EBP2
Critical Appraisal
Application Review

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Before you begin...

It would be helpful to go ahead and print out this article if you haven’t already.

**Article to Appraise**

And this practice sheet:

**Appraisal Practice Handout**

Fill it out as you work through this PowerPoint, your search, & critical appraisal of the article! The practice sheet replicates the critical appraisal application you’ll do soon (but with added information)!
Objectives

• Review steps in the EBM process
• Review validity criteria for randomized controlled trials (RCTs)
• Critically appraise an article about an intervention
• Define absolute and relative risk reductions
• Review EBM2 Week 4’s Critical Appraisal Application process
While we are focusing on the Appraisal aspect, EBM begins and ends with the patient…so let’s meet Roberta!
Your patient is Roberta an 87-year-old female who is being treated for mild hypertension but is otherwise healthy, with no chronic diseases. She is a widow who lives at home with a young family that provides her with companionship. She has very little sensation in her lower legs, due to poor circulation, and walks with a cane. She is very concerned about falling. Her son, the “health nut”, just read an article about Vitamin D. He strongly urges her to start taking Vitamin D because the article said it can prevent accidental falls. However she finds it difficult to remember to take pills every day. After watching a commercial for an osteoporosis medication that is taken once a year, the son asks if taking a mega dose of Vitamin D once a year would help.
A recap...

- 87-year-old female
- Mild hypertension but otherwise healthy
- Poor circulation, walks with a cane
- Concerned about falling
- Asks about a yearly Vitamin D mega dose
Take a minute to consider your PICOTT

<table>
<thead>
<tr>
<th>Patient Problem</th>
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<tbody>
<tr>
<td>Intervention</td>
<td></td>
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<tr>
<td>Comparison</td>
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<tr>
<td>Outcome</td>
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<tr>
<td>Type of question</td>
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<tr>
<td>Type of Study</td>
<td></td>
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<tr>
<td>Patient Problem</td>
<td>Elderly female, fear of falls</td>
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<tr>
<td>------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Intervention</td>
<td>Vitamin D mega dose annually</td>
</tr>
<tr>
<td>Comparison</td>
<td>None or placebo</td>
</tr>
<tr>
<td>Outcome</td>
<td>Reduce risk of falls</td>
</tr>
<tr>
<td>Type of question</td>
<td>Prevention/Therapy</td>
</tr>
<tr>
<td>Type of Study</td>
<td>RCT &lt; Systematic Review &lt; Meta-Analysis</td>
</tr>
</tbody>
</table>
In elderly females, would a large annual dose of Vitamin D reduce the risk of falls?
Time to find the evidence!

Go to PubMed
Search for the evidence to address the clinical question
Note your search (keywords, MeSH, filters, etc)
Come back to the PowerPoint to review the search and begin appraisal process
Choosing articles: which are best?

• Matches your PICO
• Right study design
• In English language
• Accessible via Duke subscriptions

*After you make your initial article selections based on the above criteria, your next step is to ensure the researchers have done all they can to eliminate bias (more on that after the searching section).
The search process...

My initial search was:  falls AND vitamin D

*note that falls finds the MeSH term accidental falls (that’s good!)

There were a lot of articles, with many related to daily doses, etc.

So my next search was narrower:

falls AND vitamin D AND (annual OR high dose OR mega OR yearly)

*Include other relevant synonyms that you find in the literature!

The last step is to filter by study type & age (according to PICOTT)
The filters on the right are for the best type of evidence. The filters on the left are for Ages, English, Humans, Date. NOTE: Skip Text Availability!
Now that you have done a search & have articles that match your PICO to review, let’s talk about the next step, the critical appraisal.

You need to consider the validity of the studies to guide your clinical practice and, more specifically, your care of Roberta. Your job is determine if the researchers did all they could to eliminate bias.

Before we practice appraising a specific article, let’s review the therapy validity criteria (FRISBE).
Appraisal: FRISBE

- **Follow-up**
- **Randomization / Concealed allocation**
- **Intention-to-Treat**
- **Similar baseline characteristics**
- **Blinding**
- **Equal treatment**

Now let’s talk about each one using the Users Guide...
Validity Criteria

User’s Guides for an Article About Therapy: Are the Results Valid?

1. Did the intervention and control groups start with the same prognosis?
   a. Were patients randomized?
   b. Was randomization concealed?
   c. Were patients in the study groups similar with respect to known prognostic factors?

2. Was prognostic balance maintained as the study progressed?
   a. To what extent was the study blinded?
   b. Aside from the experimental intervention, were the groups treated equally?

3. Were the groups prognostically balanced at the study’s completion?
   a. Was follow up complete?
   b. Were patients analyzed in the groups to which they were randomized? (i.e., was it an intention-to-treat analysis?)
   c. Was the trial stopped early?
1. Do the experimental and control groups begin the study with a similar prognosis?

Randomization
Allocation concealment

Similar at baseline
Which of these methods is considered randomized?

1. Assigning patients by odd/even birth dates
2. Assign patients by toss of coin
3. Assign patients sequentially
4. All of these
Which of these methods is considered *randomized*?

1. Assigning patients by odd/even birth dates
2. Assign patients by toss of coin
3. Assign patients sequentially
4. All of these
Randomization

• Spread confounding variables evenly across the groups

• Equal chance of getting into either arm of the study

• Increase likelihood that the intervention is the only difference between groups
Concealed allocation means that

1. the patients don’t know which intervention they received
2. the person enrolling patients does not know the next assignment
3. the researchers can not change the randomization sequence
4. 2 and 3
Concealed allocation means that

1. the patients don’t know which intervention they received
2. the person enrolling patients does not know the next assignment
3. the researchers cannot change the randomization sequence
4. 2 and 3
Allocation Concealment

- Investigator cannot influence (determine or change) the assignment of patients into the study arms

- Can always conceal allocation

- Reduced selection bias
Allocation Concealment

- Investigator cannot influence the allocation at the time of study entry
- RCTs lacking a statement about allocation concealment are associated with larger effect-size bias (33% if unclear, 41% if not done)
- Not typically done (55% of RCTs in “best” journals, 7% of RCTs in “poorer” journals)

Concealed allocation?!

The patient’s condition fits the trial, and she has consented. Which treatment pack should I give her?

Nope!
Similar at Baseline

- Known prognostic factors should be balanced between groups
  - Typically “Table 1”
2. Do the experimental and control groups retain a similar prognosis after the study started?
Blinding

• Reduces assessment bias

• Who to blind?
  ➢ Subjects
  ➢ Clinicians
  ➢ Data collectors
  ➢ Outcome adjudicators
  ➢ Data analysts

Fig. 1: The double-blind nature of the study was maintained throughout the trial. Dr. Innes is shown sitting.
Equal Treatment

• The experimental intervention should be the only thing that differs between groups.
• Any other factor which differs systematically between groups is called a “co-intervention”, and may obscure true effects.
3. Do the experimental and control groups **end** with a similar prognosis?

- Follow up Complete
- Intention to Treat
- Trials Stopped Early
Follow-up

• Account for all patients in the study

• Study duration long enough to manifest the target outcome
Follow-up Complete

• Loss of subjects creates missing data, which threatens the balance of randomization
• Those lost may have different prognosis than those who stayed
• Methods for managing missing data vary in strength
Intention to Treat

• Analyzed in groups to which they were randomized, whether they received the intervention or not
• Don’t allow cross-over (it introduces bias!)
• **Maintains randomization**
• True measure of the “Effectiveness” – this is how it works in the real world

*Euphemisms for breaking ITT: “per protocol analysis”, “as treated analysis”, “efficacy analysis”*
Analyzed in groups to which they were randomized, whether the intervention received or not.
Not analyzed in groups to which they were randomized. The randomization is lost and bias was introduced.
Trials Stopped Early

- Fewer observed outcomes
- Greater chance of random error
- Truncating RCTs accounts for differences in effect size, in a systematic review
- Magnitude is greatest with fewer than 500 outcome events

Bassler et al. JAMA 2010;303(12):1180-1187
ANALYZING THE RESULTS
How are results presented?

- **Risk** = any event or outcome
- **Absolute Risk** = proportion of group with an outcome

For example: 100 people are randomized to Drug A for stroke prevention. 15 people have strokes.

- Absolute Risk of stroke with Drug A = 15%
Absolute Risk Reduction

• 100 people were randomized to Drug B, a newer medication. With Drug B, 10% of people had a stroke.

• 15% - 10% = 5%

• **ARR** is the absolute difference between groups.
Relative Risk Reduction

• “What proportion of our baseline risk have we reduced?”

• **RRR** = \( \frac{ARR}{Baseline\ Risk} \)

• RRR = 5%/15% = 33%

• Which one is more impressive?
Review the article:
http://tinyurl.com/jama-vitamind

Critically appraise using this sheet:
http://tinyurl.com/critical-app-practice
User’s Guides for an Article About Therapy: Are the Results Valid?

1. Did the intervention and control groups start with the same prognosis?
   a. Were patients randomized?
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2. Was prognostic balance maintained as the study progressed?
   a. To what extent was the study blinded?
   b. Aside from the experimental intervention, were the groups treated equally?

3. Were the groups prognostically balanced at the study’s completion?
   a. Was follow up complete?
   b. Were patients analyzed in the groups to which they were randomized? (i.e., was it an intention-to-treat analysis?)
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<table>
<thead>
<tr>
<th><strong>Follow-Up</strong></th>
<th></th>
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<tbody>
<tr>
<td>• Were all patients who entered the trial properly accounted for and attributed at its conclusion?</td>
<td></td>
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<tr>
<td>• Was follow-up complete?</td>
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<table>
<thead>
<tr>
<th><strong>Randomization</strong></th>
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<tbody>
<tr>
<td>• Was the allocation (assignment) of patients to treatment randomized?</td>
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<tr>
<td>• Was the allocation concealed?</td>
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<table>
<thead>
<tr>
<th><strong>Intention-to-Treat Analysis</strong></th>
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<tbody>
<tr>
<td>• Were patients analyzed in the groups to which they were randomized?</td>
<td></td>
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<tr>
<td>• Were all randomized patient data analyzed?</td>
<td></td>
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</tbody>
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<table>
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<tr>
<th><strong>Similar Baseline Characteristics of Patients</strong></th>
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<tbody>
<tr>
<td>• Were groups similar at the start of the trial?</td>
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<tr>
<th><strong>Blinding</strong></th>
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<tbody>
<tr>
<td>• Were patients, health workers, and study personnel &quot;blind&quot; to treatment?</td>
<td></td>
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<th><strong>Equal Treatment</strong></th>
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<td>• Aside from the experimental intervention, were the groups treated equally?</td>
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**Summary of article’s validity**
So, overall, is it valid “enough”?

Yes!
Now on to results...
Construct your 2x2 table on paper...

<p>| | | |</p>
<table>
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Hints...

Now fill in the table headers and figure out the experimental event rate and the control event rate.
Is this what yours looked like?

<table>
<thead>
<tr>
<th></th>
<th>More than 1 Fall</th>
<th>No Falls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>837</td>
<td>294</td>
</tr>
<tr>
<td>Placebo</td>
<td>769</td>
<td>356</td>
</tr>
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</table>

Experimental event rate (Y): $\frac{837}{1131} = 74\%$

Control event rate (X): $\frac{769}{1125} = 68.4\%$
What’s the absolute risk increase?

1. 74% - 68.4% = 5.6%
2. \( \frac{.74}{.684} = .108 = 11\% \)
3. \( \frac{837}{769} = 1.08 \)
4. Not sure
The absolute risk increase

1. $74\% - 68.4\% = 5.6\%$

2. $\frac{.74}{.684} = .108 = 11\%$

3. $\frac{837}{769} = 1.08$

4. Not sure

**Absolute Risk Reduction (ARR)** is the difference in risk between the control group and the treatment group. 
\[
ARR = X - Y
\]

Note that since the outcome for the experimental group actually resulted in a higher risk, it is an Absolute Risk Increase (rather than Reduction) by 5.6%. 
What is the relative risk increase?

1. $74\% - 68.4\% = 5.6\%$
2. $5.6 / 68.4 = 8\%$
3. $74 / 68.4 = 11.3$
4. Not sure
The relative risk increase is

1. \( 74\% - 68.4\% = 5.6\% \)

2. \( \frac{5.6}{68.4} = 8\% \)

3. \( \frac{74}{68.4} = 11.3 \)

4. Not sure

Relative Risk Reduction (RRR) is the percent reduction in risk in the treated group compared to the control group.

\[
RRR = \left[ \frac{(X - Y)}{X} \right] \times 100\%
\]

Again, note that it is a Relative Risk Increase (rather than Reduction) by 8\%.
What’s the Number Needed to Treat?

1. 20
2. 18
3. 6
4. Not sure

Rather than an NNT (Number Needed to Treat) we are working with the NNH (Number Need to Harm), or the number of patients that need to be treated with the intervention to have one additional bad outcome.
Clinicians would need to treat 18 patients with a mega dose of Vitamin D to result in 1 additional patient having a fall.
Results: 2x2 table

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Absolute Risk Increase: 74% - 68.4% = 5.6% increase in risk

Number Needed to Harm: 1 / 5.6 = 18
So based on this article as well as others you may have reviewed, should Roberta take the yearly mega dose of Vitamin D?

EBM only takes you so far... To answer this question, you also use values and preferences.
Critical Appraisal Application Process

• Email link to assignment sent out Monday 4pm
• The assignment will replicate the process from this PowerPoint
• Submit completed assignment by Tuesday 11am
• Meet with Librarian to present the case, your PICOTT, PubMed search and your critical appraisal of the article