Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Treatments for Acute Pain: A Systematic Review*

Draft report available for public comment from August 31, 2020, to September 28, 2020.

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Comments to Draft Report

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each draft report is posted to the EHC Program website or AHRQ website for public comment for a 3- to 4-week period. Comments can be submitted via the website, mail, or email. At the conclusion of the public comment period, authors use the commentators' comments to revise the draft report.

Comments on draft reports and the authors' responses to the comments are posted for public viewing on the website approximately 3 months after the final report is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

This document includes the responses by the authors of the report to comments that were submitted for this draft report. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Summary of Peer Reviewer Comments and Author Response

This research review underwent peer review before the draft report was posted for public comment on the EHC website.

We received comments from eight peer reviewers on the draft report of Treatments for Acute Pain: A Systematic Review. We made individual edits where indicated for clarity or spelling. The following more substantive changes were also made in response to peer reviewer comments:

Overview of peer review comments
We received 10 sets of comments on the draft report from four peer reviewers, five members of the technical expert panel, and the AE. Seven reviewers gave the report a top rating of "superior," and the other three gave it the next-tier rating, "good." The comments were generally positive and acknowledged the heterogeneity of the available data.

The following is a summary of the most common/pertinent comments:

1. **Comments about the limited evidence.** There were few studies included for long-term opioid use, mostly because they did not include the specific conditions determined *a priori* or were for chronic, mixed, or nonspecified pain. Several reviewers noted that the paucity of studies was not attributable to the quality of the review but rather the limited evidence available.

2. **Suggestions for additional studies.** There were few included studies for sickle cell pain. A reviewer suggested additional primary studies and a systematic review. The authors reviewed these suggestions and the reference list of the systematic review and none met inclusion criteria. The majority of the suggested studies were placebo controlled and thus out of scope. In response the authors added an explanation to the discussion that the inclusion criteria limited the number of studies for sickle cell pain.

3. **Inconsistency in reporting findings throughout the report.** There were some comments related to strength of evidence statements and ensuring they were consistent with the results throughout. This was done.

4. **Requested details for clarification.**
    a. Lack of detail about conclusions in summary points. There was a comment related to reporting results in the summary bullets at the beginning of each KQ and choosing between including only qualitative statements or adding quantitative results to each KQ. Quantitative statements were added when available and when the evidence was stronger.
    b. Dosing of nonsteroidal anti-inflammatory drugs (NSAIDS). The language in the Evidence Summary was edited to clarify that the doses of NSAIDs in each arm differed in some studies.
    c. Study types that informed long-term data. In response to the comment from the Food and Drug Administration, a number of sections throughout the report were updated to clarify that long-term use data was from observational studies.
    d. Individual study descriptions. Additional detail provided in the results to better describe studies and findings (e.g., duration of pain for nonsurgical pain conditions, revised bullet points to indicate if findings in Key Findings were

for surgical pain, primarily surgical pain, or mixed [surgical or nonsurgical] pain).

e. Inappropriate groupings of pain conditions, in particular musculoskeletal pain conditions and surgical and nonsurgical dental pain. In response the authors clarified conclusions that were comprised of studies related to surgical, nonsurgical, or mixed patient groups with dental pain. For musculoskeletal conditions, detail was added to the limitations section about the variability within the acute pain conditions, including musculoskeletal pain.

5. **Additional details about limitations of the evidence base and systematic review process.** The discussion was updated to explicitly address the variability within predefined acute pain categories (musculoskeletal pain including fractures and post-surgical pain) that could obscure potential differential effects by specific conditions. Also clarified the lack of homogeneity amongst studies which made it difficult to stratify results based on duration of the pain.

6. **Inconsistent language in Main Points to convey certainty of evidence.** There was a comment related to the use of the words "probably," "might be," and "possibly." This language corresponds to suggested language in AHRQ's "Describing Effects Roadmap" workgroup for informative statements to communicate results of systematic reviews. Language in the report was revised to be more consistent within the document using "might be" to describe low strength of evidence (SOE) rather than also using "possibly" to describe low SOE. Text to explain the meanings of the plain-language statements were added in Appendix B, Methods, on page B-6.

7. **Concurrence with conclusions of the review.** Several reviewers noted that the paucity of studies was not attributable to the quality of the review but rather the limited evidence available. What is notable are the absence of comments disputing the conclusions of the systematic review.

8. **Succinct presentation of findings**. Multiple reviewers noted that the findings were clear and the report succinct.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Margaret Spiller / 1	NA	General	I can only speak for me. I cant take anymore injections (osteoporosis). They also dont work. Cant take anymore aleve (ulcers). Tylenol is bad for my liver. If opioids are working best, then, that should be the treatment. I want to be able to live a functional life. These meds make that possible. Let the patient and their doctor make treatment decisions on chronic pain that is incurable. PLEASE.	Thank you for sharing your story. We are sorry to hear about your pain. Your pain appears to be chronic pain. This report summarizes the published evidence on benefits and harms of treatments for acute pain
Margaret Spiller / 1	NA	General	Many many pain patients have been harmed by the CDC guidelines mainly because doctors are fearful to prescribe the only and most effective opioid medicines that work and have been used successfully for centuries without harm. Some patients have turned to street drugs for their pain out of desperation and got meds laced with deadly fentanyl and died!	Thank you for the comment. This report is not a guideline; it summarizes the published evidence on benefits and harms of treatment for acute pain.
Margaret Spiller / 1	NA	Description of the problem and evidence	No	Noted.
Margaret Spiller / 1	NA	Difficult to read	Yes	Noted.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Bailey Parker / 2	NA	Evidence summary	There are a lot of nights and maybes in this. I find it barbaric to put someone through a tooth being pulled without proper medicine. I find it even worse to tell a failed cervical fusion patient that the only thing they need is a massage.	"Might" and "maybe" are suggested "plain language" descriptors that indicate a low level of evidence. The report does not make recommendations, but summarizes the published evidence on benefits and harms of treatments for acute pain. Treatment of failed cervical fusion is a chronic pain condition not addressed in this report.
Bailey Parker / 2	NA	References	No one would undergo surgery ever if they knew they wouldn't get proper pain management.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain.
Bailey Parker / 2	NA	General	You are being pretty cavalier in the face of pain patients and people with serious health conditions. People will die. They will kill themselves due to unmanaged uncontactable pain. Your narrative is wrong.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not address treatment of intractable (chronic) pain.
Bailey Parker / 2	NA	Understand results and conclusions	Nope. You might as well have told people in need of skilled doctors that they would be better of with mindful meditation. Western medicine will be a joke.	Thank you for the comment.
Annie Shoger / 3	NA	Introduction	The reports is fairly easy to follow but as a non professional there may be things I do not quite understand totally. But their findings I did not agree with at all.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. We utilized plain language suggested by the Cochrane EPOC group and an AHRQ Methods Workgroup to describe findings, to the extent possible.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Annie Shoger / 3	NA	Methods	Studies do not really address long term chronic pain in patients and usually they are done for a long period of time to get the whole picture.	The focus of this report is on acute pain-- it does not address chronic pain.
Annie Shoger / 3	NA	Results	"Again, I do not agree with the results as NSAIDAS do not work for me. Even opiates have their limitations as they do not take all the pain away but it does takes enough away (if given enough as you become tolerant of them and they do not possess any risks is taken as prescribe) to take the deliberating pain to a more manageable level so that I can do things. Otherwise everything is a struggle and one has to really plan their day around their pain for that day."	Thank you for the comment. You appear to be referring to management of chronic pain, which can be challenging. The focus of this report is on acute pain.
Annie Shoger / 3	NA	General	Reports such as these are grabbed by PROP (Physicians for responsible opioid prescribing) and CDC (Center for Disease Control) which are harming patients as myself. For some reason, opiates are being portrayed as the devil itself when on the contrary it has been around for thousands of years and really are one of the safest medications on the market.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain.
Annie Shoger / 3	NA	Description of the problem and evidence	I believe I understand what was being described as the problem and evidence but I believe it is false from my perspective.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain.
Annie Shoger / 3	NA	Difficult to read	Yes, a little as least from a non professional health care provider reader.	Noted.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Annie Shoger / 3	NA	Understand results and conclusions	I believe so.	Noted.
Penny Volosin / 4	NA	General	"I wholeheartedly disagree with the findings in this report. [....] Please remember that everyone is different and a “cookie cutter” style to pain management does not work for everyone and you will be discriminating against people. Pain management patients are not abusers of the medication. Thank you for allowing comments"	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not address long-term or ongoing management of chronic pain such as persistent pain following back surgery.
Penny Volosin / 4	NA	Description of the problem and evidence	Yes	Noted.
Penny Volosin / 4	NA	Difficult to read	No	Noted.
Penny Volosin / 4	NA	Understand results and conclusions	Yes	Noted.
Anonymous / 5	NA	Evidence Summary	I don't know how you came about getting this evidence. I do know that I have had kidney stones and in no way, shape, or fashion does an NSAID work for that kind of pain.	Thank you for your comment. We are sorry to hear about your kidney stone pain. The methods section describes the approach to identifying studies for inclusion in the report. The findings regarding NSAIDs versus other medications for kidney stone pain are based on published evidence.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 5	NA	Introduction	Nsaids create a lot of problems for those of us that are Allergic to them. I have ibs-d and a mitral valve prolapse. Nsaids make the symptoms of both increase. Why are you trying to push Nsaids when the public has been warned about the stomach and heart issues they can create.	Thank you for your comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not make recommendations on clinical management. Clinicians must consider benefits and harms in individual patients when choosing medications for acute pain.
Anonymous / 5	NA	Methods	I live with pain everyday. I have 7 bulging discs, 2 slightly herniated, with nerve involvement sacroiliac joint dysfunction, radiculopathy, lumbosacral spondylosis, degenerative disc disease and I just had a total knee replacement. It is because of studies like this that I have lost any kind of normalcy in my life. Opiods have their place in helping people from staying bed ridden Since the CDC guidelines came down the pendulum had swung too far and it feels like we are back in the draconian age. I have had shots in my back, 2 nerve ablations, physical therapy, chiropractic care, I have worn a brace, but I am allergic to NSAIDS and Tylenol won't cut it. Are you trying to kill the chronic pain patients? We are not to blame. We see our drs, take our meds accordingly, and take random drug tests. The addicts get better pain relief than we do."	Thank you for sharing your story. We are sorry to hear about your pain. Your pain appears to be chronic pain. This report summarizes the published evidence on benefits and harms of treatments for acute pain

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 5	NA	Results	Not everyone metabolizes medication the same. No one feels pain the same. Don't put us in a box and expect us all to turn out the same. Can all of you wear the same size shirt pants, shoes? No you are all different. If you were to have kidney stones that were so big that you had to have lithotripsy done, you would not have to take an Nsaid or Tylenol. I guarantee that you would be screaming for pain meds. I know. I have been there. I am on disability and I wish I wasn't like this. No one grows up wanting to have these issues. All of you are one accident away from needing something other than an Nsaid or Tylenol. This is crazy. Don't punish pain patients or the disabled.	Thank you for your comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not make recommendations on clinical management. Clinicians must consider benefits and harms in individual patients when choosing medications for acute pain. Findings regarding effectiveness of NSAIDs and acetaminophen for kidney stone pain are based on the available literature.

Anonymous / 5	NA	Discussion	This is a farce. Nsaids and Tylenol. Are you going to treat diabetics with water instead of insulin. If a patient has a heart attack and they are in tremendous pain, are you going to give them Tylenol? It appears that you guys have no respect for the disabled or the chronic pain patients. No not everyone who is on an opiod ends up on street drugs. That is something that you tell yourself so the paperwork looks good. Come walk in my shoes. Throw yourself down at least 3 flights of stairs, get back up and do it again. Then have someone hit you all over, then give birth. Yep. I have had 3 kids, they are older now,and everytime I bend.over it feels like I having contractions. Now give yourself a Tylenol. What I am trying to say is that back pain, like I have, keeps me in the bed often. It's easy to sit up there and say severe back pain is not worth mentioning and just give these people a Tylenol and they will go away or we will judge them and make them look like addicts. Chronic pain patients and those of us on disability have been yelled at, judged, dehumanized, labeled, and abandoned and you guys want to make it worse. This has got to stop. Recognize pain, treat it with something other than OTC medication, and don't this the baby out with the bathwater just so your paperwork looks great. Is the pat on the back going to be worth the pain you allow people to go through. I am only 54 and I don't want to be in pain till I die. Would you? What about your family members?	Thank you for your comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not make recommendations on clinical management. Clinicians must consider benefits and harms in individual patients when choosing medications for acute pain.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 5	NA	References	All I can say here is that people need to think I am allergic to NSAIDS and Tylenol don't work. The amount that I would have to take would kill my liver. Which Tylenol can do. Don't punish pain patients and those of us that are on disability due to intense pain. You are hurting a whole population of people that didn't ask to be in pain. You are turning your back for the big atta boy, and you are also turning your backs on thousands of honest Americans who did nothing wrong but get caught up in the net with the illicit drug users. I hope you guys can sleep with that because I and thousands of others wake up all through the night in pain.	Thank you for sharing your story. We are sorry to hear about your pain. Your pain appears to be chronic pain. This report summarizes the published evidence on benefits and harms of treatments for acute pain. It does not make recommendations.
Anonymous / 5	NA	General	I think that you have read enough of what I had to say. Don't let it fall on deaf ears.	Thank you for the comment.
Anonymous / 5	NA	Description of the problem and evidence	I understand all right. Hurt the chronic pain patients and those.on disability some more.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not address treatment of intractable (chronic) pain.
Anonymous / 5	NA	Difficult to read	No it wasn't difficult. It was downright sad.	Thank you for the comment.
Anonymous / 5	NA	Understand results and conclusions	Nope. Your conclusions and results mean nothing to those of us that suffer.	Thank you for the comment. This report summarizes the published evidence on benefits and harms of treatment for acute pain. It does not address treatment of intractable (chronic) pain.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Julie Killingworth / 6	NA	Evidence Summary	Low quality Or very low quality evidence is NOT evidence!! You're just a bunch of linguistic tricksters trying to act like you know what you're talking about but you don't. You don't even treat bodily diseases. You're mostly a bunch of PHD quacks!	Thank you for the comment. The report summarizes the published evidence on benefits and harms of treatment for acute pain. In many cases, the evidence is of low quality, though higher quality evidence is highlighted when available. Several investigators on the review team are health workers (physicians and nurses).
Julie Killingworth / 6	NA	Introduction	Bunch of nonsense garbage from a bunch of pain fetishists psychopaths	Thank you for the comment.
Julie Killingworth / 6	NA	Appendices	I couldn't even be bothered because I'm in agony since being cut off the lowest dose Tramodol. The only thank you give me a will to live right now is to see you all in a federal prison for antitrust and depraved mind murder of incurable disabled.	Thank you for sharing your story. We are sorry to hear about your pain. The report summarizes the evidence on benefits and harms of treatments for acute pain. Your pain appears to be chronic, which this report does not address.
Julie Killingworth / 6	NA	Difficult to read	It is extremely difficult to read because it's nonsensical cult creepiness written by a bunch of creeps	Thank you for the comment. We used "plain language" as recommended by the Cochrane EPOC group and an AHRQ methods work group to the extent possible to summarize findings.
Cathy Marquardt / 7	NA	Evidence Summary	I'm seriously wondering where you found this many people who say opioids are less effective for pain.	Findings regarding opioids are based on published studies evaluating opioids.
Cathy Marquardt / 7	NA	Introduction	I disagree with most everything noted.	Thank you for the comment. Our findings are based on the published literature.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Cathy Marquardt / 7	NA	General	No one who has ever had kidney stones is getting relief at the height of the pain, when the stone is moving. It is important to not prescribe these meds unnecessarily, yes. It's also very important to not be so afraid of a less than 2% chance of addiction if the meds are prescribed, stored, and used correctly. These meds were around long before now and are safe and effective for most people. Please stop the war on pain patients!!	Thank you for the comment. Findings regarding medications for kidney stone pain are based on the published literature.
Jonathan Courtrney / 8	NA	Evidence Summary	I don't know where you get these subjects, but I find it odd there is no mention of patients getting ulcers from NSAID medications.	Thank you for the comment. The report summarizes evidence on benefits as well as harms of treatments for acute pain. As described in the report, serious adverse events such as bleeding or ulcers were not reported with NSAIDs. In most trials, NSAIDs were given as a single dose or for a few days, which is common for most acute pain conditions and generally not enough exposure to cause ulcers.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Jonathan Courtrney / 8	NA	Results	There is no mention of the damage NSAID medications cause long term. The current system that measures MME is flawed. Medications have different half lives.D50E81D48:D49D48:D51	Thank you for the comment. As described in the report, serious adverse events such as bleeding or ulcers were not reported with NSAIDs. In most trials, NSAIDs were given as a single dose or for a few days, which is common for most acute pain conditions and generally not enough exposure to cause ulcers. Opioids were converted to mg morphine equivalents using published conversion ratios in order to be able to compare the strength of the opioid therapy used in different studies.
Jonathan Courtrney / 8	NA	Discussion	You are drafting rules that are causing more harm than good with incomplete science. Shame on you.	This report summarizes the published evidence on benefits and harms of treatments for acute pain. It does not make recommendations.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Charmaigne Cross / 9	NA	General	I noticed that the studies mentioned were all “fair” quality, and from a range of years. Why did the authors not use “excellent” quality studies? I also noticed cases were not consistent in the drug comparison. For example, some studies used Tramadol where others used Oxycodone. Some compared the opioid to Ketoprofen, which is Toradol, a stronger NSAID, where others used Tylenol. I believe better and more consistent studies are needed before imposing pain and suffering on post op patients. I have had several surgeries and can say with confidence the NSAIDS or Tylenol would not have been adequate to relieve the pain. In fact, one time a doctor released me from the hospital with only Tylenol and the pain was unbearable! I had to call and get something stronger or I would have had to go to the ER.	The report did include good quality studies; unfortunately, most studies had methodological limitations (as described in the Quality Rating tables) and were downgraded to fair or poor. Good quality studies are discussed in the Results and highlighted when available. We evaluated studies that compared an opioid versus an NSAID (such as Toradol) separately from acetaminophen (Tylenol). Findings regarding medications for postoperative pain are based on the published literature.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Charmaigne Cross / 9	NA	Description of the problem and evidence	It appears to me that the authors were picking and choosing studies to prove their point rather than using a scientific approach to learn more about the effectiveness of opioids vs. non-opioid medication for post operative pain. Certainly, the risk of misuse is a concern, but as the studies showed, only 1% of patients prescribed opioids post op displayed this behavior. Although the report says that demographic and sociological data were collected, it does not break down the results by age group. For example, are younger people more likely to misuse the medications vs. other age groups? This information would be helpful to understand how prescribers can help avoid the risk of addiction or misuse.	We included studies that met pre-defined inclusion criteria as described in the Methods. Demographic criteria were recorded but as noted in the Results, there was insufficient data to determine how benefits or harms varied in groups defined by demographic factors (including age), social, or clinical factors. Addiction and misuse were not reported as outcomes in the studies included in this report, which focuses on treatment of acute pain, which is typically short-term.

Redacted / 10	NA	General	My family has 3 generations of a genetic problem called Elhers Danlos Syndrome. Each generation has worse symptoms than the last. The collagen in our bodies does not work well. The only medication that works for us is Opioids for pain. The only exception for me was when my teeth were removed was Brand Advil, it helped the most and it had to be the brand not generic. Which brings me to my point. We do not all fit in the same box as humans. In my family each generation has gotten worse. There are alot of comorbidities that go along with Elhers Danlos. Such as cysts, hernias, subluxing and dislocating of joints, arthritis starting at a young age and worsening over a lifetime. Herniation and bulging of spinal discs. Just a few of our problems. We have been genetically tested for medications that work good for us and medications we should not use. My point is that we do not all fit in the same box. Doctors do not know enough about our problems and do not treat us as a whole system with pieces not working correctly. We spend our lives going from body part specialist to specialist. Each with a different answer. I am the grandmother. The spinal injections do not work for me and they do not last more than a week, if at all. Over my lifetime I have had so many NASIDS, my gastro system can not tolerate them anymore. I have gone from a physically hard working woman to being disabled by the time I was in my late 30's. By my 40's I was in so much pain after 3 spinal surgeries, I could no longer function without help. I went to my PCP, who also	Thank you for sharing your story. We are sorry to hear about your pain and loss. The report focuses on treatments for acute pain. You appear to have chronic pain, which is not addressed in this report.

			had trained himself in Pain Management, but was not an actual Pain Management Clinic. He put me on an antidepressant because people who have pain that is never going to get better, are depressed. He had me take a Coated Asprin, which I tolerated, for inflammation. And he started me on the dreaded Oxycontin Extended Release for pain. With trial and error we found the dosage that worked for me. It gave me back a quality of life. I was able to function finally. I was by no means pain free and never will be, but it was tolerable. Once we found the correct amount of Oxycontin Extended Release, I was stable on that medication for 15 years. I did not have to up the dose, I did have from the doctor a "As needed opioid medication for times when the extended release did not last 12 hours and I could not tolerate the pain. All of this was monitored by him, We did a contract and urine tests years before these were "in vogue" We had a great working relationship and I never abused my medication. I kept my word on our contract. I only used one pharmacy and if I had to change I would notify him. If I had to have a surgery I would notify him and ask permission to take the medications the other doctor would prescribe. He knew everything about me and I saw him every three months. His office would send my prescriptions to my pharmacy as they were due to be filled. His system was great and I was finally able to have a life. Then the 2016 CDC Guidelines were published. I was referred to a Pain Management Clinic and dropped by my PCP. I was in the	

			process of moving from NH to Florida to retire to the home I had just bought and was looking forward to a nice retirement. Needless to say my retirement has gone from a dream to hell. People with Elhers Danlos do not use lidocaine patchs, creams,etc. We do not get Novacaine at a dentist because it does not work on us at all. I was 8 years old and having my teeth drilled for a cavity without Novacaine because the needle and pain from the Novacaine was worse than getting my teeth drilled. I never knew why, until Elhers Danlos was discovered in the 1990's. It explained why me and my siblings spines fell apart and why we could not do things because our joints dislocated. My 8 month old baby daughter's elbow would dislocate and we had to keep it wrapped so it would stay in place, Now everything made sense! You can not make MME's the same for everybody. We are all different. We all metabolize different medications at different rates. But when I found the right dose for me, it worked for 15 years! I had no other choice than to go on Suboxone. I was dependant on Opioids not addicted to them. I never craved them like an addict would. But I used them because they worked good for me. I would much rather have a decent quality of life. Quantity of life is not worth anything if the quality is not there.the pain medication I was taking gave me no side effects. The Suboxone made my arms, legs and feet swell. It made my stomach sick. It gave me mouth sores because you have to use it as a sublingual pill. It does nothing for my pain.	

			All it does it keep me from going into horrible withdrawals because no one would wean me down off the Oxycontin that actually worked for me with no side effects. But no one wants to hear that. I asked the Suboxone doctor to change me to buprenorphine because I was one of the 2% of people who was having side effects to the Naloxone in the Suboxone. At least now the swelling, mouth sores and sick stomach are gone. The DEA, CDC and FDA do not belong between me and my doctor, My PCP handled my medications with caution and educated me before I made choices. All was good and my PCP knew me better than any Pain Clinic that runs patients in and out like cattle. And the people who are saying that Opioids do not work or make pain worse over time are just plain lying. I'm sorry that people loose family because someone made a bad decision and became addicted to heroin, fentanyl, alcohol,methamphedamines,etc. Believe me I know. I just lost my 19 year old grandaughter who was in college to become a nurse and was one of the most wonderful, caring persons you would ever meet. The drunk driver who was also on Cocaine, slammed into the car she was a passenger in, at 65 MPH and hit her side of the car. She was brain dead on the scene. She was in the Trama Unit for 3 days before doctors did a test to show us the blood was stopping at her neck and not getting to her brain. Per her wishes we donated her organs. She saved the lives of 5 people and her heart was used to make valves for babies to be given a chance at	

			life. So I have been there. I have lost one of the most precious things a person can loose and all because someone made a bad decision. Yes, I am angry as hell about it. I want to see him go to jail for the rest of his miserable life, but I do not see the government making alcohol illegal. They tried it once during Prohibition and it did not work. Pretty much the same here with Opioids. Portugal has the right idea. Make it all legal and treat the depressed and mentally ill. This war on drugs came into existence during the Nixon era. We as a country have spent billions on the war on drugs and we are worse off 40 years later. The USA should follow Portugal's example. They have it right, not just a quick fix by politicians before an election year. And it has not worked. We still have more people overdosing on drugs and alcohol than ever before. Follow the money and you will have your answers. The people behind the CDC Guidelines, I will bet they all own tons of stock or businesses in the Substance abuse business. Whether it be the drugs like suboxone or actual facilities addicts go to for rehabilitation. Yes, I agree that other things like physical therapy, yoga, tai chi all help but they are just not enough and the insurance companies won't pay for them. I would love to be active again, but I need the pain relief from the Opioids to be able to lower the pain enough to be able to move. That would maybe make it so I would need to take a lower dose, but again that decision is between me and my doctor who knows me best. I have a swimming	

			pool which helps me all summer long but I do not have the money to be able to heat it to use during the winter months, so I can not get the swimming I need because of the money issue. It is a great therapy for my whole family who all have Elhers Danlos, but I can not even write it off as a medical deduction on my taxes. The CDC Guidelines were enacted as laws and not the guide it was meant to be. Everyone panicked because they wanted to blame something on the Fentanyl crisis. Individual decisions are part of why a person is an addict. They should be paying the price, not the Intractable Pain Patient.The addict is getting help, but the pain patient is not and is also being treat like a drug addict and not like a diabetic who is dependent on a medication. The suicide rate has gone up from taking away pain medications from pain people. Does the CDC take those people into account when they do their numbers of people overdosing? Do they take into consideration the alcohol and other drugs in the Opioid overdose person? Were they taking other drugs or drinking large amounts of alcohol while they were taking Opioids in whatever form? When I read the statistics on overdoses, most have more than one substance in their body. The true prescription overdose figure is down around 2-4% while just alcohol overdoses are around 6-8%. Alcohol is a bigger killer than Opioids! I do not see any restrictions on alcohol other than an age limit of 21. The man who killed my granddaughter is 24 years old.Age did not make him any	

			more responsible of a person, he still drove drunk and murdered her. People in intractable pain are mostly in an age group of 55 and up. The people overdosing are between 17 and 25 years of age. Why is the CDC not putting out a new guideline? Their first one was wrong and used wrong by states and alot of people are suffering needlessly because of it. A board of Intractable Pain Patients, Doctors like PCP's and Mental Health workers should be made up to make these new decisions. Not just people and doctors who are involved ONLY in rehab facilities , drug companies and insurance companies. All sides of this issue should be part of the CDC board's discussions. More people are going on to disability because they can no longer function without their medications that allow their pain levels to be at a manageable level enough to work and care for their families. My family now has to help me to do the everyday things I can no longer do for myself. I went from a useful, functioning person to a person who needs help just to live everyday. It is more than depressing, and there is no logical reason for it. You have actually taken my life from me. I hate the fact I am in a position at 63 years old that I need help everyday from my family. I would still be functioning and have a semblance of a life if the CDC and state laws did not take away the only medication that gave me that life. I did nothing wrong! I followed the rules but here I sit, wasting away and miserable. I can not go out for an evening to a movie or to visit friends. The pain	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			stops me from doing everything I loved. All because you all get to decide how I should have to live. This is America, land of the free. I do not feel free at all anymore. This is wrong and needs to be fixed by people with common sense and not an agenda to fulfill.	
Anonymous / 11	NA	General	When words like "are probably" and "some patients" are used, it dilutes and refutes the science behind risk vs. benefits in treating patients. There are patients in which NSAIDS are contraindicated. Acute pain can range from mild to severe. Please do not increase barriers to care, so that clinicians and patients can make informed choices based on the condition(s) presented.	We used "plain language" as recommended by the Cochrane EPOC group and an AHRQ Methods Working Group to summarize findings as "probably" (moderate level of evidence) or "might be" (low level of evidence) associated with outcomes. The phrase "some patients" is used twice in the report: once when noting that acute pain persists in some patients in the Background section and once to note that in a poor quality trial some patients were randomized multiple times. We think both of these uses is appropriate. The report summarizes evidence on benefits as well as harms of NSAIDs. The report does not make recommendations. Clinicians should consider benefits and harms in individual patients when selecting treatments.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Isaac Arnett / 12	NA	Evidence Summary	There are a lot of might and maybe statements in this report which intimates a lack of science based evidence.	We used "plain language" as recommended by the Cochrane EPOC group and an AHRQ Methods Working Group to summarize findings as "probably" (moderate level of evidence) or "might be" (low level of evidence) associated with outcomes.
Isaac Arnett / 12	NA	General	There are a lot of might and maybe statements in this report which intimates a lack of science based evidence. Being a CPP and having gone through a large number of medications with severe side affects, before being prescribed a narcotic, I can speak from experience. I suspect that my case of Cushings was caused by and originated from the use of SSRI, SNRI, antidepressants, and anticonvulsants that I was given, though I can not prove it. There is science evidence that Cushings has be caused through medications. even now, after years of medical probing, testing, and surgeries..., I live with chronic pain, and observe that pain management has become more focused on pill count management; a one size fits all approach, regardless of pain levels.	Thank you for your comment. We are sorry to hear about your pain. The report summarizes evidence on benefits and harms of treatments for acute pain. You appear to have chronic pain, which is not addressed in this report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions (postoperative pain, surgical dental pain, and kidney stones) and might be similarly effective to NSAIDs for low back pain. E54 My response: One of the more subtle reporting biases found in this report is that opioids are rarely a treatment of first choice in low back pain not associated with surgery. It is thus to be expected that NSAIDs will be a default first treatment in mild to moderate low back pain. The inclusion of single-dose trials in the data review introduces a bia against opioids, in that no opportunity is offered for appropriate dose titration to reach effective levels of medication.	The report summarizes the evidence on opioids vs. NSAIDs for various acute pain conditions. Many of the trials used single doses, which we noted is a limitation of the evidence. Dose titration is not relevant for initial treatment of acute pain, the topic of almost all trials in the report. The purpose of evaluating the evidence for various medications for acute pain is to help determine first- versus second-line medications.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • An opioid might be more effective than Gabapentin for acute neuropathic pain. My Response: This is one of the few areas of the report in which "might" is appropriately used. During 24 years of online support group moderation as a non-physician subject matter expert in chronic neuropathic face pain, I have observed that Gabapentin is widely used off-label in management of such pain. Some patients respond positively to titrated/divided doses over 1200 mg/day; others receive no pain relief from this medication; some are initially relieved only to have pain recur within weeks or months for no explained reason. A few display allergic reactions to the med. "Brain fog" (cognitive disorganization) and word finding difficulty are common side effects in many. For significant numbers of patients, opioids offer improved outcomes for both effectiveness and fewer side effects.	Thank you for the comment. The findings regarding opioid versus gabapentin are based on the published evidence.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • Opioids are probably associated with increased risk of short-term adverse events versus non-opioid pharmacologic therapy for acute pain, including any adverse event, study withdrawal due to adverse events, nausea, dizziness, and somnolence, but serious adverse events are uncommon in randomized trials. My Response: Although serious short term adverse events may be uncommon in randomized trials, withdrawal by patients placed on placebo is common due to uncontrolled breakthrough pain. Moreover, many adverse events associated with non-opioid pharmacologic therapy are not observed in hospital settings, but instead occur later in re-admissions for liver toxicity, cardiac irregularities, ulcers or colitis reactions. Failure to acknowledge this obvious confound compromises the integrity of the observation.	The report summarizes the evidence on harms of medications for acute pain, including withdrawal due to adverse events. Placebo-controlled trials of medications were not eligible for inclusion, as this report focused on studies that compared one medication versus another. As noted in the report, medications were not associated with serious adverse events, likely due in part to the short duration that medications were used in the studies. Clinicians should consider potential benefits and harms in individual patients when choosing therapies for acute pain.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • Being prescribed an opioid for acute low back pain or postoperative pain might be associated with increased likelihood of use of opioids at long-term follow-up versus not being prescribed. My Response: This assertion is almost certainly an example of the post hoc ergo propter hoc fallacy. Prevailing medical practice looks upon prescription opioids as an option for relatively severe pain that is unresponsive to other interventions. Initial high severity and protracted duration of pain are associated with later emergence of chronic pain syndromes. Since opioids are used in more severe or intractable pain, we would expect continuing use during long-term follow-up compared to cases where pain is less severe and opioids are not initially tried. Large-cohort studies (not referenced by the AHRQ report) of post surgical pain are also available that demonstrate rates of long-term prescription (>90 days continuous renewals) in opioid-naïve post-surgical patients on the order of 1% or less. Within this 1%, some proportion reflects not exposure to opioids in any habituating sense, but rather the failure of a surgical procedure to fully address the original cause of pain. This distinction is not acknowledged in the AHRQ report as a confound, and it should be.	Our findings do not reflect the post hoc fallacy because they do not suggest that causality is present, rather, findings regarding the association between opioid use for acute pain and long-term use are based on studies showing this association. Although the association could be related to confounding such as severity of baseline pain or other factors associated with development of long-term pain, the association was present in studies that adjusted for potential confounders. As described in the Methods, we included studies that compared rates of long-term use in persons prescribed and not prescribed opioids for acute pain. Uncontrolled studies that did not compare long-term use in persons prescribed versus not prescribed opioids for acute pain were not eligible for inclusion. Although the Results focus on relative estimates, rates of persistent use are reported (e.g., Thiels et al reported persistent use in 0.27% prescribed 1 to 199 MME and 1.3% in those prescribed ≥500 MME).

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • Heat therapy is probably effective for acute low back pain, spinal manipulation might be effective for acute back pain with radiculopathy, massage might be effective for postoperative pain, and a cervical collar or exercise might be effective for acute neck pain with radiculopathy. My Response: Radiculopathy pain is associated with nerve pinch or lesions. Spinal manipulation in such cases must be administered with profound caution to avoid further damaging nerves that may already be compressed or damaged. Studies which mix patient populations with and without radiculopathy introduce potential confounds that should be acknowledged and assessed before drawing any general conclusions on effectiveness or treatment risks.	We reported results for spinal manipulation for low back pain stratified by presence or absence of radiculopathy when the evidence permitted. As noted in the Results, severe adverse events were not noted with spinal manipulation in patients with radiculopathy. Studies of spinal lumbar manipulation in general (not necessarily restricted to acute low back pain) report that neurological complications are very rare in patients with low back pain with or without radiculopathy (neurological complications are more common with cervical manipulation).

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	• • Research is very limited on the comparative effectiveness of therapies for sickle cell pain, acute neuropathic pain, neck pain, and management of postoperative pain following discharge. My Response: these research limitations are no less applicable for other categories of pain addressed by the AHRQ report and have in fact been highlighted in a Cochrane Review of the 2016 CDC Guidelines on prescription of opioids to adults with chronic non-cancer pain. In fact, the current AHRQ review unintentionally offers significant support for an assessment that the current state of medical trials literature lacks methodological rigor to such a degree that generalizations drawn by AHRQ writers are clearly inappropriate and should be withdrawn outright.	This statement cited by the commenter highlights the very limited evidence for these conditions. Other acute pain conditions were supported by more robust evidence, though limitations were also noted. We did not locate a "Cochrane Review of the 2016 CDC Guideline," as Cochrane does not typically conduct systematic reviews of a guideline. It is unclear what the reviewer is referring to.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Evidence Summary	TECHNICAL Expert Panel "In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts." My Response: If these important defining elements of the study do not represent the views of individual technical and content experts, then whom DO they represent? And precisely how were they arrived at? In areas of research where conclusions may be controversial, it is customary to entertain a "minority report". However, the AHRQ report instead opts for an effort to create the illusion of collegial unanimity. Treatments for Acute Pain Systematic Review [Structured Abstract] My Response: Remarks on the Key Points apply equally to the structured abstract.	The Technical Expert Panel provides info the scope, Key Questions, and methods of the report. They are not responsible for the results or conclusions, which are the responsibility of the authors.

Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Introduction	___ ___ ___ "The 2016 Centers for Disease Control and Prevention (CDC) guideline focused on chronic pain, but included one recommendation to limit opioids for acute pain in most cases to 3 to 7 days. This recommendation was based on evidence indicating an association between use of opioids for acute pain and long-term use. 35" My Response: This earlier recommendation has likewise been challenged by the AMA in its recent comments concerning needed revisions to the 2016 guidelines. ___ ___ ___ "In the last several years, over 25 states have passed laws restricting prescribing of opioids for pain; nearly half of the states with limits specify that they apply to acute pain.20,36 Although data indicate some effects of policies in reducing opioid prescribing, studies on clinical outcomes are lacking." My Response: June 2020 AMA comments to the CDC likewise challenge CDC to actively advocate for repeal of these laws. As a final observation on this section of the AHRQ draft report, I note that the introduction is remarkable not only for what it says, but for what it doesn't. The report ignores well established contradictions to its own politically pre-determined messages. Notably, neither the authoritative work of Dr Nora Volkow and the National Institute	The report does not state or imply that tolerance or physical dependence is a predictable result of opioid prescribing, nor are tolerance or physical dependence discussed as adverse consequences of opioids. The quote cited by the commenter discusses DSM criteria, which is not addressed in the report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			on Drug Abuse nor the published commentaries of the American Medical Association are discussed. Specifically, Dr Volkow and a co-author state in the New England Medical Journal: “Unlike tolerance and physical dependence, addiction is not a predictable result of opioid prescribing. Addiction occurs in only a small percentage of persons who are exposed to opioids — even among those with pre-existing vulnerabilities...Older medical texts and several versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) either overemphasized the role of tolerance and physical dependence in the definition of addiction or equated these processes (DSM-III and DSM-IV). However, more recent studies have shown that the molecular mechanisms underlying addiction are distinct from those responsible for tolerance and physical dependence, in that they evolve much more slowly, last much longer, and disrupt multiple brain processes.” Nora D Volkow, MD and Thomas A McLellan, Ph.D., “Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies” . NEMJ 2016; 374:1253-1263 March 31, 2016]. http://www.nejm.org/doi/full/10.1056/NEJMra1507771	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Methods	Author's Notes: With eight key questions, it should immediately have become apparent that many would go unanswered when review of published trials narrowed down the eligible trials set to 151 out of 20,000. However, the review team appears not to have made an effort to refine their focus.	The focus and scope of the report was determined a priori with input from a Technical Expert Panel, AHRQ, and the funder (CDC). Describing areas where evidence is lacking is an important function of systematic reviews.

Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Methods	Author's Notes: Among the 115 trials that survived AHRQ quality review, the assessed strength of medical evidence (SOE) was "low" in 52, "low to moderate" in 3, "moderate" in 15, and "insufficient" in 29. This level of evidence does not engender confidence in generalizations from such results. The report section on Applicability is worth repeating and parsing (bold emphasis by the author): Applicability "A number of issues could impact the applicability of our findings. Most randomized trials were conducted in emergency department or postoperative care unit settings, which might reduce applicability to outpatient management of acute pain. Further, trials of pharmacologic therapy frequently evaluated a single dose and some trials of nonpharmacologic therapy evaluated a single treatment session, potentially limiting the applicability of findings to a multidose course of treatment. Trials excluded important patient subgroups, such as persons with a history of substance use disorder, prior opioid use, and psychological or medical comorbidities, or did not report information regarding these factors. In addition, trials were not designed to evaluate how benefits or harms varied in subgroups defined by these factors or others, such as age, sex, and race/ethnicity. Another limitation to applicability is that most trials—particularly trials of pharmacologic	The findings are based on the available evidence. The strength of evidence ratings reflect the strength of the available evidence. The strength of evidence indicates the degree of uncertainty in findings--e.g., "low" strength of evidence indicates high uncertainty and "moderate" strength evidence indicates moderate uncertainty. This is reflected in the language used to describe findings (e.g., "might be" associated with indicates "low" strength of evidence, "probably" associated with indicates "moderate" strength of evidence). The applicability issues are important for interpreting the evidence and understanding to whom it applies. An important function of systematic reviews is to highlight areas of uncertainty and issues of applicability. Withdrawing or not publishing a review because evidence is lacking is inappropriate and akin to not publishing a randomized trial because it does not provide the desired result.

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			therapy—were designed to assess short-term (<1 week, and often <1 day) effects on pain, with few trials evaluating effects on non-pain outcomes or at longer term followup. Finally, the applicability of findings for one pain condition addressed in this review to another pain condition in this review, or to acute pain conditions not addressed in this review, is uncertain. For example, opioids were associated with decreased pain versus acetaminophen for dental pain, but increased pain versus acetaminophen for kidney stone pain. The applicability of findings from one acute pain condition to others may vary depending on the type and nature of the pain. For example, evidence on pharmacologic therapy for low back pain may have high applicability to neck pain, another musculoskeletal condition in the spine, but less applicable to sickle cell pain, neuropathic pain, or abdominal pain." My Response: Potential limitations on applicability summarized above seem to fly directly in the face of stated "Key Findings" earlier addressed. It may not be going too far to suggest that these limitations should prompt outright withdrawal of this AHRQ report, in light of the profound weaknesses revealed in medical trials literature. The many confounds revealed here contradict the top level key findings of the report with respect to comparative effectiveness of opioid analgesics versus NSAIDS or other non-opioid treatments. We simply cannot say from such weak	

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Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			evidence whether non-opioid therapies “probably” or “may” be superior to opioids. Such statements in the report are highly irresponsible and ill-supported.	

Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Results	Research Gaps "It is important for future studies on opioids to evaluate longer-term outcomes, including long-term use and potentially associated harms (e.g., opioid use disorder, overdose, impaired social and emotional cognition, and workforce nonparticipation). Well-designed clinical registries that prospectively enroll patients with acute pain prescribed and not prescribed opioids could complement randomized trials evaluating long-term outcomes." My Response: Wording of this text reflects an uncritical anti-opioid bias and assumption of harms that is unsupported by medical literature. It also ignores a reality of randomized controlled trials involving a placebo arm. As we are informed by a Cochrane Review, the relative paucity of long-term trials on opioid effectiveness is for the most part a research artifact: many pain patients placed on placebos drop out of conventional randomized trials. To obtain a more balanced trial, it may be necessary to instead perform "enriched enrollment" trials. See Baraa O. Tayeb, Ana E. Barreiro, Ylsabyth S Bradshaw, Kenneth K H Chui, Daniel B Carr, "Durations of Opioid, Nonopioid Drug, and Behavioral Clinical Trials for Chronic Pain: Adequate or Inadequate?" Pain Medicine, Volume 17, Issue 11, 1 November 2016, Pages 2036–2046.	Assessment of long-term outcomes of opioids is appropriate due to the unique characteristics of opioids related to tolerance, physical dependence and potential long-term harms such as overdose and opioid use disorder. Our suggestion for research explicitly suggests observational designs to evaluate long-term outcomes, including clinical registries. However, longer-term opioid studies than are currently available (a single trial is 1 year in duration) are certainly feasible. The cited article is not a Cochrane review, it is a review of a Cochrane review that noted that most studies of non-opioid interventions are also relatively short-term. For acute pain, this may be appropriate, given that long-term harms are not expected from non-opioid interventions.

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			https://academic.oup.com/painmedicine/article/17/11/2036/2447887	

Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	References	In the section on Opioid Therapy, the AHRQ team missed or perhaps deliberately ignored a landmark study which contradicts their conclusions concerning the centrality of medical opioids in our public health crisis: Eric C. Sun, Beth D. Darnall, Laurence C. Baker, Sean Mackey, "Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period", JAMA Internal Medicine 2016;176(9):1286-1293. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2532789 In another of the references, AHRQ writers chose to emphasize the appearance of a dose-dependent relationship between initial opioid use in acute pain and long-term use in chronic pain. They ignored the absolute numbers of patients in which such a relationship was inferred. Likewise, they jumped to conclusions on cause and effect that were unsupported by the data offered. See Gabriel A Brat, Denis Agniel, Andrew Beam, Brian Yorkgitis, Mark Bicket, Mark Homer, Kathe P Fox, Daniel B Knecht, Cheryl N McMahill-Walraven, Nathan Palmer, Isaac Kohane, "Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study", BMJ 2018;360:j5790 http://www.bmj.com/content/360/bmj.j5790.long	The study by Sun et al. does not meet inclusion criteria because it does not compare long-term use between persons prescribed and not prescribed opioids for postoperative pain. It evaluated rates of chronic opioid use after surgery but not in relation to use or non-use of opioids in the postoperative period. The study by Brat et al. also does not meet inclusion criteria because it does not compare long-term use between persons prescribed and not prescribed opioids for postoperative pain (it only evaluates patients prescribed opioids).

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			Although the draft report of the HHS Task Force on Pain Management is referenced, its central conclusion that there is no one-size-fits-all pain patient or treatment plan is conveniently ignored.	

Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	General	I write and speak as a technically trained non-physician patient advocate for people with chronic pain with 24 years experience in this field. I have published over 100 papers, articles, public addresses and conference proceedings in a mix of mainstream medical journals and mass media. I sit as an invited participant on two editorial boards, neither of which has reviewed or approved the remarks below. Overall Observations by the Author: Use of the terms “are probably” or “might be” to describe outcomes of trials suggests to me a systemic anti-opioid bias throughout the report and its appendices. When reported details of the referenced trials are examined with care, we find no protocols, methods, or analysis to establish either probability or possibility of the claimed outcomes, from the original sources. What we find instead are assessments of “medical evidence weak” or “no evidence”, describing the majority of 151 randomized controlled trials summarized in the report (from more than 20,000 candidate trials initially flagged from medical literature database search, of which 1871 were subjected to full text review). It must be assumed that such terms were introduced as opinions by the AHRQ report writers, or peer reviewers, or both. Given that the draft report fails to identify names and affiliations of the writers, it becomes practically impossible to research	The evidence levels are based on the published literature. We summarized the findings using "plain language" as suggested by the Cochrane EPOC group and an AHRQ Methods Working Group. "Probably" indicates moderate level of evidence and "might be" indicates low level of evidence/low certainty, based on assessments using the AHRQ framework for grading strength of evidence. Methodological limitations, including confounding, are a key domain when grading strength of evidence. The review protocol was developed with input from a Technical Expert Panel. Input and comments from the public, including patients and patient representatives, was solicited during a public comment process and taken into consideration prior to finalizing the report. All investigators declared conflicts of interests and were not found to have conflicts precluding participation by AHRQ. As described in the Results, there was insufficient evidence to determine how benefits and harms varied according to clinical or demographic factors. No study reported how genetic variability impacted benefits or harms of treatment. We revised the

			their professional publications for known biases and predispositions. Likewise important is that there is no evidence of participation in this review process by any patient advocate or representative. A major shortcoming of this report is its failure to adequately acknowledge confounds in the medical literature and in the analysis of the AHRQ writing team, which significantly compromise any ability to generalize results meaningfully in prescription guidelines or policy. Specifically, there is no mention of the terms “genetic” or “genomic” anywhere in this report. Yet we now know from other sources that there is high variability in individual responses to prescription opioid medications, due to polymorphism in the expression of six liver enzymes which mediate opioid (and 90% of other medications) metabolism. This medical reality is plausibly a major underlying reason why no currently available patient profiling instrument has demonstrated reliable prediction accuracy for risk of dependence, tolerance, addiction or mortality in medical patients managed on opioid therapy. Lack of such instruments is acknowledged in the report, but no explanation for the reasons associated therewith is offered. The practical impact of natural patient metabolic variability is that it is literally impossible to generalize conclusions concerning opioid safety or effectiveness,	Research Gaps to note this as a limitation. The report utilized the standard process for posting. AHRQ does not disclose investigator names while reports are in progress in order to maintain the scientific integrity of the review process. Further, there was a notice in the Federal Register when the review was initiated to solicit information on supplementary evidence from nonpublished studies.

			based on any fixed dose or duration criteria. As acknowledged by both the May 2019 report of the HHS Interagency Task Force on Pain Management, and the American Medical Association in its June 2020 comments to a CDC Call for Stakeholder Comment in the Federal Register, there can be no one-size-fits-all patient or therapy plan. Trying to generalize a single standard of pain care – even for a single disorder – is a fool's errand and very likely to remain so for the foreseeable future. A clear implication from HHS and AMA findings current as of September 2020 is that fundamental premises and assumptions embedded in the AHRQ systematic review concerning risks or harms must be withdrawn and reconsidered from the ground up. AMA is now on public record challenging the US CDC to undertake nothing short of an across-the-board repudiation and withdrawal of all legislated hard limits on prescription opioid daily dose or duration. This challenge in effect renders much of the AHRQ outcomes review moot. Also of concern is the process by which this draft report has been issued. AHRQ has circulated it only to their internally managed email distribution lists, with a review period of 30 days. In an outcomes review of this magnitude, a more appropriate venue would be the US Federal Register, for a period of at least 60 days. However, the draft – if it is issued at	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			all – will require major revision and refocus along lines suggested herein, before any public review is announced.	
Richard Lawhern / 13	Alliance for the Treatment of Intractable Pain	Description of the problem and evidence	Although the report describes a problem and reviews evidence, its conclusions are biased and substantially divorced from the many confounds revealed in the trials that it purports to review and synthesize.	Thank you for the comment. The report summarizes the published evidence on benefits and harms of treatment for acute pain. In many cases, the evidence is of low quality, though higher quality evidence is highlighted when available. The limitations of the notice are described and evidence rated using AHRQ methods.
Maureen Roland / 14	NA	Evidence Summary	Each patient needs to be treated according to the protocols for that specific patient. The patient's physician should be the one deciding what therapies are most effective for that particular patient, not arbitrary research. People also metabolize medications differently and what works for one patient may not work at all for another.	Thank you for your comment. The report summarizes published evidence on benefits and harms of treatments for acute pain. As noted in the Results, evidence on how benefits and harms vary based on demographic or clinical characteristics is extremely limited. The report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing treatment.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Maureen Roland / 14	NA	Introduction	I read a LOT of, "mights", "probably's" and so on.	We summarized the findings using "plain language" as suggested by the Cochrane EPOC group and an AHRQ Methods Working Group. "Probably" indicates moderate level of evidence/low evidence and "might be" indicates low level of evidence/low certainty, based on assessments using the AHRQ framework for grading strength of evidence and corresponds to the strength of evidence for specific interventions.
Maureen Roland / 14	NA	Results	Recommendations based on vague assumptions.	Thank you for the comment. The report was conducted using pre-defined methods as detailed in a protocol that was posted prior to conducting the review.
Maureen Roland / 14	NA	General	Most people have no idea of the difference between acute and chronic pain. Most alternative therapies are not covered by insurance. A pain sufferer cannot walk around all day applying heat to an area of pain and, often, that is ineffective. There's very little evidence that opioid medication for acute pain leads to long term use of opioids.	Thank you for your comment. We defined acute pain, the focus of this report, as pain lasting 4 weeks or less. The findings of the review regarding heat and the association between use of opioids for acute pain and long-term use are based on the published literature.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Maureen Roland / 14	NA	Description of the problem and evidence	I think there are assumptions that there is a "problem" in the first place. If we had to be so concerned about acute pain patients somehow becoming addicted to opioids prescribed for post-surgical pain due to kidney stones, for example, there would be a much higher incidence of seniors being addicted, when, in fact, the majority of people in the demographic for addiction and overdose are young males in their late teens/early twenties using illicit recreational street drugs. I also didn't see any reference to the study of 645,000 post op kidney stone patients who showed no long term dependence on opioid medication.	The report addresses evidence on the benefits and harms of treatments for acute pain. Data on the adverse events associated with use of opioids are summarized in the Introduction/Background.
Maureen Roland / 14	NA	Difficult to read	Yes. Too vague. Too many assumptions.	Thank you for the comment. The report was conducted using pre-defined methods as detailed in a protocol that was posted prior to conducting the review.
Maureen Roland / 14	NA	Understand results and conclusions	Yes.	Noted.
Mikal Casalino / 15	NA	Evidence Summary	I think you are so off base on how well opioids help with acute pain. I can not agree with your assessment of what things are best for the acute care patient. It is misleading and not true for most people. You didn't use test subjects who were in the hospital or post-surgery. You used Medline. and other different sources that published their findings. That is just not a great way to do research.	Thank you for the comment. We used published studies on treatments for acute pain. Some studies did include patients who were in the hospital following surgery, though the focus was primarily on the outpatient setting. Key Discussion focuses solely on acute post-operative pain.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Mikal Casalino / 15	NA	Introduction	It is geared to finding out what is best analgisic to use after certain procedures.	Thank you for the comment.
Mikal Casalino / 15	NA	Methods	there was no method, you just took info from other peoples' work.	Thank you for the comment. The report was conducted using pre-defined methods as detailed in a protocol that was posted prior to conducting the review. Systematic reviews by definition summarize the evidence based on previously published literature.
Mikal Casalino / 15	NA	Results	There is not enough paitient information to make these judgement. It is as if you purposely want people to be in pain. Each person is different and you can not say one type of treatment for a specific problem.	Thank you for your comment. The report summarizes published evidence on benefits and harms of treatments for acute pain. As noted in the Results, evidence on how benefits and harms vary based on demographic or clinical characteristics is extremely limited. The report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing treatment.
Mikal Casalino / 15	NA	Discussion	didn't see this.	Noted.
Mikal Casalino / 15	NA	References	didn't see this	Noted.
Mikal Casalino / 15	NA	Abbreviations and Acronyms	didn't see any	Noted.
Mikal Casalino / 15	NA	General	the general comments are base on bad research. Actually you didn't do the research yourself.	Noted.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Mikal Casalino / 15	NA	Description of the problem and evidence	not really	Thank you for the comment.
Mikal Casalino / 15	NA	Difficult to read	no	Thank you for the comment.
Mikal Casalino / 15	NA	Understand results and conclusions	yes, but can not believe how you came to the conclusions.	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.
Anonymous / 16	NA	Evidence Summary	The word, "possibly" is not evidence.	We summarized the findings using "plain language" as suggested by the Cochrane EPOC group and an AHRQ Methods Working Group. "Possibly" indicates low level of evidence/low certainty, based on assessments using the AHRQ framework for grading strength of evidence.
Anonymous / 16	NA	Methods	For patients who suffer from diseases such as Trigeminal Neuralgia or Optical Neuralgia- it's akin to having gasoline poured over their heads and set on fire on an hourly basis. No aspirin or Tylenol type pain reliever would come close to relieving an iota of their pain.	The report summarizes the evidence on benefits and harms for acute neuropathic pain, which is unfortunately very limited.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 16	NA	Results	Absolutely absurd. Longterm real studies have proven those that are given true pain medication have faster recovery time with less harmful side effects. Those living with chronic pain must have real, true pain medications for survival.	Thank you for your comment. The report summarizes the research literature on benefits and harms of treatment for acute pain. Chronic pain is not addressed in this report.
Anonymous / 16	NA	Discussion	Imagine, if you will, having gasoline poured over your entire head then lit on fire. Or being consistently electrocuted. You'll be begging for something stronger than what's suggested here for treatment.	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.
Anonymous / 16	NA	General	I sincerely believe this is the most ridiculous piece on true pain treatment I've ever reviewed.	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.
Anonymous / 16	NA	Description of the problem and evidence	"Not in the least. Only because it's completely illogical and unethical.	
Anonymous / 16	NA	Difficult to read	Only in that it is absolutely not accurate.	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 16	NA	Understand results and conclusions	I found them and cannot believe the results or conclusions to be truly accurate. While I agree massage and Chiropractic therapy are helpful in some cases, overall they're completely ineffective in pain treatment of surgeries, many diseases, kidney stones, and others listed. I actually found it insulting.	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.

Redacted / 17	NA	Evidence Summary	Please stop pushing the false narrative that insaids and tylenol may be better that opiate pain medication. May be is not going to guarantee I get up for work every day or be able to function..ur may be is not good enough when I know and all pain patients know what helps us to function!! Everyone response to meds and disease different, we are not 1 size fit all!! By u continuing false narrative that some how lowering all pain patients meds, or cutting them off will stop overdosing of illegal street drugs is outright lie!! The only ones impacted by targeting pain meds is legitimate pain patients! My husband has adhesive arachnoiditis, degenerative disc disease, chronic kidney disease, alldonyia and more..he has had same high stable dose for 20yrs..he works full time plus!! He can't be more functioning!! Yet he has been forced tapered, neglected by doctor, abused, talked down too and abandoned!! He was almost killed from a doctor that lied and said they are only allowed to write suboxone!! We were fine until the weaponized guidelines!! No one should have power over his function!! Yet because of bias guidelines and others, many agencies, government, insurance companies, states, doctors, pharmacists and more are all holding his ability to function over our whole family heads!! How can anyone live life with diseases and have someone u don't know have power over ur function..please stop trying to kill my husband and other pain patients with bias poor science!!	Thank you for sharing your story. We are sorry to hear about your husband's pain. The review synthesizes available evidence on treatments for acute pain. Your husband appears to have chronic pain, which is not addressed in this report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Redacted / 17	NA	Description of the problem and evidence	No , the evidence is poor and bias, and we know they are against pain meds by bias statements	The report summarizes the research literature on benefits and harms of treatments for acute pain. The report was conducted using pre-specified methods as detailed in a protocol that was posted prior to conducting the review.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 18	NA	Discussion	I am not commenting on every section. I am here to state that most of this is not true. I have severe neck pain from a old injury and 18mos ago it came back with a vengeance. I also had a ligament removed from the bottom of my foot along with arthritis and a bone cyst on top of the same foot. Surgery is out of the question because at 62 I could lose my foot due to circulation. I went through weeks of physical therapy for my neck, which made it worse. My doctor wouldn't prescribe anything for pain even though my mri's showed the permanent damage to my neck. The pain was so excruciating that I no longer wanted to live with it and ended up in er, which they gave me half a tramadol. I finally found a doctor that would help me. He prescribed hydrocodone after we exhausted every alternative which he had to record. When I mentioned above going to the er I didn't want to live anymore with that pain in my neck radiating into the back of my skull. I thought I was going to lose my mind. I wanted to die. So think about people like me, and others who are so much worse off and the suffering they are enduring unnecessarily because of this so called opioid crisis.	Thank you for sharing your story. We are sorry to hear about your pain. The review synthesizes available evidence on treatments for acute pain. Your husband appears to have chronic pain, which is not addressed in this report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Anonymous / 18	NA	Description of the problem and evidence	I don't think it was a very good study. The problem is chronic pain and your evidence is biased to fit your anti-opiod agenda.	Thank you for sharing your story. We are sorry to hear about your pain. The review synthesizes available evidence on treatments for acute pain. Your husband appears to have chronic pain, which is not addressed in this report.
Anonymous / 18	NA	Understand results and conclusions	What is the conclusion? Take a couple advil and grab a heating pad? Obviously whoever conducted this study wasn't very thorough.	Thank you for your comment. The report describes the evidence on benefits and harms for various acute pain conditions, including pharmacological and nonpharmacological therapies that are supported by low, moderate, or high level evidence.
Robert Carlson / 19	National Comprehensive Cancer Network	Document	Please see attached file	We revised the Discussion to note that few studies evaluated patients with acute pain related to cancer. Thank you for providing references to guidelines on management of cancer pain. However, the report is not a summary of guidelines on pain and many of the guidelines address chronic pain, which is not addressed in the report.

Steve Postal / 20	American Physical Therapy Association	Evidence Summary	APTA provides the following comments to statements (in quotes) from AHRQ's Evidence Summary. "Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions (postoperative pain, surgical dental pain, and kidney stones) and might be similarly effective to NSAIDs for low back pain." (And, other references to "effective") • APTA seeks clarification from AHRQ as to what it considers "effective". Is effectiveness measured as "lower pain scale scores"? Or is effectiveness also referring to function (a beneficiary's ability to drive a car, go to work, take care of family . . .)? "Opioids are probably associated with increased risk of short-term adverse events versus nonopioid pharmacologic therapy…" • This type of qualifying statement is much more helpful. It provides a specific outcome, versus a generic use of "not effective." "Being prescribed an opioid for acute low back pain or postoperative pain might be associated with increased likelihood of use of opioids at long-term follow-up versus not being prescribed." • APTA believes that "might be" is not strong enough, as there is a significant correlation between prescription and long-term use of opioids.	Thank you for your comments. The outcomes and methods for classifying magnitude of response are described in the Methods. The primary outcomes were pain and function. We used "plain language" to summarize findings, as recommended by the Cochrane EPOC group and an AHRQ Methods Working Group. This includes the term "might be," which refers to low quality/low certainty evidence. The findings on heat therapy for acute low back pain are based on research literature that showed consistent benefits. The findings on massage are based on low level of evidence on benefit for postoperative pain. Thank you for the references on the effectiveness of spinal manipulation; we did not find additional studies meeting inclusion criteria. The report summarizes evidence on the benefits and harms of treatment for acute pain; it does not make recommendations on treatment, including use of biophysical agents. The review addressed the 8 pre-specified acute pain conditions, which were determined with feedback from a Technical Expert Panel.

			"Heat therapy is probably effective for acute low back pain, spinal manipulation might be effective for acute back pain with radiculopathy, massage might be effective for postoperative pain, and a cervical collar or exercise might be effective for acute neck pain with radiculopathy." • Heat therapy: APTA advocates for not using (superficial or deep) heat to obtain clinically important long-term outcomes in musculoskeletal conditions. - There is limited evidence for use of superficial or deep heat to obtain clinically important long-term outcomes for musculoskeletal conditions. While there is some evidence of short-term pain relief using heat, the addition of heat should be supported by evidence and used to facilitate an active treatment program. • Heat therapy and massage: - A carefully designed active treatment plan has a greater impact on pain, mobility, function, and quality of life. There is emerging evidence that passive treatment strategies can harm patients by exacerbating fears and anxiety about being physically active when in pain, which can prolong recovery, increase costs, and increase the risk of exposure to invasive and costly interventions such as injections or surgery.	

			• Spinal manipulation: APTA has research that describes the effectiveness of spinal manipulation. See: https://pubmed.ncbi.nlm.nih.gov/21292148/#:~:text=There%20is%20moderate%20quality%20evidence,is%20low%20or%20very%20low. (This is a systematic review) https://pubmed.ncbi.nlm.nih.gov/16018809/ https://link.springer.com/article/10.1186/1471-2296-6-29 • Further, APTA stresses that the use of biophysical agents as a standalone intervention, or the use of multiple biophysical agents with a similar physiologic effect, is not considered physical therapy nor is it considered medically necessary without documentation that justifies the use of the biophysical agents for those purposes. The medical necessity of physical therapist services is determined by a licensed physical therapist based on the results of the physical therapist's evaluation. Medically necessary physical therapist services improve, maintain, or slow the decline of the current level of function; or prevent, minimize, slow the progression of, or eliminate impairments of body functions and structures, activity limitations, or participation restrictions. “This review focused on eight acute pain conditions: low back pain, neck pain, other	

Source: https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/research
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Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			musculoskeletal pain, neuropathic pain, postoperative pain (excluding inpatient management of pain after major surgical procedures),[…]" • Within scope of physical therapy, neuromusculoskeletal pain also is important. APTA requests further research on neuromusculoskeletal pain.	

Aimee Cegelka / 21	American Geriatrics Society	Evidence Summary	We are writing to comment on AHRQ's draft systematic review on Treatments for Acute Pain. AGS is a not-for-profit organization of over 6,000 health professionals devoted to improving the health, independence, and quality of life of all older people. We very much appreciate this opportunity to provide feedback on a topic that is particularly important to our members. We shared your call for comments with member experts on the topic. Our comments on the draft systematic review are outlined below. Age We found it difficult to determine what the breakdown in demographics was from the studies included. We advocate ensuring that older adults are included in (rather than excluded from) the studies surveyed as this will improve the generalizability of the studies to the older adult population. We additionally felt that the review appeared at times to collapse the older adult population in with other special populations; we believe that that it would be strengthened by addressing older adults as a distinct population. Comparative studies of analgesics in older adults with multimorbidity are sorely needed to guide treatment decisions. Fractures It was unclear whether acute fracture pain was included in the "other	Information regarding the age of patients in the trials was abstracted and available in the Evidence Tables in the Appendix. As noted in the Results, there was insufficient evidence to determine how benefits and harms varied in populations defined by age or other clinical or demographic factors. We agree that more evidence is needed on benefits and harms in older adults. This is discussed as a Limitation. As described in the methods, acute fracture pain was included as "other musculoskeletal pain" and some trials evaluated patients with acute fracture pain. Regarding specific treatments, the report summarizes the research literature on benefits and harms. The review summarized evidence on benefits as well as harms of NSAIDs. Renal harms were not reported in the trial, likely in part because of the short duration of symptoms. The guideline does not make treatment recommendations. Clinicians should consider potential benefits and harms in individual patients when selecting therapies, including cervical colors and opioids.

			musculoskeletal" category. This is an important form of pain that acutely affects older adults and we advocate including it in any future reviews. NSAIDs We advocate ensuring that acute kidney injury and other renal issues are included in the adverse effects section of the NSAID papers; we were unclear whether they were included. This is a key issue for older adults and may prevent use of NSAIDs in the patients treated by geriatrics healthcare professionals. Opioids We advocate that healthcare professionals treating older adults balance patient and family goals while using their best judgement of the individual's risks and benefits. While opioids remain an important tool that may improve functional status, older adults need judicious personalized dosing as pharmacokinetics vary greatly with aging. Cervical Collars We have concerns about the recommendation for use of cervical collars and how these recommendations would affect older adults. The collars can be uncomfortable and difficult to wear. In addition, they may cause issues with impaired sleep, increase the risk of aspiration, and even cause delirium in some patients. We find that this is the case for Physical Medicine and Rehabilitation patients as well and do not recommend	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			use of cervical collars in this population either.	
Brian Callahan / 22	National Safety Council	Evidence Summary	See attached document	The systematic review cited by the commenter was reviewed for potentially relevant references, which were added if they met inclusion criteria.

Kristin McGarity / 23	NA	Evidence Summary	The Main Points section of "Treatments for Acute Pain: A Systematic Review" has the same issue as previous AHRQ reports on chronic pain: The studies cited do not support the broad, general statements in the Main Points, Implications and Conclusions, or Structured Abstract sections. I have seen how policymakers use AHRQ reports. I have been in the room when state agencies have written policy based on these reports. They do not read the Limitations section. They do not read the Applicability section. They write one-size-fits-all policy, based solely on the generalizations in the Main Points and Conclusions sections. In particular, opioid medication has a tremendously wide variation in response between individuals. Wide variation in individual response limits applicability of cited studies to clinical practice, but this factor was not mentioned in the Evidence Summary. Most Americans have either taken a prescription opioid for acute pain or know people who have. Anecdotally, it's common knowledge that some people get good pain relief from opioid medication, some people suffer symptoms of addiction, and some people get no pain relief and/or intolerable side effects. It is reasonable to assume that studies include the same wide variation in	Thank you for the comments. The report summarizes the research literature on benefits and harms of therapy for acute pain. As noted in the report, evidence to determine how benefits and harms vary according to demographic or clinical factors, which would be helpful for individualizing therapy, are lacking. This is noted as an important Research Gap in the Discussion.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			response between participants (whether due to genetic factors, metabolism, or some other reason). Averaging pain scores leads to deceptive conclusions. In a study where half the participants get 100% relief and the other half get 0%, the final result would appear identical to a study where all participants get 45-55% relief. To conclude that "[o]pioid therapy was associated with decreased or similar effectiveness for pain versus an NSAID," we would need to know that NSAIDs and opioids perform similarly *in the same individuals.* These studies, as presented, do not rule out the possibility that opioids perform better in some individuals and NSAIDs perform better in other individuals. To prevent misunderstandings from becoming harmful policy, AHRQ should include more limitations and applicability issues directly in the Main Points and Implications and Conclusions sections, rather than in separate sections. Further, because AHRQ's work affects everyone, including exceptions and outliers, AHRQ should explicitly warn that their conclusions do not account for wide variations in individual response to treatment. AHRQ should explicitly warn that the conclusions in this evidence review do not support one-size-fits-all policy.	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Kristin McGarity / 23	NA	Introduction	It is indeed helpful to shift attention away from chronic pain to acute pain, as excessive prescribing for acute pain has been the main source of excess pills for diversion and non-medical use. However, the statement “some studies indicate that opioids may not be more effective than nonopioid therapies for some acute pain conditions” is not supported by the evidence presented.	Thank you for the comment. The findings regarding opioids versus nonopioids are based on research literature showing that benefits are larger with nonopioids than with opioids.
Kristin McGarity / 23	NA	Methods	Each Key Question focuses on a specific acute pain condition. Opioids do not perform better or worse than NSAIDs for particular *conditions,* they perform better or worse for particular *individuals.* Study results cannot be assumed applicable to all individuals with a particular acute pain condition.	Thank you for the comment. The report is based on the research literature on benefits and harms for different treatments for acute pain. The findings are necessarily based on results in populations of studied patients. As noted in the report, evidence to determine how benefits and harms varied according to patient demographics or clinical factors was not available. This report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing therapy.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Kristin McGarity / 23	NA	Results	Studies cited in the evidence base average all patients with a certain diagnosis together, and do not account for individual variations in response.	Thank you for the comment. The report is based on the research literature on benefits and harms of different treatments for acute pain. The findings are necessarily based on results in populations of studied patients. As noted in the report, evidence to determine how benefits and harms varied according to patient demographics or clinical factors was not available. This report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing therapy.

Kristin McGarity / 23	NA	Discussion	Applicability Opioid medication has a tremendously wide variation in response between individuals. Wide variation in individual response limits applicability of cited studies to clinical practice, but this factor was not mentioned in either the Limitations or Applicability sections. For instance, “opioids were associated with decreased pain versus acetaminophen for dental pain, but increased pain versus acetaminophen for kidney stone pain” might suggest that opioids are ineffective for kidney stone pain, *or* it might suggest that kidney stones have a wider variation in pain severity, such that the most severe cases benefit from opioid medication. This section correctly notes “[m]ost randomized trials were conducted in emergency department or postoperative care unit settings, which might reduce applicability to outpatient management of acute pain.” This is such a monumental applicability issue, it seriously weakens AHRQ’s conclusions, and should be mentioned in the Conclusions, Main Points, and Structured Abstract sections. This section correctly notes “evidence on pharmacologic therapy for low back pain may have high applicability to neck pain, another musculoskeletal condition in the spine, but less applicable to sickle cell	Thank you for the comment. The report is based on the research literature on benefits and harms of different treatments for acute pain. The findings are necessarily based on results in populations of studied patients. As noted in the report, evidence to determine how benefits and harms varied according to patient demographics or clinical factors was not available. This report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing therapy. The applicability issues are addressed in the Discussion section of the report.

			pain, neuropathic pain, or abdominal pain," but this qualifier does not go far enough. Evidence on pharmacologic therapy for *any individual* has little applicability to evidence on pharmacological therapy for *any other individual,* regardless of diagnosis, because responses range so broadly between individuals (whether due to genetic factors, metabolism, or some other reason). Implications for Clinical and Policy Decisionmaking Because AHRQ's work affects everyone, including exceptions and outliers, AHRQ should explicitly caution that their conclusions do not account for wide variations in individual response to treatment, and this evidence review does not support one-size-fits-all policy. Limitations of the Evidence Base Studies involve averaging participants together. A study reports one number for "pain reduction" for an entire group, made up of a wide range of individuals. Within that group it's reasonable to suppose some patients found opioids intolerable, some patients found them helpful, and some (due to genetics or metabolism) found the dosage inadequate. Results from a heterogenous group of people with (for instance) kidney stone pain cannot be generalized to a broader population of	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			individuals with such wide variation in response to treatment. The evidence base does not account for differences in individual response to treatment. The evidence base, as summarized here, tells clinicians and policymakers nothing whatsoever about outliers who might be harmed when such broad average generalizations are written into policy.	

Kristin McGarity / 23	NA	General	The report concludes, “Opioid therapy was associated with decreased or similar effectiveness for pain versus an NSAID for postoperative pain, surgical dental pain, kidney stone pain, and low back pain.” Yet, as the Discussion section explains: “For postoperative pain, dental pain, and kidney stone pain, most comparative effectiveness trials of pharmacologic therapy (opioid or nonopioid) evaluated effects of a single dose on pain at <1 day (usually 8 hours or less) followup.” Results from a single intravenous dose at 8 hours cannot be assumed to represent results for every other situation falling under “acute pain.” As defined by most state laws and regulations, “acute pain” could include any new pain lasting up to 7-10 days, or even longer. A policymaker, seeing the conclusion “[o]pioids were less effective than nonopioid analgesics for some acute pain conditions,” would likely assume this conclusion applies to all patients with these conditions, for up to 7-10 days (or longer), including outpatients. Longer-lasting and recurring acute pain conditions do not respond to treatment the same way as a single time-limited illness or injury. A policy that covers “acute pain” in general does not make this distinction. This generalization is particularly concerning for conditions (such as sickle-	Thank you for the comment. The report is based on the research literature on benefits and harms for different treatments for acute pain. The findings are necessarily based on results in populations of studied patients. As noted in the report, evidence to determine how benefits and harms varied according to patient demographics or clinical factors was not available. No study specifically focused on persons with acute recurrent pain. Issues related to single dose trials are detailed in the Results and Discussion section and findings are separated out from trials of multidose courses of therapy. No study evaluated therapies administered as first line versus second line interventions. This report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing therapy. The applicability issues are addressed in the Discussion section of the report. The Abstract and Conclusions summarize the key findings from the report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			cell disease) that disproportionately affect people of color and people with disabilities. Studies ask the question “are opioids or non-opioids more effective in a single dose,” but that isn’t the question clinicians are faced with in practice. The question isn’t necessarily “I need to give a single dose, should it be opioid or non-opioid?” In current practice, clinicians typically try non-opioids first, then move to opioids if time goes by with little improvement in pain or function. The questions that actually reflect typical practice are left unasked: “If opioids are equal or less effective as first-line therapy, are opioids more effective as a second-line (or later) intervention?” “Do some people find opioids more effective, and do other people find nonopioid analgesics more effective? Why?” It is the Structured Abstract and Conclusions sections that will influence federal and state policy. If limitations and applicability issues are missing, or mentioned but left out of the Conclusions section, harmful policy will be the predictable result.	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Kristin McGarity / 23	NA	Description of the problem and evidence	yes	Noted.
Kristin McGarity / 23	NA	Difficult to read	no	Noted.
Kristin McGarity / 23	NA	Understand results and conclusions	Yes, although AHRQ's stated conclusions do not necessarily follow from the results.	Thank you for the comment. The report is based on the research literature on benefits and harms for different treatments for acute pain. The findings are necessarily based on results in populations of studied patients. As noted in the report, evidence to determine how benefits and harms varied according to patient demographics or clinical factors was not available. This report does not make recommendations. Clinicians should consider potential benefits and harms when individualizing therapy.

Angie Stengel / 24	American Society of Regional Anasthesia and Pain Medicine (ASRA)	Evidence Summary	Comments from letter: General comments on the draft reports ASRA appreciates AHRQ's evaluation of the effectiveness and comparative effectiveness of opioid, nonopioid, pharmacologic, and nonpharmacologic therapy for treatment of acute pain, which we recognize reflects a significant effort on the part of AHRQ's expert panel, reviewers, and staff. ASRA offers the following comments for consideration as AHRQ finalizes its review. Acute Neck Pain with Radiculopathy. The report notes that both cervical collars and exercise might be effective for acute cervical radiculopathy. In response to this finding, we note the following: • Guidelines for chronic back pain almost universally recommend against bed rest, as do most guidelines for acute back pain. Although the etiologies for acute neck pain are not the same as low back pain, there is considerable overlap. • Exercise, by its very nature, involves increased activity, while cervical collars result in immobilization and decreased activity. Therefore, these recommendations are, in many respects, contradictory. • The evidence for cervical collars is based on limited evidence. • Treatments should be geared towards etiologies (similar to mechanism-based treatment) if possible, rather than symptoms (i.e. neck pain).	The limitations (low level of evidence) regarding cervical collars is noted in the Results. Findings regarding acetaminophen versus opioids for renal colic are based on a large, good-quality trial, and met criteria for moderate level of evidence. Trials of gabapentin versus opioids were not designed to address respiratory depression or associated harms (e.g., overdose). Harms of opioids are well-described in the report.

			Based on the above, we therefore recommend that the report more clearly specify which scenarios (if any) might benefit from the application of a cervical collar. Renal colic. The authors assert that opioids, which have been the reference standard for severe acute pain for centuries, are probably less effective than acetaminophen for renal colic, one of the most painful conditions known. In response to this finding, we note the following: • The effectiveness of acetaminophen as an analgesic is modest at best, with systematic reviews finding no evidence of efficacy for low back pain and osteoarthritis. • There is no pathophysiological basis for acetaminophen to be more effective than opioids for renal colic when opioids are widely acknowledged to be more effective than acetaminophen for other acute pain conditions. • Acetaminophen is not a risk-free drug. In addition to its known liver toxicity, a recent highly publicized study found it increases risk-taking behaviors. • Delays in treatment for severe acute pain may lead to long-term sequelae that include psychological consequences and persistent pain. Based on the above, we recommend that this statement be further tempered to reflect that the finding is based on a single study, and that there is a lack of extensive	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			research to address whether acetaminophen or opioids are more effective for renal colic. Acute neuropathic pain. The report states that an opioid might be more effective than gabapentin for acute neuropathic pain. Based purely on number needed to treat from a meta-analysis, this statement is true. However, we recommend that this statement be qualified to note that the risk of addiction is lower with gabapentin and pregabalin compared to opioids and that the risk of respiratory depression from these drugs alone is lower than that of opioids.	
William Shaffer / 25	American Association of Orthopaedic Surgeons	Evidence Summary	The conclusion that opioids were less effective than nonopioid analgesics for some acute pain conditions and were associated with increased risk of short-term adverse events' is critical to inform pain alleviation care and policy moving forward. The AAOS supports ongoing research in specific areas of post-operative pain, acute neuropathic pain, neck pain, and non-pharmacologic therapies. Furthermore, the AAOS strongly supports the optimization of multi-modal pain management strategies to effectively alleviate pain postoperatively.	Thank you for your comment.
William Shaffer / 25	American Association of Orthopaedic Surgeons	Document	See attached document.	Thank you for your comment.

Ashley Walton / 26	American Society of Anesthesiologists	Evidence Summary	The statement: An opioid might be more effective than gabapentin for acute neuropathic pain. Based purely on number needed to treat from a meta-analysis (Finnerup NB, et al. Lancet Neurol 2015; 14: 162-173), this statement is true. However, ASA would argue that it should be qualified by stating that the risk of addiction is lower with gabapentin and pregabalin compared to opioids and that the risk of respiratory depression from these drugs alone is lower than that of opioids. Therefore, in some situations the risk-benefit ratio may favor gabapentinoids over opioids for acute neuropathic pain. The statement: Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions (postoperative pain, surgical dental pain, and kidney stones) and might be similarly effective to NSAIDs for low back pain. As written, the statement is overly broad. It groups an extremely diverse group of medications (NSAIDS), as well as a diverse group of acute medical conditions with one overarching conclusion. While there are certain mechanistic similarities between the various NSAIDS, the specific clinical effects, toxicities, contraindications and other properties of the drugs preclude their being considered as a single class when dealing with diverse indications. Moreover, each of the acute pain	Thank you for your comment. The findings on gabapentin are based on the research literature that met inclusion criteria. Respiratory depression and other associated outcomes (e.g., overdose) were not addressed in the published studies. Potential harms of opioids are described in the Background section. We revised the Discussion to more clearly indicate that there are potential differences within classes of medications and acute pain conditions (including postoperative pain) that could impact assessments of benefits and harms. The report does not address multimodal therapies and in many cases treatments were not administered as part of multimodal therapy. Therefore, we did not use the suggested language.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			conditions mentioned in the statement has a distinct set of contributing physiological factors. Surgical pain, for example, has a set of inflammatory mediators and neurobiological processes distinct from those of acute low back pain and other acutely painful injuries. As written, this statement will be misinterpreted in any widely circulated guideline or document. ASA suggests alternate wording for this statement within the evidence summary: NSAIDS may be similarly effective to opioids when used in multimodal analgesic strategies for some types of postoperative pain. This statement, we believe, highlights accurately the possibility that opioids can be avoided at least in part after some surgeries. It also avoids discouraging the use of opioids in the setting of serious or unrelieved pain and introduces the notion that postoperative analgesia is not a matter of a simple choice of prescribing either an opioid or an NSAID when there are a range of options.	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Ashley Walton / 26	American Society of Anesthesiologists	Discussion	Specific to the inclusion of postoperative pain, the evidence cited in the body of the report is wholly inadequate to comment all-inclusively on the comparative effects of NSAIDS and opioids for postoperative pain for the diverse range of surgical procedures performed. Tens of millions of surgical procedures are performed each year with recovery periods ranging from hours with little need for strong analgesia, e.g. cataract surgery, to months with extensive painful rehabilitation requirements, e.g. spine surgery. The differences in analgesic types, doses and durations of treatment are highly specific to the situation. An NSAID may in fact be adequate for pain after a minor procedure where other modes of analgesia, e.g. nerve blocks and icepacks are available. The state of the art is in optimizing "multimodal" therapy in which the best combination of analgesic techniques is tailored to the surgery and individual.	We revised the Discussion to clarify that postoperative pain is a heterogeneous condition and that benefits and harms could vary based on severity of pain and other factors. The report does not address multimodal therapies and in many cases treatments were not administered as part of multimodal therapy.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Ashley Walton / 26	American Society of Anesthesiologists	References	The literature cited is deficient in scope and quality with respect to the NSAIDS and opioids included in the studies. Despite the inclusion of more than 150 publications in the review, only 4 were listed as pertinent to the postoperative NSAID versus opioid question. Of those, two used tramadol, a relatively weakly effective agent, i.e. a "weak opioid." Furthermore, both tramadol studies used sub-maximal doses of the drug, and no attempt was made to adjust for well-described genetic factors strongly influencing tramadol's effects. The comparator NSAID celecoxib was used at a dose 50% above its current maximal recommended dose in one of the selected studies. Importantly, opioids whether weak or strong were given in all studies at a single dose and in 3 of 4 studies at a dosing interval greater than recommended and commonly used. Issues related to choice of outcome tools and corporate sponsorship further complicate interpretation of the data. A key property of opioids as a class is that unlike NSAIDS, they lack an analgesic ceiling effect when used for acute pain, and opioid dose was not examined in any study cited. Thus, while side effects may at some point limit opioid doses, the relatively low doses used in the few studies cited do not allow a comparison of potential analgesic effects.	Opioid doses were converted to mg morphine equivalents using published conversion ratios to provide information about relative potency; the mg morphine equivalents are reported in the Results and Evidence Tables. There was insufficient evidence to determine how relative benefits and harms of opioids versus other medications varied according to opioid dose, NSAID type, or NSAID dose. However, research has generally not shown differential effects of equivalent doses of different NSAIDs, on average.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Ashley Walton / 26	American Society of Anesthesiologists	Understand results and conclusions	The conclusions of the manuscripts did not include the claim that the NSAIDS under study were superior to the opioids used as comparators. It is critical to emphasize that the thrust of the summary statement, "Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions…" as it pertains to postoperative pain was not the conclusion of the authors of the cited papers. For the authors of the review to extend the conclusions to rank NSAID effects above opioid effects is inappropriate and should be stricken from the conclusions of the review document.	The findings are based on all of the available evidence, not individual studies (or interpretation of findings from individual studies). The results for opioids versus NSAIDs for postoperative pain are based on the body of literature on opioids versus NSAIDs. Because the evidence was somewhat mixed (opioids associated with increased likelihood of rescue medication use, but inconsistent effects on pain intensity) we removed the conclusion that opioids are less effective than NSAIDs for postoperative pain. We revised the Discussion to clarify that findings are applicable to the surgical procedures evaluated in the trials and could differ for other procedures. As noted in the Methods, the focus was on management of postoperative pain at or near the time of discharge.

Andrey Ostrovsky / 27	AppliedVR	General	Thank you for the opportunity to submit comment from AppliedVR. Please see the attached document for detailed comments. The following citations were suggested for review: 1) Spiegel B, Fuller G, Lopez M, et al. Virtual reality for management of pain in hospitalized patients: A randomized comparative effectiveness trial. PLoS ONE. 2019;14(8): e0219115. Accessible at https://doi.org/10.1371/journal.pone.0219115 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0219115 2) Tashjian VC, Mosadeghi S, Howard AR, et al. Virtual Reality for Management of Pain in Hospitalized Patients: Results of a Controlled Trial. JMIR Ment Health. 2017;4(1):e9. doi: 10.2196/mental.7387. Accessible at https://pubmed.ncbi.nlm.nih.gov/28356241/ 3) Gold JI, Mahrer NE. Is Virtual Reality Ready for Prime Time in the Medical Space? A Randomized Control Trial of Pediatric Virtual Reality for Acute Procedural Pain Management. J Pediatr Psychol. 2018;43(3):266-275. doi:10.1093/jpepsy/jsx129. Accessible at	Thank you for the comment. We reviewed the suggested citations. They did not meet inclusion criteria because they focused on hospitalized patients, pediatric patients, conditions not addressed in the review (labor pain), or were not randomized trials.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			https://pubmed.ncbi.nlm.nih.gov/29053848/ 4) Mosadeghi S, Reid MW, Martinez B, et al. Feasibility of an Immersive Virtual Reality Intervention for Hospitalized Patients: An Observational Cohort Study. JMIR Ment Health. 2016;3(2):e28. doi:10.2196/mental.5801. Accessible at https://pubmed.ncbi.nlm.nih.gov/27349654/ 5) Wong M, Spiegel BM, Gregory KD. Virtual Reality reduces pain in laboring women: a randomized controlled trial. American Journal of Obstetrics and Gynecology. 2020; 222(1). Page S34. Accessible at https://www.sciencedirect.com/science/article/pii/S0002937819314255	

Janelle Derbis / 28	Food and Drug Administration	General	1. The report lumps acute pain conditions together in a way that may be potentially problematic (why radicular with non-radicular pain, why surgical with non-surgical dental pain—these pathologies are completely different)? All of post-surgical pain is lumped in one category together. Additional information on results by each type of post-surgical procedure would be helpful since there is a lot of variation in post-surgical procedures. Statements such as "Opioid therapy was probably less effective than nonsteroidal anti- inflammatory drugs (NSAIDs) for postoperative pain" (pg 5) and the first point in Main Points section (pg ES1) are extremely broad and potentially misleading. 2. The report states a focus on “outpatient” management, but also include ER or pre-discharge analgesia, and creates a separate exception for sickle cell disease. We know this space is messy but the inclusion of SCD feels forced. Regardless, the setting the report intends to focus on does not appear to be cleanly captured. 3. Trying to “standardize” pain scales across studies (in order to somehow combine results) by converting to a 0-10 format is an approach they use, but do not reference. Perhaps this is standard or so well-established they feel like they don’t need to reference this. 4. There are some editorial changes to make (e.g., page numbers in Table of Contents, spelling out abbreviations vs using abbreviations should be more consistent)	1) The acute pain conditions were selected with input from a Technical Expert Panel (TEP) and organized according to the TEP input. The conditions were generally grouped clinically, taking into consideration who is managing the patient (e.g., dental providers manage both surgical and nonsurgical dental pain). 2) Although the focus was on outpatient management, as explained in the Methods, we expanded to ED and post-operative care units for sickle cell in order to capture potentially relevant literature. 3) Standardization of pain scores (to a 0 to 10 scale) is a generally accepted method and provides more consistency for users of the report to interpret findings. 4) We reviewed page numbers in the Table of Contents and reviewed abbreviations to ensure they were spelled out initially. Page numbers often do not align with the number of a PDF document due to the Front Matter and Preface. 5) As described in the Methods, we restricted inclusion to RCTs for evaluation of benefits and harms and included observational studies to evaluate the association between opioid use for acute pain and long-term use and predictors of opioid use.

			5. There seem to be very few observational studies included (7 studies). Consider more clearly stating that only RCTs were considered for some key questions and including a description of some of the main reasons for excluding observational studies for the key questions for which they were eligible. 6.Overall, the review could benefit from more discussion about how trials handled prior opioid use as this was only mentioned on pages 116 and 119. This could be mentioned more prominently throughout the other sections of the review and as a limitation since it sounds like many studies didn't report this. Also, please consider how this important limitation and the lack of information on substance use disorders might affect conclusions such as: (pg 117) "The findings of our review that opioids are not superior to NSAIDs for some commonly encountered acute pain conditions, and in some cases may be inferior, may provide indirect evidence that such policies may not adversely affect outcomes among patients with those conditions, provided that NSAIDs or other effective alternatives are utilized" 7. There is mention that the few studies that looked at long-term opioid use were based on claims data on dispensing (pg 119). This is quite limited and provides no information on opioid use outside of medical supervision. It might be helpful to more clearly highlight this as an additional limitation.	6) The lack of evidence on patients previously treated with opioids is described in the Discussion. This was reported in very few studies and we do not think it makes sense to add this information in the Results to every section on opioids. 7) We revised the Limitations section of the Discussion to note that long-term opioid use studies were based on dispensing data. 8) Thank you for the suggestions. None of the studies meet inclusion criteria because they evaluate the effects of opioid policies (e.g., state legislation), which were beyond the scope of the report.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			8. Overall there seems to be a lack of information found on the effect of interventions on opioid prescribing (sub-question h). There are a number of studies that describe the effect of an opioid prescribing intervention on prescribing rates (For example, for post-surgical outpatient opioid prescribing: Aulet et al (JAMA Facial Plastic Surgery 2019; 21 (6):487-490); Potnuru et al (Surgery. 2019; 166 (3): 375-379); MacLean (Pain Med. 2019 (epub 2018); 20 (6): 1212-1218); Zipple (J Am Coll Surg. 2019; 229 (2): 158-163). Assuming these and other studies were excluded based on review methods, it might be helpful to mention there are studies that address this question that did not meet inclusion criteria.	
Janelle Derbis / 28	Food and Drug Administration	Document	see attached document	We responded to suggested edits and comments embedded in the report. We clarified limitations of observational studies on the association between opioid use versus non-use for acute pain and long-term use and the need for research in persons previously prescribed opioids. We checked the report for spelling errors, and corrected them as needed.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Jacob Marzalik / 29	American Psychological Association	Document	Please see the attached document for comments.	Thank you for your comments. The suggested citation focuses on psychological therapies for chronic pain, which was not addressed in this report.
Sharon Grider / 30	Retired Veterans Administration	Evidence Summary	I totally disagree with your summary of evidence. Opiates are very safe and effective after surgery for low back pain. I should know I have been taking them for over 20 years off and on. After my first surgery I took him for three weeks as prescribed and I did not become addicted. Your research is incorrect unfortunately on addiction. Medicine taken for pain very rarely causes addiction. There actually studies on the subject if you research it from 1990.	Thank you for sharing your story. We are sorry to hear about your you pain. This report focuses on benefits and harms of treatment for acute pain. You appear to have chronic pain, which is not addressed in this report.
Sharon Grider / 30	Retired Veterans Administration	Introduction	I think the comment section in the introduction are is already predisposed to be against opioid therapy. This whole report is designed for alternative sources. But we must recognize the opiate problem is not from prescriptions. It is illegal drugs that are causing our problem and lack of education of our citizens. Educate is the only way.	Thank you for your comments. The background section discusses epidemiological data on opioid prescribing, opioid mortality, and opioid use disorder, which all rose rapidly over an approximate 10 year period from 2000 to 2010.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Sharon Grider / 30	Retired Veterans Administration	Methods	I totally disagree. I believe your opinions are predisposed to be against opiate pain relief. I also know that every patient is different and all medicines work differently on each individual. The physician and the patient should be the one that desires on the medications that they should take for pain. Everything has risk and that should be outlined to the patient as well. Making patients suffer or doctors be liable because I can't effectively treat patients needs to be corrected.	Thank you for your comments. This report is based on research evidence on the benefits and harms of treatment for acute pain. Studies were selected using pre-specified inclusion criteria. Clinicians should consider potential benefits and harms in individual patients when selecting treatment.
Sharon Grider / 30	Retired Veterans Administration	Results	I think the study was limited in the results. It seems to study it was written to be anti-opiate. More research needs to be done because opiates are very Effective pain medication. Pass a kidney stone and take an ibuprofen versus an opiate and I beg to differ which one works better it's the opiate.	Thank you for your comments. This report, including findings on medications for kidney stone pain, is based on research evidence on the benefits and harms of treatment for acute pain.
Sharon Grider / 30	Retired Veterans Administration	Discussion	The results were insufficient. Again I think this study is predisposed to be anti-Opiates.	Thank you for your comments. This report is based on research evidence on the benefits and harms of treatment for acute pain. Studies were selected using pre-specified inclusion criteria.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Sharon Grider / 30	Retired Veterans Administration	References	The results were Insufficient. There are many sufficient records with the pharmaceutical companies stating how effective Opiate pain medications work. Especially studies versus Tylenol or NSAIDS	Thank you for your comments. This report is based on research evidence on the benefits and harms of treatment for acute pain, including research studies on opioids versus acetaminophen or NSAIDs. Studies were selected using pre-specified inclusion criteria. Clinicians should consider potential benefits and harms when individualizing therapy.
Sharon Grider / 30	Retired Veterans Administration	Abbreviations and Acronyms	They were acceptable	Thank you for your comment.
Sharon Grider / 30	Retired Veterans Administration	Appendices	I found the appendix to support their conclusions which was biased in my opinion. There are so many contrary opinions on this very subject. Very biased report in my opinion.	Thank you for your comments. This report, including findings on medications for kidney stone pain, is based on research evidence on the benefits and harms of treatment for acute pain.
Sharon Grider / 30	Retired Veterans Administration	General	I think the report should be made it more of patients that are effectively treated with opiate pain medicine for years. There are many patients they can tell you what really works. They've taken all these medications and they know exactly what works.	Thank you for your comment. The report addresses treatment for acute pain. Chronic pain is not addressed in the report.
Sharon Grider / 30	Retired Veterans Administration	Description of the problem and evidence	I understood the report. It seem to be biased though in my opinion.	Thank you for your comments. This report is based on research evidence on the benefits and harms of treatment for acute pain. Studies were selected using pre-specified inclusion criteria.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Sharon Grider / 30	Retired Veterans Administration	Difficult to read	No	Noted.
Sharon Grider / 30	Retired Veterans Administration	Understand results and conclusions	I understood the conclusion but totally disagreed with it. If you wish to have my number please Email me and I will respond with my number.	Thank you for your comment.

Evan Kharasch / 31	NA	General	Serious acute pain is an immense problem affecting the lives of millions of Americans each year. The causes of this problem are diverse and include injuries, e.g. motor vehicle accidents and surgeries, physiological problems, e.g. gallstones and renal calculi and neurological problems, e.g. episodic migraine headaches and acute neuropathic pain. The size and scope of the problem suggest the treatments employed must be carefully tailored to the specific condition, circumstances and individual patient. We are also highly cognizant of the devastating opioid crisis responsible for the loss of hundreds of thousands of lives and the relationship of this crisis to injudicious approaches to pain management. In this regard we congratulate AHRQ on commissioning the work entitled, "Treatments for Acute Pain: A Systematic Review" now made available for comment. The comments of this letter are focused on the first listed Main Point found in the Evidence Summary section (ES-1) of the manuscript: "Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions (postoperative pain, surgical dental pain, and kidney stones) and might be similarly effective to NSAIDs for low back pain." We believe the statement as written is overly broad, inaccurate and detrimental to timely, effective medical treatment of pain after surgery.	We revised the Discussion to more clearly indicate that there are potential differences within classes of medications and acute pain conditions (including postoperative pain) that could impact assessments of benefits and harms. However, research on NSAIDs have generally not showed differential benefits on average. We revised the Discussion to clarify that postoperative pain is a heterogeneous condition and that benefits and harms could vary based on severity of pain and other factors. Opioid doses were converted to mg morphine equivalents using published conversion ratios to provide information about relative potency; the mg morphine equivalents are reported in the Results and Evidence Tables. There was insufficient evidence to determine how relative benefits and harms of opioids versus other medications varied according to opioid dose, NSAID type, or NSAID dose. The findings are based on all of the available evidence, not individual studies (or interpretation of findings from individual studies). The results for

			The principal reasons for the revision are as follows: 1. The statement inappropriately attempts to combine conclusions regarding the use of an extremely diverse group of medications (NSAIDS) on an even more diverse group of acute medical conditions. While there are certain mechanistic similarities between the various NSAIDS, the specific clinical effects, toxicities, contraindications and other properties of the drugs preclude their being considered as a single class when dealing with diverse indications. Moreover, each of the acute pain conditions mentioned in the statement has a distinct set of contributing physiological factors. Surgical pain, for example, has a set of inflammatory mediators and neurobiological processes distinct from those of acute low back pain and other acutely painful injuries. Please consider that no widely promulgated set of pain management guidelines attempts to lump together such a diverse group of drugs and pain types under a single rule. 2. Specific to the inclusion of postoperative pain, the evidence cited in the body of the report is wholly inadequate to comment all-inclusively on the comparative effects of NSAIDS and opioids for postoperative pain for the diverse range of surgical procedures performed. Tens of millions of surgical procedures are performed each year with recovery periods ranging from hours with little need for strong analgesia, e.g. cataract surgery, to months with extensive painful rehabilitation requirements, e.g. spine surgery. The	opioids versus NSAIDs for postoperative pain are based on the body of literature on opioids versus NSAIDs. Because effects of opioids versus NSAIDs were somewhat mixed (increased rescue analgesic use but inconsistent effects on pain intensity) we removed postoperative pain as a condition for which opioids were less effective than NSAIDs. We revised the Discussion to clarify that findings are applicable to the surgical procedures evaluated in the trials and could differ for other procedures. As noted in the Methods, the focus was on management of postoperative pain at or near the time of discharge.

			differences in analgesic types, doses and durations of treatment are highly specific to the situation. An NSAID may in fact be adequate for pain after a minor procedure where other modes of analgesia, e.g. nerve blocks and icepacks are available. Absolutely no evidence would support the conclusion that an NSAID by itself provides adequate analgesia after joint replacement surgery or highly invasive procedures. Note – even highly invasive procedures are now being done on an outpatient basis, the apparent target of the statement in question. The state of the art is in optimizing "multimodal" therapy in which the best combination of analgesic techniques is tailored to the surgery and individual; we seldom now face a decision of prescribing an NSAID versus an opioid exclusively. 3. The literature cited is further deficient in attributes of its scope and quality with respect to the NSAIDS and opioids included in the studies. Despite the inclusion of more than 150 publications in the review, only 4 were listed as pertinent to the postoperative NSAID versus opioid question. Of those, two used tramadol, a relatively weakly effective agent, i.e. a "weak opioid." Worse, both tramadol studies used well sub-maximal doses of the drug, and no attempt was made to adjust for well-described genetic factors strongly influencing tramadol's effects. The comparator NSAID celecoxib was used at a dose 50% above its current maximal recommended dose in one of the selected studies. Importantly, opioids whether weak	

			or strong were given in all studies at a single dose and in 3 of 4 studies at a dosing interval greater than recommended and commonly used. Issues related to choice of outcome tools and corporate sponsorship further complicate interpretation of the data. A key property of opioids as a class is that unlike NSAIDS they lack an analgesic ceiling effect when used for acute pain, and opioid dose was not examined in any study cited. Thus, while side effects may at some point limit opioid doses, the relatively low doses used in the few studies cited do not allow a comparison of potential analgesic effects. 4. The conclusions of the manuscripts did not include the claim that the NSAIDS under study were superior to the opioids used as comparators. It is critical to emphasize that the thrust of the summary statement, “Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for several acute pain conditions…” as it pertains to postoperative pain was not the conclusion of the authors of the cited papers. For the authors of the review to extend the conclusions to rank NSAID effects above opioid effects is inappropriate and should be stricken from the conclusions of the review document. While it is clear primacy of NSAIDS over opioids for acute postsurgical pain should not be included in the Evidence Summary section, we would like to suggest an alternative statement crafted to address the existing data such as it is in the context of acute postoperative pain management	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			as it is currently practiced. That statement is: "NSAIDS may be similarly effective to opioids when used in multimodal analgesic strategies for some types of postoperative pain. For moderate to severe postoperative pain, opioids may be needed for effective analgesia, and should be used in conjunction with NSAIDS." This statement, we believe, highlights accurately the possibility that opioids can be avoided at least in part after some surgeries. It also avoids discouraging the use of opioids in the setting of serious or unrelieved pain. Most importantly, it introduces the notion that postoperative analgesia is not a matter of a simple choice of prescribing either an opioid or an NSAID to a patient when a range of options appropriate to the surgery and specific patient exist. Thank you for considering our comments on the critical need for clarification of the conclusions resulting from this landmark review.	
Evan Kharasch / 31	NA	Document	See document.	See response to above comments from this commenter.
Anonymous / 32	NA	Document	I think this was written by people who have never been in pain.	Thank you for the comment.

Brian Rabinovitz / 33	NA	Evidence Summary	Reading over the report I have serious concerns that the construction of the report was designed to reach a specific conclusion. I am concerned that you had a goal of stating that opioids were less beneficial than other options and that this is part of a motivation to generally reduce availability of opioids because of general concerns regarding addiction. For example, in the conclusion of the abstract you state "Opioids were less effective than nonopioid analgesics for some acute pain conditions." This indicates that in fact opioids were not less effective for some other pain conditions and yet you refrain from stating this. In doing so you are framing the issue against the value of opioids. I have strong concerns that this framing will negative impact chronic pain patients who rely on opioid therapy. As someone who has taught psychopharmacology classes, I am familiar with the mechanisms of action of both opioids and NSAIDs and recognize that activation of opioid receptors allows for stronger pain reduction than NSAIDs. I saw that no study you evaluated examined the effectiveness of opioids for chronic pain conditions like complex regional pain syndrome. This is important because publications such as this one may be used to justify removal of opioid options for people suffering from chronic pain (even if that is not your original intent) and there may be no other option that is as effective. I noticed that in the section on peripheral neuropathic pain you found that opioids	The conclusions highlight key findings. In addition to conditions and comparison for which opioids were less effective than other medications, we also highlighted situations for which opioids were more effective (e.g., opioids were more effective than acetaminophen for acute dental pain). To focus on key findings, we did not highlight all findings related to opioids with insufficient evidence or that found opioids similarly effective compared with other medications. However, these are detailed in the report. Chronic pain is not addressed in this report. The literature did not permit stratifying studies on benefits and harms for postoperative pain by the severity of postoperative pain. We revised the Discussion to note this as a limitation of the evidence.

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
			provided superior pain relief compared to gabapentin, and yet an observation like this is conveniently absent from the general summary section. Even in your evaluations of the efficacy I see flaws. For example, in the section on postoperative pain you have not been able to divide the studies between more and less intense levels of postoperative pain and that might be a significant factor in the efficacy of opioids versus other therapies. Thus, I worry that the way you have presented your meta-analysis may be used to unjustly remove opioids as an option for individuals who genuinely have no other option that is as effective.	

Brian Rabinovitz / 33	NA	General	Reading over the report I have serious concerns that the construction of the report was designed to reach a specific conclusion. I am concerned that you had a goal of stating that opioids were less beneficial than other options and that this is part of a motivation to generally reduce availability of opioids because of general concerns regarding addiction. For example, in the conclusion of the abstract you state "Opioids were less effective than nonopioid analgesics for some acute pain conditions." This indicates that in fact opioids were not less effective for some other pain conditions and yet you refrain from stating this. In doing so you are framing the issue against the value of opioids. I have strong concerns that this framing will negative impact chronic pain patients who rely on opioid therapy. As someone who has taught psychopharmacology classes, I am familiar with the mechanisms of action of both opioids and NSAIDs and recognize that activation of opioid receptors allows for stronger pain reduction than NSAIDs. I saw that no study you evaluated examined the effectiveness of opioids for chronic pain conditions like complex regional pain syndrome. This is important because publications such as this one may be used to justify removal of opioid options for people suffering from chronic pain (even if that is not your original intent) and there may be no other option that is as effective. I noticed that in the section on peripheral neuropathic pain you found that opioids	The conclusions highlight key findings. In addition to conditions and comparison for which opioids were less effective than other medications, we also highlighted situations for which opioids were more effective (e.g., opioids were more effective than acetaminophen for acute dental pain). To focus on key findings, we did not highlight all findings related to opioids with insufficient evidence or that found opioids similarly effective compared with other medications. However, these are detailed in the report. Chronic pain is not addressed in this report. The literature did not permit stratifying studies on benefits and harms for postoperative pain by the severity of postoperative pain. We revised the Discussion to note this as a limitation of the evidence.

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			provided superior pain relief compared to gabapentin, and yet an observation like this is conveniently absent from the general summary section. Even in your evaluations of the efficacy I see flaws. For example, in the section on postoperative pain you have not been able to divide the studies between more and less intense levels of postoperative pain and that might be a significant factor in the efficacy of opioids versus other therapies. Thus, I worry that the way you have presented your meta-analysis may be used to unjustly remove opioids as an option for individuals who genuinely have no other option that is as effective.	

Kristen Aquino / 34	Kristen Aquino / 34	Document	See document. This is an admirable effort from Agency for Healthcare Research and Quality to perform a systemic and comprehensive review of the current literatures on the treatments for acute pain and the authors should be congratulated for the achievements. However, there are several limitations that should be discussed in the systemic review. First of all, pain is a very complex phenomenon of the nervous system. For example, multiple different complex etiologies could present as low back pain and each different etiology might demand different treatment. Low back pain could be caused from spinal arthritis, paraspinal muscular and ligament strain, spinal nerve roots compression from either spinal stenosis or disc herniation, spinal mechanical instability, spinal deformity, sacroiliac joint pain, spinal tumor, trauma or infection. The optimal pain treatment for different etiologies is likely to be different. Secondly, the definition of acute pain, especially acute pain related to low back pain and neck pain, is relatively vague. Is it only limited to acute new low back or neck pain, or does it also include the acute exacerbation of intermittent or chronic low back pain or neck pain? Does chronic low back pain or neck pain excluded in the literature review? Do all the reviewed abstracts that are included in the systemic review exclude the chronic low back pain or neck pain patients?	The report included acute back or neck pain; although it would have included studies on acute exacerbations of chronic pain no such studies met inclusion criteria. Chronic pain was excluded, as described in the methods. Gabapentin, pregabalin, and duloxetine were included interventions. However, these medications are not usually used for acute pain, with the possible exception of gabapentin or pregabalin for acute neuropathic pain. Reporting bias is a possibility; however, we were unable to formally assess for reporting bias using statistical or graphical methods due to small numbers of studies and heterogeneity in populations, interventions, outcomes, and methods. This is discussed in the Limitations of the Review Process section

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			In addition, one noticeable omit of the systemic review is the lack of an important category of pain medication, such as gabapentin, pregabalin or duloxetine is comparison to either narcotic pain medications or other pain treatment options. Neuropathic pain medications such as gabapentin has been gaining popularity in recent years in treating low back pain or neck pain, in an attempt to minimize the use of narcotic pain medications. It would be important to know whether these medications have similar effects in controlling acute back or neck pain compared to other pain treatment options. Lastly, a clear potential limitation of the systemic review is the reporting bias. Generally only positive results are published. Especially in the study with pain, the authors usually had the interests in proving the effectiveness of non-pharmacological treatments or non-narcotic pain medications compared to pharmacological treatments or narcotic pain meds. Therefore, the sum of the published results would likely be biased as a result.	

Public Commenter Name / Number	Organization	Report section	Comment	EPC Response
Ruth Koznecki / 35	NA	Document	I tried NSAIDS, they did nothing for my pain (no relief at all), massages relief for 20 minutes pain comes right back, steriods no relief at all and suffered severe side effects that last for 6 months. Physical therapy caused more pain no matter how long I did physical therapy. I found that prescription opioids gave me my life back I do not have to live in bed. Now I am being forced to taper and know that eventually I will be back to not living. I will be sentenced to living in bed. I know this because I was forced to taper before and I ended up in so much pain that I was bedridden again until I found a doctor to help me and up my prescription medications now he has to force me to taper because I am to high according to the "government." I am pleading with you please help the chronic pain patients get our lives back.	Thank you for sharing your story. We are sorry to hear about your pain. This report focuses on benefits and harms of treatment for acute pain. You appear to have chronic pain, which is not addressed in this report.
Anonymous / 36	NA	Document	The CPC folks with incurable painful disabilities are being severely victimized and harmed ! CP with its severity left untreated is deadly ! We need attention brought to this pain pandemic that's been killing us long before the covid virus hit. It's shameful, ignorant and it Needs to Be Stopped! Painful disabilities deserves respect, and most of all they deserve proper medications that actually work , to sustain our lives! Pushing for harmful drugs that haven't worked to reduce incurable suffering is unacceptable.. .	Thank you for sharing your story. We are sorry to hear about your pain. This report focuses on benefits and harms of treatment for acute pain. You appear to have chronic pain, which is not addressed in this report.