Meeting Minutes

HB 21-1317 Sixth Meeting of the Scientific Review Council

June 15, 2022; 12:30 pm - 2:30 pm MT

General Remarks and Welcome

- Dr. Chris Urbina, Chair of the Scientific Review Council (SRC), called to order the sixth meeting of the SRC on June 15, 2022, at 12:30 pm MT.

Scientific Review Council Introductions and Update on Conflicts of Interest

- The Chair conducted a roll call for both the Council and the Colorado School of Public Health project team members.
- The following Council members were present and introduced:
    - Chris Urbina
    - Greg Kinney
    - Archana Shrestha
    - David Brumbaugh
    - Erica Wymore arrived 20 minutes late with advanced notice and apologies.
    - Kennon Heard
    - Paula Riggs
    - Susan Calcaterra
    - Kent Hutchison arrived 75 minutes late with advanced notice and apologies.
- The following Council members were absent:
    - Lesley Brooks, with advanced notice and apologies
    - Joseph Schacht, with advanced notice and apologies
- The following SPH team members were present and introduced:
    - Jonathan Samet arrived 30 minutes late with advanced notice and apologies
    - Greg Tung, leaving early with advanced notice and apologies
    - Tianjing Li
    - Rosa Lawrence
    - Neeloo Soleimanpour
    - Louis Leslie
    - Thaistsara Rittiphairoj
    - Sam Wang
    - Meghan Buran
    - Bobbi Ortega
- The following SPH team members were absent:
    - Ashley Brooks-Russell
    - Lisa Bero
    - Jean-Pierre Oberste
    - Christi Piper, with advanced notice and apologies
- Changes to COI forms for any Council members
    - None
- No questions for Chair Chris Urbina.

Review of Agenda, Meeting Minutes, and Response to SRC Recommendations

- Chair Chris Urbina reminded everyone in attendance that meeting minutes and the response to SRC recommendations are available on the project website under the resources tab.
- Review of agenda with Council
    - Agenda shown on screen for the panelists (Council and Colorado SPH) as well as public attendees.

No questions for Chair Chris Urbina.

Progress Update from the Cannabis Research & Policy Project

- Dr. Tianjing Li presented on the progress to date of the scoping review.
- Dr Tianjing Li presented on the progress of the data extraction process where the initial literature search resulted in 46,000 titles and abstracts reduced through screening to 489 observational studies and randomized control trials in addition to 264 systematic review case reports/case series for data extraction. For the 489, all study characteristics have now been extracted. Currently, we have finished extraction of the study characteristics from 145 of 489 articles collected by our student workers assisting with the study. 75 articles have been verified by one of the methodologists on the team, primarily looking for concentrations in association with health outcomes. A full verification for all 489 studies will occur with regard to the exposure, outcomes, and associations.

Questions and Answers

- Chair Chris Urbina asked if this verification process will continue for all 489 studies.
    - Dr Tianjing Li confirmed this process will continue for all studies reviewed by the student and methodologist team and will need at least a couple more weeks to get this accomplished to ensure we are reporting accurate information on exposure, outcomes, and association.

No further questions for Dr. Tianjing Li.

SRC Discussion of General Plans and Overview of the Draft Report

- Dr. Jonathan Samet provided a review of the Draft Report for the Legislature developed by the Cannabis Research and Policy Team. Reviewed the outline and discussed the relatively finished sections.
- Dr. Jonathan Samet requested feedback on the: discussion about the terminology of using potency vs concentration seeking firm guidance. He acknowledged that HB 1317 has potency in it's name. However, from a pharmacologic perspective potency refers to the pharmacological properties of an agent and does not refer to concentration or the amount/dose.
    - As an example, Dr. Greg Kinney previously made the comment that fentanyl is more potent than a variety of opioids in its pharmacological action.
- For context, Dr. Jonathan Samet presented Figure 1a and 1b from the draft report and how it is used in the framework of exposure, dose, and risk in relation to the outcome whether adverse and/or beneficial. Dr. Jonathan Samet notes that the figures are useful for how we frame the

discussion and the language we use. Dr. Jonathan Samet described each part of Figure 1b in posing it as a paradigm for cannabis products.

- Dr. Jonathan Samet desires guidance on language we (Cannabis Research & Policy Team) use in the text with regard to potency and concentration, giving consideration to the title HB 1317 and the terminology used by CDPHE in its prior report. From a pharmacological perspective potency has been misused in replacing concentration. Dr. Jonathan Samet asked the SRC to comment on the terminology to be used.

Questions and Answers

- Chair Chris Urbina asked the group if the language is correct in this report and to offer guidance?
    - Dr. Susan Calcaterra mentioned from a report she read on the methamphetamine drug supply and their evaluation system where they look at two aspects: 1. Potency and 2. Purity. Dr. Susan Calcaterra understands these to be two different concepts but are considered when thinking about the harms of a substance. Purity relates to the % of THC and contaminants and potency is the affinity of the product for the receptor. Do we think concentration covers this concept of potency and purity?
        - Dr. Greg Kinney mentioned that if we say purity in terms of THC, he does not think that most people who are creating products are doing so with only THC in mind. He indicated that people purchase a plant product that has additional components that are inherent to the product. Subtleties may be lost by focusing only on THC.
        - Dr. Susan Calcaterra mentioned that there may be many components in the product, e.g., oils and butane. Do these components increase risk and can their additions to risk be considered?
        - Chair Chris Urbina mentioned that this diagram Figures 1a & 1b are outlining what we are trying to define. Consider adding terpenes where cannabinoids are listed as there are influences on the product, and on the selection and use of the product. Chris does not consider the appropriate term to be purity and gave preference for concentration.
        - Dr. Kennon Heard emphasized how much THC is in the product, commenting that the diagram does not include contaminants that may be relevant to adverse consequences, eg., carcinogenesis. He acknowledged that such effects may not be the focus of this report.
        - Dr. Sam Wang mentioned that data on how other cannabinoids interact with THC is relevant. Products are available with THC and CBD because of perceived and claimed mellowing effects of the combination. We might mention in the report of how other THC products may affect health impacts in relation to other characteristics we are evaluating. However, such interactions are not relevant to our charge. The primary goal is to look at THC concentrations and how they relate to health outcomes, but acknowledged that Dr. Susan Calcaterra brings up a valid point.
        - Dr. Jonathan Samet responded to Dr. Susan Calcaterra's comment and stated that we should add other product characteristics to cannabinoids in figure 1B.

He returned to the central question of whether to use potency or not throughout the report.

- Dr. Kennon Heard, Dr. Greg Kinney, Dr. David Brumbaugh, and the SRC members present agreed with using the term concentration. The group was unanimous.
- Chair Chris Urbina agreed and mentioned that we will need to redefine concentration within the report and change the conversation with the public so that this focuses on more concentrated THC, the percentage of the product is in greater amounts of THC. Chair Chris Urbina noted that this will also be a topic mentioned in the letter that the SRC writes up in response to the report from the Cannabis Research and Policy Team.
- Dr. Sam Wang agreed on this idea of using concentration as well and as we move forward in this research and topic, there will be more clarity from what this team has worked on.
- Chair Chris Urbina reemphasized Kennon's comment about including terpenes and potential contaminants in the figure.
- Dr. Greg Kinney mentioned that we should acknowledge that the state has done a forward-thinking job of setting up good testing for known and expected contaminants. Figure 1b takes the assumption that every product available for purchase has already been tested unless produced by oneself.
- Chair Chris Urbina thinks nothing is absolute and worth mentioning Dr. Greg Kinney's comment in the report.
- Dr. Jonathan Samet said that we have not highlighted in general all the different product emissions that could be generated. This should be acknowledged.
    - Dr. Paula Riggs mentioned that combustion emissions depend on the route of administration but agrees that the topic is not specifically called out. Emissions will depend on combustion of the product vs. vaping vs. using concentrates w/ butane or butane hash oil.
    - Dr. Jonathan Samet asked if there are any studies on metabolomics where they have evaluated compounds after the use of these different products.
        - Chair Chris Urbina seconded that this would be a great future research question.

No further questions for Dr. Jonathan Samet.

- Dr. Jonathan Samet pointed out that we added a paragraph in the report about variation in effects across populations and highlighting that there are health equity considerations where some populations are impacted more than others with increased exposure. However, most studies identified to date have very little information on the population that is under investigation. Nonetheless, the issues in the paragraph are important. He asked if there are key references to include?

Questions and Answers

- Dr. Susan Calcaterra mentioned we should avoid using the term marijuana and stick with cannabis throughout and especially in this paragraph based on the history of the term despite not being able to change the bill's terminology.
- Dr. Paula Riggs notes we have not described the demographics of medical marijuana users despite their prescribed need and they may or may not be different from non-medical marijuana users as medical use may rent lead to different profiles of concentration use.
- Chair Chris Urbina asked Dr. Paula Riggs if that creates another category of users.
    - Dr. Paula Riggs believes it does and could not find in prior material or the charge to the committee if the focus is to look at the medical marijuana users or recreational users. Dr. Riggs also mentioned that there are important differences between the groups when evaluating the benefits/adverse effects, exposure, concentration, and other characteristics. They have different exposures based on the grouping.
    - Chair Chris Urbina commented that we didn't include this in the characteristics of the study when looking at the dashboard.
    - Dr. Paula Riggs mentioned that it is a group that has a different kind of exposure compared with non-medical marijuana users.
    - Dr. Greg Kinney notes consideration of a third group not being recognized, specifically those not purchasing the products from dispensaries and untested for contaminants. Such uses might increase disparities.
        - Chair Chris Urbina acknowledged Dr. Greg Kinney's comment and thinks that not everything is being tested and people are using high concentrations of products they are growing themselves.
    - Dr. Jonathan Samet asked if there are any studies/data regarding this matter for those using marijuana for medical purposes.
    - Louis Leslie mentioned that they have broadly categorized it into medical use on the dashboard.
    - Dr. Kennon Heard noted that through license information or the state collects data on those who use marijuana products for medical purposes.
    - Dr. Sam Wang mentioned that there is a public report from either CDPHE or the Dept of Revenue on who has obtained a card for use of medical cannabis.
    - Dr. Paula Riggs mentioned that this is not a formal registry.
    - Dr. Greg Kinney notes that some have licenses for different reasons and choose not to be on the lists.
    - Chair Chris Urbina highlighted it as a grey area. Early on the accepted and legal use was only through medical licensing.
    - Dr. Paula Riggs, not all have converted and potentially due to taxes and experience.
    - Dr. Tianjing Li said that of the included studies not all have reported who have a medical usage license and some studies are testing for medical use where some of their participants are unhealthy or have some conditions, but license status is unclear.
- Chair Chris Urbina notes that we may need to include a general statement about the population of individuals using cannabis for therapeutic reasons going forward and potentially present it as future research or as recommendations that we look more carefully at that individual population.

    - Dr. Jonathan Samet mentioned that we will add another paragraph regarding this matter

No further questions for Dr. Jonathan Samet.

- Dr. Jonathan Samet pointed out that a paragraph in the introduction about the systematic evidence map, is this clear and sufficient?

Questions and Answers

- Chair Chris Urbina thinks this much improved over the previous draft and it is useful to have for those not well versed on this material.
- Dr. Greg Kinney suggested we discuss why we excluded so many studies when we start from ~46,000, and what can show up in a large literature review, no description of why it went down to 489 studies.
- Dr. Jonathan Samet mentioned that this emphasizes the systematic review process, and asked if we should we add a general PRISMA diagram for the purpose of describing the flow in the systematic review process?
    - Dr. Tianjing Li comments that the exclusion reasons are included in the flow diagram in the report, but we could add text for additional explanation.
    - Dr. Jonathan Samet clarified that we are in the introduction section, not the methods.
    - Dr. Greg Kinney said we should add an explanation to prep the reader in the method section, i.e. the abstracts won't have complete extractable data, explain what we see as researchers.
    - Dr. Paula Riggs suggested briefly describing the bar of evidence that leads to inclusion of how the review moves from 46,000 titles and down to 489 studies.
    - Dr. Jonathan Samet thinks adding a generic PRISMA diagram with explanation in the introduction would prepare the audience.
    - Dr. Tianjing Li agrees that adding a figure describing the process of conducting a systematic review, framing the question with your eligibility criteria selection of studies preserves the quality and then synthesizing the data may be helpful for the reader.
    - Chair Chris Urbina mentioned that was helpful from initial research protocol.
    - Dr. Tianjing Li referred to Greg's question and notes that the figure does illustrate the reasons for exclusion from the full text report, but we do not do so for the titles/abstract exclusion due to multiple reasons and do not reconcile that.
    - Dr. Greg Kinney noted that for a reader who is not familiar with the processes of systematic reviews might think that there are many studies that may fit for evaluation and not understand the basis for their exclusion.
    - Chair Chris Urbina suggested adding an asterisk with a general sentence below the diagram might work.
    - Dr. Jonathan Samet mentioned that we should say earlier in the report what a systematic review is and why one starts with a large study number and narrows it down. Also, we should address why 40,942 title/abstracts are excluded. Notably the protocol

has the criteria outlined in more detail, but we can expand upon it in the report to reach a wider audience.

- Chair Chris Urbina asked if there are any other questions or comments about these sections.
    - No further questions or comments.
- Chair Chris Urbina asked if there are any general questions on the report?
    - Dr. Susan Calcaterra notes that she provided comments on the June 9th draft version and expressed her general comments. She notes that on the overview of the report regarding the overview of approach, second paragraph (sentence starting with "the resulting database could then...") should we discuss the value of some of the qualitative relationships that we've identified in the studies, particularly for those with insufficient details.
        - Dr Tianjing Li agreed and noted that it was a good point to highlight.
    - Dr. Susan Calcaterra notes under the section of theoretical framework for how potency is related to health effects in the third paragraph (sentence starting with "in figure 1b...") should we add the characteristics we are talking about i.e., frequency of use, route of use, etc.
    - Also, Dr. Susan Calcaterra mentioned in the next paragraph in this document regarding individual's tolerance to the effects of THC; do we want to note that having tolerance or withdrawal symptoms does not mean they have a use disorder, do we want to talk about this?
        - Chair Chris Urbina asked if Dr. Susan Calcaterra is defining this as an adverse effect of not using THC?
        - Dr. Susan Calcaterra answered with concern that confusion may arise with the development of tolerance versus having a use disorder. Similarly, having a dependence does not mean that they have a use disorder. So having tolerance is not necessarily associated with a use disorder and desires clarification to be made so the reader does not make inferences.
            - Dr. Paula Riggs highlights that you can have dependence on a medication that is prescribed too. Although true that symptoms that count towards use disorders are adverse effects of the drug.
            - Dr. Greg Kinney notes that everyone as a medical user might be considered as having a "problem" based on how the question is phrased and using cannabis therapeutically.
            - Dr. Paula Riggs said that the criteria does not mean they have a use disorder.
            - Chair Chris Urbina asked how to handle this, is it beyond our review or do we need to consider this as a future discussion?
            - Dr. Paula Riggs stated that the committee is charged with looking at benefits and adverse effects of higher potency products. She believes that potency/concentration can be related to addictive potential and perhaps adverse effects and

withdrawal, but we were not charged with this or if we need to address use disorder.
    - Dr. Greg Kinney acknowledged Dr. Paula Riggs's statement that this occurs with potentially all medications.
    - Dr. Paula Riggs pointed to benzodiazepines and opioids as having abuse liability, as do other medications.
    - Dr. Greg Kinney thinks a paragraph addressing this matter would be helpful to add to the report because of it being a negative outcome. But it identifies that it is not the emphasis of the report.
    - Dr. Sam Wang asked if the group thinks it could be briefly added that an individual's tolerance to the effects of THC similar to other pharmaceuticals can change the amount of drug dose use, etc...and a sentence added that tolerance does not necessarily indicate substance use disorder or tolerance.
      Dr. Susan Calcaterra said that not all tolerance and withdrawal symptoms are associated with an adverse event/outcome. It needs to be stated in the report.
    - Chair Chris Urbina summarized that this conversation focused on results and we have not gotten to that point yet unless it should be mentioned earlier on in the report to inform the reader.
- Dr. Jonathan Samet explained that defining the adverse effects can become challenging, but it is important to do so in some legal regulatory structures. If we discuss that tolerance does not imply use disorder, then we will have to classify consequences identified in the literature review associations of the health effects (adverse and beneficial) and the general classification.
    - Dr. Paula Riggs mentioned that they are many drugs with the potential for abuse liability and in consideration with prescribing medications there is thought of weighing the risk vs benefit. Is tolerance what we want to focus on or abuse liability? It has an addictive potential and if we are not differentiating from recreational use then we cannot say that they are not potential for abuse, there is abuse liability.
    - Chair Chris Urbina acknowledged the importance of this conversation and asked do we capture it in the discussion around therapeutic benefit and adverse effects which can be true for THC and what condition they are using it for.
    - Dr. Erica Wymore, do we characterize this in terms of pharmaceutical or recreational? Needs to be clear between medical vs recreational use and differentiate the pharmaceutical/adverse effects.
    - Dr. Paula Riggs comments that for the scope of this literature review it is relevant to acknowledge that the higher the concentration for a product with abuse liability, the greater the addiction potential to develop a use disorder. What are the potential adverse effect in relation to higher potency?

- Dr. Susan Calcaterra thinks this should be added to the theoretical framework paragraph where higher potency leads to development of tolerance, higher potency leads to development of dependence and those two things are not necessarily adverse effects.
- Dr. Paula Riggs emphasized that the greater the concentration the higher the potential for developing the use disorder. Despite tolerance individually does not constitute a use disorder but potency is related to addiction.
- Dr. Susan Calcaterra agreed.

- Chair Chris Urbina summarized the discussion on the issue of tolerance and when we discuss outcomes that we should address the potential for tolerance, dependence, and substance use disorder.
- Dr. Jonathan Samet agreed and asked Dr. Sam Wang if we have enough to write this paragraph about the high concentration would lead to the greater abuse liability and greater risk for a use disorder.
    - Dr. Sam Wang mentioned that we might be putting more of the "horse before the cart" when we are charged to determine if that is even the case.
    - Dr. Paula Riggs notes that is part of the literature review and a priori claims are not inherent to the literature review.
    - Dr. Jonathan Samet highlights the general comment that the greater the exposure the more likelihood of addiction/ abuse liability and compared this to findings in with nicotine-containing products. Dr. Jonathan Samet asked if Dr. Sam Wang would pose some questions to the SRC for addition to the introduction regarding these matters.
    - Dr. Sam Wang said he will read this more thoroughly and has been reviewing the document and trying to change some of the terminology of potency/concentration in the document. Tolerance is important and the exposure-dose framework will be adjusted with consideration of Susan's point on tolerance and dependence. Dr. Sam Wang expressed concern about introducing apparent conclusions up front.
    - Dr. Paula Riggs proposed that background and significance for other substances in relation to abuse liability. Include something that already has abuse liability may lead to greater tolerance and progress to significant addiction.
    - Chair Chris Urbina offered that Dr. Jonathan Samet and Dr. Sam Wang consider the comments made and not preempt the conclusions.
- Dr. Jonathan Samet mentioned that we can expand on the comments made and clarify the context for the review and it might be emphasized in the outline of the scientific review questions.
- Chair Chris Urbina asked if there were any more questions for Dr. Jonathan Samet and the research team about the current draft of the report.
- Dr. Jonathan Samet commented that what was added to the report was the description of the methods without replicating the protocol but allude to it enough. The PRISMA diagram and the table of study characteristics are included. Still to be added are the findings as further data is extracted and the evidence map developed. We will probably

have to freeze what data extraction we have before the deadline and then continue after submission of the report.
    - Chair Chris Urbina asked what would be the best format for receiving the feedback.
        - Dr. Jonathan Samet mentioned sending it to Neeloo, Chris, and himself for review of the comments

No further questions or comments

Discussion of SRC Letter

- Chair Chris Urbina mentioned that the SRC suggested developing a letter to accompany the report stating that the research team incorporated feedback, particularly the distinction between potency vs concentration, discussing the tentative format and highlighting SRC recommendations.
    - Chair Chris Urbina proposes developing a list of proposed recommendations (policies and education especially in terms of health equity and exposure awareness). Also, do we or do we not agree to the report from the Cannabis Research and Policy Team while emphasizing important points from the report.
    - Dr. Kennon Heard asked how strong of recommendations made by the SRC should be. For example, would the SRC make contributions on strength of evidence, e.g., as strong/weak? Or on policy?
        - Chair Chris Urbina mentioned the recommendations can be as strong as we want, if the SRC finds it necessary to say.
    - Dr. Erica Wymore asked about comments on the limitations and challenges of the literature review, documentation in the studies, and definitions of potency and how to define it adequately via gaps in the literature.
    - Chair Chris Urbina acknowledged Erica's comments and emphasized that Dr. Jonathan Samet will include limitations in the team's report as well. SRC should produce a letter on the highlights of the report.
    - Dr. Jonathan Samet mentioned that the team has a deadline, July 1, while the SRC does not have a statutory deadline.
        - Chair Chris Urbina mentioned that the SRC does not have a deadline but it is important to develop and send a letter.
        - Dr. Paula Riggs supported an approach of digesting the report and then formulating a thoughtful letter from the SRC and not rushing to produce a report before the end of June. The timing might be to produce the report by the middle of July after reading the full report and avoid repetition from the report.
        - Dr. Kennon Heard states that it would be important to review the report first and then writing the SRC letter, depending when the legislature is back in session to develop an overview of future policy implementation.
    - Chair Chris Urbina mentioned issues that are important to address that are not able to be discussed in this systematic review that we may want to address and add them into our letter.
    - Dr. Jonathan Samet said that both groups have a wide range to develop recommendations and evidence-based policies.

    - Chair Chris Urbina stated that the consensus was to not rush the development of the SRC's product to the legislature. There is a possibility that we have a future meeting in the summer too.
    - Dr. Kent Hutchison offered his help and agreed with Dr. Paula Riggs to not rush their final product.

No further questions or comments for Chair Chris Urbina.

SRC Plans and Approach

- Chair Chris Urbina encouraged the group to interact with the dashboard and send comments to Jon, Chris, and Neeloo. SRC members unable to participate in the next meeting should send comments to Jon, Chris, Neeloo. Neeloo and Chris will distribute comments we receive amongst the group to review.

Next Meeting Timing and Closing Remarks

- June 21st and June 29th meeting is scheduled
- No final questions or comments