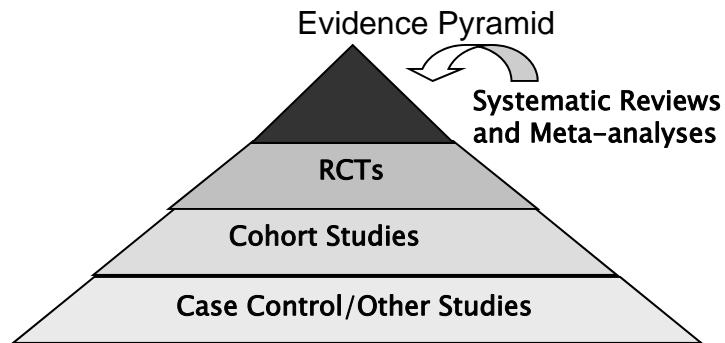
<u>General Format</u>	
Double space the entire document.	
Indent the first line of each paragraph. Do not use extra blank lines between paragraphs.	
<u>Citing Abbreviations</u>	<u>Examples</u>
The first time you use an abbreviation you must write the complete phrase first and follow the phrase with the abbreviation in parentheses. From then on, use only the abbreviation	The Residency Review Committee (RRC) is the entity that accredits residency training programs. The RRC requires programs to conduct faculty/residency collaborative research for accreditation.
<u>Numbers in Text</u>	<u>Examples</u>
<p>Spell out numbers one through nine.</p> <p>Except percentages (9%)</p> <p>Medication dosages (15 mg BID)</p> <p>Laboratory values (162.4 ml/min)</p> <p>Dates (June 30, 2014)</p> <p>Time frame (39 weeks, 3 years)</p> <p>Ages (individuals 13 yrs or older).</p> <p>More than one number in a sentence</p>	<p>In this study, nine children aged 4 months to 2 years received ear tubes.</p> <p>In this study, the first 8 children received ear tubes and the second 8 were placed on Bactrim for 2 weeks.</p>
<u>Articles from the Medical Literature</u>	<u>Examples</u>
<ul style="list-style-type: none"> • Recent review article(s), no more than 2, on which to base your summary of issues. • Recent evidence articles, 2, on which to base your Summary of Evidence and your answer. • All articles should be from medical journals preferably published in 2008 or newer. If you have problems, a trained medical librarian consultant can help you. Be sure to bring this workbook and your Clin-IQ question to the librarian. 	<p><u>Review article:</u></p> <p>1. Wilson R, Gazzala J, House J. Aspirin in primary and secondary prevention in elderly adults revisited. [Review] South Med J. 105(2):82-82, 2012.</p> <p><u>Evidence article:</u></p> <p>2. Berger JS, Krantz MJ, Kittelson JM et al. Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease: a meta-analysis of randomized trials. JAMA 301(18): 1909-1919, 2009.</p>

ATTACHMENT 3. GUIDELINES FOR AUTHORS

<p><u>In Text Citations</u></p> <p>If you cite, paraphrase, mention or quote directly from a published article, book, website, etc. you must cite the material in the text (and include the citation information in the Reference List). <u>Failure to do so constitutes plagiarism and copyright infringement.</u></p>	<p><u>Examples</u></p> <p>Use of combined oral contraceptives increases the risk of venous thrombosis two-to-six <u>fold</u>.^{1,2} Both the estrogen and progestogen of combined oral contraceptives contribute to the increased thrombotic <u>risk</u>.¹ On top of this, smoking doubles the risk of venous <u>thrombosis</u>.² It has been established that women over age 35 who smoke should not use combined oral contraceptives due to the risk for cardiovascular <u>disease</u>.³</p>
<p><u>Reference Lists</u></p> <p>Reference lists are placed at the end of the paper. References are listed <u>in the order in which they are cited in the text of your article.</u></p> <div style="border: 1px solid red; padding: 10px; margin-top: 10px;"> <p>Clin-IQ Reference TIP: </p> <p>Reference 1 is always the first article cited and is always reference ¹ no matter how many times it is cited in the text.</p> </div>	<p><u>Examples</u></p> <p><u>Both</u> the estrogen and progestogen of combined oral contraceptives contribute to the increased thrombotic <u>risk</u>.¹</p> <p>... in these 56 women when APC resistance was re-tested 3 months later (mean baseline 2.75 vs. mean three months later 2.47; difference -0.29; 95% CI -0.04 to <u>-0.53</u>).¹</p>
<p style="text-align: center;">Complete Reference Examples (based on the Uniform Requirements for Medical Manuscripts)</p>	
<p><u>Journal Article Example</u></p>	<p>1. Mold JW, Holtzclaw BJ, McCarthy LH. Night sweats: a systematic review of the literature. J Am Board Fam Med 25(6): 878-893, 2012.</p>
<p><u>Book Chapter Example</u></p>	<p>2. Lim LL, Foldvary-Schaeger N. Sleep Disorders. Ch. 10 In: Carey WD, ed. Current Clinical Medicine, 2nd ed. New York: Elsevier (Saunders); 2010:914-921.</p>
<p><u>Website Example</u></p>	<p>3. Felland LE, Lechner AE, Sommers A. Improving access to specialty care for Medicaid patients: policy issues and options. A Commonwealth Fund Report. Center for Studying Health System Change, June 2013. (Accessed June 27, 2013, at www.hschange.com).</p>
<p>A sample completed Clin-IQ, which meets the style, formatting and publication requirements, can be found in Attachment 7.</p>	

ATTACHMENT 4. GLOSSARY OF STUDY TYPES

Figure 1. Glossary of Study Types

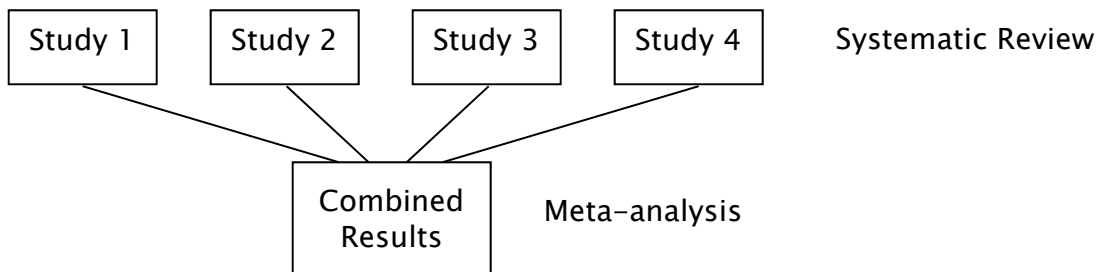


1. Systematic Review: Level 1 Evidence

- a. A comprehensive survey of a topic in which all the primary studies of the highest evidence (e.g., randomized controlled trials, prospective cohort studies (see below)) are identified, appraised and summarized using explicit inclusion and exclusion criteria.
- b. Results should be reproducible

2. Meta-analysis: Level 1 Evidence

- a. Similar to a systematic review in that a comprehensive search of the topic is conducted.
- b. If the results of the review of all included studies are similar enough statistically, the results are combined and analyzed as if they were one study
- c. Results should be reproducible.

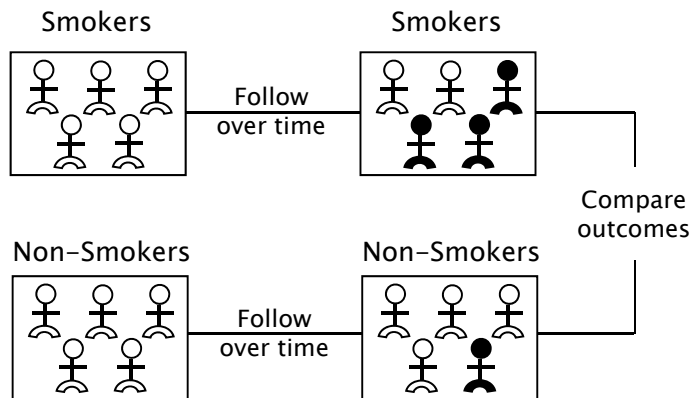


3. Randomized Controlled Trial (RCT): Level 1 Evidence

- a. 2 groups: 1 treatment group and 1 control group. Treatment group received treatment under investigation. Control group receives either no treatment (placebo) or gold standard treatment.
- b. Patients are randomly assigned to each group.
- c. Best type of study to answer questions about therapy.
- d. Sometimes there can be 3 or even 4 groups (called arms) depending on the study question. Example of a 4-arm RCT: Allergy treatment.
 - i. Claritin alone
 - ii. Flonase alone
 - iii. Claritin + Flonase
 - iv. Placebo

ATTACHMENT 4. GLOSSARY OF STUDY TYPES

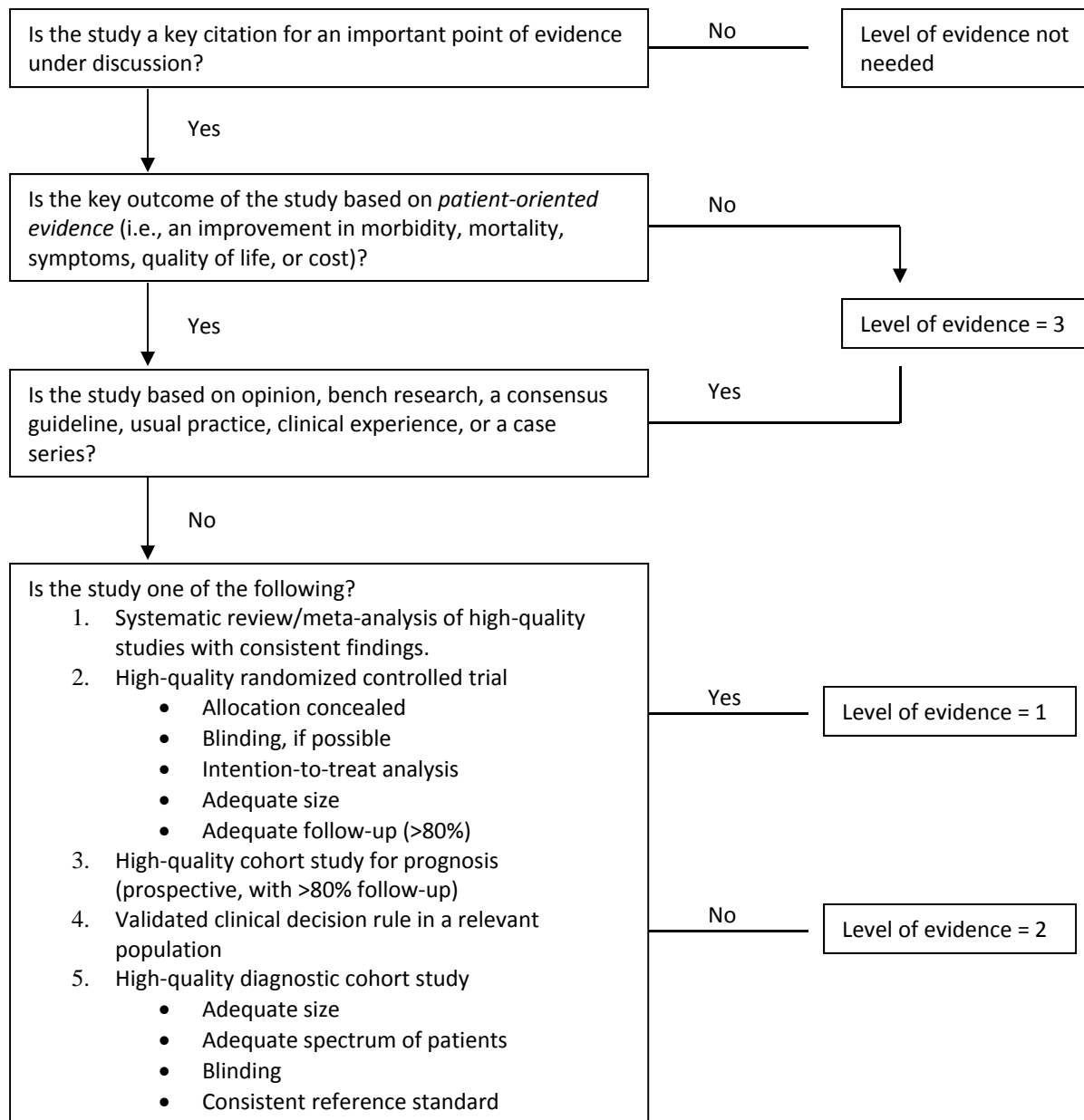
4. Cohort Study: Level 1 or 2 Evidence based on question and study design
- A study in which patients who presently have a condition and/or receive a particular treatment are observed over time and compared with another group who do not have the condition being studied.
 - Example:



Examples adapted from SUNY Downstate Medical Center (<http://library.downstate.edu/EBM2>)

ATTACHMENT 5. DETERMINING LEVELS OF EVIDENCE

Figure 2. Algorithm for determining level of evidence for an individual study



Levels of Evidence

A = Consistent level 1 studies

B = Consistent level 2 or 3 studies or extrapolations from level 1 studies

C = Level 4 studies or extrapolations from level 2 or 3 studies

D = Level 5 studies or troubling inconsistent or inconclusive studies of any level

Source: <http://www.aafp.org/afp/2004/0201/p548.html>

ATTACHMENT 6. CLIN-IQ REVIEW FORM

Peer Reviewers, Faculty Reviewers, and Mentors

Reviewer: _____

Authors _____

Brief Title (first few words) _____

General Instructions to Reviewers

- Objective is to help authors improve the manuscript.
- Suggest how to make the manuscript more clear, concise and relevant.
- Identify possible areas of confusion for the reader and make specific suggestions.
- Verify that at least one reference is accurately interpreted.
- Identify any glaring grammatical or format problems, in a supportive manner.
- Sprinkle PRAISE along with recommendations for change.

Answer:

Does the answer accurately represent the evidence given? [☐] Needs improvement [☐] Yes

Reviewers Comments:

Level of Evidence:

Does the level of evidence accurately represent the references cited?

[☐] Needs improvement [☐] Yes

Reviewers Comments:

Summary of Issues: Clinical significance, prevalence and relevance based on recent review article(s).

Is the writing clear and logical? [☐] Needs improvement [☐] Ready to publish

Is the length appropriate (200-300 words)? [☐] Needs improvement [☐] Ready to publish

Reviewers Comments:

ATTACHMENT 6. CLIN-IQ REVIEW FORM

Summary of Evidence: Describes studies, outcomes, interventions. A figure or table will be added.
Evidence articles should be cited.

Is the writing clear and logical? ☐ Needs improvement ☐ Ready to publish

Is the length appropriate (500-700 words)? ☐ Needs improvement ☐ Ready to publish

Review at least one evidence article and comment:

- Are the evidence articles all current (**2008-present**)? ☐ Needs improvement ☐ Yes
- Is the information appropriated represented in the text? ☐ Needs improvement ☐ Yes
- Have the statistics been accurately represented and explained? ☐ Needs improvement ☐ Yes
- If present, do the figures or tables accurately present the data and contribute to your understanding of the material? ☐ Needs improvement ☐ Yes

Reviewers Comments:

Conclusions: Conclusion should be clinically relevant and wrap up evidence.

Is the writing clear and logical? ☐ Needs improvement ☐ Ready to publish

Is the length appropriate (50-100 words)? ☐ Needs improvement ☐ Ready to publish

Does the conclusion state clearly how the answer will impact practice? ☐ Needs improvement ☐ Yes

Reviewers Comments:

Reference List:

Are all references cited in the body of the report according to the instructions in the Workbook (superscripted numbers)? ☐ Needs improvement ☐ Yes

Is the reference list in order numerically according to the order the articles are cited in the text?
☐ Needs improvement ☐ Yes

Reviewers Comments:

Additional comments to the author

ATTACHMENT 7. SAMPLE CLIN-IQ

Clin-IQ Project

Clinical Question: In women over 35 years of age who smoke, does Mirena (levonorgestrel-releasing intrauterine system) reduce the risk of DVTs compared to oral contraceptives?

Authors: M. M., MD (PGY-3) and K. J., MD (PGY-2)

Faculty Mentor: J. L. B., MD

Residency Program: [YOUR PROGRAM NAME HERE]

Answer: Yes

Level of Evidence for the Answer: B

Search Terms: intrauterine device, venous thrombosis, oral contraceptives

Date Search was Conducted: September 2012

Inclusion and Exclusion Criteria:

Inclusion Criteria: Published systematic reviews/meta-analysis, cohort studies, and clinical research trials comparing risk of venous thrombosis in women using a levonorgestrel-releasing intrauterine device versus oral contraceptives.

Exclusion Criteria: Women less than 18 years of age

Summary of the Issues

Use of combined oral contraceptives increases the risk of venous thrombosis two-to-six fold.^{1,2} Both the estrogen and progestogen of combined oral contraceptives contribute to the increased thrombotic risk.¹ On top of this, smoking doubles the risk of venous thrombosis.² It has been established that women over age 35 who smoke should not use combined oral contraceptives due to the risk for cardiovascular disease.³ Therefore, in this subset of patients, other forms of contraception with other routes of administration are being evaluated to see if they have reduced risks.

ATTACHMENT 7.

SAMPLE CLIN-IQ

The levonorgestrel-releasing intrauterine device (LNG-IUD) is a T-shaped plastic contraceptive that is inserted in the uterine cavity where it continuously releases the progestogen levonorgestrel.² More than eight million women have used the LNG-IUD worldwide. Plasma levels of levonorgestrel during use of a LNG-IUD are lower than during the use of progestogen-only pills. Studies of progestogen-only pills suggest that there is little or no increased risk of venous thrombosis, therefore it is expected that LNG-IUD will have little thrombotic risk. The thrombin generation-based activated protein C (APC) resistance assay is a global coagulation test that enables quantification of the net prothrombotic effect of combined oral contraceptives and can also be used to predict the thrombotic risk of the LNG-IUD.¹

Summary of the Evidence

A 2009 study assessed the thrombotic risk of the LNG-IUD. In this study, the thrombotic risk was evaluated by comparing the APC resistance before and after insertion of a LNG-IUD in 56 women. High resistance to APC is associated with an increased risk of thrombosis. In contrast to combined oral contraceptives which increase APC resistance, it was observed that the use of the LNG-IUD slightly decreased the resistance to APC in these 56 women when APC resistance was re-tested 3 months later (mean baseline 2.75 vs. mean three months later 2.47; difference -0.29; 95% CI -0.04 to -0.53).¹ In women who switched from a combined oral contraceptive to the LNG-IUD, there was an even larger decrease in resistance to APC (difference -1.48; 95% CI -0.85 to -2.11). This decrease in APC resistance suggests that the LNG-IUD does not have a prothrombotic effect and suggests that it does not increase the risk of venous thrombosis. The non-randomized design is possibly a limitation of this study. In this study, researchers compared resistance to APC before and after insertion of an IUD in the same women so the comparison groups were equal except for the studied intervention which

ATTACHMENT 7.

SAMPLE CLIN-IQ

is the IUD. However, due to the non-randomized design, the observed decrease in APC resistance after insertion of the LNG-IUD can only be attributed to the intrauterine device.¹

In 2010, analyses were done on a large case-control study on risk factors for venous thrombosis. Risk factors for venous thrombosis associated with non-oral contraceptives including injectable depot-medroxyprogesterone acetate (DMPA) and LNG-IUDs were evaluated for this specific analysis. The original study was a large population-based case-control study on risk factors for venous thrombosis where patients younger than 70 years with a first episode of deep venous thrombosis or pulmonary embolism were analyzed from the files of six anticoagulation clinics in the Netherlands. For this specific study, premenopausal women were selected, aged 18 to 50 years, who were not pregnant nor within four weeks postpartum and were not using oral contraceptives. In this study, 446 patients and 1146 controls were included. The use of injectable DMPA contraceptives were associated with a 3.6-fold increased risk of venous thrombosis compared with nonusers of hormonal contraceptives. The use of a LNG-IUD was not associated with an increased risk (odds ratio 0.3; 95% CI, 0.1 to 1.1). Further adjustment for BMI, positive family history of deep venous thrombosis, or smoking habit only marginally affected the risk estimates. It was concluded that LNG-IUD seems to be the safest option regarding the risk of venous thrombosis, however the study was limited to first thrombotic events.²

A 2012 cohort study was done to assess the risk of venous thrombosis in users of non-oral hormonal contraception. Participants included all Danish non-pregnant women aged 15-49 free of previous thrombosis or cancer who were followed from 2001 to 2010. In this study, 1,626,158 women contributed to 9,429,128 woman years of observation, during which time 3,434 first ever venous thrombosis events were confirmed. Risk of thrombosis of users of transdermal, vaginal, intrauterine, and subcutaneous hormonal contraception was compared to users of oral contraceptives and non-users of contraception. It was concluded that

ATTACHMENT 7. SAMPLE CLIN-IQ

compared to non-users of hormonal contraception, transdermal patches increase the risk of venous thrombosis eight times, vaginal rings increase the risk of venous thrombosis 6.5 times, but the LNG-IUD did not cause any increased risk of venous thrombosis and may even be protective (relative risk 0.6, 95% CI 0.4 to 0.8) (see Table).⁴

Contraception type	Relative Risk (95% CI)
Non-use	1.00 (reference)
COC with levonorgestrel and oestrogen	3.21 (2.70 to 3.81)
COC with norgestimate	3.57 (2.98 to 4.27)
Levonorgestrel IUD	0.57 (0.41 to 0.81)
Patch	7.90 (3.54 to 17.65)
Vaginal ring	6.48 (4.69 to 8.94)

*Adapted from Lidegaard and Hougaard, 2012.⁴

(For all results above, $p < 0.05$.)

Conclusion

Based on our research of literature, we conclude that in women over 35 years of age who smoke, Mirena (levonorgestrel-releasing intrauterine device) reduces the risk of deep vein thrombosis compared to oral contraceptives. The LNG-IUD was found to decrease the resistance to APC which indicates that this device does not have a prothrombotic effect. In all studies reviewed, the LNG-IUD did not cause any increased risk of venous thrombosis. This information will indeed change the way we practice; we will advise women over age 35 who smoke to consider Mirena for contraception.

ATTACHMENT 7.

SAMPLE CLIN-IQ

Reference List:

1. Vliet H, Tchaikovski S, Rosendaal F. The effect of the levonorgestrel-releasing intrauterine system on the resistance to activated protein C (APC). *Thromb Haemost* 2009; 101: 691-695.
2. Veljkovic M. Contraception for women with medical disorders. *Acta Facultatis Medicae Naissensis* 2009; 26 (4): 211-216.
3. Hylckama Vlieg A, Helmerhorst F, Rosendaal F. The risk of deep venous thrombosis associated with injectable depot-medroxyprogesterone acetate contraceptives or a levonorgestrel intrauterine device. *Arterioscler Thromb Vasc Biol* 2010; 30: 2297-2300.
4. Lidegaard O, Hougaard L. Venous thrombosis in users of non-oral hormonal contraception: follow-up study, Denmark 2001-10. *BMJ* 2012; 344 (2990) 1-9.

ATTACHMENT 8.

EXAMPLES OF PUBLISHED CLIN-IQS

In Adult Smokers Unwilling or Unable to Quit, Does Changing From Tobacco Cigarettes to Electronic Cigarettes Decrease the Incidence of Negative Health Effects Associated With Smoking Tobacco? A Clin-IQ

Jennifer Brown, MD, Brandon Brown, MD, Peter Schwiebert, MD, Kalyanakrishnan Ramakrishnan, MD, Laine H. McCarthy, MLIS

Family Medicine Residency Program, Department of Family & Preventive Medicine, University of Oklahoma College of Medicine, Oklahoma City, OK

Abstract

Data from a randomized controlled trial and systematic review support the claim that switching from tobacco cigarettes to electronic cigarettes (e-cigarettes) can reduce the short-term negative health effects of smoking. In adult smokers unwilling or unable to quit, exhaled carbon monoxide levels, total number of cigarettes smoked, and exposure to nitrosamine chemicals were reduced within a 12-month period. While the e-cigarette industry remains largely unregulated thus far, these studies provide encouraging hope in the uphill battle toward helping patients make informed and healthy choices. (*J Patient-Centered Res Rev.* 2014;1:99-101.)

Keywords

electronic cigarettes, e-cigarettes, tobacco, smoking, smoking cessation

Search Terms

adult, smoking, adverse effects of smoking, nicotine administration, nicotine dosage, smoking psychology, smoking cessation

Clinical Question

In adult smokers unwilling or unable to quit, does changing from tobacco cigarettes to electronic cigarettes decrease the negative health effects associated with smoking tobacco?

Answer

Probably, based on current evidence. More research is needed.

Date answer was determined: December 2013

Level of evidence for the answer: A

Inclusion Criteria

Published systematic reviews, meta-analyses, randomized controlled trials and cohort studies comparing the short-term and relatively long-term health effects of electronic cigarettes with tobacco cigarettes.

Exclusion Criteria

Pregnant women, children, and individuals with preexisting lung disease.

Summary of the Issues

Tobacco use is projected to kill 1 billion people in the 21st century, making it the single greatest cause of preventable death globally.¹ Tobacco use in any form has negative health consequences, the severity of which depends on the amount and duration of smoking as well as the type of nicotine delivery system employed.¹ Tobacco cigarette smoke contains thousands of chemical byproducts (including 45 known or suspected carcinogens) that bind to DNA causing genetic mutations. Tobacco also contains nicotine, a highly addictive and psychoactive drug.

Electronic cigarettes (e-cigarettes) or electronic nicotine delivery systems, first introduced in China in 2006, have spread worldwide.² Often made to resemble traditional cigarettes, e-cigarettes vaporize a solution containing nicotine and flavor in an agent such as diethylene glycol. The result is a relatively clean nicotine delivery system that should, in theory, have fewer adverse health effects when compared with traditional cigarettes. However, extensive data is lacking, and there remain significant concerns regarding the purity of the ingredients, device functionality, user modification and general lack of oversight regarding manufacturing and marketing.²

As popularity of e-cigarettes continues to increase, studies comparing the effects of e-cigarettes and traditional cigarettes on acute adverse health outcomes are emerging.³ This data is essential for recommending their use, particularly in smokers unwilling or unable to quit. The Jan. 8, 2014, tobacco-themed

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ATTACHMENT 8.

EXAMPLES OF PUBLISHED CLIN-IQS

issue of *The Journal of the American Medical Association* focused on a number of different challenges that health care providers have encountered in the last 50 years regarding tobacco abuse and cessation attempts, and included a call for more research and regulation of e-cigarettes.⁴

Summary of the Evidence

Studies have shown that risks of these negative health effects are related to the length of time a person smokes and how much they smoke.¹ As such, we chose to infer that reducing the extent and duration of tobacco cigarette smoking would, in turn, decrease these negative health effects. While more than 100 online and print publications were reviewed, only one randomized control trial was found that studied e-cigarette use in smokers unwilling or unable to quit.⁵ Various other publications that studied the safety of e-cigarettes referenced each other, and we chose to use information from two of the most comprehensive resources.^{3,5}

Since long-term effects of e-cigarettes are unavailable, we chose to focus on measurable physiological and chemical parameters that have been scientifically linked to adverse health effects of smoking. Nitrosamine is a chemical compound found in latex, rubber, cosmetics and pesticides, as well as in tobacco smoke, snuff and snus, a moist powdery variation of snuff.³ More than 90% of nitrosamine derivatives are known to be highly carcinogenic and have been shown to cause a wide range of cancers.³ Carbon monoxide (CO), another byproduct of the combustion process, reduces the body's oxygen-carrying capacity and alveolar elasticity, promoting the development of emphysema and chronic obstructive pulmonary disease.³

Cahn et al.,³ examining the evidence concerning the safety and efficacy of e-cigarettes, stated that only a minority (5,300 of the 10,000-100,000) of the chemicals in cigarette smoke have been detected, whereas all components in e-cigarette vapor have been identified using gas chromatography and mass spectrometry. Only two substances in e-cigarettes (nitrosamines and diethylene glycol) are believed to have negative health effects. The researchers noted that maximal levels of nitrosamine in e-cigarettes are comparable to those in a nicotine patch and are much lower than in tobacco cigarettes (Table 1).³ Diethylene glycol is a relatively benign substance commonly used in concert smoke machines, but it also has been associated with lethal toxicity at high levels.⁶

Caponnetto et al.⁵ designed a 12-month, prospective, randomized controlled trial to evaluate smoking reduction and/or abstinence among 300 smokers unwilling to quit using two different nicotine strength e-cigarettes: 2 groups

Table 1. Nitrosamine levels in various nicotine delivery systems³

Nicotine delivery systems	Nitrosamine level*
Nicotine gum (4 mg)	2.00
Nicotine patch (4 mg)	8.00
Electronic cigarettes	8.18
Snus (moist powdery smokeless tobacco)	~2,010
Light cigarettes	~4,800
Full-strength cigarettes	~6,200
Dipping or smokeless tobacco (straight long cut)	~9,300

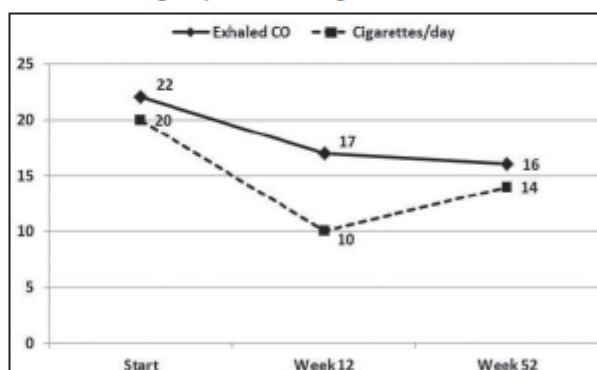
*Levels are reported as total nanograms in 1 gram of product.

(n=100 each) received nicotine cartridges of different strengths; the third group (n=100) received non-nicotine cartridges for 12 weeks. Participants were not required to change their current smoking habits.

Over the 12-month period, nine follow-up visits were used to determine number of cigarettes smoked daily and exhaled CO levels. Both parameters decreased in the groups using e-cigarettes (Figure 1). A significant number of "reducers" (smokers who reduced daily cigarette use by more than 50%) and "quitters" (those abstaining from smoking and had exhaled CO level <7 ppm) did not experience side effects commonly associated with quitting tobacco smoking. Rates of hunger (6.5%), insomnia (4%), irritability (3.5%), anxiety (3%) and depression (2%) were lower than that expected with traditional tobacco smoking cessation methods.⁴ In addition, no weight gain was reported during this study.

Even though it is a relatively clean nicotine delivery system, e-cigarettes still contain nicotine. Nicotine is an addictive and psychoactive agent that causes physical dependence and tolerance while enhancing attention, concentration

Figure 1. Amount of exhaled carbon monoxide (in parts per million) and total cigarettes per day in electronic cigarette users that are unwilling to quit tobacco cigarette use.⁵



ATTACHMENT 8. EXAMPLES OF PUBLISHED CLIN-IQS

and mood. It is also a sympathomimetic drug that releases catecholamines, increasing heart rate and blood pressure, constricting blood vessels and reducing sensitivity to insulin.¹ Nicotine thus has its own negative health effects, but long-term use of nicotine replacement products (gum, patch, etc.) have been shown to be generally well tolerated without evidence of serious adverse consequences.¹

Conclusion

In tobacco smokers unwilling to quit, switching to e-cigarettes decreases exhaled CO level and number of tobacco cigarettes smoked. Furthermore, users of e-cigarettes are exposed to less carcinogenic nitrosamine than tobacco cigarette smokers. A reduction in exposure to CO and nitrosamines, as well as an overall reduction in smoking, helps reduce smoking-related negative health effects.

However, further studies are needed to evaluate the long- and short-term effects of the diethylene glycol chemicals used as delivery agents in e-cigarettes. Improved product regulation and standardization of nicotine levels, safety, use and commercialization are required before e-cigarettes can be called a "safe" alternative to tobacco cigarette smoking.⁴ In the meantime, these early studies shed exciting new information on an addiction that has defied traditional treatment approaches.

Acknowledgments

Clin-IQ (Clinical Inquiry) is a required resident/faculty scholarly activity that takes questions from community practitioners and feeds the answers back out to improve patient care. L.H.M. received support from Oklahoma Shared Clinical & Translational Resources, funded by grant number NIGMS U54GM104938, NIGMS/NIH.

Conflicts of Interest

None

References

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2. O'Connor RJ. Non-cigarette tobacco products: what have we learnt and where are we headed? *Tob Control*. 2012;21:181-90.
3. Cahn Z, Siegel M. Electronic cigarettes as a harm reduction strategy for tobacco control: a step forward or a repeat of past mistakes? *J Public Health Policy*. 2011;32:16-31.
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5. Caponnetto P, Campagna D, Cibella F, et al. Efficiency and Safety of an eElectronic cigarette (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS One*. 2013;8:e66317.
6. Sosa NR, Rodriguez GM, Schier JG, Sejvar JJ. Clinical, Laboratory, Diagnostic, and Histopathologic Features of Diethylene Glycol Poisoning-Panama, 2006. *Ann Emerg Med*. 2014 Jan 15 [Epub ahead of print].

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Aurora.org/clin-iq

ATTACHMENT 8. EXAMPLES OF PUBLISHED CLIN-IQS



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<p>Clin-IQ Project Clinical Question: In adults with chronic insomnia, is melatonin as effective as prescribed medications in promoting sleep, but with fewer side effects?</p> <p>Authors: Beth Hites, DO (PGY-2)</p> <p>Answer: Inconclusive for effectiveness; Yes, for fewer side effects</p> <p>Level of Evidence for the Answer: B</p> <p>Search Terms: melatonin, melatonin agonist, insomnia, chronic insomnia, comparison, sleep, benzodiazepine, benzodiazepine receptor agonist, and antidepressant</p> <p>Inclusion and Exclusion Criteria: Inclusion: Humans, English, Age 19+, Randomized Control Trials, Clinical Trials and Meta-analysis Exclusion: Case Studies</p> <p>Summary of Issues: The most common sleep disorder, insomnia, can have a major impact on an individual's physical and psychological health, personal life, and career. It is defined as difficulty in initiating and/or maintaining sleep, or waking too early, and occurs despite adequate opportunity and circumstances for sleep.¹ A study by Singareddy, et al., of 1,246 individuals followed for seven years, who did not report insomnia at baseline, found the overall incidence of chronic insomnia to be 9.3%, with a higher incidence among women than men. Factors found to increase the risk of chronic insomnia were younger age (20-35 years), non-white</p>	<p>ethnicity, and obesity. Predictors of chronic insomnia included: poor sleep, mental health – maladaptive personality traits, and excessive use of coffee at baseline. Surprisingly, short sleep duration and sleep apnea were not found to be predictors of chronic insomnia.²</p> <p>The most common self-reported daytime complaints by those suffering from chronic insomnia include fatigue/malaise, poor concentration, social/vocational dysfunction, mood disturbances, daytime sleepiness, decreased energy, increased errors and/or accidents, headache, gastrointestinal disturbances, and worry/anxiety about sleep. An ambulatory assessment conducted by Varkevisser, et al., on chronic insomnia and daytime functioning found that, while subjective well-being was compromised in insomniacs vs. control participants, the objective performance level between the two groups was comparable. This study's findings were comparable overall to multiple other studies, with only minor deviations in performance noted by a few (i.e., decreased balance, decreased performance in conditions lacking external stimuli, etc.).³</p> <p>Summary of Evidence: A review of published data that directly compared both the efficacy in promoting sleep and/or patient reported side effects between melatonin and one or more prescribed medications for insomnia was conducted. Only one randomized controlled trial (RCT) was found that met the criteria for side effect comparison. There were no RCTs found that directly</p>	<p>compared the efficacy of melatonin to benzodiazepines, non-benzodiazepine agonists, melatonin agonists, or antidepressants in the treatment of chronic insomnia. There were several RCTs and meta-analysis that compared prescriptive medications for chronic insomnia with each other and/or cognitive behavioral therapy (CBT), or compared classes of prescribed medications to CBT.</p> <p>A 2003 study by Rogers, Kennaway, and Dawson looked at the neurobehavioral performance effects of daytime melatonin compared with temazepam administration. Sixteen healthy individuals with a mean age of 21.4 were given melatonin 5 mg, temazepam 10 mg, or placebo at 1200 (noon) in a randomized double-blind crossover fashion. Neurobehavioral performance tasks (unpredictable tracking, spatial memory, vigilance, and logical reasoning) were completed and assessed hourly from 0800 – 1100, and every two hours from 1300 – 1700. Results showed more negative changes in performance with temazepam than with melatonin ($p < 0.05$). Subjective sleepiness levels were greater with temazepam and melatonin than with placebo ($p \leq 0.05$), with temazepam's greatest sleepiness level from 1300-1400, and melatonin's greatest sleepiness level from 1300-1700. These results demonstrating fewer negative cognitive effects while patients are awake suggest that melatonin may be preferable to benzodiazepines in sleep disorder management.⁴</p> <p>One review comparing melatonin and placebo suggests that melatonin is effective</p>
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tive in decreasing sleep onset latency, advancing sleep onset/offset time, and increasing total sleep time in circadian rhythm sleep disorders such as those seen in jet lag or shift work.⁵ One RCT of 43 participants evaluated the effectiveness of a melatonin, magnesium, and zinc combination against placebo. This study showed significant subjective improvement in ease of getting to sleep ($p<0.001$), quality of sleep ($p<0.001$), hangover on awakening from sleep ($p=0.005$), alertness and behavioral integrity next morning ($p=0.001$), and total sleep time ($p<0.001$) for those taking the melatonin, magnesium and zinc combination.⁶

Conclusion:

In adults, there are few, if any, trials directly comparing the effectiveness of melatonin to prescribed medications for the treatment of chronic insomnia. Given the prevalence of sleep disorders and the health care costs of treating chronic insomnia, this is an area that is in need of more research. In adults with chronic insomnia, it does appear that melatonin has fewer reported side effects than temazepam. Against placebo, melatonin appears to be safe and effective in decreasing sleep onset latency and increasing total sleep time, without significant adverse effects.

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The Journal of the Oklahoma State Medical Association

In adults (ages 20 – 50) with gastroesophageal reflux disease taking a proton pump inhibitor daily who present with new onset headache, are there common co-morbid conditions?

Patricia Dunlap, MD (PGY 3); Sameer Zafar, MD (PGY 2); Pamela Tietze, MD; Toney L. Welborn, MD, MS

Answer: Inconclusive

Date answer was determined: September 10, 2010

The level of evidence for the answer: B

Program Name: University of Oklahoma Health Sciences Center, Family Medicine Residency Program, Oklahoma City, Oklahoma

SUMMARY OF THE ISSUES

The most successful class of drugs for the treatment of gastroesophageal reflux disease (GERD) is the proton pump inhibitor (PPI). PPIs have proven to be highly effective and have a consistent effect on gastric acid suppression. They have an excellent adverse effect profile after more than 20 years of clinical use. The most common side effects are diarrhea, headache, and skin reactions. These side effects are experienced by 0.5% to 5% of PPI users.¹ PPIs are FDA approved as first-line treatment of GERD.²

It is well documented that headache is one of the most common side effects of PPI use. The cause of these headaches is not known although at times these headaches have resulted in discontinuation of the medication. All PPIs act by inhibiting the H⁺/K⁺ ATPase pump. Gastric acid secretion is regulated by three types of receptors: histamine, gastrin, and acetylcholine. These receptors all reside on the parietal cells in the stomach. Activation of these receptors leads to activation of the H⁺/K⁺ ATPase pump. PPI administration therefore results in increased pH in the stomach.²

Omeprazole was the first PPI to be introduced in Sweden in 1987, followed by lansoprazole in 1992 (France) and pantoprazole in 1994 (Germany). There have been several others since.³ GERD is a term used to describe any symptomatic or histopathologic changes within the esophagus due to gastroesophageal acid reflux. It is estimated that 60 million people in the United States suffer from GERD. GERD is experienced on a daily basis by 7% of adults within the United States, and another 14% have weekly symptoms. Forty percent of adults have symptoms of GERD monthly. If 5% of PPI users suffer side effects, it can be estimated that up to 3 million people could be suffering from new onset headaches secondary to PPI use.⁴

SUMMARY OF THE EVIDENCE

We found three studies; a nested case-control study, a cohort

study, and prospective follow-up study. A nested case-control study is a case-control study that is nested (or embedded) within a cohort study. The cases are usually all of the cases in the cohort while the controls are selected at random from the non-cases. The prospective follow-up study was designed according to guidelines for Safety Assessment of Marketed Medicines (SAMM).

The nested case-control design was used to compare PPI users reporting headaches versus those reporting no headaches. The data was obtained from a prospective, observational study performed in the Netherlands in which 10,008 lansoprazole users were followed between January 1994 and April 1998. The purpose of the study was to investigate not only the incidence but also the characteristics of headaches in lansoprazole users along with any cofactors.⁵

In this study 2.5% (246 of 10,008) of lansoprazole users reported headaches. Tension headaches were the most common affecting two-thirds of those reporting headaches. Migraine headaches made up the other one-third. Females and subjects with a history of analgesic use were at a higher risk of developing headaches with the use of lansoprazole. The cessation of headaches after a dose reduction or discontinuation of lansoprazole strongly suggested that headache was indeed an adverse effect of lansoprazole use.⁵

The cohort study, performed in England, involved omeprazole, lansoprazole and pantoprazole. Esophageal reflux / esophagitis was the reason for prescribing a PPI to approximately two-fifths of the subjects of each cohort. The omeprazole cohort included 12,205 subjects, out of a total of 28,496 subjects, who received a prescription for omeprazole between June 1989 and June 1990. Omeprazole was prescribed for peptic ulcer disease, esophageal reflux and hiatal hernia more frequently than lansoprazole and pantoprazole. The lansoprazole cohort consisted of 17,329 subjects, out of a total of 36,722 subjects who received a prescription for lansoprazole between May and November 1994. Lansoprazole was prescribed for dyspepsia more often than omeprazole. The pantoprazole cohort included 11,541 subjects, out of a total of 28,159 subjects, who received a prescription for pantoprazole between December 1996 and June 1997. Pantoprazole was prescribed for dyspepsia more often than omeprazole and lansoprazole.⁶

The most common adverse event reported in all three cohorts was diarrhea. The next most frequently reported adverse events were abdominal pain and nausea/vomiting. The fourth most common adverse event was headache with an incidence

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rate of 0.10 per 1000 days of exposure for omeprazole, 0.17 per 1000 days of exposure for lansoprazole, and 0.15 for 1000 days of exposure for pantoprazole. Comorbidities and adverse events were not linked.⁶

The prospective follow-up study was performed in the Netherlands. A total of 5,669 lansoprazole users were included. The purpose of this study was to determine the safety and effectiveness of lansoprazole in the general public. The most common adverse events were diarrhea, headache and nausea. Commonalities among subjects reporting adverse events were female and consumption of 1-4 alcoholic beverages per day. Prior use of a PPI or mucosaprotectives and concomitant use of over-the-counter (OTC) acid-related preparations were also more common among those reporting adverse events. Co-morbidities assessed by the practitioner were by systems: gastrointestinal, cardiovascular, endocrine, respiratory, musculoskeletal, and psychiatric. The most common comorbidity was cardiovascular followed by gastrointestinal. The most common underlying diseases were hypertension, asthma/chronic obstructive pulmonary disease and diabetes mellitus. A relationship between a comorbidity, PPI use and new onset headache was not addressed.⁷

COMMENT

PPI use is associated with new onset headaches. In evaluating a patient with new onset headaches a good place to start one's investigation is the patient's medication list. This should include all OTC preparations as some PPIs are now OTC. Whether there are comorbidities among PPI users and new onset headaches is unclear. More research needs to be done.

SEARCH TERMS

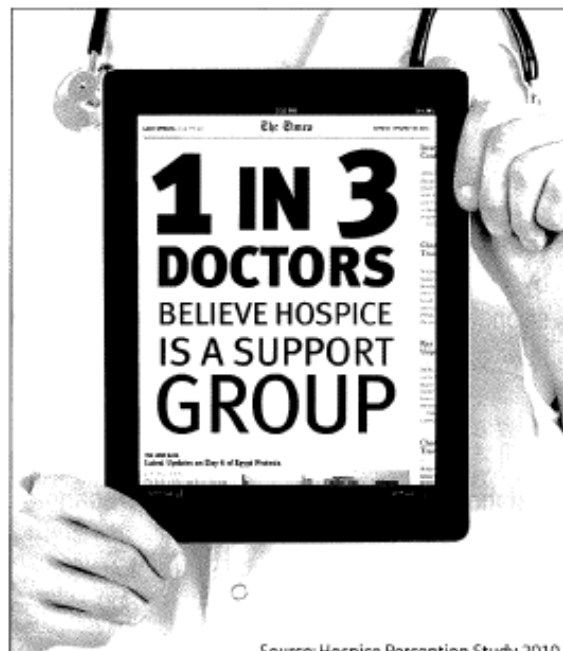
PPI associated headaches, PPI adverse events, GERD.

INCLUSION/EXCLUSION CRITERIA

Articles published in English about GERD and PPI use in humans; age 20 -50. Articles about the use of PPIs in animals were not considered.

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Source: Hospice Perception Study 2010

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