Drug Information PRN Focus Session—Keeping Up with Drug Information Resources and Skills: The Effective Utilization of Innovative Drug Information Tools, and Strategies to Evaluate Meta-analyses and Systematic Reviews

Activity Number: 0217-0000-16-127-L04-P, 1.50 hours of CPE credit; Activity Type: An Application-Based Activity

Monday, October 24, 2016
3:15 p.m. to 4:45 p.m.
Regency Ballroom 2

Moderator: Andrew M. Abe, Pharm. D.
Clinical Assistant Professor of Pharmacy Practice, University of Kansas, Kansas City, Kansas

Agenda

3:15 p.m. Looking Beyond Traditional Drug Information Resources: Making the Most of Innovative Tools in Pharmacy Practice
Conor T. Hanrahan, Pharm. D., BCPS
Manager, Drug Information Services, Intermountain Healthcare, Salt Lake City, Utah

4:00 p.m. Innovative Strategies and Techniques to Evaluate Meta-analyses and Systematic Reviews When Making Patient Care Decisions
J. Russell May, Pharm. D., FASHP
Clinical Professor, Medical College of Georgia, Augusta, Georgia

Conflict of Interest Disclosures
Andrew M. Abe: no conflicts to disclose
Conor T. Hanrahan: no conflicts to disclose
J. Russell May: no conflicts to disclose

Learning Objectives

1. Differentiate the value of social media and other innovative tools (e.g., Google FOAM, Iodine.com) compared with traditional resources in answering drug information questions.
2. Identify how social media and other innovative tools can be effectively applied in daily practice.
3. Evaluate the limitations and risks of social media and other innovative tools when used to answer clinical questions.
4. Identify essential elements of a meta-analysis and systematic review that can be used by the busy practitioner.
5. Evaluate potential limitations and methodological problems with a qualitative systematic review and meta-analysis.
6. Compare and contrast different frameworks and scoring systems for evaluating the quality of clinical trials.

Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/am

© American College of Clinical Pharmacy
Looking Beyond Traditional Drug Information Resources

Conor Hanrahan, PharmD, BCPS
Manager, Drug Information Services
Intermountain Healthcare, Salt Lake City, UT
Monday, October 24, 2016

Conflict of Interest

• None

Learning Objectives

• Differentiate the value of social media and other innovative tools compared with traditional resources in answering drug information questions.
• Identify how social media and other innovative tools can be effectively applied in daily practice.
• Evaluate the limitations and risks of social media and other innovative tools when used to answer clinical questions.

Outline

• Web 2.0 and social media
• Applicability to health care
• Risk and quality assessment
• Examples of innovative social media tools
  • FOAMSearch (formerly GoogleFOAM)
  • iForumRx
  • Iodine

Web 2.0

The new generation of the Internet focused around user-generated content and user interactions

Web 1.0

Web 2.0

Social Media

• Electronic communication platforms through which users co-create, share, discuss, and modify user-generated content
  • Blogs
  • Microblogs
  • Wikis
  • Media-sharing sites
  • Social networking sites
  • Virtual reality environments
Social Media Characteristics

1. Identity: Extent to which users reveal themselves
2. Conversations: Extent to which users communicate with one another
3. Sharing: Extent to which users exchange content
4. Presence: Extent to which users know if other users are available
5. Relationships: Extent to which users relate to each other
6. Reputation: Extent to which users know the social standing of others
7. Groups: Extent to which users are ordered or form communities

Blogs

• Oldest and most established form of social media
• Create and post content for others to consume and comment on
• Content can take many forms

Microblogs

• Considered the most dynamic form of social media
• Users post a large number of brief messages or updates over a short period of time

Wikis

• Collaborative Web sites that can be directly edited by anyone with access to the site (crowdsourced)
• Information can be accessed, added, or edited quickly

Media-Sharing Sites

• Designed to view and share embedded digital media content
• Also includes commentaries, profiles, etc.

Assessment Question 1

Wikis are best defined as which one of the following:
A. Audio or audiovisual social media that can be downloaded to a computer or mobile device.
B. A collaborative social media platform that can be directly edited by anyone with access to the site.
C. An interactive social media platform maintained by an individual or an organization that posts regular entries of commentaries and events.
D. A social media platform that allows users to send short, quick messages to other subscribers.
Applicability to Health Care
Social media and you...

Use Cases

• Professional networking
• Organizational promotion
• Patient care
• Public health programs

• Professional education
• Patient education

Advantages of FOAM

• Disseminate, discuss, and dissect scientific research
• Free, real-time, and more up-to-date
• Access to diverse array of topics
• Explore issues where research is lacking
• Collaboration
• More engaging learning experience

Limitations of FOAM

• Variable quality and accuracy of the content
• Variable degree of scholarship
• Reliance on post-publication peer review
• Heavy reliance on reader to discern legitimacy
• Qualifications and conflicts of interest may or may not be known
• Brevity may lead to omission of important nuances

FOAM (FOAMed)

• Free open access medical education
• Communicate and educate medical content through a variety of social media platforms
• Content is created organically by individuals from various disciplines
• Typically more dynamic and less formal than traditional educational materials
• Quality often vetted in real-time by users

FOAM

• Exponential rise in the number of FOAM resources
• As of 2013, there were 141 documented FOAM blogs and 42 podcasts for emergency medicine and critical care
• Extensive use of FOAM content
• Academic Life in Emergency Medicine (ALiEM) Web site
• 84,570 hits per month from 195 countries between June 2013 to Dec 2013

© American College of Clinical Pharmacy
Assessing FOAM Quality

<table>
<thead>
<tr>
<th>Credibility</th>
<th>Content</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transparency</td>
<td>Professionalism</td>
<td>Aesthetics</td>
</tr>
<tr>
<td>Process</td>
<td>Engagement</td>
<td>Interaction</td>
</tr>
<tr>
<td>Use of other resources</td>
<td>Academic rigor</td>
<td>Functionality</td>
</tr>
<tr>
<td>Trustworthiness</td>
<td>Orientation</td>
<td>Ease of use</td>
</tr>
<tr>
<td>Bias</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Is the editorial process independent from sponsors, conflicts, and other sources of bias?
- Is there transparency about who was involved in its creation? Is the identity of the author clear?
- Does the resource cite up-to-date references and are they consistent with the data presented?
- Is the information presented accurate and of a consistent quality?
- Are limitations about the topic acknowledged?

Assessing FOAM Quality

- Is the content presented in a logical, clear, and coherent way?
- Does the resource use correct grammar/spelling?
- Is there a way to provide feedback?
- Are there comments from other contributors that either endorse or refute the information presented?
- Is there a well-defined purpose or topic?
- Is the content of the resource professional?

Applicability in Daily Practice

- Useful to stay up-to-date on current issues
- Useful forum for communication and debate
- Never rely on it as the sole source of truth
  - Always assess quality
  - Always verify and validate

Assessment Question 2

Compared with traditional medical references, FOAM content is typically
A. Shorter, more dynamic, easily accessible, and relies heavily on post-publication peer review.
B. Highly evidence-based with a strong pre-publication peer review process.
C. Consistent with regard to the degree of scholarship and author/commenter qualifications.
D. Focused on core, foundational practice principles as opposed to current or controversial topics.

Assessment Question 3

You are a pharmacist staffing in the ED when you receive a STAT order for an intravenous lipid emulsion 1.5 mL/kg bolus, followed by a continuous infusion of 0.25 mL/kg/min for 60 minutes.

Not having heard of this therapy before, you ask the physician for his clinical rationale and more details. The physician then provides you with a FOAM blog post about the therapy (see case handout).

Describe how you would assess the quality of this resource and your next steps before completing the order.
Innovative Tools
New and shiny things for medical information...

FOAMSearch
• Developed by Todd Raine, MD
• Custom search engine that curates emergency medicine/critical care FOAM resources from
  • Blogs
  • Podcasts
  • Screencasts (video podcasts)
  • Wikis
  • Journals
  • Other social media tools


Limitations of FOAMSearch
• Advertisements in search results
• Ambiguous vetting process for resource inclusion and risk of bias
• Lack of transparency
• Broken links
• Lack of data comparing utility of custom versus traditional search engines

Common EMCC FOAM Sites
• Life in the Fastlane
• Academic Life in Emergency Medicine
iForumRx

- Hosted by the University of Mississippi School of Pharmacy
- Robust editorial and advisory board
- Goals
  - Inform ambulatory care pharmacy specialists about high-quality, practice-changing evidence
  - Empower practitioners to apply the best evidence to patient care in ambulatory care settings
  - Uses interactive blogs, podcasts, polls, panel discussions, etc.

iForumRx Considerations

- Content is referenced and evidence-based
- Commendable editorial process
- Covers broad range of topics focused on ambulatory care
- Timely and interactive
- Free of commercial influence

Iodine

- Founded in 2013 by Thomas Goetz and Matt Mohebbi
  - Medical team primarily includes nurses and pharmacists
  - "Create feedback loops between the patient experience and the intended outcome"
  - Combines clinical information with patient reviews of medications (crowdsourced reviews)
Iodine Considerations

• Novel and cutting-edge approach to patient-oriented crowdsourcing in medicine
• Information is provided in a patient-friendly manner
• Encourages reliance on patient opinion
• Sample bias?
• May overly emphasize medication downsides
• No comparisons or information on untreated disease
• Questionable disease-related data

Other Similar Sites

• RxWiki
• Everyday Health
• Patientslikeme
• Omada Health
• Ginger.io
• Propeller Health

Assessment Question 4

Which one of the following is the most accurate statement regarding FOAMSearch:
A. Custom search algorithms typically lead to slow search result speeds, limiting real-world utility.
B. FOAMSearch could be useful for oncology practitioners looking for FOAM resources.
C. Practitioners should not rely solely on FOAMSearch due to an ambiguous vetting process and lack of transparency.
D. FOAMSearch appears to be an efficient, non-commercial way to find FOAM resources.

Concluding Thoughts

• Social media is becoming a frequently used outlet for medical information
• May supplement, but not replace traditional medical resources
• Many advantages and disadvantages
• Continued diligence is needed to ensure quality

Looking Beyond Traditional Drug Information Resources

Conor Hanrahan, PharmD, BCPS
Manager, Drug Information Services
Intermountain Healthcare, Salt Lake City, UT
Monday, October 24, 2016
Strategies and Techniques to Evaluate Meta-analysis and Systematic Reviews When Making Patient Care Decisions

J. Russell May, Pharm.D., FASHP
University of Georgia College of Pharmacy
Augusta, GA
October 24, 2016

Learning Objectives
After attending this session the audience should be able to:
• Identify essential elements of a meta-analysis and systematic review that can be used by the busy practitioner
• Evaluate potential limitations and methodological problems with a qualitative systematic review and meta-analysis
• Compare and contrast different frameworks and scoring systems for evaluating the quality of clinical trials

Terminology: Common Question...
• What is the difference between a systematic review, a meta-analysis, and a review article?
  • Systematic review: a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research and to collect and analyze data from studies that are included in the review.
  • Contrast this to a "review article"
    • A broad overview of a clinical condition
  • Often, systematic reviews include statistical techniques (meta-analysis) to synthesize the data from several studies into a single quantitative estimate of summary effect size

Importance of This Topic
• Systematic reviews and meta-analysis
  • Essential tools for summarizing data
  • Help keep clinicians up-to-date
  • Provide evidence for
    • Policy makers
    • Clinicians
    • Guideline developers
  • Provide summaries of previous research for funders of potential new research
  • Helps editors judge merits of publishing new studies

Systematic Review Examples
• Included in the top 10 at Cochrane Library
  • http://www.cochrane.org/ as of August, 2016
  • Gabapentin for chronic neuropathic pain and fibromyalgia in adults
  • Sun protection for preventing basal cell and squamous cell skin cancers
  • Paracetamol for low back pain

Conflict of Interest
• Dr. May has nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) mentioned in this presentation.
**Gabapentin for chronic neuropathic pain and fibromyalgia in adults**

- **Objective:** to assess analgesic efficacy and adverse effects of gabapentin in these conditions
- **Search:** MEDLINE (1966 – March 14, 2014), EMBASE (1980 – 2014 week 10), and CENTRAL, Internet and specifically Clinicaltrials.gov (most recent search March 17, 2014)
- **Selection:** Randomized, double-blind studies of analgesic and adverse effects in adults

**Results:**
- 5633 participants in 37 studies of “reasonable quality”
  - No top tier evidence that was unequivocally unbiased
  - Second tier evidence with potential important residual bias: doses of 1200 mg or more was effective for some people, gabapentin (35%) and placebo (21%)
  - Over half those treated will not have worthwhile pain relief
  - Persons taking gabapentin could expect to have at least one adverse event (62%)

**Sun protection for preventing basal cell and squamous cell skin cancers**

- **Objective:** to assess the effects of sun protection strategies for preventing keratinocyte cancer in the general population
- **Search:** Cochrane Skin Group Specialized Registry, CENTRAL, MEDLINE, EMBASE, and LILACS. Also 5 trial registries, and bibliographies of relevant trials (up to May 2016)
- **Selection:** randomized controlled trials in adults and children

**Results:**
- One RCT study, factorial design with 1621 participants
  - Studied sunscreens
    - With or without beta-carotene administration
    - No difference in development of basal cell or squamous cell carcinoma (RR = 1.03 and 0.88, respectively)
  - Certainty of evidence low: lack of histological confirmation of carcinoma
  - Further assessment of sunscreens and other barrier methods needed

**Paracetamol for low back pain (LBP)**

- **Objective:** to investigate the efficacy and safety of paracetamol for non-specific LBP
- **Search:** CENTRAL, MEDLINE, EMBASE, CINALHL, AMED, Web of Science, LILACS, IPA from inception through August 7, 2015. Also, reference lists from eligible papers and trial registry websites
- **Selection:** RCTs versus placebo for non-specific LBP

**Results:** Three trials (n = 1825), two trials included in a meta-analysis
  - For acute LBP: high quality evidence for no difference using meta-analysis combining two studies
  - For chronic LBP: low quality evidence (study with 1 gm IV dose for immediate effect) for no effect. Note study has been retracted.
Tools for Evaluating Systematic Reviews/Meta-analysis

• Some easy-reading literature sources
  • Murad MH, et al. How to Read a Systematic Review and Meta-analysis and Apply the Results to Patient Care. JAMA 2014;312:171-179

How a Systematic Review/Meta-Analysis Should Be Performed

• Over 2,500 new systematic reviews published in English annually
• Key information is often poorly reported
• Development of QUOROM
  • Quality Of Reporting Of Meta-analysis
  • Reporting guidance for authors
  • Published in 1999
  • Evolved into PRISMA in 2009
    • Preferred Reporting Items for Systematic Reviews and Meta-analysis

Tools for Evaluating Systematic Reviews/Meta-analysis

• Evaluating a systemic review/meta-analysis by knowing how one should be performed

How a Systematic Review/Meta-Analysis Should Be Performed

• PRISMA: 27 item checklist “to include when reporting a systematic review or meta-analysis”
• JAMA: 9 Step Process for conducting a systematic review and meta-analysis

9 Step Process for Conducting a Systematic Review and Meta-analysis

• To evaluate, one might ask, "How did they...?":
  • Formulate the question
  • Define the criteria for study inclusion (PICO + study design)
  • Develop a priori hypothesis to explain heterogeneity
  • Conduct literature search
  • Screen titles and abstracts for inclusion
  • Review the full text of possible eligible studies
  • Assess the risk of bias
  • Abstract the data
  • Perform the meta-analysis (more on this later)

Evaluating...

• Methodology
  • Should be a clear clinical question addressed by the systematic review
    • Defined by PICO
      • Type of patients
      • Type of interventions
      • Type of comparisons
      • Type of outcomes
Evaluating...

- Clear clinical question?
  
  **Example:**
  
  
  - Too broad, too narrow?
    - Induction of remission in patients with perianal fistula
    - Single drug, combination therapy?
    - Etc...

Evaluating...

- Methodology
  
  - How was the search for relevant studies conducted?
    - Comprehensive
    - Tools for search listed (PubMed, Cochrane, EMBASE, etc.)
    - Terms used
    - Reasonable limitations placed on search (e.g., English language)
    - Manual search through references of articles
    - Attempt to identify unpublished data

Evaluating...

- Search for relevant studies thorough?
  
  **Example:**
  
  
  - Pubmed, EMBASE, Cochrane Library
  - Terms: (ciprofloxacin or quinolone or antibiotic) AND (Crohn’s disease or inflammatory bowel disease)
  - Any language
  - Manual search of references retrieved

Evaluating...

- Data abstraction
  
  **Example:**
  
  
  - Two investigators abstracted data (differences resolved “by consensus”)
  - Characteristics evaluated: study design, demographics, interventions, duration, extent of disease, and co-therapy
  - 987 studies identified > 951 excluded on basis of title and abstract> 36 studies evaluated > 31 excluded (reviews, retrospective, uncontrolled, postoperative studies, lack of placebo) >>>5 studies included

Now for the hard (fun?) parts...

- Evaluation of heterogeneity ($I^2$ statistic)
- Evaluation of publication bias (Funnel Plot)
- Evaluation of effect size and overall effect size (Forest Plot)
- Drawing your conclusions
Evaluation of Heterogeneity (I² statistic)

- The statistical model used is based on how heterogeneous or homogenous the included studies are.
- An I² statistic assesses heterogeneity
  - Values <25%: homogeneous group
  - Values >75%: heterogeneous group

Evaluation of publication bias (Funnel Plot)

- Studies with a positive effect are more likely to be published.
- Assessment of publication bias: funnel plot
- Displays each trial according to its effect size (X-axis) and weight (y-axis)
- Assumption: no bias
  - More precise trials clustered at the top and smaller trials will spread out near the bottom
  - Result: an upside down funnel

Evaluation of effect size and overall effect size (Forest Plot)

- Effect size is the targeted difference between groups in each study
- Typically expressed as OR, RR, or HR with 95% CI
- Effect size is weighted for each study
  - Large RCTs weighted higher
- Overall treatment effect calculated
- Results displayed: Forest Plot

Forest Plot*

<table>
<thead>
<tr>
<th></th>
<th>Drug A/Drug B</th>
<th>Drug A/Drug C</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith AB et al</td>
<td>3/63</td>
<td>2/53</td>
<td>1.26 (0.22 to 7.27)</td>
</tr>
<tr>
<td>Jonse CD et al</td>
<td>7/18</td>
<td>2/28</td>
<td>5.44 (1.27 to 22.34)</td>
</tr>
<tr>
<td>Brown EF et al</td>
<td>5/44</td>
<td>3/51</td>
<td>1.93 (0.49 to 7.63)</td>
</tr>
<tr>
<td>Green GH et al</td>
<td>7/52</td>
<td>5/59</td>
<td>1.59 (0.34 to 7.70)</td>
</tr>
<tr>
<td>Black K et al</td>
<td>8/27</td>
<td>4/24</td>
<td>1.78 (0.61 to 5.17)</td>
</tr>
<tr>
<td>Johnson KL et al</td>
<td>12/34</td>
<td>3/36</td>
<td>4.24 (1.31 to 13.72)</td>
</tr>
<tr>
<td>Allen MN et al</td>
<td>28/100</td>
<td>9/94</td>
<td>2.92 (1.46 to 5.87)</td>
</tr>
<tr>
<td>Overall Effect</td>
<td></td>
<td></td>
<td>2.30 (1.65 to 3.21)</td>
</tr>
</tbody>
</table>

Favors A/B      Favors A/C

I² = 10%

*Designed for illustration purposes only

Other Considerations

- How generalizable are the results?
  - For a clinical trial: “results of a study can only be applied to patients who are similar to those in the study”
  - For a systematic review: a little more complex
- Funding source(s) for the review
- Disclosures
Conclusions

- Systematic Reviews/meta-analysis
  - Excellent way to summarize evidence for making patient (or other) judgements
  - Provides a way to interpret disparate results
  - Reлиant on criteria for inclusion of previous studies and statistical methods to assure validity
- Using guidelines for how to conduct a systematic review provide tools to evaluate the quality of a systematic review

Strategies and Techniques to Evaluate Meta-analysis and Systematic Reviews When Making Patient Care Decisions

J. Russell May, Pharm.D., FASHP
University of Georgia College of Pharmacy
Augusta, GA
October 24, 2016

Questions?
jmay@augusta.edu