



# Quick Literature Searches

National Pediatric Nighttime Curriculum

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# Case 1

It's 1:00am and you have just received the following text page from an RN:

"pt in 234, bronchiolitis, now wheezing and O2 up to 2L, do you want to give albuterol trx?"

# Case 2

It's 2:00am and you have just received the following call from the intern:

"Pt in 422, 4 yo with pneumonia and pleural effusion is having persistent fevers, now day 6, should I do additional work-up for source of fever?"



← Click to  
continue Case 2

# Objectives

- Learn how to ask an answerable question
- Create a successful literature search by identifying:
  - what type of question is being asked
  - and the best studies to answer it
- Quickly appraise an article for its validity

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# Applying Evidence Based Medicine...After Midnight

- What do you think about in this situation?
  - What are your previous clinical experiences?
  - What does the literature say regarding bronchodilators and bronchiolitis?



Initial steps to take:

You quickly review the patient's chart and see he's a previously healthy 10 month old, with RSV bronchiolitis, on hospital day 2. He has no prior history of wheezing. When you perform your exam, he is mildly tachypneic on 2L NC O<sub>2</sub>, up from 1L earlier in the day, and you appreciate intermittent wheezes.

Now...do you give him an albuterol treatment?

# Creating an Answerable Question

- **P: Population or problem**
  - Includes descriptors of the type of patients or problems you are inquiring about, can include
- **I: Intervention, prognostic factor, or exposure**
  - Includes what you want to do for the patient
  - May include factors that can influence the patient's prognosis
  - May include exposures the patient has had
- **C: Comparison**
  - Defines what you want to use as measurement for contrasting your intervention
  - Not always applicable
- **O: Outcome**
  - The variables you are interested in measuring

# Creating an Answerable Question

- For your bronchiolitis patient, you may ask:

P In previously healthy children with bronchiolitis,

I does using albuterol (bronchodilators)

C compared to no bronchodilator treatments

O improve their oxygen status or clinical outcome?

# Objectives

- Learn how to ask an answerable question
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# Creating a Successful Search

To quickly sort through the literature, you must know the type of question being asked and the best studies to answer it.

Questions can be divided into four basic categories:

<b>Diagnosis</b>	how to select and interpret diagnostic tests
<b>Therapy</b>	how to select treatments to offer patients that do more good than harm and that are worth the efforts and costs of using them
<b>Prognosis</b>	how to estimate the patient's likely clinical course over time and anticipate likely complications of disease
<b>Harm/Etiology</b>	how to identify the negative impact of a medical intervention/environmental agent OR the causation of disease

# Creating a Successful Search

Type of Question:	Suggested best type of study:
Diagnosis	prospective, blind comparison to a gold standard
Therapy	RCT > cohort > case control > case series
Prognosis	cohort study > case control > case series
Harm/Etiology	RCT > cohort > case control > case series



For your bronchiolitis patient, what type of question are you asking?

What will be the best type of study to search?

# Creating a Successful Search

- **Select a database**
- **Form search using MeSH terms**
  - Two types of search terms exist
    - MeSH (Medical Subject Heading) terms
    - Text terms
      - Example: searching for “swine flu outbreak” finds about 630 articles in MEDLINE. However, searching for “influenza A virus, H1N1 subtype” and “disease outbreak”, both MeSH terms, generates a more comprehensive search with over 1800 articles.
- **Connect search terms**
  - AND, OR, and NOT
  - In all capital letters
- **Use Clinical Queries**
  - Select the Category of question
  - Select the Scope of search
- **Run the search**
- **Limit your results, if desired**

# Creating a Successful Search

P	In previously healthy children with <b>bronchiolitis</b> ,
I	does using albuterol ( <b>bronchodilators</b> )
C	compared to no bronchodilator treatments
O	improve their oxygen status or clinical outcome?

- Identify MeSH terms: Bronchiolitis and “Bronchodilator Agents”
- Select Clinical Queries
- Enter and Connect search terms
- Identify the type of question and the best study to answer it
- Select Therapy for category
- Select Broad for study scope

# Objectives

- Learn how to ask an answerable question
- Create a successful literature search by identifying:
  - what type of question is being asked
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- Quickly appraise an article for its validity

# Quickly appraise the article

- Validity: closeness to the truth
- Statistical accuracy: results soundly derived
- Applicability: usefulness to your patient
- Threats to the truthfulness of an article are termed biases, and three broad categories of bias exist in medical studies.

Bias	Definition	Ways to minimize bias
Selection bias	<ul style="list-style-type: none"><li>•When the groups of patients being compared differ in ways other than what is being studied</li></ul>	<ul style="list-style-type: none"><li>•Random selection and random allocation of patients</li><li>•Maximizing follow-up</li><li>•Ensuring participants stay in the groups they were originally allocated (intention-to-treat analysis)</li></ul>
Measurement bias	<ul style="list-style-type: none"><li>•When the outcome measured is inaccurate, either due to inaccuracy in the measurement instrument or a bias in the expectations by study participants or researchers</li></ul>	<ul style="list-style-type: none"><li>•Blinding of study participants and researchers</li></ul>
Confounding bias	<ul style="list-style-type: none"><li>•When an associated factor other than the one being studied is confused with or altering the true results</li></ul>	<ul style="list-style-type: none"><li>•Randomization and statistical techniques can help minimize this bias</li></ul>

# Quickly appraise the article

- Studies vary in their methodology as do the questions required to assess them
- In the middle of the night, it's not essential to memorize the ideal questions
- BUT, you should at least think about the validity, results, and applicability of the study
- To quickly to do this, glance at the abstract paying particular attention to
  - the type of study
  - the patients studied
  - the methods section to screen for bias
  - the results section
- Finally, make a decision about how applicable the study seems to your patient
- Scan the articles for your bronchiolitis search, and select the one titled "**Bronchodilators for bronchiolitis.**" Gadomski AM, Brower M. Cochrane Database Syst Rev. 2010 Dec 8;12:CD001266.
- Quickly glance at the abstract for the article's validity, results, and applicability

## Quick Appraisal

Type of study: Systematic review (of randomized controlled trials)

Patient description: infants, outpatient and inpatient

Screen for bias: Yes, as part of Cochrane systematic review

Results: No difference between bronchodilators, and placebo for admission, length of hospitalization and oxygen saturation

Applicable to your 10 month old, previously healthy, inpatient with bronchiolitis? Yes.

**BACKGROUND:** Bronchiolitis is an acute, viral lower respiratory tract infection affecting infants and often treated with bronchodilators.

**OBJECTIVES:** To assess the effects of bronchodilators on clinical outcomes in infants with acute bronchiolitis.

**SEARCH STRATEGY:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2010, Issue 1) which contains the Acute Respiratory Infections Group's Specialized Register, MEDLINE (1966 to March week 2 2010) and EMBASE (2003 to March 2010).

**SELECTION CRITERIA:** Randomized controlled trials (RCTs) comparing bronchodilators (other than epinephrine) with placebo for bronchiolitis.

**DATA COLLECTION AND ANALYSIS:** Two authors assessed trial quality and extracted data. Unpublished data were obtained from trial authors.

**MAIN RESULTS:** We included 28 trials (1912 infants) with bronchiolitis. In 10 inpatient and 10 outpatient studies, oxygen saturation did not improve with bronchodilators (mean difference (MD) -0.45, 95% confidence interval (CI) -0.96 to 0.05, n = 1182). Outpatient bronchodilator treatment did not reduce the rate of hospitalization (12% in bronchodilator group versus 16% in placebo, odds ratio (OR) 0.78, 95% CI 0.47 to 1.29, n = 650). Inpatient bronchodilator treatment did not reduce the duration of hospitalization (MD 0.06, 95% CI -0.27 to 0.39, n = 349). In seven inpatient and eight outpatient studies, average clinical score decreased slightly with bronchodilators (standardized mean difference (SMD) -0.37, 95% CI -0.62 to -0.13, n = 1006). Oximetry and clinical score outcomes showed significant heterogeneity. Including only studies at low risk of bias significantly reduced heterogeneity measures for oximetry ( $I^2$  statistic = 17%) and average clinical score ( $I^2$  statistic = 26%), while having little impact on the overall effect size of oximetry (MD -0.38, 95% CI -0.75 to 0.00, P = 0.05) and average clinical score (SMD -0.26, 95% CI -0.44 to -0.08, P = 0.005). Effect estimates for outpatients were slightly larger than for inpatients for oximetry (outpatients MD -0.57, 95% CI -1.13 to 0.00 versus inpatients MD -0.29, 95% CI -1.10 to 0.51) and average clinical score (outpatients SMD -0.49, 95% CI -0.86 to -0.11 versus inpatients SMD -0.20, 95% CI -0.43 to 0.03). Adverse effects included tachycardia and tremors.

**AUTHORS' CONCLUSIONS:** Bronchodilators do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. The small improvements in clinical scores for outpatients must be weighed against the costs and adverse effects of bronchodilators

# Take Home Points

- Ask an answerable question, using the PICO format
- Create a successful literature search by identifying what type of question is being asked and the best studies to answer it
- Quickly appraise an article for its validity, statistical results, and applicability

# References

- Duke University Medical Center Library . (2011). *Introduction to Evidence Based Medicine*. Retrieved Jan 11, 2010 from <http://www.mclibrary.duke.edu>.
- Onady, GM, Raslich, MA. Evidence-based Medicine: Searching Literature and Databases for Clinical Evidence (Search Tools). *Pediatrics in Review*. 2004; 25: 358-363
- Raslich, MA, Onady, GM. Evidence-based Medicine: Critical Appraisal of the Literature (Critical Appraisal Tools). *Pediatrics in Review* . 2007; 28: 132-138

# Case 2: Applying Evidence Based Medicine...after Midnight

- What do you think about in this situation?
  - What are your previous clinical experiences?
  - What does the literature say regarding typical course for a patient with parapneumonic effusion?



Initial steps to take:

You quickly get additional information regarding the patient from your intern and learn he's a previously healthy 4 year old with pneumonia, effusion, and fever for 6 days. The effusion was drained 4 days ago, and the culture grew *Streptococcus pyogenes*, susceptible to ampicillin, which he has been receiving. He was weaned off oxygen yesterday, and his respiratory status is stable. He has a new peripheral IV and other than the fever, has no new complaints or symptoms.

Now...should you pursue an additional source for the fever or, after 6 days, can it still be due to the effusion?

# Creating an Answerable Question

- For your pneumonia patient, you may ask:

P	In previously healthy children with pneumonia and pleural effusions,
I	Is prolonged fever (>5 days)
C	
O	an expected clinical course?

# Creating a Successful Search

Type of Question:	Suggested best type of study:
Diagnosis	prospective, blind comparison to a gold standard
Therapy	RCT > cohort > case control > case series
Prognosis	cohort study > case control > case series
Harm/Etiology	RCT > cohort > case control > case series



For your pneumonia patient, what type of question are you asking?

What will be the best type of study to search?

# Creating a Successful Search

P	In previously healthy children with <b>pneumonia</b> and <b>pleural effusions</b> ,
I	Is prolonged <b>fever</b> (>5 days)
C	
O	An expected clinical course?

- Identify MeSH terms: Pneumonia, “Pleural Effusion”, and Fever
- Select Clinical Queries
- Enter and Connect search terms
- Identify the type of question and the best study to answer it
- Select Prognosis for category
- Select Broad for study scope
- From the Clinical Studies category, click on the “See All” hyperlink to reveal the comprehensive search
- Limit to pediatric studies

# Quickly appraise the article

- Validity: closeness to the truth
- Statistical accuracy: results soundly derived
- Applicability: usefulness to your patient
  
- To quickly do this, glance at the abstract paying particular attention to
  - the type of study
  - the patients studied
  - the methods section to screen for bias
  - the results section
  
- Find the article from your search titled "**Predictive factors of morbidity in childhood parapneumonic effusion-associated pneumonia: a retrospective study.**" Picard E, Joseph L. Pediatr Infect Dis J. 2010 Sep;29(9):840-3.
- Quickly glance at the abstract for the article's validity, results, and applicability.

- STUDY OBJECTIVE: To find the clinical and laboratory criteria that best predict a prolonged fever in children with parapneumonic effusion-associated pneumonia treated conservatively.
- DESIGN: **Retrospective, cohort study.**
- PATIENTS: **Children admitted to the Shaare Zedek Medical Center between January 1, 1997, and December 31, 2006, and who had been discharged with a diagnosis of empyema and pleurisy.**
- MEASUREMENTS AND RESULTS: **One hundred-twenty children were included, all of whom were treated with antibiotics; in 80 patients, a thoracic drain was introduced; in 23, pleural tap was performed; and in 17 patients, no special procedure was performed.** In no case was video-assisted thoracic surgery performed. The mean total days of fever was  $12.8 +/ - 5.9$  (2-29 days), and the mean length of stay at the hospital was  $11.5 +/ - 4.9$  (3-25) days. In 44 patients (37%), a bacterial culture was positive either in blood or in pleural fluid or both. A positive blood or a positive pleural fluid culture was significantly associated with a prolonged fever as was a history of an underlying disease. Platelet counts, serum Na, serum protein, pleural lactate dehydrogenase (LDH), pleural glucose, pleural/serum LDH ratio, pleural/serum glucose ratio, and pleural fluid pH were the only factors significantly but weakly correlated with the total duration of fever or duration of fever after admission. A "fever duration" score using platelet count, pleural fluid pH, pleural/serum LDH ratio, and pleural/serum glucose ratio predicted a prolonged course of fever ( $>7$  days) with a sensitivity of 91% (95% confidence interval: 60%-100%) and a specificity of 47% (95% confidence interval: 25%-71%).
- CONCLUSIONS: **In children with parapneumonic effusion-associated pneumonia, a positive bacterial culture and an underlying disease are associated with prolonged fever.** A low score based on platelet count, pH pleural fluid and glucose, and LDH pleural/serum ratio is associated with a prolonged fever. We speculate that children with the risk factors mentioned earlier may be the best candidates for an early aggressive approach.

## Quick Appraisal

Type of study: **Cohort, retrospective**

Patient description: **admitted children in Jerusalem, majority had special procedure performed**

Screen for bias: **retrospective, unclear**

Results: **Positive blood or pleural fluid culture was significantly associated with a prolonged fever**

Applicable to your 4 year old, previously healthy, inpatient with fever and pleural effusion?

Possibly, you elect to read the article to assist with your decision.