Analgesics ≥18 years of age (Non-Steroidal Anti-Inflammatory Drugs, & Acetaminophen):

Primary:

1. **Bertin L, Pons G, d'Athis P, Lasfargues G, Maudelonde C, Duhamel JF, Olive G. Randomized, double-blind, multicenter, controlled trial of ibuprofen versus acetaminophen (paracetamol) and placebo for treatment of symptoms of tonsillitis and pharyngitis in children. J Pediatr 1991; 119:811-14.**

Extended Abstract:

***Study objectives**:* To evaluate the ability of ibuprofen or acetaminophen to improve sore throat in children aged 6 to 12 years of age.

***Methods**:*

***Design**:* Randomized.

***Allocation**:* Eligible patients were distributed using a computer-generated randomization list to three treatment arms: ibuprofen, acetaminophen, or placebo.

***Blinding**:* This trial was double-blinded.

***Follow-up period**:* The total duration of this study was 48 hours.

***Setting**:* Study performed in multiple sites located in a community setting.

***Participants**:* Children with sore throat secondary to bacterial tonsillitis were included considered for inclusion. Exclusion criteria included patients with cardiac, hepatic, or renal disorders, gastroduodenal disease, known hypersensitivity to non-steroidal anti-inflammatory drugs and penicillins. Patients were excluded with a history of receiving antibiotic, analgesic, diuretic, or anti-inflammatory drugs within 1 week before the study. Patients with sore throat lasting longer than 48 hours were excluded. No local treatments were allowed.

Table 1. Number of patients enrolled per group

Group	Enrolled Population
Ibuprofen	77
Acetaminophen	78
Placebo	76
Total patients enrolled	231

***Intervention**:* Treatments were ibuprofen (200, 300, 400, or 500 mg), acetaminophen, or placebo. Drugs were given orally at a dose of 10 mg/kg three times a day for 48 hours. All patients received phenoxymethylpenicillin for 7 days. If a patient experienced fever of greater 39°C, non-pharmacological interventions were attempted to reduce temperatures.

***Outcomes**:* Primary outcomes include decrease in pain, both pain during swallowing (with the child drinking a little water), and spontaneous pain. Other outcomes involved looking at self-assessment of increasing well-being, overall evaluation by the physician, and overall evaluation by parents of the quality of life for the child. Tolerability was assessed after 48 hours of treatment. Measures of tolerability included nausea, vomiting, abdominal pain, and cutaneous rash.

***Patient follow-up**:* Patients were assessed after 48 hours.

***Main results**:* Both treatment arms were better than placebo at reducing pain and pain with swallowing. Ibuprofen showed to be more effective than acetaminophen for reducing pain and pain with swallowing.

***Conclusions**:* Children (6-12 years of age) with sore throat can achieve symptomatic pain improvement with ibuprofen or acetaminophen. Children may get better sore throat pain relief with ibuprofen compared to acetaminophen.

***Comments/critical appraisal (including assessment of internal and external validity)**:*

Internal validity: Children were randomized to receive ibuprofen, acetaminophen, or placebo. All drugs were dosed the same. This can potentially bias results because ibuprofen and acetaminophen are different drugs. Ibuprofen is a more potent analgesic than acetaminophen. Hence, at equivalent doses, ibuprofen would provide more relief of sore throat pain compared to acetaminophen. Patients were allocated by a computer-generated randomization list. This study was double-blinded. All patients received medication and completed the trial as intended. Baseline characteristics were similar across treatment groups.

External validity: This study included children experiencing sore throat pain secondary to bacterial tonsillitis. The study site was based in Europe. Cultural variations can possibly influence generalizability to North American patients. Based on the inclusion criteria, children in this study are likely to be self-care candidates in community settings. As such, results from this study can be included in the EBSCR algorithm. The rating scales incorporated patient-derived assessment of sore throat pain. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. Although subjective ratings cannot be directly extrapolated to the general population, the results of this study were consistent using different sore throat outcomes. In terms of safety, no adverse events were noted in this study. Mild adverse events were seen in all treatment arms, including placebo. In the end, if children meet the appropriate criteria, this study provides sufficient evidence to recommend ibuprofen or acetaminophen as initial treatment for sore throat pain.

2. **Ruperto N, Carozzino L, Jamone R, Freschi F, Picollo G, Zera M, Della Casa Alberighi O, Salvatori E, Del Vecchio A, Dionisio P, Martini A. A randomized, double-blind, placebo-controlled trial of paracetamol and ketoprofen lysine salt for pain control in children with pharyngotonsillitis cared by family pediatricians. Ital J Pediatr 2011; 37:48-54.**

Study objectives: To evaluate the efficacy and safety of paracetamol syrup and ketoprofen lysine salt in children with pharyngotonsillitis compared to placebo.

Methods:
***Design**:* Randomized.
***Allocation**:* Microsoft Access 2000 was used to randomized eligible patients into three treatment arms: paracetamol, ketoprofen, or placebo.
***Blinding**:* This trial was double-blinded.
***Follow-up period**:* The total duration of this study was 4 days.
***Setting**:* Study performed in multiple sites located in a community setting.
***Participants**:* Children (6-12 years of age) with sore throat secondary to tonsillitis were included considered for inclusion. The maximum allowed duration of symptoms was 7 days. Children were required to score greater than 5 in the Tonsillo-Pharyngitis Scale (TPS) and greater than 120 mm in the Children's Sore Throat Pain (CSTP) Thermometer. Exclusion criteria included patients with known hypersensitivity to study medications, or other known conditions to interfere with the assigned drugs.

Children were excluded with a history of receiving antipyretic drugs, or throat lozenges in the past 6 hours. Children were excluded if an analgesic or any "cold" medication was taken in the past 8 hours.

Table 1. Number of patients enrolled per group

Group	Enrolled Population	Evaluable Population
Paracetamol	34	32
Ketoprofen	33	33
Placebo	32	32
Total patients enrolled	99	97

***Intervention**:* Treatments were paracetamol 12mg/kg syrup, ketoprofen lysine salt 40 mg (open label), or placebo syrup 1mL/2kg. Children were given one of the three study medications. No further dosing was allowed for the first 4 hours. After initial treatment, pain intensity assessment was performed a primary care facility. Study medications were to be continued at home after the first 4 hours. Paracetamol was to be used as 12mg/kg up to 4-5 times daily. Ketoprofen was to be used as 40mg every 8 hours for maximum of 3 administrations daily. At day 4 children came back to the primary care facility for final assessment.
***Outcomes**:* Primary outcome of this study was to measure the pain intensity difference (PID) sum of pain intensity difference (SPID), and total pain relief (TOTPAR). Tolerability was assessed at 1 and 4 hours after initial treatment.
***Patient follow-up**:* Patients were assessed after 4 days.

***Main results**:* Both treatment arms were better than placebo at reducing pain associated with sore throat. No major adverse events were reported with paracetamol.

***Conclusions**:* Children (6-12 years of age) with sore throat can achieve symptomatic pain improvement with paracetamol or ketoprofen.

Comments/critical appraisal:
Internal validity: Children were randomized to receive paracetamol, ketoprofen, or placebo. Drugs were dosed appropriately based on effective concentrations found in literature for this population. Ketoprofen was used as an open-label control because the delivery of medication could not be concealed. Patients were randomly allocated into the different treatment arms using Microsoft Access. This study was double-blinded. Two patients were re-allocated into the paracetamol arm after development of pharyngotonsillitis. The trial summary indicates 2 patients were excluded from analysis due to protocol violation. Baseline characteristics were similar across treatment groups. Each treatment arm had about 50% of children with a positive Strep-test. Thus, it can be assumed the underlying cause of sore throat was distributed evenly.

External validity: This study included children experiencing sore throat pain. The study site was based in Europe. Cultural variations can possibly influence generalizability to North American patients. Based on the inclusion criteria, children in this study are likely to be self-care candidates in community settings. As such, results from this study can be included in the EBSCR algorithm. The rating scales incorporated patient-derived assessment of sore throat pain. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. Although subjective ratings cannot be directly extrapolated to the general population, the results of this study were consistent using different sore throat outcomes. Along with subjective outcomes, generalizability can be further complicated by the

relatively small sample size. In terms of safety, no major adverse events were noted in this study. In the end, if children meet the appropriate criteria, this study provides sufficient evidence to recommend acetaminophen syrup as initial treatment for sore throat pain.

Tertiary/Secondary:

3. **Drutz JE. Symptomatic relief of sore throat in children and adolescents. UpToDate. Accessed on Feb 3 2013 from: www.uptodate.com.**

Source Description: A clinical decision support service, UpToDate provides evidence-based information to healthcare professionals. Physician editors continually monitor publications to ensure UpToDate articls reflects the most accurate information. Often, authors that are recognized in a particular field of study are encouraged to write expert opinions about a subject manner. As such, UpToDate articles are primarily expert opinions supported by recent evidence. The article on acute sore throat was updated on July 2012 and current as of January 2013.

Summary: In terms of pain medication, UpToDate lists acetaminophen, and non-steroidal anti-inflammatory agents (such as ibuprofen) as acceptable therapeutic options to manage acute sore throat pain in children. The article cautions against the use of acetylsalicylic acid in this population due to risk of Reye syndrome. The other agents mentioned involve prescription medications.

Comments/critical appraisal: UpToDate authors are not instructed to describe the search strategies used to select references used to support personal opinions. There might be potential selection bias in the literature used to guide therapeutic discussions. This particular article provides healthcare professionals with a practical approach to sore throat management in patients younger than 18 years of age. Unfortunately, the article fails to provide detailed information about individual treatment options (dose, dosage form, duration, etc.). Also, preferred agents for treatment are not systematically ranked. Overall, this article provides fundamental information about acute sore throat. However, this article should not guide therapeutic decisions for management of acute sore throat in an outpatient setting.

Analgesics ≥18 years of age (Non-Steroidal Anti-Inflammatory Drugs, Acetaminophen, & Acetylsalicylic Acid ± Caffeine):

Primary:

1. **Schachtel BP, Fillingim JM, Thoden WR, Lane AC, Baybutt RI. Sore throat pain in the evaluation of mild analgesics. Clin Pharmacol Ther 1988; 44(6):704-11.**

***Study objectives**:* To evaluate the ability of a refined model to assess the effectiveness of ibuprofen or acetaminophen to treat sore throat.

***Methods**:*
***Design**:* Randomized, single-dose parallel study.
***Allocation**:* Eligible patients were distributed using a computer generation randomization code to receive ibuprofen 400 mg, acetaminophen 1000 mg, or placebo.
***Blinding**:* This trial was double-blinded.
***Follow-up period**:* The total duration of this study was 6 hours.
***Setting**:* Study performed in single-centre located in community setting.
***Participants**:* Adults seeking medical attention from a family physician for an upper respiratory tract infection (URTI) with an acute sore throat were considered for inclusion. To meet the inclusion criteria, patients were required to have a relatively severe sore throat pain (score greater than 66 mm on the 100 mm Sore Throat Pain Intensity Scale) associated with other symptoms of an upper respiratory infection. Also, patients had to show objective evidence of tonsillopharyngitis (score of 4 or more on the 10-point tonsillopharyngitis assessment). Exclusion criteria included history of hypersensitivity to ibuprofen, aspirin, or acetaminophen, previous use of any "cold medication", mood-altering drugs or alcohol within 8 hours, consumption of caffeine-containing medications or beverage within 6 hours, and any respiratory function compromise.

Table 1. Number of patients enrolled per group

Group	Enrolled Population
Ibuprofen 400 mg	39
Acetaminophen 1000 mg	40
Placebo	41
Total patients enrolled	120

***Intervention**:* Treatments were ibuprofen 400 mg, acetaminophen 1000mg, or placebo. Patients received the study medication and were evaluated in a physician's office. Patients were evaluated at 1, 2, and 3 hours. After 3 hours, post-treatment assessment was continued outside the study site.
***Outcomes**:* Primary outcomes involved total pain relief summed over 6 hours calculated from the pain relief ratings scales: the Sore Throat Pain Intensity Scale and the Sore Throat Relief Rating Scale. The Sore Throat Pain Intensity Scale involved absolute differences and the sum of pain intensity differences (SPID). The Sore Throat Relief Rating Scale recorded total pain relief after 6 hours. Secondary outcomes involved looking at rating scale results for patients with severe degrees of swollen throat and difficulty swallowing (defined as baseline scores greater than 66 mm).
***Patient follow-up**:* Patients returned 3 hours after discharge to complete the rating scales and report any adverse effects to study medications.

***Main results**:* Ibuprofen was more effective than acetaminophen at improving all rating scale elements. Both analgesics provided better symptomatic control compared to placebo.

***Conclusions**:* Adults experiencing sore throat can achieve symptomatic relief with either ibuprofen or acetaminophen. Ibuprofen appears to provide a larger effect size compared to acetaminophen.

Comments/critical appraisal (including assessment of internal and external validity):

Internal validity: Eligible patients were randomized to receive ibuprofen 400 mg, acetaminophen 1000 mg, or placebo. Patients were screened by one family physician. This introduces a potential bias. Patients were allocated by a computer-generated randomization list. This study was double-blinded. All patients received the study medication. The baseline demographic values were similar across all treatment arms. The study design failed to mention if there were any dropouts. If unstated dropouts were excluded from the final analysis, this can bias the results in favor of treatments with ibuprofen or acetaminophen.

External validity: This study included adults experiencing subjective sore throat pain secondary to URTI associated with tonsillopharyngitis. The source of the tonsillopharyngitis was not specified as either bacterial or viral. However, majority of patients in the community are unlikely to know the source of the sore throat. This study included patients likely to be self-care candidates in community settings. As such, results from this study can be included in the EBSCR algorithm. The study evaluated the usefulness of two subjective rating scales to determine efficacy of ibuprofen and acetaminophen. The rating scales incorporated patient-derived assessment of sore throat pain. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. Although subjective ratings cannot be directly extrapolated to the general population, the results of this study were consistent using different sore throat outcomes. In terms of safety, no adverse events were noted in this study. In the end, if patients meet the appropriate criteria, this study provides sufficient evidence to recommend ibuprofen or acetaminophen as initial treatment for management of sore throat pain.

2. **Benrimoj SI, Langford JH, Christian J, Charlesworth A, Steans A. Efficacy and tolerability of the anti-inflammatory throat lozenge flurbiprofen 8.75mg in the treatment of sore throat. Clin Drug Invest 2001; 21(3):183-193.**

***Study objectives**:* To evaluate the efficacy and tolerability of flurbiprofen lozenges (8.75 mg or 12.5mg) for achieving total pain relief associated with an upper respiratory tract infection (URTI). The study also examined changes associated with throat soreness, and swollenness.

***Methods**:*
***Design**:* Randomized, parallel group study
***Allocation**:* A computer-generated randomization list assigned patients to flurbiprofen 8.75mg, flurbiprofen 12mg, or placebo.
***Blinding**:* This trial was double-blinded. Treatment and placebo were indistinguishable. Study medications were unmarked; and identical in size, taste, and odor.
***Follow-up period**:* The total duration of the study was 5 days.
***Setting**:* Study performed in single-centre located in community setting.
***Participants**:* Prior to allocation, patients were selected based on the following inclusion criteria: male or female patients aged 18 years or over with a sore throat associated with a URTI of ≤7, objective evidence of tonsillopharyngitis, and subjective rating scores above predetermined values. Subjective rating scores included a throat soreness ≥6 (0-10 ordinal scale), patient perception of swollen throat ≥60mm (0-100mm visual analogue scale), and/or moderately hurting neck glands (5-category scale). Exclusion criteria included history of NSAID-induced bronchospasm, sore throat > 7 days, suspected bacterial infection, asthma, disease complicating breathing, previous use of topical throat treatment within 2 hours of study entry, any sore throat medication containing a local anaesthetic within 4 hours of study entry, or long-acting or slow-release analgesics within 24 hours of study entry, pregnancy, women of childbearing potential not taking oral contraceptives. Investigators excluded patients who were thought to be non-compliant to trial requirements or patients who have participated in another clinical trial within the previous 30 days.

Table 2. Number of patients enrolled per group

Group	Enrolled Population	Evaluable Population
Placebo	128	125
Flurbiprofen 8.75mg	128	120
Flurbiprofen 12.5mg	64	63
Total patients enrolled	320	308

***Intervention**:* Treatments were flurbiprofen 8.75mg or 12.5mg, and placebo. Patients received the study medication and were instructed to consume lozenges by sucking until completely dissolved. Measurements of throat soreness, swollen throat, and pain relief were performed by the patient at 15-minute intervals over the first 2-hour period. At 2 hours, the patient completed an overall lozenge rating scale. After 2 hours, the assessment continued outside the study site. Patients used rating scales to assess lozenge at 3, 4, 5, and 6 hours post-treatment. After 6 hours, the patients were instructed to take one lozenge every 3 hours as required up to a maximum of eight lozenges within a 24-hour period. Patients were instructed to record administration times, concomitant medications, and any adverse events before returning to the clinic on day 5.

***Outcomes**:* Primary outcomes involved total pain relief summed over 15 to 120 minutes calculated from the pain relief ratings scale. Secondary outcomes involved total pain relief summed over 15 to 360 minutes, changes from baseline for throat soreness and swollen throat over 15 to 120 minutes and 15 to 360 minutes, and the overall lozenge rating at 120 minutes.
***Patient follow-up**:* Patients returned on day 5 to submit study medication administration data (described in *Intervention*).

***Main results**:* There was a significant difference in the time to achieve total pain relief (determined over 15-120 minutes), reducing throat soreness over 2 hours, and reducing throat swollenness over 2 and 6 hours with flurbiprofen (8.75mg or 12.5mg) compared to placebo. There was no significant difference in the time to achieve total pain relief between the two flurbiprofen doses. There was no significant difference in tolerability between flurbiprofen groups and placebo.

***Conclusions**:* The use of flurbiprofen 8.75mg accelerates time to pain relief, reduces soreness and swollenness over placebo. Use of flurbiprofen 8.75mg lozenges provides adequate sore throat relief to patients that can last up to 4 hours. Flurbiprofen did not present any increased harm to patients.

Comments/critical appraisal (including assessment of internal and external validity):

Internal validity: Eligible patients were randomized to receive flurbiprofen 8.75mg, flurbiprofen 12.5mg, or placebo. Patients were allocated by a computer-generated randomization list. This study was double-blinded. All patients received the study medication. All tonsillopharyngitis assessments were made by a single physician. A single physician assessment may have biased entry into the study. The flurbiprofen 12.5mg group contained a higher proportion of smokers. There were 2 patients excluded in the per protocol analysis due to taking prohibited additional medications (panadol and further lozenges) between 2 and 6 hours. Table 1 contains the final number of evaluable patients. Patients were excluded due to non-compliance. Excluded patients were included in the intent-to-treat (ITT) population using zero for missing entries. ITT analysis reduces the bias to validate statistical findings. The study was completed as intended.

External validity: This study included patients 18 years of age or older experiencing pain secondary to non-bacterial URTI. The study site was based in Europe. Cultural variations can possibly influence generalizability to North American patients. The majority of viral throat infections in healthy individuals are self-limiting. As such, the patient population from this study can be applied to the EBSCR algorithm. This study focused on patient-perceived improvement of symptoms associated with URTI, including throat soreness. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. Nevertheless, the pain relief model used in this study to determine analgesic effectiveness has been validated in literature. In terms of safety, no adverse events were noted in the study. Interesting, the placebo arm (using sugar lozenges) provided symptomatic relief of sore throat pain. Compared to flurbiprofen, the placebo arm showed a smaller effect size with a slow onset of action. Sugar lozenges may provide some benefit through demulcent activities. More importantly, this study used flurbiprofen lozenges. Flurbiprofen is not available in Canada. As such, this product would have to be compounded with another NSAID product available in Canada. NSAIDs exhibit different analgesic and anti-inflammatory properties. If NSAID lozenges are desired, an NSAID with similar potency and safety profile would have to be chosen to replace flurbiprofen.

3. **Bachert C, Chuchalin AG, Eisebitt R, Netayzhenko VZ, Voelker M. Aspirin compared with acetaminophen in the treatment of fever and other symptoms of upper respiratory tract infection in adults: a multicenter, randomized, double-blind, double-dummy, placebo-controlled, parallel-group, single-dose, 6-hour dose-ranging study. Clin Ther 2005; 27(7):993-1003.**

***Study objectives**:* To study the efficacy, safety, and tolerability of aspirin (ASA; 500 mg and 1000 mg) and acetaminophen (500 mg and 1000 mg) compared to placebo in adult patients with acute febrile upper respiratory tract infection (URTI) of viral origin.

***Methods**:*
***Design**:* Randomized, double-dummy, placebo-controlled, parallel-group study.
***Allocation**:* Eligible patients were randomized to receive a single dose of aspirin 500 or 1000 mg, acetaminophen 500 or 1000 mg, or placebo. Patients were allocated by permuted block randomization (block size of 5).
***Blinding**:* This trial was double-blinded.
***Follow-up period**:* The total duration of the study was 6-hours. Patients were assessed at baseline 2, 4, and 6 hours after dosing.
***Setting**:* Patients were recruited at 7 clinics in Moscow, Russia, and 10 clinics in Kyiv and Lugansk, Ukraine. Patients stayed in the clinic for the whole 6 hour observation period.
***Participants**:* Prior to allocation, patients were selected based on the following inclusion criteria: men and women between the ages of 18 and 65 years with an acute, uncomplicated, febrile URTI of suspected viral origin. Patients had to experience URTI for 5 days with fever (38.5°C to 40°C) and other symptoms of URTI (including sore throat). See Table 3 for patient enrollment. Demographic and baseline characteristics were similar in the groups. Fifty one percent of patients were male. The mean age of patients in this study was 37.4 years of age. The mean body weight of the patients was 74.3kg. Patients were excluded based on (1) bacterial infection (pneumonia, otitis media, bacterial sinusitis, any other bacterial infection of the respiratory tract needing antibiotics), (2) current use of antibiotics or antibiotic use within a 1 week period, (3) history of asthma or hypersensitivity to acetylsalicylic acid, salicylates, or other NSAIDs or acetaminophen, (4) history of peptic ulceration or bleeding, (5) hepatic and/or renal dysfunction, (6) diagnosis of Gilbert's disease, (7) Quincke's edema. Investigators could exclude any individuals based on risk, or potential gastrointestinal compromise. Pregnant or lactating women, individuals with known drug dependency or alcohol abuse, and patients participating in another clinical study within the previous 4 weeks were not recruited.

Table 3. Number of patients enrolled per group

Group	Intention-to-Treat (ITT) Population	Per Protocol (PP) Population*
Placebo	78	78
ASA 500mg	78	78
ASA 1000mg	78	78
Acetaminophen 500mg	79	79
Acetaminophen 1000mg	79	79
Total patients enrolled	392	386

*Six patients were excluded from the PP final analysis. These patients were excluded because they failed to provide adequate documentation at 4 hours after dosing.

***Intervention**:* The placebo group received 2 bottles containing two 500 mg tablets of aspirin placebo and two 500 mg tablets of acetaminophen placebo. Study medication consisted of the contents of both bottles (4 tablets), taken with 200 mL tap water. Medication was taken in the presence of the investigator or study nurse, who recorded the administration and compliance with the study protocol. No hot or cold drinks or meals were allowed during the 6 hour observation period. Water at room temperature was supplied to a limit of 1 L per patient, but was not allowed within 10 minutes before measurement of body temperature. Oral temperature was measured at baseline (directly before intake of study medication) and at varying time points (0.5, 1, 1.5, 2. 2.5, 3. 3.5, 4, 5, and 6 hours) after treatment. Headache, frontal, and maxillary sinus sensitivity to percussion, sore throat, achiness, and feverish discomfort were rated by patients using an ordinal scale (from 0 = none to 10 = severe) at baseline and again at 2, 4, and 6 hour observation period. Adverse events were recorded throughout this period. After 6 hours, a physical examination was performed and patients were discharged.
***Outcomes**:* The primary outcome for this study was AUC for the change in orally measured body temperature from baseline until 4 hours after dosing. Secondary outcomes involved maximum temperature difference between baseline and the lowest measured body temperature, the time to the maximum temperature difference, the temperature differences between baseline and each measured time point after dosing, and the intensity of the URTI symptoms of headache, frontal and maxillary sinus sensitivity to percussion, sore throat, achiness and feverish discomfort. Safety and tolerability were also evaluated by occurrence of adverse events.
***Patient follow-up**:* Patients were assessed for efficacy and safety 6 hours after receiving study medication. There were 386 patients included in the per protocol analysis. Six patients were excluded due to incomplete documentation of the primary end point at 4 hours after dosing.

***Main results**:* For the primary outcome, all active treatments were significantly superior to placebo ($P < 0.001$, 1-sided *t* test), with no significant differences between them. Significant reductions were seen in the mean intensity of headache, achiness, and feverish discomfort with all active treatments at most time points, but not in sinus sensitivity to percussion or sore throat. All treatments were equally well tolerated, and no clinically significant adverse events occurred.

***Conclusions**:* Aspirin and acetaminophen were more effective against fever and other symptoms (not sore throat) associated with URTI compared to placebo. This study did not find a significant reduction in the intensity of sore throat with aspirin or acetaminophen.

Comments/critical appraisal (including assessment of internal and external validity):
Internal validity: Eligible patients were randomized to receive ASA (500mg or 1000mg), acetaminophen (500mg or 1000mg), or placebo. Patients were allocated by block randomization (block size of 4). This study was double-blinded. Hence, there was no bias. All patients took the study medication and provided data for efficacy analysis. However, 6 patients were excluded for incomplete or inadequate documentation of the primary end point at 4 hours after dosing, creating a per-protocol analysis population of 386 patients. Main analysis used the intention-to-treat (ITT) population. The study was completed as intended.

External validity: This study included patients 18-60 years of age experiencing sore throat pain secondary to non-bacterial URTI. The study site was based in Europe. Cultural variations can possibly influence generalizability to North American patients. The majority of viral throat infections in healthy individuals are self-limiting. As such, the patient population from this study can be applied to the EBSCR algorithm. However, this study was powered to assess the antipyretic effects of the therapeutic agents. Resolution of sore throat was a secondary outcome. Also, the baseline sore throat rating score was

below 6. Compared to other sore throat pain management studies, this represents a lower cut off for inclusion. Relative to other studies, patients in the study did not experience a decreased quality of life secondary to sore throat. The findings of this study should not discourage use of aspirin or acetaminophen for treatment of sore throat.

4. **Eccles R, Loose I, Jawad, M, Nyman L. Effects of acetylsalicylic acid on sore throat pain and other pain symptoms associated with acute upper respiratory tract infection. Pain Med 2003; 4(2):118-124.**

***Study objectives**:* To evaluate the efficacy and safety of acetylsalicylic acid (ASA) in the treatment for sore throat associated with upper respiratory tract infections (URTI).

***Methods**:*
***Design**:* Randomized, single-centre, prospective, parallel group, placebo-controlled study.
***Allocation**:* Eligible patients were randomized to receive ASA 800mg or placebo. Patients were allocated by permuted block randomization (block size of 4).
***Blinding**:* This trial was double-blinded. The effervescent tablets used were physically identical in appearance, taste, and degree of effervescence.
***Follow-up period**:* The total duration of the study was 3 days. Patients were evaluated at 2, 4, and 6 hours for sore throat outcomes (described below). Study was in two phases. First, a 2 hour lab phase. This was followed by a 3 day home phase. Efficacy was measured during the 2 hour lab phase and for the first 4 hours of the home phase. Safety was investigated over both the lab and home phase.
***Setting**:* Study was designed as a single-center study in an out-patient setting (UK Centre). Protocol was amended to allow recruitment of patients from a second out-patient site (Sweden Centre). In total, 279 patients were recruited. For the per protocol analysis, 272 patients were analyzed.
***Participants**:* The center from United Kingdom (Center 1) recruited 161 valid patients. The center from Sweden (Center 2) recruited 111 valid patients. Prior to allocation, patients were selected based on the following inclusion criteria: patients aged 18 and 60 years with a history of URTI for 12-120 hours. Patients had to have at least 4 symptoms from the list of 16 provided by investigators in the previous 24 hours (sore throat, runny nose, sneezing, wet cough, dry cough, earache, ear fullness, sinus pain, sinus pressure, muscle aches/pains, feverish discomfort, chills, hoarseness, scratchy throat, and headache). Patients also had to score ≥6 on an 11-point ordinal scale for throat pain severity and score ≥5 on a tonsillopharyngitis scale. Exclusion criteria included pregnant or lactating females, contraindications to ASA, any medications that could influence sore throat, unable to breathe through their nose, history of mouth breathing, and any condition that required medical attention. Investigators excluded patients who previously participated in this study or another clinical trial within the previous 30 days. The intervention and control groups were similar. There were no significant differences in demographics or vital signs.

Table 4. Number of patients enrolled per group

Group	Enrolled Population	Evaluable Population*
Placebo	-	133
ASA 800mg	-	139
Total patients enrolled	279	272

*Seven patients were excluded from the final analysis. Investigators state 279 patients received treatment, but only 272 were protocol valid cases.

***Intervention**:* Treatments were ASA 800mg and placebo. Patients received the study medication as an effervescent tablets dissolved in 6 ounces of water. In the 3-day home phase, patients were instructed to take 1-2 effervescent study medications dissolved in water every 4-6 hours as needed up to six tablets per day. No special instructions were given regarding intake of food. During the 6-hour post dosing period, patients were instructed not to take any other medications, candies, lozenges, gum, cigarettes, inhale substances, and using menthol based products. Eating and drinking was prohibited during 6-hour post dosing evaluation. Patients rates sore throat pain at baseline at 15, 30, 60, 90, and 120 minutes, and at 3, 4, 5, and 6 hours.
***Outcomes**:* The primary outcome for this study has rating of sore throat pain using an 11-point ordinal scale. The scale was used to determine if ASA was superior to placebo for decreasing sore throat pain over 2 hours. Secondary outcomes involved sore throat relief scale using a seven-category ordinal scale. This scale was used to determine if ASA was superior to placebo for decreasing sore throat pain over 4 and 6 hours, relieving sore throat pain over 2, 4, and 6 hours, decreasing the intensity of headache, and muscle aches and pains over 2 hours. Another outcome included severity of common cold symptoms at baseline and 2 hours following completion of all sore throat scales. Safety of ASA was also evaluated by occurrence of adverse events.
***Patient follow-up**:* Patients were assessed for efficacy and safety 6 hours after receiving study medication. Patients were assessed for safety after the 3-day home phase. 279 patients were recruited and obtained treatment. 272 were protocol valid cases for efficacy analysis.

***Main results**:* ASA 800mg provided statistically significant results in all primary and secondary outcomes compared to placebo. There was a significant decrease in the primary outcome of total sum of pain intensity differences (SPIDs) up to 2 hours with ASA 800mg compared to placebo. ASA 800 mg provided statistically significant reduction in SPIDs up to 4 and 6 hours. ASA 800mg provided statistically significant reduction in sore throat pain intensity over 2 hours ($P<0.001$), reducing sore throat pain intensity over 4 and 6 hours, relieving sore throat pain over 2, 4, and 6 hours. ASA 800mg provided statistically significant relief of muscle aches and pain and headache over 2 hours compared to placebo ($P< 0.01$). No safety issues were identified. P values from the results listed above indicate statistical significance.

***Conclusions**:* The use of ASA 800mg can provide relief from sore throat pain associated with URTI. ASA did not present any increased harm to patients. Therefore, it is a safe and effective treatment option for sore throat pain from URTI.

***Comments/critical appraisal (including assessment of internal and external validity)**:*

Internal validity: Eligible patients were randomized to receive ASA 800mg or placebo. Patients were allocated by block randomization (block size of 4). This study was double-blinded. Due to randomization and blinding performed, this study was internally valid. All patients received the study medication. There were 7 patients who were considered invalid protocol cases. Table 4 contains the final number of evaluable patients. Main analysis used the intention-to-treat (ITT) population. The study was completed as intended. Outcomes were assessed using a significance level of less than 5%. Blinding was also excellent because appearance, taste, and degree of effervescence were the same for the drug and placebo. This was a well-designed study; it was well thought out.

External validity: This study included patients 18-60 years of age experiencing sore throat pain secondary to URTI. The study site was based in Europe. Cultural variations can possibly influence

generalizability to North American patients. The investigators excluded suspected bacterial infections. Microbiological assessments were not done to rule out bacterial infections. Hence, patients in this study most likely had URTI due to either bacterial or viral infections. However, majority of patients in the community are unlikely to know the source of sore throat. Results from this study could be applied to your adult patients who have sore throat from URTI. The investigators of this study allowed patients to take the study medication on demand. On demand administration of the study medication allows generalizability of results. Medication was allowed to be taken at any time during the study, with no specific instructions on whether to take with food, so that it mimicked real life. Concomitant medications were not allowed, as this could have affected results. This study focused on patient-perceived improvement of sore throat. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. However, the analgesic assessment method for sore throat improvement used in this study has been validated in literature. This study used ASA effervescent tablets. According to the Health Canada Drug Database, the highest strength ASA effervescent tablets available are 325mg. As such, the ASA 325mg effervescent tablets would have to be re-constituted to an approximate concentration of 4.4 mg/ml.

5. Boureau F, Pelen F, Verriere, F, Paliwoda A, Manfredi R, Farhan M, Wall R. Evaluation of ibuprofen vs paracetamol analgesic activity using sore throat pain model. Clin Drug Invest 1999; 17(1):1-8.

***Study objectives**:* To evaluate the validity of a sore throat pain model by comparing the analgesic efficacy of ibuprofen and paracetamol.

***Methods**:*
***Design**:* Randomized, double-dummy study.
***Allocation**:* Eligible patients were randomized through a computer-generated randomization code to receive ibuprofen 400 mg or paracetamol 1000 mg.
***Blinding**:* This trial was double-blinded.
***Follow-up period**:* The total duration of the study was 2 days.
***Setting**:* Study was designed as a multicenter study in out-patient settings.
***Participants**:* Prior to allocation, patients were selected based on the following inclusion criteria: patients presenting with onset of sore throat within 2 days, subjectively identified moderately severe throat pain associated with an obvious diagnosis of tonsillo-pharyngitis. Exclusion criteria included history of hypersensitivity to ibuprofen, aspirin, paracetamol or any other NSAID or any contraindication to treatments, previous use of local sore throat treatment within 2 hours, any analgesic treatment within 6 hours and/or any anti-inflammatory treatment within 3 days prior to the initial consultation, patients with mouth breathing as a result of nasal congestion. Patients were excluded if antibiotics were used within the week prior to the initial consultation.

Table 5. Number of patients enrolled per group

Group	Enrolled Population	Per-Protocol Population*
Ibuprofen	57	52
Paracetamol	56	52
Total patients enrolled	113	104

*Nine patients had major deviations from the protocol during the study and were excluded from per-protocol analysis.

***Intervention**:* Treatments were ibuprofen 400 mg or paracetamol 1000 mg. The first dose of the study medication was administered in the physician's office. After the initial dose, patients were discharged. Patients evaluated throat pain every 6 hours. No other medications were allowed within this 6 hour period. Additional doses of the study medication were allowed after the 6 hour period. Patients recorded the results of their hourly assessments on a diary card. Patients returned for a final consultation after 2 days. If antibiotics were considered necessary, this was given 6 hours after the initial dose of the study medication.
***Outcomes**:* The primary outcome for this study has rating of sore throat pain using three indices: pain on swallowing, relief of sore throat pain, and difficulty swallowing. Other assessments involved tonsillopharyngitis score, and global evaluation of treatment efficacy.
***Patient follow-up**:* Patients were assessed for efficacy and safety 48 hours after the initial dose of the study medication.

***Main results**:* Ibuprofen 400 mg was shown to be more effective than paracetamol 1000 mg in all primary outcomes after 2 hours.

***Conclusions**:* The use of ibuprofen 400mg can provide better symptomatic sore throat relief than paracetamol 1000 mg.

Comments/critical appraisal (including assessment of internal and external validity):

Internal validity: Eligible patients were randomized to receive ibuprofen 400 mg or paracetamol 1000 mg. Patients were allocated by computer-generated randomization. This study was double-blinded. All patients received the study medication. There were 9 patients who were considered invalid protocol cases. This study lacked a placebo arm to assess effectiveness of sore throat treatments. Hence, this study can only confirm if one analgesic is superior to another. The study was completed as intended.

External validity: This study included adults experiencing tonsillopharyngitis confirmed by clinical diagnosis. The study site was based in Europe. Cultural variations can possibly influence generalizability to North American patients. This study included patients likely to be self-care candidates in community settings. As such, the patient population from this study can be applied to the EBSCR algorithm. This study focused on patient-perceived improvement of sore throat. Hence, the main weakness of this study was the use of subjective parameters to assess effectiveness. The analgesic assessment method for sore throat improvement used in this study has been validated in literature. Also, the baseline sore throat rating score was below 6. Compared to other sore throat pain management studies, this represents a lower cut off for inclusion. Without a placebo arm, establishing a true benefit from either agent becomes difficult. The results are largely driven by the superior analgesic effect of ibuprofen over paracetamol. Thus, this study can only confirm that ibuprofen has better analgesic properties compared to acetaminophen.

6. **Schachtel BP, Fillingim JM, Lane AC, Thoden W, Baybutt RI. A double-blind study comparing aspirin with caffeine to aspirin and placebo in patients with sore throat. Arch Intern Med 1991;151:733-737.**

***Study objectives**:* To evaluate the use of caffeine as an analgesic and antipyretic adjuvant in patients with acute sore throat due to tonsillopharyngitis.

***Methods**:*
***Design**:* Randomized controlled trial.
***Allocation**:* Patients were assigned to receive ASA with caffeine, ASA alone, or placebo via computerized randomization, based on presenting with URTI with a sore throat that began a maximum of 4 days prior.
***Blinding**:* This trial was double-blinded.
***Follow-up period**:* Two hours following administration of treatment.
***Setting**:* Study was designed as a single-center study in an out-patient setting (UK Centre). Protocol was amended to allow recruitment of patients from a second out-patient site (Sweden Centre).
***Participants**:* 210 adult patients with URTI and acute sore throat, with confirmed tonsillopharyngitis and severe throat pain.
***Intervention**:* Patients in the combination therapy group received 800mg of aspirin with 64mg of caffeine; patients in the aspirin monotherapy group received 800mg of aspirin; patients in the placebo group received a placebo treatment which was not described in the study.
***Outcomes**:* Sum of pain intensity differences (SPID) from baseline, total of pain relief (TOTPAR) ratings, change in pain scale (CPS), change in difficulty swallowing, change in swollen throat, antipyretic activity (measured by mean change in oral temperature from baseline).
***Patient follow-up**:* Patients remained in the physician's office for 2 hours after administration and reported on efficacy outcomes at 15, 30, 45, 60, 90, and 120 minutes after administration.

***Main results**:* For SPID, TOTPAR, CPS, difficulty swallowing, and swollen throat, both ASA + caffeine and ASA were significantly better than placebo. Additionally, ASA + caffeine was significantly better than ASA monotherapy in these outcomes. The increase in analgesia with the combination product versus the ASA-only product for each outcome was as follows: SPID: 44%, TOTPAR: 34%, CPS: 34%, difficulty swallowing: 33%, change in swollen throat: 23%. It is also worth noting that the differences in individual relief scores and pain scores favored combination therapy over ASA monotherapy at 30 minutes ($p<0.05$) and at each time interval thereafter ($p<0.01$). ASA + caffeine and ASA monotherapy were both effective as antipyretic agents when compared to placebo (both agents caused a change in oral temperature of -2°C while placebo yielded a change of +1°C; $p<0.01$) but caffeine did not offer added efficacy in antipyretic activity of ASA.

***Conclusions**:* Caffeine as an adjunct to ASA provides greater pain relief than ASA alone (and placebo) within 30 minutes, for up to 2 hours.

***Comments/critical appraisal (including assessment of internal and external validity)**:* This study did not address the method of use of placebo interventions- it is not known whether the monotherapy arm or the placebo arm were given a caffeine placebo, or just ASA/ASA placebo. Additionally, the dose of 800mg ASA may not be appropriate for all patients, thus these study results may not be externally valid.

Tertiary/Secondary:

7. **Pelucchi C, Grigoryan L, Galeone C, Esposito S, Huovinen P, Little P, Verhij V. Guideline for the management of acute sore throat. Clin Microbiol Infect 2012; 18 (Suppl. 1):1-27.**

Study objectives: The European Society for Clinical Microbiology and Infectious Disease (ESCMID) reviewed primary and secondary literature to develop a guideline to diagnose and treat acute sore throat.

Scope:
Inclusion criteria: Guidelines were limited to duration of acute sore throat of less than 14 days, and uncomplicated sore throat in adults and children in Europe.
Exclusion criteria: Guidelines excluded recurrent or persistent cases of sore throat, complicated pharyngitis, severe co-morbidities, immunosuppression, or history of acute rheumatic fever. Furthermore, sore throat associated with travel outside of Europe, and/or sexually transmitted diseases were excluded.
Outcomes: Different classes of analgesics were compared to each other and placebo. Specific outcome criteria were not outlined in the guideline.
Recommendations: First-line diagnostics, symptomatic and antibiotic treatment.
Treatment options: Analgesics, corticosteroids, zinc, herbals, acupuncture, and antibiotics.

Methods:
Source: Articles (primary and secondary literature) were retrieved from Medline, PubMed, and Cochrane Database. Search terms were based on keywords/MeSH terms from previous clinical guidelines. Searches spanned from 2000-2009. A total of 1000 articles were found. Abstracts and unpublished studies were excluded. Weak designs or data quality were not excluded.
Assessment of evidence in the literature*:* Studies were evaluated based on the design, potential bias, and validity. See Table 6 below.

Table 6a. Hierarchy of literature search

Study Design	Evidence rank
Systematic reviews and meta-analysis	1
Randomized trials	2
Prospective cohort	3
Case – control, cross-sectional, retrospective cohort	4
Case reports	5
Expert Opinion	6

Table 6b. Suffix designations

Suffix	Description
First Suffix	
A	Low risk of biased results; all or most of the validity criteria are met
B	Moderate risk of biased results; half of the validity criteria are met
C	High risk of biased results; most of the validity criteria are not not
Second Suffix	
+	Numerical results unequivocally support a positive answer to the research question
-	Numerical results unequivocally do not support a positive answer to the research question

?	Numerical results are unclear

Recommendation Grading: Based on the assessment of evidence, the investigators graded recommendations based on consistency of evidence and study design. See Table 7 below.

Table 7a. Checklist for grading

Grading	Description
A	Consistent evidence; clear outcome
B	Inconsistent evidence; unclear outcome
C	Insufficient evidence; consensus

Table 7b. Recommendations based on quality of evidence

Study Design	Recommendation rank for preventative and therapeutic intervention trials	Other Studies
Systematic reviews (SR) or meta-analysis (MA) of randomized control trials (RCT)	1	1
One RCT or more than one RCT (no SR or MA)	2	---
One cohort study or more than one cohort study (no SR or MA)	3	2
Other	4	3

Main results: The authors determined that analgesics were better than placebo. Either ibuprofen or acetaminophen are recommended for relief of acute sore throat symptoms (grade: A1, see checklist for grading above and Table 7). Therefore, systematic reviews or meta-analyses of RCTs showed consistent evidence with clear outcomes. For aspirin, there were two studies listed in this review. Both attained levels of 2A+ which equates to randomized trials with low risk of bias (all or most of the validity criteria are met) and the numerical results unequivocally support a positive answer to the research questions; ASA (effervescent tablet) is effective and safe for treating sore throat pain associated with upper respiratory infections (Eccles R, Loose I, Jawad, M, Nyman L. Effects of acetylsalicylic acid on sore throat pain and other pain symptoms associated with acute upper respiratory tract infection. Pain Med 2003; 4(2):118-124.), and aspirin (tablet formulation) is not as well tolerated as ibuprofen or acetaminophen (Moore N, Le Parc JM, Van Ganse E, Wall R, Schneid H, Cairns R. Tolerability of Ibuprofen, aspirin and paracetamol for the treatment of cold and flu symptoms and sore throat pain. IJCP, Dec 2002; 56(10): 732-734.

Conclusions: Acute sore throat pain can be treated with NSAIDs (including aspirin, ibuprofen, flurbiprofen) or paracetamol (acetaminophen).

Comments/critical appraisal:
Internal validity: This guideline used a commonly used framework to determine quality of evidence, and considered bias. However, the authors failed to acknowledge the importance of clinical outcomes in grading selected articles. Funding for this guideline was provided by Pfizer.

External validity: The search criteria used by the authors captured an extensive list of articles evaluating the role of analgesics in treating acute sore throat. The wide search parameters allowed selection of different analgesics agents, age ranges, and treatment durations. Final recommendations did not provide specific details regarding products, age groups, or duration of therapy. This guideline supports the role of analgesics to treat acute sore throat. Unfortunately, due to a lack of clinically relevant information, this guideline should not be used to decide one analgesic over another.

8. Thomas M, Del Mar C, Glasziou P. How effective are treatments other than anti-biotics for acute sore throat.

Study objectives: To compare efficacy of non-antibiotic medications versus placebo in the treatment of acute sore throat.

Scope:
Inclusion criteria: Articles were limited to randomized control trials from 1966 onwards. Keywords used for the search included 'tonsillitis', 'pharyngitis', 'sore throat', 'randomized controlled trial', 'drug therapy', 'therapeutic use', or 'random'.
Exclusion criteria: This review excluded articles if acute sore throat was not investigated, active treatment was an antibiotic, trial performed in a non-clinical setting, excessive dropouts, no suitable control, no treatment, and unclear randomization or blinding.
Outcomes: Different classes of non-antibiotic medications were compared to each other and placebo.
Treatment options: Analgesics, corticosteroids, influenza vaccines, and streptococcal bacteria oral spray.

Methods:
Source: This review article limited searches to Cochrane databases, and Medline searches.
Grading of evidence: A universal scale was used to score each symptom described in the articles. Each symptom was graded as 100 at baseline. Efficacy was determined by the percentage change of symptom score in the intervention group relative to placebo.

Main results: The authors found that NSAIDs, including combination with caffeine, appears to be effective in treating symptoms associated with acute sore throat. Based on the standardized symptom scale, ibuprofen 400 mg single dose showed the most symptomatic improvement. ASA 800 mg in combination with caffeine 64 mg also decreased throat pain after 1 hour.

Conclusions: NSAIDs, including combination with caffeine, represents an effective alternative to manage symptoms associated with acute sore throat.

Comments/critical appraisal:
Internal validity: This review used an internally derived grading scheme for symptomatic improvement. Only randomized controlled trials were included for this review.
External validity: The studies reviewed in this article used different intervals to measure efficacy of non-anti-bacterial agents for acute sore throat. This inconsistency makes it difficult to recommend a therapeutic duration of an analgesic that showed benefit to resolve acute sore throat. Finally, the majority of trials measured outcomes within a very short time span (less than 24 hours). Thus, patients with acute sore throat for longer than 24 hours may not benefit from non-antibacterial pharmacologic agents.

9. Derry CJ, Derry S, Moore RA. Caffeine as an analgesic adjuvant for acute pain in adults. Cochrane database of systematic reviews 2012, Issue 5.

Study objectives: To assess the efficacy of caffeine as an adjuvant to an analgesic versus the analgesic alone in the treatment of acute pain.

Scope: This systematic review looked at the use of caffeine as an adjuvant to any type of analgesic medication (including ASA, ibuprofen, diclofenac, and paracetamol), regardless of pain condition. Studies for a variety of acute pain conditions were included, such as migraine headaches and postpartum pain. Patients were at least 16 years old with any level of pain, and there was no restriction on dose for either caffeine or the primary analgesic. The primary outcomes for this review were number of participants with at least 50% of maximum pain relief within 4-6 hours, number of participants reporting "very good" or "excellent" pain treatment on a patient global evaluation of treatment 5-point scale, number of participants reporting clinically meaningful pain relief, and number of patients with headache relief at two hours.

Methods: The reviewers searched the online databases Cochrane Central Register of Controlled Trials, Medline, EMBASE, and Oxford Pain Relief Database. Additionally, the reviewers contacted manufacturers of caffeine-combination products who were known to possess unpublished trials of caffeine as an adjuvant to analgesic therapy.

Main results: For at least 50% of maximum pain relief, caffeine provided additional analgesia above that of an analgesic alone, regardless of pain condition (67% vs. 61%). This yielded a NNT of 16.

Conclusion: Caffeine provides added relief for acute pain, regardless of pain condition or type of analgesic. Doses of 100mg or greater confer a benefit of an extra 5-10% of pain relief.

10. Stead W. Sore throat in adults (beyond the basics). UpToDate. Accessed on Feb 3 2013 from: www.uptodate.com.

Source Description: A clinical decision support service, UpToDate provides evidence-based information to healthcare professionals. Physician editors continually monitor publications to ensure UpToDate articles reflect the most accurate information. Often, authors that are recognized in a particular field of study are encouraged to write expert opinions about a subject manner. As such, UpToDate articles are primarily expert opinions supported by recent evidence. The article on acute sore throat was updated on October 2011 and current as of January 2013.

Summary: In terms of pain medication, UpToDate lists acetaminophen, and non-steroidal anti-inflammatory agents (such as ibuprofen or naproxen) as acceptable therapeutic options to manage acute sore throat pain.

Comments/critical appraisal: UpToDate authors are not instructed to describe the search strategies used to select references used to support personal opinions. There might be potential selection bias in the literature used to guide therapeutic discussions. This particular article provides healthcare professionals with a practical approach to sore throat management. Unfortunately, the article fails to provide detailed information about individual treatment options (dose, dosage form, duration, etc.). Also, preferred agents for treatment are not systematically ranked. Overall, this article provides fundamental information about acute sore throat. However, this article should not guide therapeutic decisions for management of acute sore throat in an outpatient setting.

11. Sore throat: what you need to know. Available at http://www.mydr.com.au/respiratory-health/sore-throat-what-you-need-to-know. Accessed Mar 27 2013.

Source Description: *mDr* represents an extension of a global healthcare publishing company called UBM Medica. This website was designed to help Australian residents make informed healthcare decisions. The articles are written by Australian healthcare providers recognized by Australian health organizations. The content on the website is reviewed by Australian clinicians.

Summary: In terms of pain relief, this article recommends paracetamol (with or without codeine) or codeine with aspirin, or aspirin alone to manage sore throat pain. The article states aspirin cannot be used in patients younger than 16 years of age due to the risk of Reye syndrome. Ibuprofen is also listed as an option to treat sore throat pain. However, ibuprofen or aspirin cannot be used in patients with peptic or duodenal ulcers, bleeding conditions, or currently taking anti-coagulant medications.

Comments/critical appraisal: Primary literature was not used to support the recommendations contained within this article. The references listed at the end of the article compromised of tertiary resources. Hence, applicability of this material for an evidence-based algorithm becomes difficulty. This particular article provides healthcare professionals with a practical approach to sore throat management. Unfortunately, the article fails to provide detailed information about individual treatment options (dose, dosage form, duration, etc.). Also, preferred agents for treatment are not systematically ranked. Overall, this article provides fundamental information about acute sore throat. However, this article should not guide therapeutic decisions for management of acute sore throat in an outpatient setting.