實證醫學 病例討論報告
Evidence-Based Medicine

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報告日期: 101.10.9

肝膽胰內科

Outline

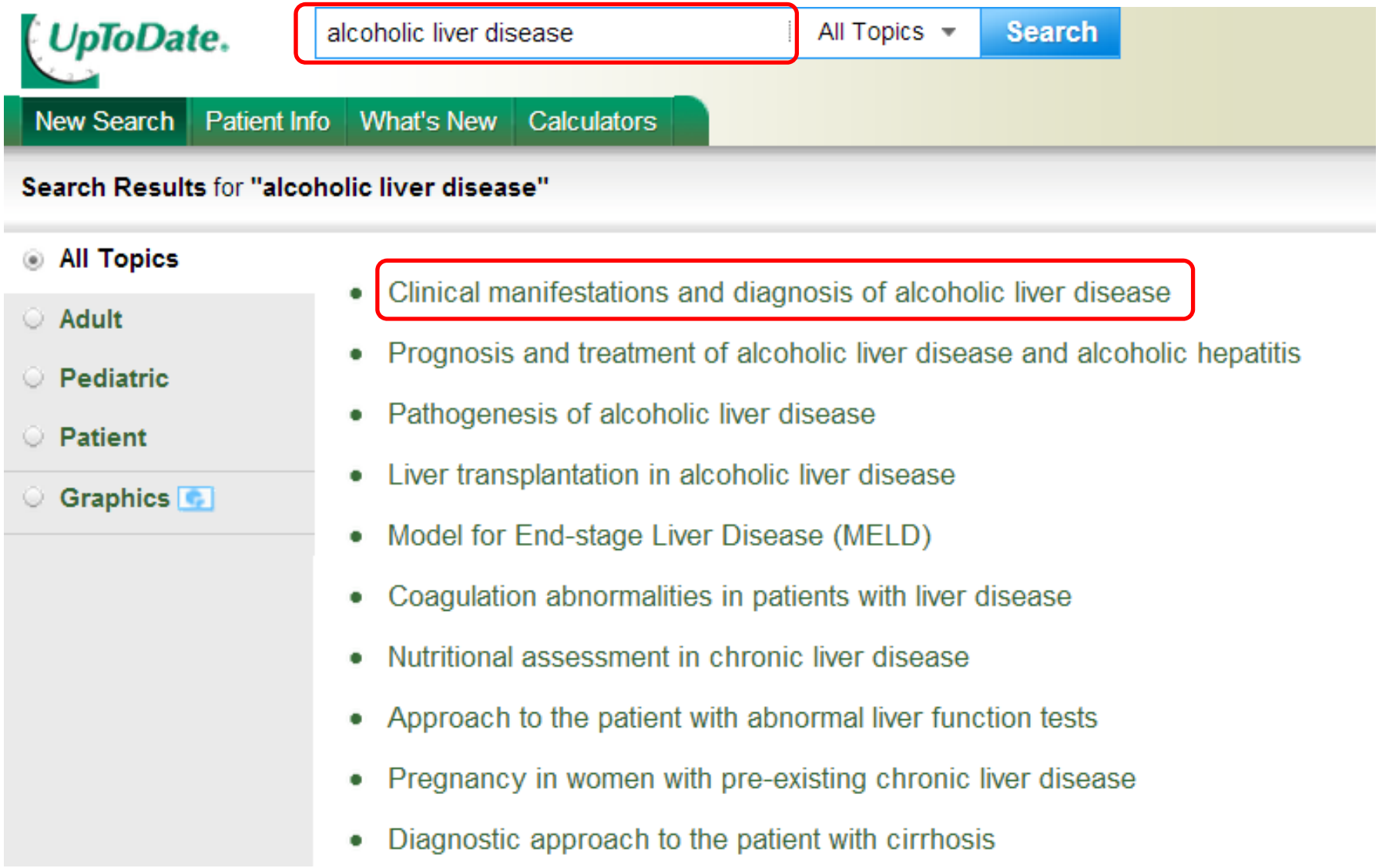
- Clinical scenario-臨床場景
- Asking-提出問題
- Acquire- 搜尋資料
- Appraisal-嚴格評讀
- Apply-臨床應用
- Audit-自我評估

Clinical scenario

- 張先生，45歲，長期飲酒習慣已有20多年，紅酒、高粱不忌。在三年前的健康檢查中診斷出來酒精性肝炎，沒有其他系統性疾病。最近兩三天，人感覺疲倦，身體微微發燒，沒有畏寒感，特別提到上周末過中秋時跟朋友飲酒作樂，有多喝兩杯。去家庭醫學科診所求助。

Clinical scenario

- Associated s/s: fever without chillness, cough(-), rhinorrhea(-), sore throat(-), diarrhea(-), abdominal pain(-),burning sensation(-)
- PE:
  - BP: 127/82 mmHg,
  - HR: 88bpm
  - RR:20cpm
  - BT: 38.2 ^{o}C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Clinical manifestations and diagnosis of alcoholic liver disease
Prognosis and treatment of alcoholic liver disease and alcoholic hepatitis
Pathogenesis of alcoholic liver disease
Liver transplantation in alcoholic liver disease
Model for End-stage Liver Disease (MELD)
Coagulation abnormalities in patients with liver disease
Nutritional assessment in chronic liver disease
Approach to the patient with abnormal liver function tests
Pregnancy in women with pre-existing chronic liver disease
Diagnostic approach to the patient with cirrhosis

Alcoholic liver disease

- **ALCOHOLIC FATTY LIVER** — Alcoholic fatty liver (steatosis) is rarely diagnosed clinically because most patients are asymptomatic and do not seek medical attention. However, up to 90 percent of alcoholics have steatosis.
- **ALCOHOLIC HEPATITIS** — Alcoholic hepatitis is defined by both clinical and pathologic criteria. It should be suspected clinically in patients with heavy alcohol use and compatible clinical and laboratory findings.
  - **Clinical manifestations** — The characteristic clinical features of alcoholic hepatitis are fever, hepatomegaly, jaundice, and anorexia. Patients can also present with right upper quadrant/epigastric pain, hepatic encephalopathy, and bleeding.

- **ALCOHOLIC CIRRHOSIS AND FIBROSIS** — The clinical and laboratory features of alcoholic cirrhosis are similar to those seen in other causes of cirrhosis with one exception: affected patients may have concurrent histologic evidence of alcoholic hepatitis. In addition, reversibility of alcoholic fibrosis may be greater than other forms of liver disease if there is a significant inflammatory component due to recent alcohol ingestion.

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Acute liver failure

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Acute liver failure

Acute renal failure

Acute heart failure

Acute fatty liver of pregnancy

Hepatitis C (acute)

Acute portal vein thrombosis

Acute cholecystitis

Renal replacement therapy for acute renal failure

Acute renal failure - differential diagnosis

Acute variceal hemorrhage

Cirrhosis of the liver

Diastolic heart failure

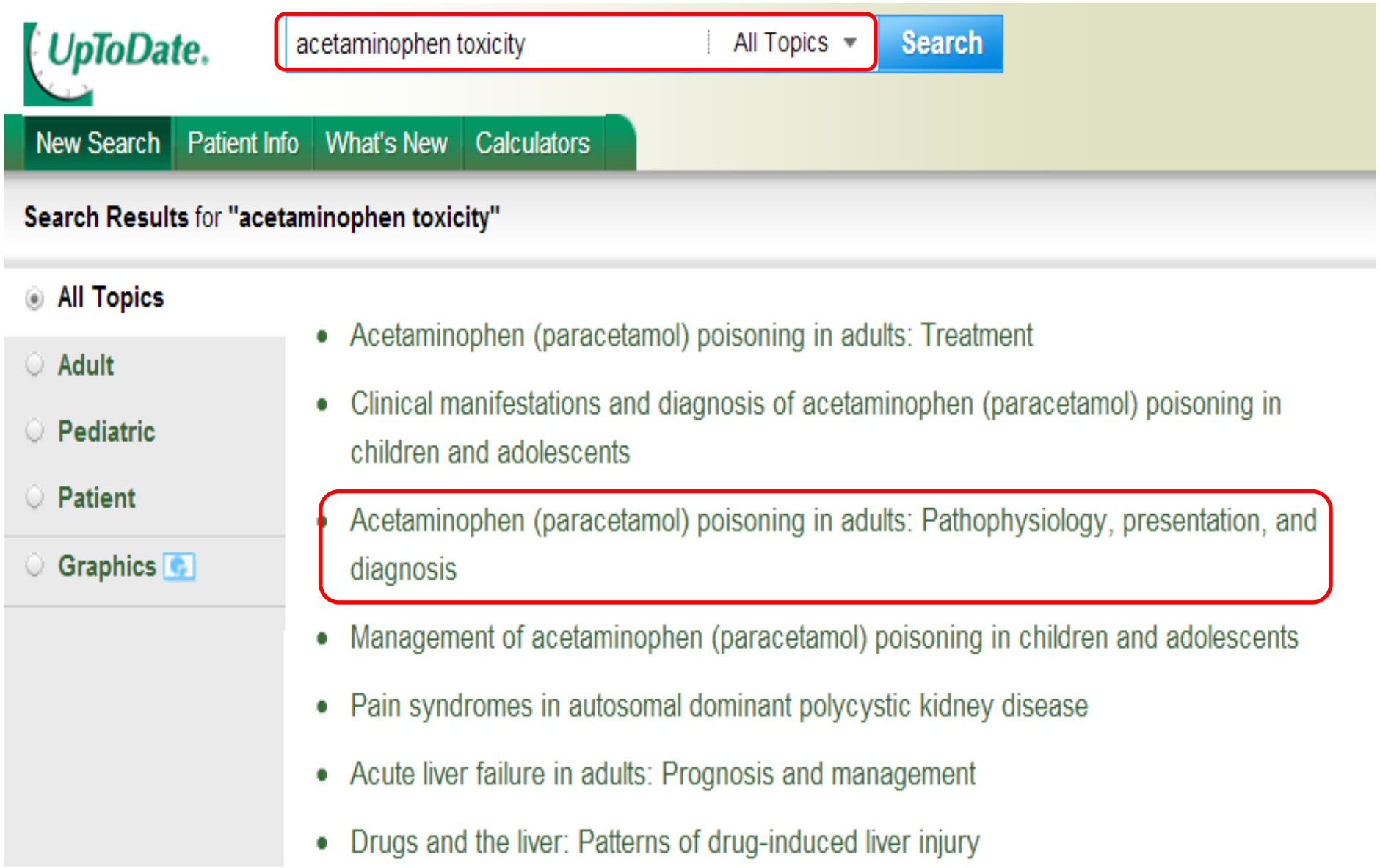
Heart failure

Acute liver failure

- acute liver failure (fulminant hepatic failure) is coagulation abnormality (INR ≥ 1.5) and any degree of mental alteration in patient with new-onset liver disease (< 26 weeks duration)
- common causes are drugs and toxins (especially acetaminophen or mushroom poisoning) and viral hepatitis
- diagnostic evaluation
  - all patients with moderate to severe acute hepatitis should have immediate measurement of prothrombin time (INR) and mental status evaluation (to determine grade of hepatic encephalopathy if present)
  - initial testing in acute liver failure includes prothrombin time/INR, electrolytes, glucose, liver function tests, renal function tests, arterial blood gas, complete blood count, blood type, acetaminophen level, toxicology screen, viral hepatitis serologies, pregnancy test, arterial ammonia, autoimmune markers, HIV, amylase, lipase
  - additional testing may include head computed tomography (CT), liver biopsy (especially if autoimmune hepatitis, malignancy or Wilson disease), electroencephalogram (EEG), and cause-specific testing if considering Wilson disease or Budd-Chiari syndrome

Acute liver failure

- acetaminophen causes 40%-50% of cases of acute liver failure acetaminophen overdose cause in 42% of cases of acute liver failure
  - based on prospective cohort study
  - 662 consecutive patients with acute liver failure in United States over 6 year period were evaluated
  - 275 cases (42%) attributed to acetaminophen
    - 131 cases (48%) unintentional
    - 122 cases (44%) intentional (suicide attempts)
    - 22 cases of unknown intent
  - Reference - Hepatology 2005 Dec;42(6):1364 full-text, editorial can be found in Hepatology 2005 Dec;42(6):1252, commentary can be found in Hepatology 2006 Apr;43(4):880, Gastroenterology 2006 Sep;131(3):963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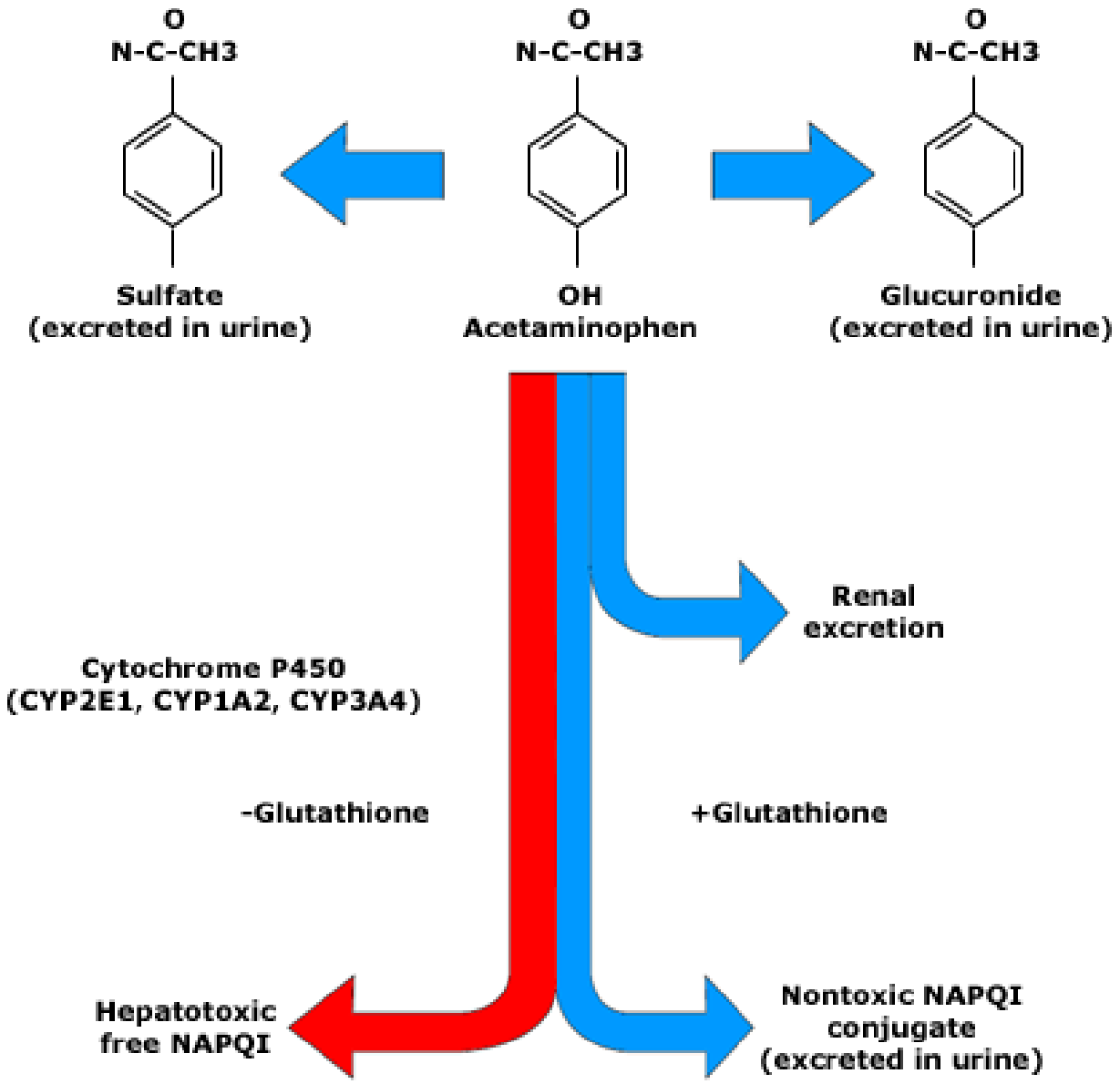
Clinical manifestations and diagnosis of acetaminophen (paracetamol) poisoning in children and adolescents
Acetaminophen (paracetamol) poisoning in adults: Pathophysiology, presentation, and diagnosis
Management of acetaminophen (paracetamol) poisoning in children and adolescents
Pain syndromes in autosomal dominant polycystic kidney disease
Acute liver failure in adults: Prognosis and management
Drugs and the liver: Patterns of drug-induced liver injury

Acetaminophen metabolism



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PHARMACOKINETICS

- The therapeutic dose is 10 to 15 mg/kg per dose in children and 325 to 1000 mg per dose in adults, given every four to six hours, with a maximum recommended daily dose of 80 mg/kg in children or 4 g in adults.
- Toxicity is unlikely to result from a single dose of less than 150 mg/kg in a child or 7.5 to 10 g for an adult.
- Toxicity is likely to occur with single ingestions greater than 250 mg/kg or those greater than 12 g over a 24-hour period.
- Virtually all patients who ingest doses in excess of 350 mg/kg develop severe liver toxicity (defined as peak aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels greater than 1000 IU/L) unless appropriately treated

- **CLINICAL FACTORS INFLUENCING TOXICITY** — Liver damage from acetaminophen ingestion can occur in four circumstances:
- Excessive intake of acetaminophen
- Excessive cytochrome P450 activity
- Decreased capacity for glucuronidation or sulfation
- Depletion of glutathione store

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Acetaminophen poisoning

- **Pathogenesis:**
- following acetaminophen overdose
  - glucuronosyltransferase and sulfotransferases are saturated
  - toxic metabolite N-acetyl-p-benzoquinoneimine (NAPQI) accumulates and depletes glutathione
  - NAPQI can covalently bind with cellular proteins and modify their structure and function
  - hepatotoxicity develops in next 24-48 hours

Acetaminophen poisoning

- **Possible risk factors:**
- risk factors that may increase susceptibility to acetaminophen poisoning
  - chronic alcohol use
  - use of enzyme-inducing drugs (such as phenytoin and carbamazepine)
  - fasting state (such as patients with malnutrition or anorexia nervosa)
  - chronic use of antituberculous therapy, specifically isoniazid

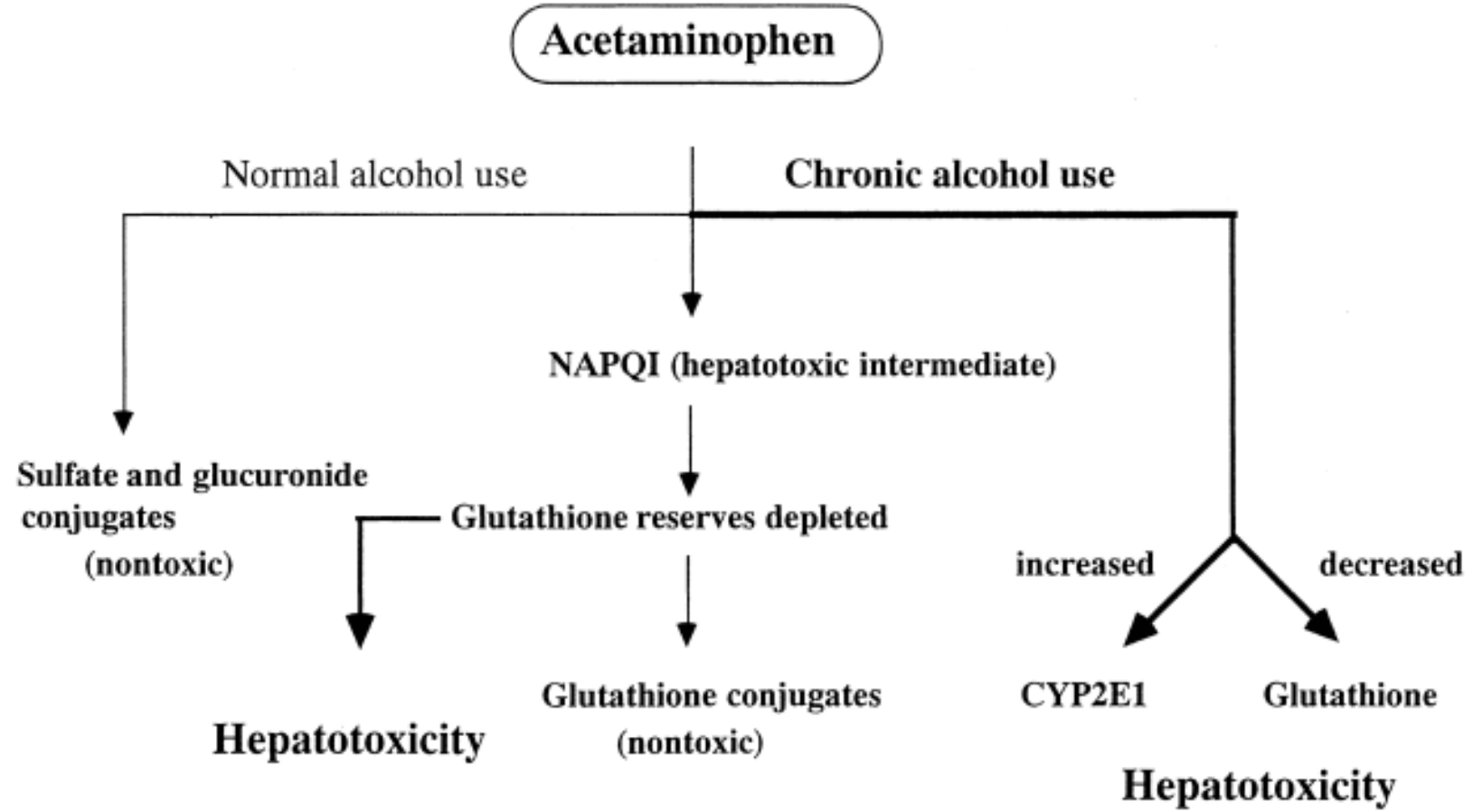


Fig. 1. Effects of normal and chronic alcohol use on acetaminophen metabolism. NAPQI: N-acetyl-p-benzoquinone imine.

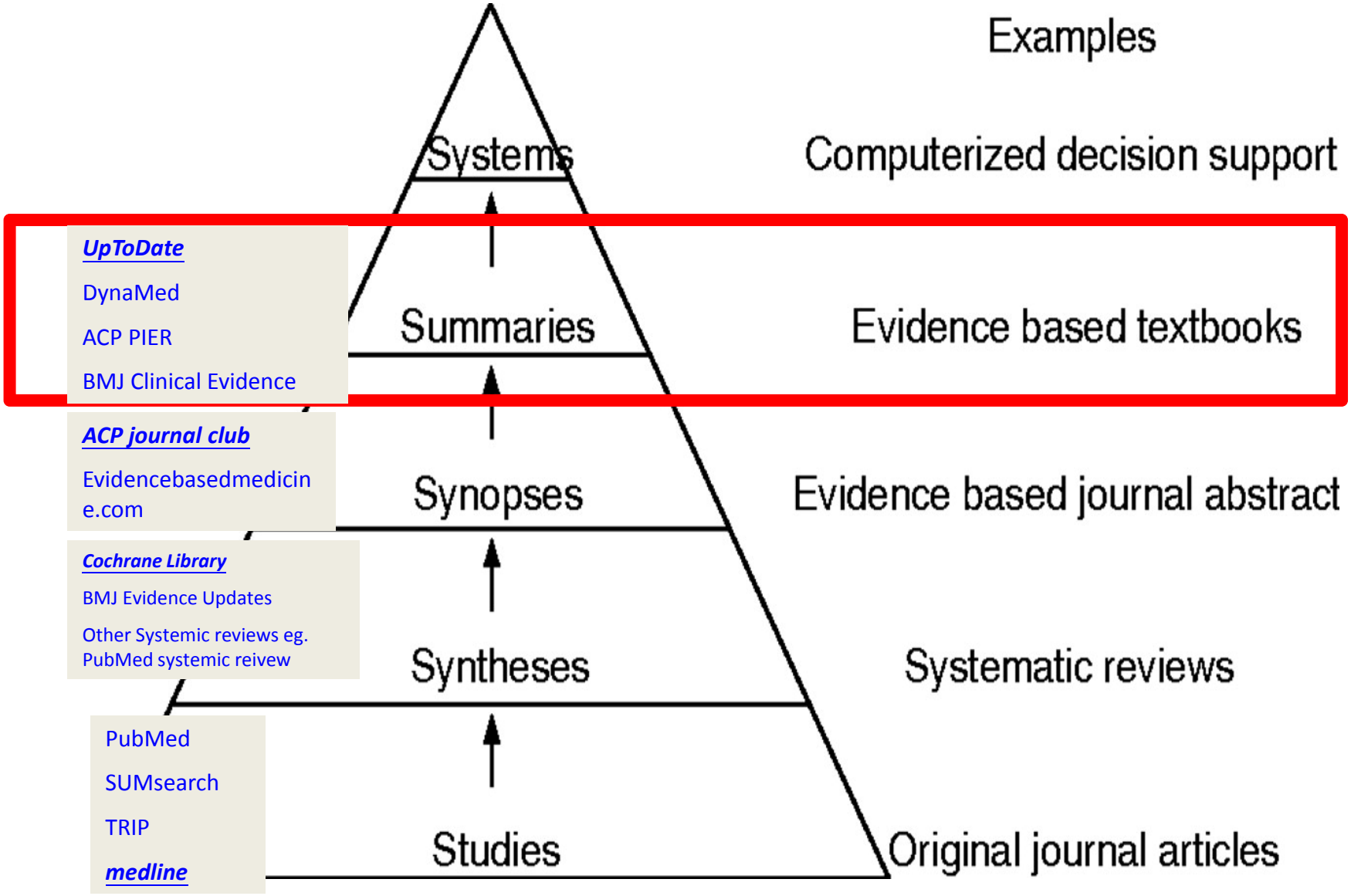
Foreground questions

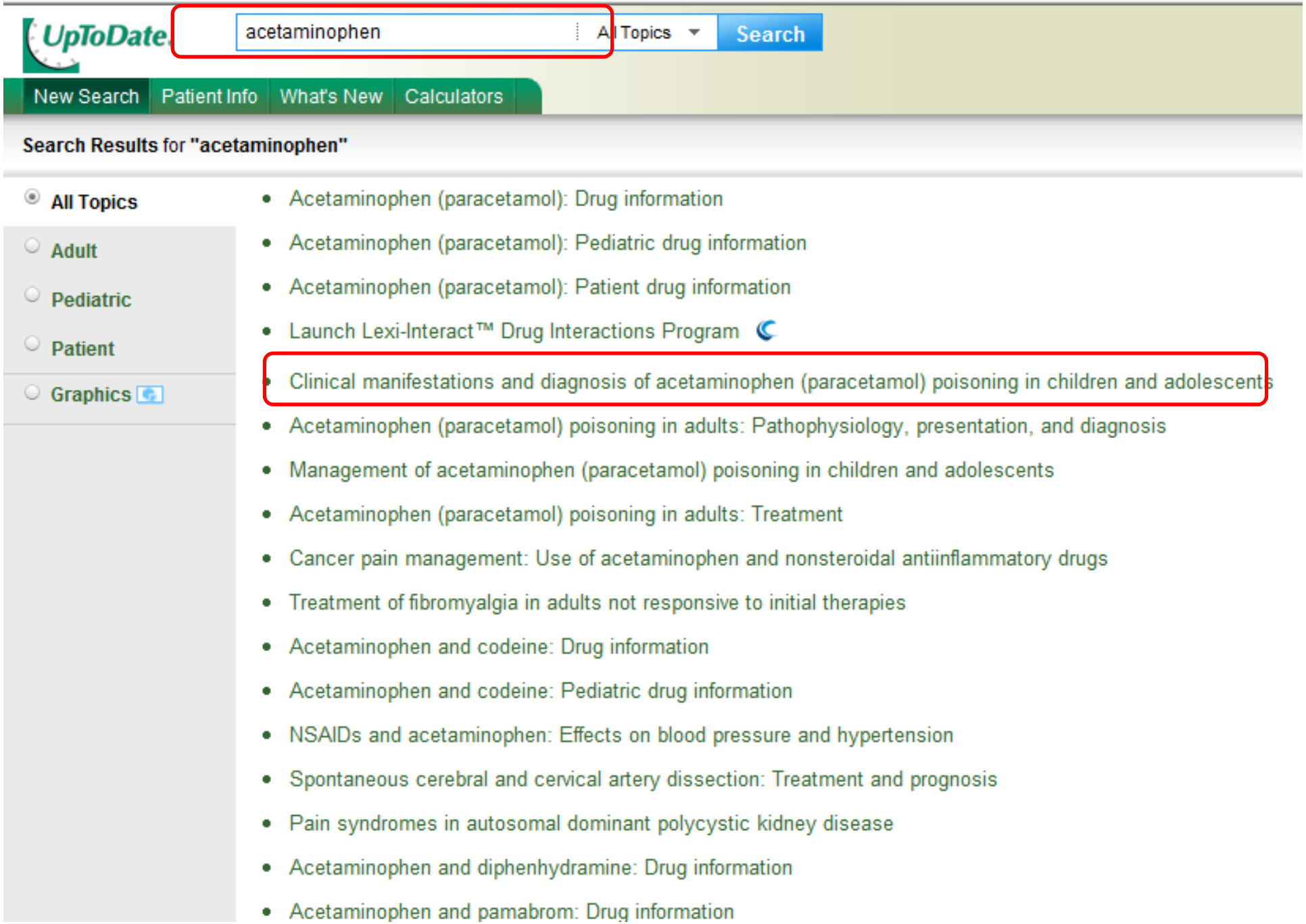
Would therapeutic dose of acetaminophen cause abnormal liver function in patients with alcoholic hepatitis ?

PICO

Patient	This 45 year-old male with alcoholic hepatitis had fever
Intervention	Acetaminophen in therapeutic dose(<4g/day)
Comparison	Placebo effect
Outcome	Liver function test

Search strategy: 5S model

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Acetaminophen (paracetamol): Pediatric drug information
Acetaminophen (paracetamol): Patient drug information
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Acetaminophen (paracetamol) poisoning in adults: Pathophysiology, presentation, and diagnosis
Management of acetaminophen (paracetamol) poisoning in children and adolescents
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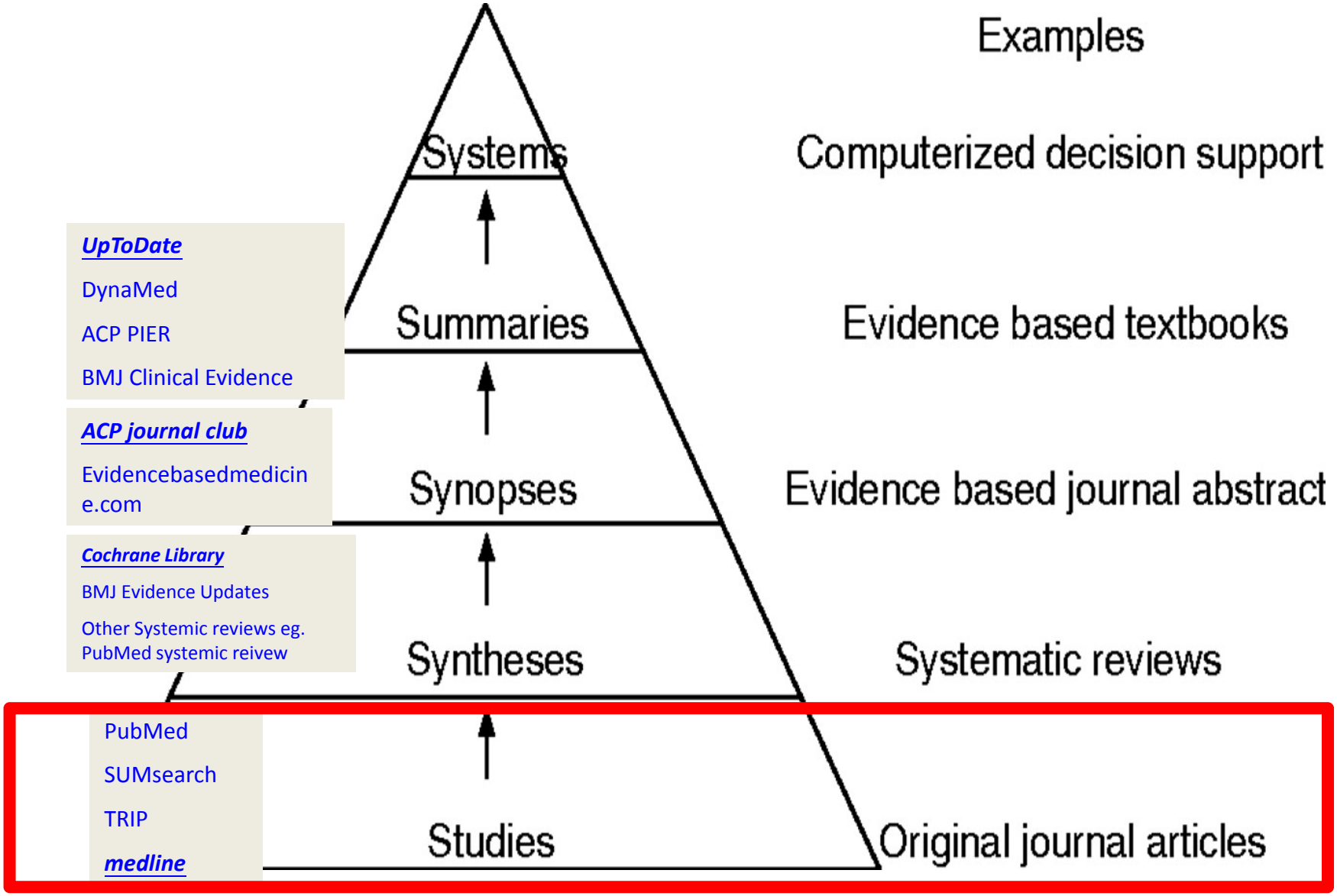
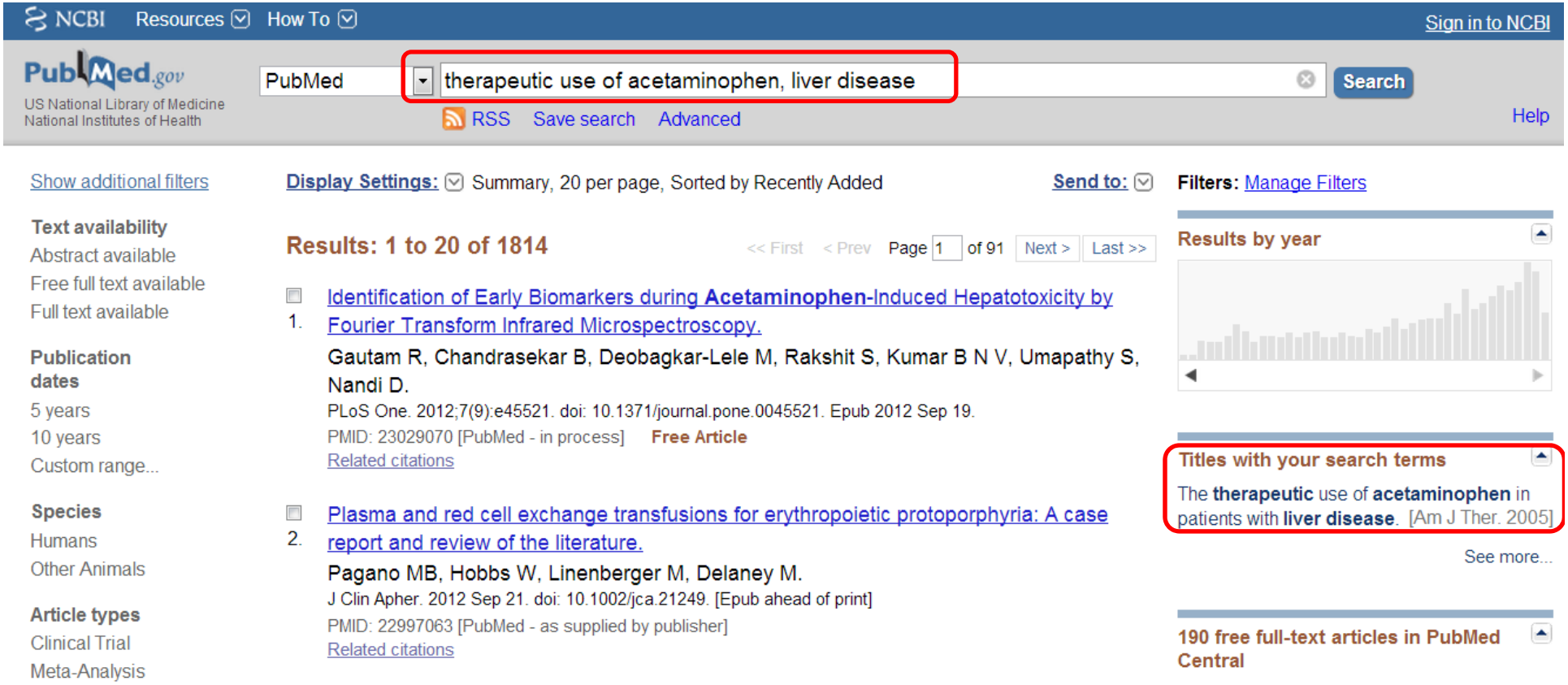
Cancer pain management: Use of acetaminophen and nonsteroidal antiinflammatory drugs
Treatment of fibromyalgia in adults not responsive to initial therapies
Acetaminophen and codeine: Drug information
Acetaminophen and codeine: Pediatric drug information
NSAIDs and acetaminophen: Effects on blood pressure and hypertension
Spontaneous cerebral and cervical artery dissection: Treatment and prognosis
Pain syndromes in autosomal dominant polycystic kidney disease
Acetaminophen and diphenhydramine: Drug information
Acetaminophen and pamabrom: Drug information

- Acetaminophen (paracetamol) is a widely available over-the-counter medication used for analgesic and antipyretic purposes. It is well established to be hepatotoxic in large doses.
- When ingested in suicide attempts at doses greater than 10 grams, it causes severe hepatic necrosis and fulminant hepatic failure.
- Doses of less than 6 grams per day are considered non-toxic and the recommended upper limit for use is 4 grams per day.

Search strategy: 5S model

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PLoS One. 2012;7(9):e45521. doi: 10.1371/journal.pone.0045521. Epub 2012 Sep 19.
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The therapeutic use of acetaminophen in patients with liver disease. [Am J Ther. 2005]
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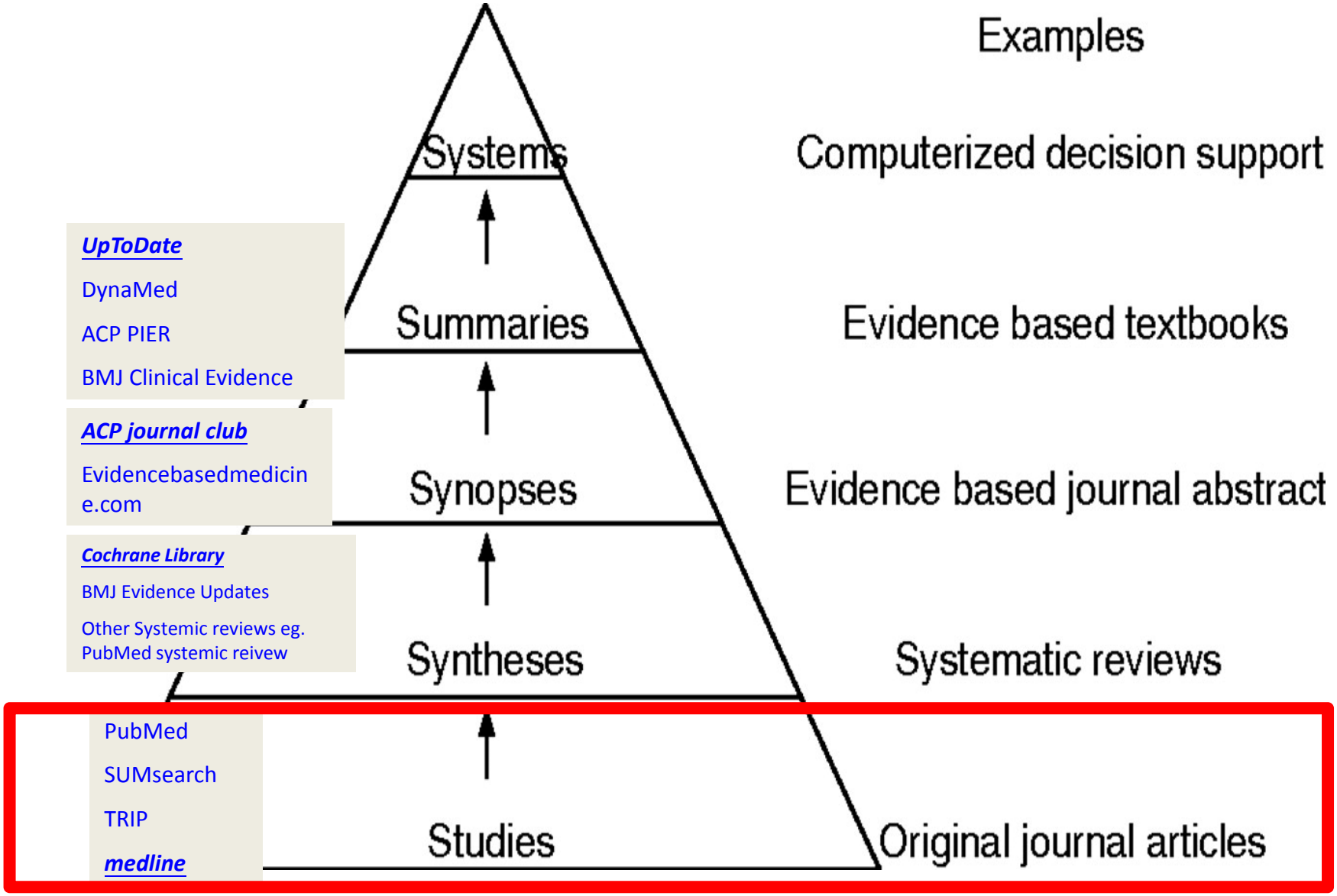
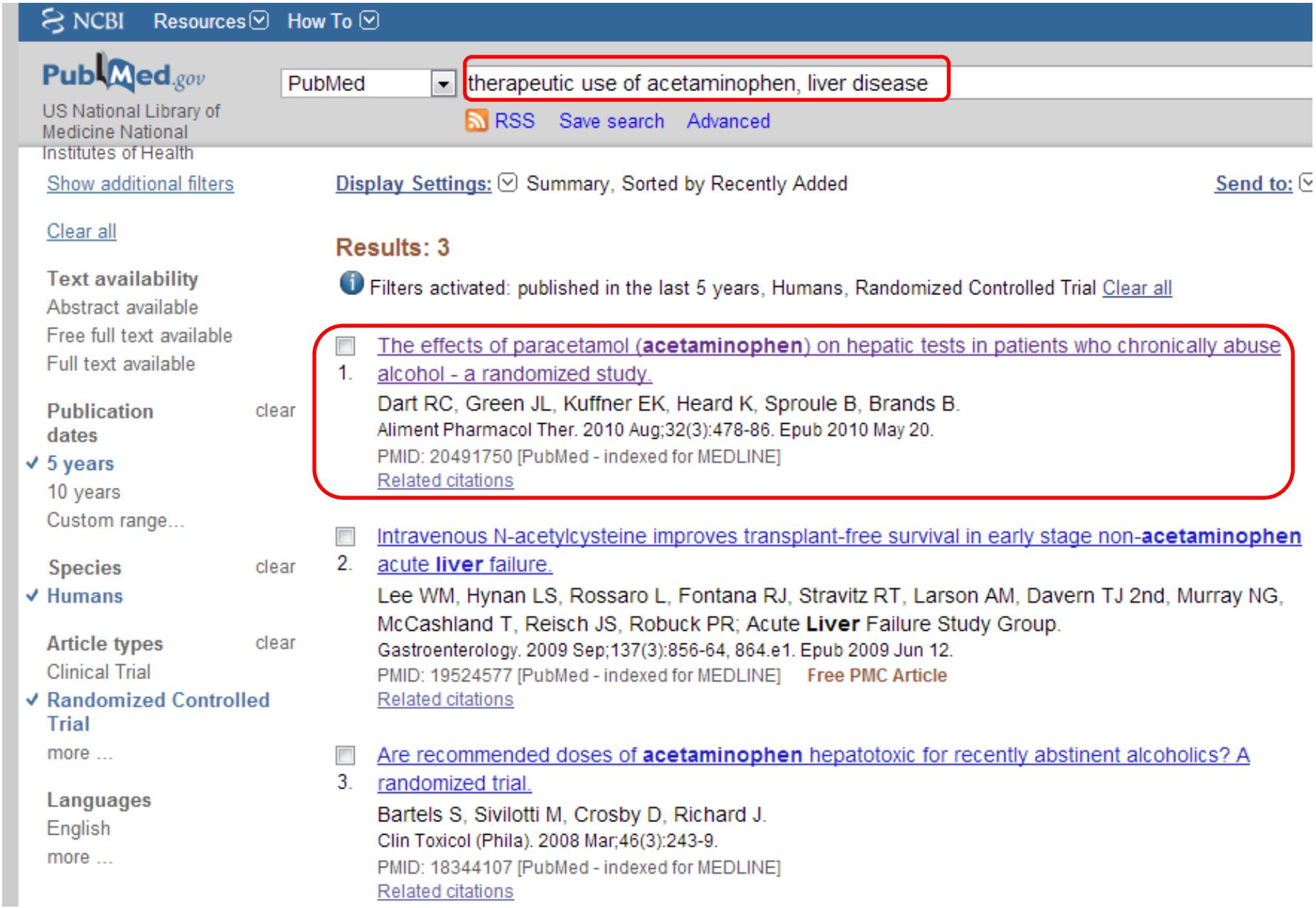
The therapeutic use of acetaminophen in patients with liver disease

- Available studies in patients with chronic liver disease, however, have shown that although the half-life of acetaminophen may be prolonged, cytochrome P-450 activity is not increased and glutathione stores are not depleted to critical levels in those taking recommended doses.
- Therefore, acetaminophen can be used safely in patients with liver disease and is a preferred analgesic/antipyretic because of the absence of the platelet impairment, gastrointestinal toxicity, and nephrotoxicity associated with nonsteroidal antiinflammatory drugs.

Search strategy: 5S model

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1. The effects of paracetamol (acetaminophen) on hepatic tests in patients who chronically abuse alcohol - a randomized study.
Dart RC, Green JL, Kuffner EK, Heard K, Sproule B, Brands B.
Aliment Pharmacol Ther. 2010 Aug;32(3):478-86. Epub 2010 May 20.
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2. Intravenous N-acetylcysteine improves transplant-free survival in early stage non-acetaminophen acute liver failure.
Lee WM, Hynan LS, Rossaro L, Fontana RJ, Stravitz RT, Larson AM, Davern TJ 2nd, Murray NG, McCashland T, Reisch JS, Robuck PR; Acute Liver Failure Study Group.
Gastroenterology. 2009 Sep;137(3):856-64, 864.e1. Epub 2009 Jun 12.
PMID: 19524577 [PubMed - indexed for MEDLINE] Free PMC Article
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3. Are recommended doses of acetaminophen hepatotoxic for recently abstinent alcoholics? A randomized trial.
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PMID: 18344107 [PubMed - indexed for MEDLINE]
Related citations

AP&T Alimentary Pharmacology and Therapeutics

The effects of paracetamol (acetaminophen) on hepatic tests in patients who chronically abuse alcohol – a randomized study

R. C. Dart[*,†], J. L. Green[*,‡], E. K. Kuffner[*], K. Heard[*,†], B. Sproule[§,¶] & B. Brands[¶]

- **Background**
- Retrospective accounts suggest that therapeutic doses of paracetamol can produce severe hepatic injury in patients with putative high-risk conditions, including alcoholism and infectious hepatitis.
- Metabolism of paracetamol to its hepatotoxic metabolite is enhanced in patients who abuse alcohol, who also have compromised liver defences from depressed hepatic glutathione.

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- **Aim**
- To determine the effect of paracetamol on serum liver tests of newly abstinent subjects who abuse alcohol, including subjects with hepatitis C infection.
- **Methods**
- A randomized, double-blind, placebo-controlled study. Adult alcohol abusers with a current drinking episode longer than 7 days received either placebo or paracetamol 4 g / day for 5 days.

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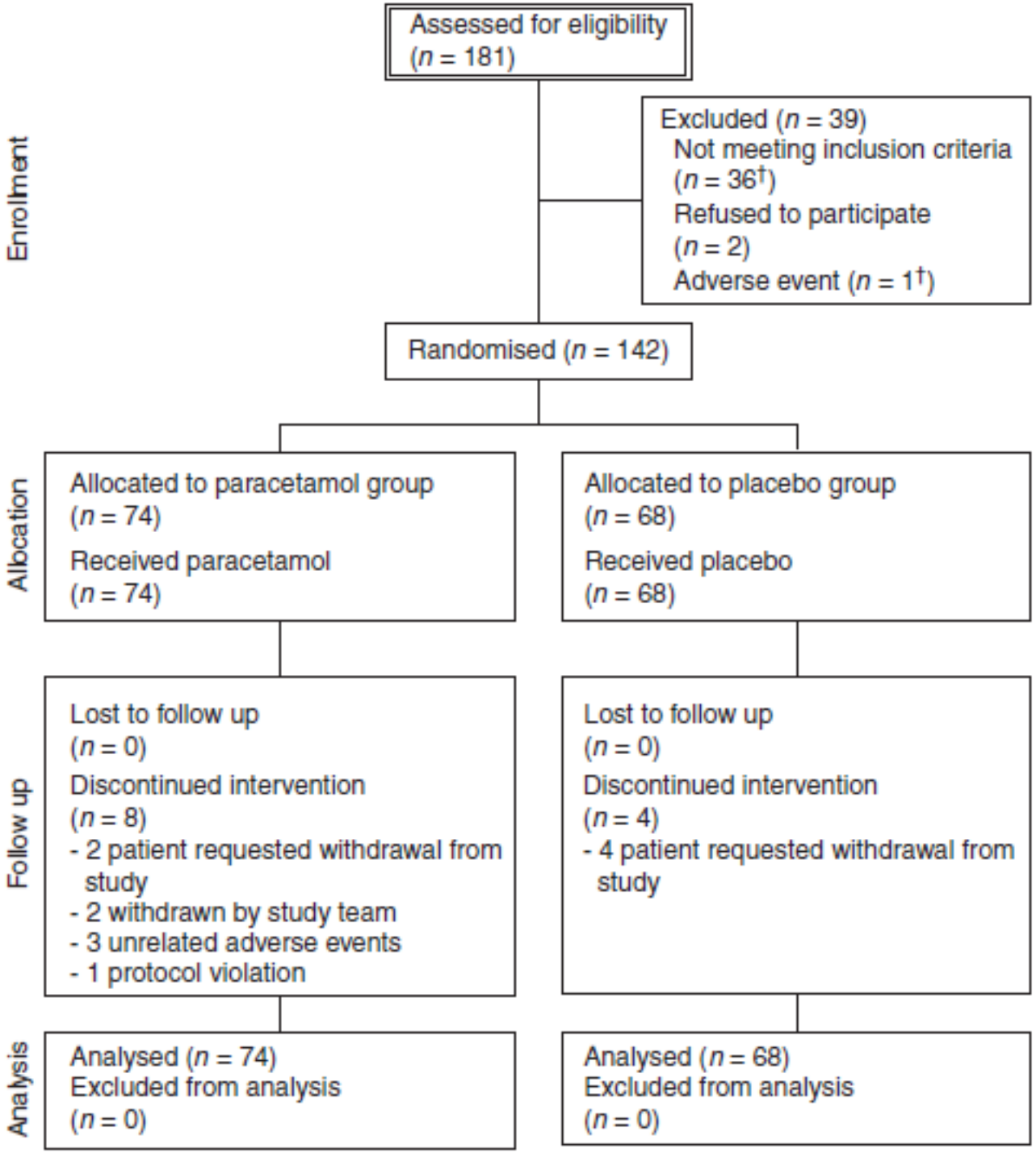
Assessed for eligibility
(n = 181)
Excluded (n = 39)
Not meeting inclusion criteria
(n = 36†)
Refused to participate
(n = 2)
Adverse event (n = 1†)
Randomised (n = 142)
Enrolment
Allocation
Allocated to paracetamol group
(n = 74)
Received paracetamol
(n = 74)
Allocated to placebo group
(n = 68)
Received placebo
(n = 68)
Follow up
Lost to follow up
(n = 0)
Discontinued intervention
(n = 8)
- 2 patient requested withdrawal from study
- 2 withdrawn by study team
- 3 unrelated adverse events
- 1 protocol violation
Lost to follow up
(n = 0)
Discontinued intervention
(n = 4)
- 4 patient requested withdrawal from study
Analysis
Analysed (n = 74)
Excluded from analysis
(n = 0)
Analysed (n = 68)
Excluded from analysis
(n = 0)

Randomization and interventions

- Baseline tests included complete blood count, comprehensive serum metabolic panel [sodium, potassium, chloride, serum bicarbonate, glucose, blood urea nitrogen (BUN), creatinine, total protein (TP), albumin, calcium, serum ALT, serum AST, total bilirubin (TB), alkaline phosphatase (AP)], and international normalized ratio (INR), GGT, and serum pregnancy test in female patients. Serum ALT, AST, TB and INR were repeated on study days 2, 4, 6 and 7.

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Randomization and interventions

- Exclusion criteria were evidence of
- paracetamol overuse as indicated by a baseline serum paracetamol level greater than 20 mcg ⁄mL
  (132.4 lmol ⁄ L)
- a history of ingesting more than 4 g of paracetamol per day for any of the 4 days preceding study enrolment
- baseline serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level greater than 200 IU ⁄ L
- baseline international normalized ratio (INR) greater than 1.5, or positive urine pregnancy test.

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Randomization and interventions

- Each subject received two tablets per dose, four times a day for five consecutive days. The paracetamol group received two tablets of 500 mg per dose for a total of 4 g per day.

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Table 1 | Subject demographics and baseline laboratory tests

	Paracetamol group (*n* = 74)	Placebo group (*n* = 68)
Age		
Years, mean (s.d.)	45.7 (9.4)	46.8 (8.3)
Range	21–77	26–64
Male (%)	67 (91)	64 (94)
Ethnic origin (%)		
Caucasian	38 (51)	28 (41)
Hispanic	16 (22)	12 (18)
African American	3 (4)	11 (16)
Native American	12 (16)	9 (13)
Other	5 (7)	8 (12)

Table 1 | Subject demographics and baseline laboratory tests

	Paracetamol group (*n* = 74)	Placebo group (*n* = 68)
Duration of current drinking episode (%)		
1–2 weeks	9 (12)	11 (16)
2–4 weeks	15 (20)	12 (18)
1–6 months	22 (30)	18 (27)
>6 months	27 (37)	27 (40)
Not reported	1 (1)	0 (0)
Blood ethanol at presentation, mmol/L		
Mean (s.d.)	0.041 (0.018)	0.042 (0.0196)
Range	0.001–0.099	0.001–0.105
n	73	68
Body mass index		
Mean (s.d.)	25.0 (4.1)	24.1 (4.0)
Range	18.9–42.0	17.6–46.7
n	73	68

Table 1 | Subject demographics and baseline laboratory tests

	Paracetamol group (n = 74)	Placebo group (n = 68)
Gamma glutamyl transferase (GGT), IU/L		
Mean (s.d.)	179.6 (251.2)	91.3 (79.1)
Range	15–1345	18–345
Median	82	68
n	73	68
Antibody to hepatitis A virus (IgM anti-HAV)		
Reactive (%)	23 (32)	27 (40)
n	73	67
Hepatitis B surface antigen (HbsAg)		
Reactive (%)	1 (1)	0 (0)
n	73	68
Antibody hepatitis B core antigen (HBclgm)		
Reactive (%)	11 (17)	20 (33)
n	65	60
Antibody to hepatitis C virus		
Reactive (%)	24 (33)	26 (38)
n	73	68

Statistical and analytical plans

- Four subgroups of patients who, based on prior reports, are allegedly at increased risk of hepatotoxicity from therapeutic doses of acetaminophen. These groups are:
  - (i) subjects who had serological evidence of hepatitis C infection
  - (ii) subjects who had an elevated ALT at baseline (from any cause)
  - (iii) subjects who had an AST:ALT ratio >2 (suggestive of alcoholic hepatitis) and
  - (iv) subjects with depressed GSH at baseline as evidenced by an increased GGT

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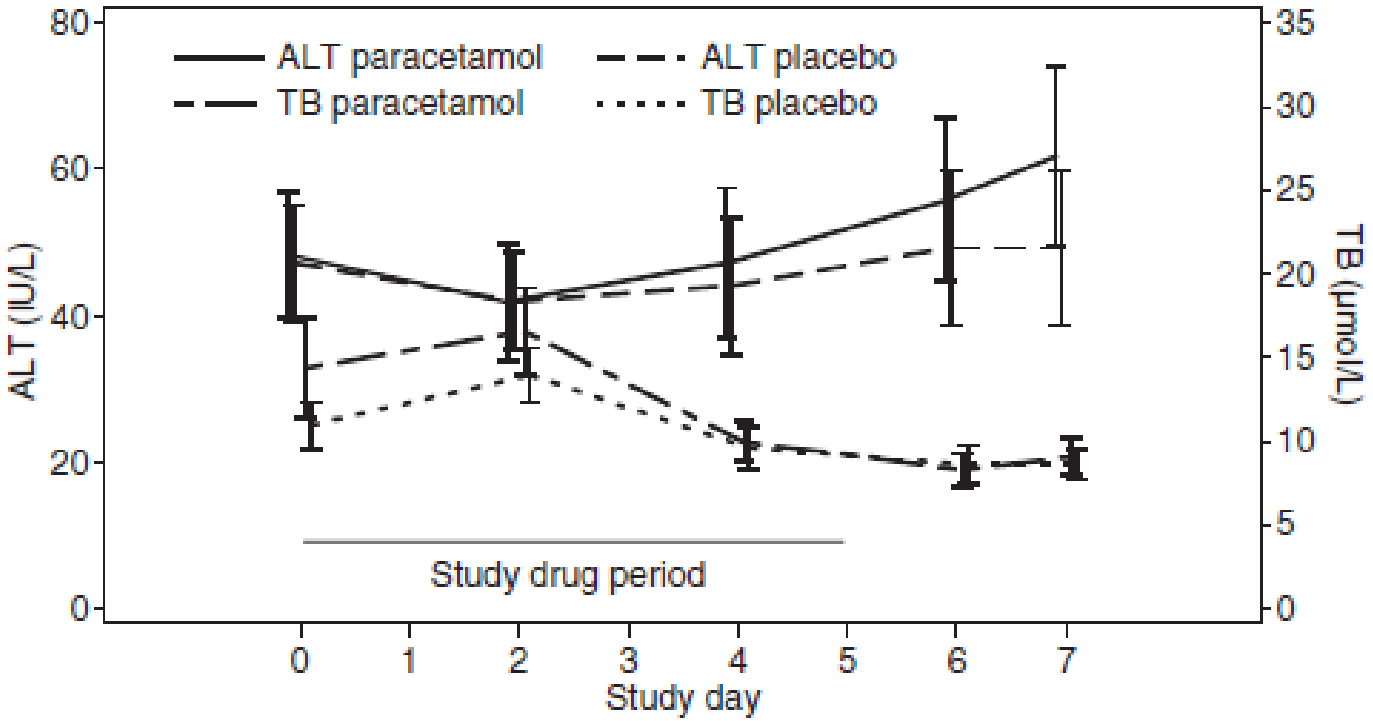
Table 2 | Hepatic laboratory tests by time and treatment group

Treatment group	Statistic	Day Baseline	2	4	6	7
Alanine aminotransferase (ALT), IU/L						
Paracetamol	Mean (s.d.)	48.2 (36.9)	41.9 (33.9)	47.2 (41.9)	55.8 (44.8)	61.8 (50.4)
	Range	8-178	8-170	11-230	9-201	12-238
	n	74	71	68	66	66
Placebo	Mean (s.d.)	47.2 (32.5)	41.9 (27.3)	44.09 (37.5)	49.3 (42.1)	49.2 (42.4)
	Range	10-159	10-131	10-218	11-237	6-249
	n	68	68	65	64	64
Aspartate aminotransferase (AST), IU/L						
Paracetamol	Mean (s.d.)	61.9 (45.3)	48.5 (38.6)	51.9 (42.3)	60.0 (42.5)	51.5 (37.3)
	Range	15-194	15-232	15-260	16-288	13-172
	n	74	71	68	66	66
Placebo	Mean (s.d.)	53.2 (34.5)	41.8 (25.3)	41.1 (31.5)	38.9 (28.3)	36.5 (25.9)
	Range	16-195	13-143	13-174	11-148	3-128
	n range	68	68	65	64	64
International normalized ratio (INR)						
Paracetamol	Mean (s.d.)	0.94 (0.12)	0.96 (0.13)	0.92 (0.08)	0.93 (0.09)	0.92 (0.06)
	Range	0.79-1.50	0.80-1.64	0.80-1.20	0.80-1.47	0.80-1.10
	n	74	72	67	66	64
Placebo	Mean (s.d.)	0.92 (0.07)	0.92 (0.06)	0.91 (0.07)	0.93 (0.07)	0.93 (0.08)
	Range	0.77-1.10	0.80-1.14	0.80-1.22	0.80-1.19	0.80-1.20
	n	68	68	65	63	63
Total bilirubin, μmol/L						
Paracetamol	Mean (s.d.)	14.38 (12.64)	16.55 (10.88)	9.95 (4.91)	8.29 (3.93)	9.05 (4.29)
	Range	3.00-80.89	4.99-71.82	2.96-27.36	3.00-22.97	3.00-23.97
	n	74	70	68	66	66
Placebo	Mean (s.d.)	10.94 (5.68)	13.94 (6.74)	9.59 (5.07)	8.59 (4.51)	8.62 (3.67)
	Range	3.42-27.36	4.99-34.20	3.42-27.36	3.00-29.07	3.42-25.65
	n	68	68	65	64	64

Normal reference ranges for serum ALT activity: Denver Health (male 40 IU/L, female 40 IU/L; Centre for Addiction and Mental Health (male and female CAMH 65 IU/L, male and female Mount Sinai 36 IU/L).



- The mean ALT activity during treatment increased from 48 IU ⁄L at baseline to 62 IU ⁄ L in the paracetamol group. The serum ALT increased from 47 IU ⁄L to 49 IU⁄ L in the placebo group.
- The mean changes for the paracetamol and placebo groups were significantly different (P = 0.04).
- The mean change in serum ALT activity from baseline to day 7 was 11.7 IU ⁄ L (95% CI 4.9, 18.6) in the paracetamol group and 1.8 IU ⁄ L (95% CI)4.8, 8.5) in the placebo group (P = 0.04).

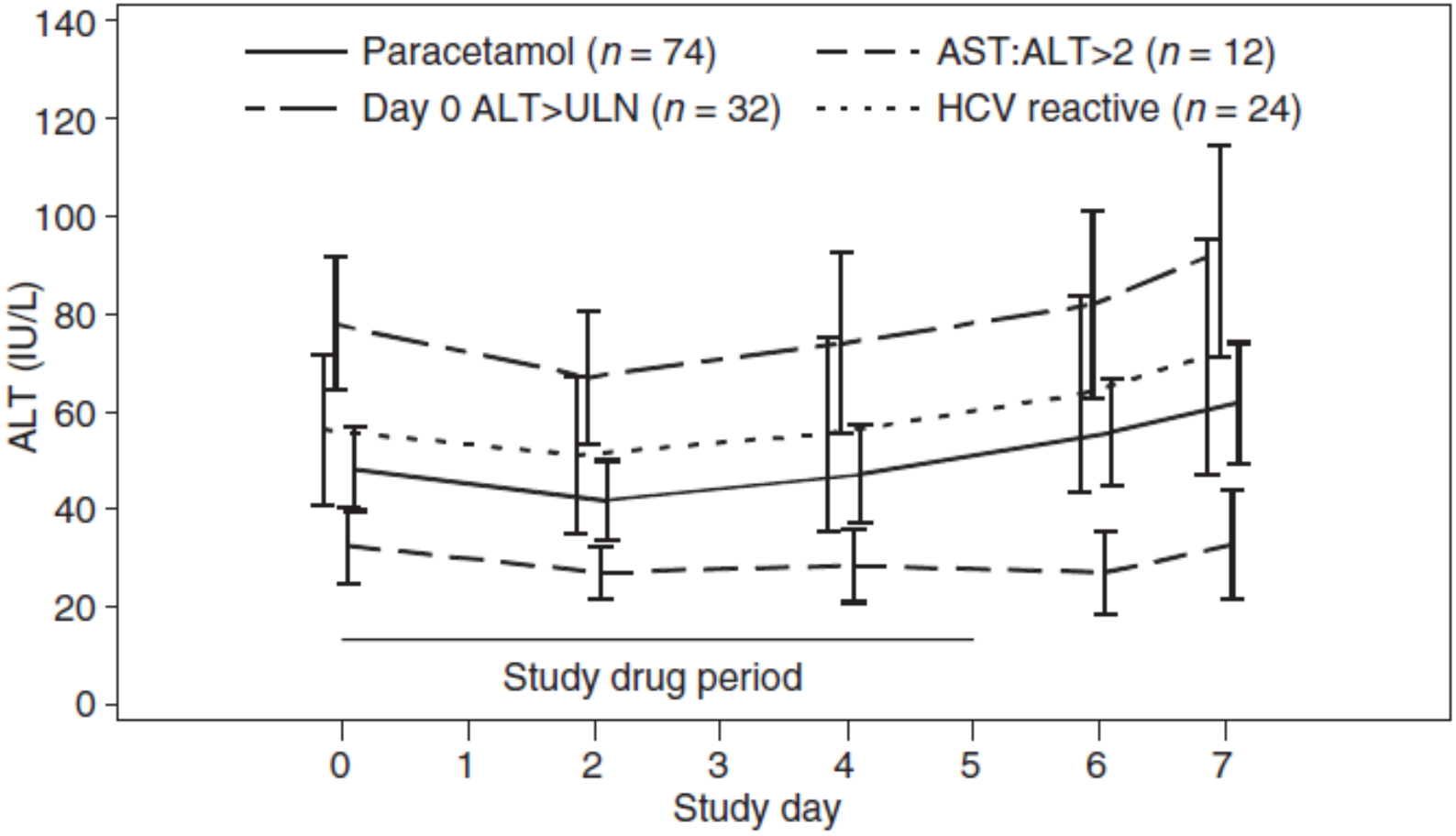


Figure 3 | Alanine aminotransferase (ALT) values for paracetamol-treated groups of patients with increased serum ALT at baseline, positive HCV or a serum AST:ALT ratio greater than 2.0.

Results

- Of 142 subjects enrolled, 74 received paracetamol and 68 received placebo. Mean ALT activity during treatment increased from 48 to 62 IU⁄L in the paracetamol group and from 47 to 49 IU⁄ L in the placebo group. Maximum ALT was 238 and 249 IU⁄ L in the paracetamol and control groups respectively.
- The INR remained unchanged and serum bilirubin decreased in both groups.
- Subgroup analyses for subjects with alcoholic hepatitis, hepatitis C virus antibody and other subgroups showed no statistical difference between groups.

AP&T Alimentary Pharmacology and Therapeutics

Conclusion

- Administration of paracetamol 4 g / day appears safe in newly abstinent patients who abuse alcohol.

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Discussion

- The results indicate that administration of paracetamol 4 g per day for 5 days to newly abstinent alcohol-abusing subjects was followed by a small increase in the serum ALT. The ALT rise was not accompanied by evidence of hepatic synthetic dysfunction.
- In a similar study, Bartels et al. administered paracetamol 4 g per day to alcoholabusing subjects for 4 days. The study found no effect on multiple hepatic measures, including serum AST, ALT and a-glutathione S-transferase, a sensitive measure of hepatocyte injury.
- Finally, Benson administered paracetamol to patients with chronic liver disease including alcoholic liver disease for 13 days in a crossover trial. There was no difference in the bilirubin, AST or ALT between paracetamol and placebo-treated arms.

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Critical Appraisal

Valid: RCT Appraisal sheets

Importance: what were the result?

證據等級

Level	與[治療/預防/病因/危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見

Grades of Recommendation

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 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

Appraisal

AAMPICOT將文獻分析

- 1a. R- Was the assignment of patients to treatments randomised?
  - YES
- 1b. R- Were the groups similar at the start of the trial?
  - YES
- 2a. A – Aside from the allocated treatment, are groups treated equally?
  - YES

- 2b. A – Are all patients who entered the trial accounted for? Are they analysed in the groups to which they were randomised?
  - YES
- 3. M - Are measures objective or are the patients and clinicians kept “blind” to which treatment was being received?
  - YES

What question did the systematic review addressed (PICO) 想要回答什麼問題？

■ 是	□ 否	□ 不清楚

評論：

- **Patient with alcoholic hepatitis had fever [P]**
- **Acetaminopen in therapeutic dose [I]**
- **Placebo or no treatment [C]**
- **The primary outcome: [O]**
  - **Liver function test**

Were the criteria used to select articles for inclusion appropriate 選擇文獻的準則適當?

■ 是	□ 否	□ 不清楚

評論：

Inclusion criteria:

(1) randomized controlled trials

(2) All review authors independently evaluated the titles and abstracts of the reports of trials identified by electronic searches. Copies of the full text were obtained for trials meeting the selection criteria.

Were the included studies sufficiently valid for the type of question asked

選擇的文獻有效回答所問的問題?

■ 是	□ 否	□ 不清楚

評論：

Summary:

Rigorously controlled data in a variety of subject groups do not support the conclusion that therapeutic doses of paracetamol can cause severe liver injury in alcohol-abusing patients. Treatment of patients with paracetamol for at least 5 days appears safe in patients who abuse alcohol, even in patients with comorbid conditions such as hepatitis C, increased baseline serum GGT, alcoholic hepatitis, or with an elevation of serum ALT before treatment.

Were the results similar from study to study
各研究的結果相似?

■ 是	□否	□不清楚

評論：

1. Are recommended doses of acetaminophen hepatotoxic for recently abstinent alcoholics? A randomized trial *(Clinical Toxicology (2008) 46,* 243–249)

2. The effect of acetaminophen (four grams a day for three consecutive days) on hepatic tests in alcoholic patients--a multicenter randomized study. (BMC medicine (2007))

3. A randomized trial to determine the change in alanine aminotransferase during 10 days of paracetamol (acetaminophen) administration in subjects who consume moderate amounts of alcohol (Alimentary pharmacology & therapeutics (2007)

APPLY

將**STUDIES**的搜尋結果應用到我病人身上

- There are evidences to determine the therapeutic dose of acetaminophen in patients with alcoholic hepatitis.
- Evidence suggests that maximal therapeutic dose of acetaminophen (4g/day) for at least 5 days does not significantly increase the risk of abnormal liver function test.
-

總結與討論

- 對於therapeutic dose of acetaminophen在alcoholic patinets使用上的研究結果是無爭議的，也就是在最大治療劑量連續使用五天下不會對alcoholic hepatitis 病人產生急性肝臟病變。
- 未來需要更多針對於有效劑量以及使用方式的探討文獻，在當下的臨床治療選擇上，acetaminophen仍然有重要的角色。

在「提出臨床問題」方面的自我評估

- 我提出的問題是否具有臨床重要性？有，因為acetaminophen 臨床上時常使用，因此更要了解使用上的限制。
- 我是否明確的陳述了我的問題？
  - 我的foreground question 是否可以清楚的寫成PICO？可
  - 我的background question是否包括what, when, how, who等字根？有，但未全能概括
- 我是否清楚的知道自己問題的定位？（亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的），並據以提出問題？知道，屬於治療範疇
- 對於無法立刻回答的問題，我是否有任何方式將問題紀錄起來以備將來有空時再找答案？有

在「搜尋最佳證據」方面的自我評估

- 我是否已盡全力搜尋？是
- 我是否知道我的問題的最佳證據來源？是
- 我是否從大量的資料庫來搜尋答案？是
- 我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋？是，學校買的版權資源非常便利，但有些paper全文仍無法取得
- 我是否在搜尋上愈來愈熟練了？是
- 我會使用「斷字」、布林邏輯、同義詞、MeSH term，限制(limiters)等方法來搜尋？部份會
- 我的搜尋比起圖書館人員或其他對於提供病人最新最好醫療有熱情的同事如何？中等程度吧

關於「嚴格評讀文獻」方面的自我評估

- 我是否盡全力做評讀了？盡力而為，但仍有不了解的項目
- 我是否了解Number need to treat 的意義？了解
- 我是否了解Likelihood Ratios的意義？約略了解
- 我是否了解worksheet每一項的意義？不太了解
- 評讀後，我是否做出了結論？是

關於「應用到病人身上」的自我評估

- 我是否將搜尋到的最佳證據應用到我的臨床工作中？是
- 我是否能將搜尋到的結論如NNT, LR用病人聽得懂的方式解釋給病人聽？可以，但還無法解釋得很清楚
- 當搜尋到的最佳證據與實際臨床作為不同時，我如何解釋？目前無不同，故暫不需解釋

改變「醫療行為」的自我評估

- 當最佳證據顯示目前臨床策略需改變時，我是否遭遇任何阻止改變的阻力？沒有，目前證據未改變臨床策略
- 我是否因此搜尋結果而改變了原來的治療策略？做了那些改變？沒有改變

效率評估

- 這篇報告，我總共花了多少時間？2.5天中共約30個小時，但是能力有限未能做有效率的全面回顧分析
- 我是否覺得這個進行實證醫學的過程是值得的？值得，疑問得到解答，也更熟悉EBM的操作
- 我還有那些問題或建議？評讀paper的方法不甚熟練

Thank you for your attention!

Liver cirrhosis

- **management of pain in patients with cirrhosis (grade C recommendation [lacking direct evidence])**based on review article
- be aware patients may also have decreased renal function
- if opioids cannot be avoided, use lowest possible dose with long intervals between doses
- tramadol reportedly safer than opioids without large studies
- acetaminophen up to 2 g daily may be safe but should not be used if patient continues to use alcohol
- nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided due to bleeding risk and decreased renal function
- Reference - Med Clin North Am 2009 Jul;93(4):901
- **use of opioids in patients with cirrhosis (level 3 [lacking direct] evidence)**
  - oxycodone may not be metabolized to oxymorphone, resulting in accumulation of oxycodone and noroxycodone
  - morphine and oxymorphone require hepatic glucuronidation and may have increased bioavailability
  - Fentanyl and methadone are not affected by hepatic impairment
  - Reference - Mayo Clin Proc 2009 Jul;84(7):613