Learning Objectives:

After working through this packet, you should be able to:
1. Apply the validity criteria for harm studies to an article concerning a question of adverse events due to pharmacotherapy.
2. Understand the methodology, strengths and weaknesses of a case-control study.
3. Understand the meaning of an odds ratio and how to apply it to a clinical case.
4. Understand the principle of confounding and be able to generate examples of possible confounders in this example.

Assessment of the Case:
You are asked to consult on a patient on the orthopedics inpatient ward. The patient is a 69-year-old Caucasian woman who is s/p total knee replacement 3 days ago. She is an active 69 year old who lived independently prior to her hospital stay. Her high level of activity (which had included a 2 mile walk three times each week) was recently halted due to her worsening osteoarthritis. Her past medical history includes hypertension and hypercholesterolemia.

Her surgery was uncomplicated, however she had considerable post-operative pain and anxiety about being hospitalized and away from home. On post-operative day #3, she became agitated, pulled out all of her intravenous lines and complained of seeing insects crawling around her room. She became abusive to hospital staff and accused the nurses of trying to poison her with her medications. A search for infection, ischemia, and metabolic abnormalities that might explain her delirium is not fruitful.

Her current medications include HCTZ 25 mg po qd, simvastatin 20 mg po qd, lorazepam 1-2 mg i.v. q2 prn agitation, and benadryl 25 mg po qhs prn sleep. She is also getting patient controlled administration of iv morphine.

The orthopedic surgery resident wonders if any of her medications might be contributing to her delirium. Specifically, she asks you whether benzodiazepines cause postoperative delirium. She is also concerned that the morphine PCA may be contributing to the patient’s delirium. However, she feels strongly that she should treat the pain aggressively and would like to know whether it is safe to continue this medication.
Asking the clinical question(s):
You frame the following clinical questions:

? In postoperative patients, are benzodiazepines associated with delirium?
? In postoperative patients, are narcotic drugs (including morphine) associated with delirium?

You are in quite a rush, so you log onto your hospital's library website and decide to search for an evidence summary in ACP Journal Club. You enter the following search strategy:

<table>
<thead>
<tr>
<th>Search History</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Postoperative</td>
<td>134</td>
</tr>
<tr>
<td>2. Benzodiazepines</td>
<td>21</td>
</tr>
<tr>
<td>3. 1 and 2</td>
<td>1</td>
</tr>
</tbody>
</table>

The single abstract that comes up is entitled Meperidine and benzodiazepines were associated with postoperative delirium. ACP Journal Club volume 122 p 80, May-June, 1995.

Within a few seconds, you pull up the page long article summary in ACP journal club. The summary does seem to address your clinical questions, specifically discussing benzodiazepines and narcotics in postoperative patients. In reading the summary, you note that it is a ‘nested case-control study’ and you quickly acknowledge (to yourself) that you are not fully comfortable with this methodology. You decide that these are important clinical questions that you will face repeatedly as a consultant on the surgical service. Therefore, you decide to print the original article. Fortunately, this is available online in full text. You print the paper (as well as the ACP journal club review) for your review this evening.

Readings and Citation:

ACP Journal Club summary: Meperidine and benzodiazepines were associated with postoperative delirium. ACP Journal Club. V122:p80, May-June, 1995.

Original Reference:

Background reading:

Users’ Guide to the Medical Literature:
Therapy and Harm: An Introduction; page 49
Harm Section 1B2; page 81