Meeting Minutes

HB 21-1317 Eleventh Meeting of the Scientific Review Council

February 24, 2023; 2:00 pm – 4:00 pm MT

General Remarks and Welcome:

- Dr. Chris Urbina, Chair of the Scientific Review Council (SRC), called to order the Eleventh meeting of the SRC on February 24, 2023, at 2:00 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
    - Joseph Schacht
    - Kennon Heard
    - Susan Calcaterra
- The following Council members were absent:
    - David Brumbaugh, with advanced notice and apologies
    - Kent Hutchison, with advanced notice and apologies
    - Erica Wymore, with advanced notice and apologies
    - Paula Riggs, with advanced notice and apologies
    - Lesley Brooks, with advanced notice and apologies
- The following SPH team members were present and introduced:
    - Jonathan Samet
    - Lisa Bero
    - Tianjing Li
    - Greg Tung
    - Christi Piper
    - Valerie Yim
    - Neeloo Soleimanpour
    - Louis Leslie
    - Rosa Lawrence
    - Christi Piper
    - Jean-Pierre Oberste
    - Thanitsara Rittihairoj
    - Meghan Buran
    - Sheana Bull
- The following SPH team members were absent:
    - Sam Wang, with advanced notice and apologies
    - Ashley Brooks-Russell, with advanced notice and apologies
    - Paige Buchanan-Hall, 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, Charge to the Colorado SPH, and Recommendations to the SRC:

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

No questions for Chair Urbina.

Overview of Draft Report from the Cannabis Research & Policy Project:

- Dr. Jonathan Samet presented the objectives of today's meeting including the outline of the draft report and the overview of the methods used to assess the four policy-motivated questions, provide an update on the educational campaign, and discuss next steps with the intent to submit a report to the legislature in the near future that will include recommendations.
- Dr. Samet highlighted the pharmacokinetic considerations section of the report and the insights that Dr. Sam Wang provided around the effects of THC and drivers that influence key receptors in the brain including various factors like product dosing, concentration, tolerance, and frequency.
- Dr. Samet broadly explained the top-down approach and how the questions used have laid the foundation for the educational campaign's objectives, future research recommendations, and potential policy recommendations. Dr. Samet reminded the group about the two approaches that the Cannabis Research & Policy Team used to analyze the evidence map.
- Dr. Samet explained the classification of extent and balance of evidence to provide an understanding of how the top-down approach was applied and how the individual findings were considered. The balance of evidence was characterized for each study outcome by the concept of equipoise and through a vote-counting approach. Votes represent individual study findings. This method will be applied to question two in the next rendition of the report. Dr. Samet provided an example of the table used to categorize equipoise and summarize the evidence.
- Dr. Samet offered to the group the opportunity to amplify any comments or pose additional questions for the Cannabis Research & Policy team.
    - Dr. Tianjing Li stated that vote counting is one way to synthesize the evidence as the studies are very heterogenous in terms of design, measurements, and quantify the size/direction of effect. She discussed the benefit of the cross-classification table. Dr. Li offered another option that can be conducted to summarize the evidence through the concept of risk of bias assessments of individual studies (e.g., RCT are stronger than observational studies) we have not looked at this yet, but it is another approach to analyze the evidence.
    - Chair Urbina asked for clarification from the report regarding some inconsistency with the direction of evidence in relation to harm/benefit and cross-classification of the studies using the vote-count approach as some study outcome conclusions were in the

affirmative direction and some study outcome conclusions were in the negative direction.

- Dr. Samet explained that the literature was considered for evidence relating to adverse consequences from use of high-concentration products that might emerge and the potential beneficial consequences from use of high-concentration products. We will provide the group with a summary of studies pointing to harm and benefit.
- Chair Urbina clarified his question in reference to the final sentence of each study outcome and where he experienced confusion when some concluding statements listed limited evidence below equipoise and limited evidence above equipoise.
- Dr. Samet discussed the directionality of effect and the nature of the effect.
- Dr. Lisa Bero explained how studies can report their results in different ways and to provide uniformity we took the outcome as it was presented in the paper, but we can flip the outcome to follow one direction with the understanding that we may encounter some double negatives.
- Dr. Susan Calcaterra recommends highlighting where the conclusions are being drawn from, especially in relation to the study design. Dr. Calcaterra advised the grading of the quality of our study if possible.
- Dr. Samet acknowledged that Dr. Calcaterra's comment built upon Dr. Li's prior comment. He disclosed that a consequence of the evidence map is the ability to identify if there is enough evidence to justify a full systematic review, we think that for some outcomes there are enough studies, but overall, the number of studies is limited therefore, the formal use of the risk of bias assessment is not necessarily warranted.
- Dr. Li said that it would be helpful but with the variety of the study designs. If we assess the risk of bias, she suspects that the risk of bias will be moderate or high risk of bias, because not every study in this review is using the appropriate study design. However, Dr. Li acknowledged Dr. Calcaterra's comment to include an additional domain relating to risk of bias with consideration to number of studies, sample size, and other factors.
- Dr. Joseph Schacht agrees with Dr. Calcaterra's comment to provide greater narrative weight to these better controlled and conducted studies. Dr. Schacht also reiterates Chair Urbina's comment related to the language surrounding the idea of equipoise. Dr. Schacht referenced the cardiometabolic conclusion statement and believes that we are missing a statement that describes the outcome as either beneficial or negative and it would be helpful to add it to the concluding statement as these were negative outcomes contributing to the judgement of equipoise. Dr. Schacht raised concern that the interpretation of the conclusion statement may be open to misinterpretation if the entire section is not reviewed, and it would be helpful to state that this is evidence that is greater than equipoise and they are not associated with negative outcomes.
- Dr. Samet acknowledged that we need to provide standard language across the report in relation to the outcome and conclusions being made.

        - Dr. Bero agreed we need to include direction of harm/benefit in the concluding statement. Additionally, she discussed the risk of bias further and identified that it involves two layers. One, we have rated studies by study design which is identified in the scoping review and detailed in a table from this draft report in addition to how the exposure was measured. If we can obtain studies with similar study designs, then we can evaluate the risk of bias of those studies of a particular design, but there is value in looking at the spread of study design when we find the relevant ones.

No further questions for Dr. Samet.

Discussion of Policy Questions 1 -4:

- Dr. Greg Tung reminded the group what the four Policy Questions were and the methods the methodologists used to analyze the data. Dr. Tung explained that question 1-3 had methods adapted from the evidence map and how they were categorized as low-, medium-, and high-relevancy, while question 4 had additional methods associated with the analysis that built upon the methods used in questions 1-3. Dr. Tung provided insight on the characterization of product concentration by stratifying studies by THC amount/concentration.
- Dr. Tung offered the group to ask any questions and feedback throughout the remainder of the presentation.

Questions and Answers

- Dr. Kennon Heard asked if an inhalation product was at 5-15% THC, then was it coded as high or low concentration?
    - Jean-Pierre Oberste disclosed how concentrations were coded. Each concentration was coded specifically, e.g., if it stated 12% then it was coded as high-concentration THC whereas 6% would be coded as low-concentration THC.
    - Dr. Tung added that we documented the specific concentrations and if a range was provided, we coded both the low end and high end of the range while acknowledging the limitations the cuts offs pose.
    - Chair Urbina asked if Dr. Tung and his team wanted additional feedback on the methods for questions 1-3 for it to be applied to question 4 or if it was just an overview he was providing.
        - Dr. Tung clarified that he wanted to provide a thorough overview of the methods used for each question for the group to understand the application before moving into the analysis section.
- Regarding Policy-Motivated Q4, Dr. Tung discussed the methods and the number of studies evaluated when we queried the evidence map for potentially relevant papers was much greater than the other three questions previously analyzed. Due to the large number of studies, we adapted our previously used methods approach for question 4, in which Dr. Tung provided an overview of how the methods differed. Dr. Tung stated that a risk of bias was not conducted for this question. Only high- and medium-relevancy studies were evaluated for this question. Dr. Tung reviewed inclusion and exclusion criteria.

    - Mr. Oberste mentioned that there were about 270 studies that referenced a concentration and 180 studies that were categorized into the low-relevancy category, thus for time purposes, they were excluded from the analysis.
    - Dr. Bero highlighted that the studies in the low-relevancy category did not directly address the question at hand regarding comparison of concentration, which is also why they were not further analyzed.
    - Dr. Tung followed up that reducing the number of text reviews was to speed up the process but also to better identify those studies that were most relevant to the question at hand.
    - Dr. Calcaterra asked how a study was categorized as low-relevancy. Was a low-relevancy study defined as a study that did not compare two different THC concentrations or studies that only compared at a single THC concentration, etc. Or were there additional categories to low-relevancy studies?
        - Dr. Tung explained that a criterion for a study to even be considered in general had to have a comparison of two different THC concentrations as the question we were trying to answer focused on a concentration level or threshold. The difference between high-, medium-, and low-relevancy studies focused on how those studies focused on the different components of dose. The high-relevancy study had a specific measure of concentration, frequency, and duration which we think will provide the best understanding of dose and the effect on concentration. Medium-relevancy would only provide two of those factors of dose while, low-relevancy studies would only provide one of those factors relating to dose.
    - Dr. Tung emphasized the need for standard language and how it was determined through the use of vote counting to classify if a study had an effect in a particular direction. Studies were classified as having an effect, no effect, or not assessed for both exposure dose and concentration while examining the final statistical test used in each study.
- Dr. Tung provided an example of the summary table illustrating the studies evaluated in relation to threshold. Dr. Tung walked through the table and highlighted that each row included the outcome domain and columns included direction of association and cannabis exposure that was pulled from the evidence map.
- Dr. Tung also provided an example of a study that was evaluated when queried from the evidence map and how the information was extracted and used to build the summary table.
    - Chair Urbina asked for clarity on his interpretation of the table and the difference between the color coordination
    - Dr. Tung added that red signifies harmful, while green signifies therapeutic/beneficial. Red square indicates a statistical association with measures of dose.
    - Dr. Samet added that the full tables are included in the appendix of the draft report due to its size and large number of studies evaluated.
    - Dr. Tung notes that there are a large number of studies and the table provides a quick visualization of the large amount of information.
        - Dr. Bero mentioned the effects are categorized by outcome.

Summary of Findings for Q4

- Dr. Samet illustrated how the evidence is limited mainly, across the board in relation to benefit, harm, and null by using the cross-classification tables. The vote count does not support an association at this point for benefit of high-concentration THC product use and the evidence is limited. Dr. Samet highlighted the limited number of studies available for these health outcomes evaluated. Dr. Samet explained that there were limited number of studies for the outcomes of interested in relation to harm. The largest number of studies were available for mental health which illustrated moderate evidence above equipoise relating to harm. Dr. Samet advised the group to review the appendix table for further detail. Finally, for outcomes that did not provide an effect lacked directionality and had limited evidence.

Question and Answers

- Chair Urbina asked that if there is no evidence, does it mean that the use of high-concentration THC products is safe or how are the summary tables interpreted?
    - Dr. Samet explained that absence of evidence is not absence of effect or evidence in safety of products used. There is lacking evidence for many health outcomes for the findings to be informative, but the limited evidence should be evident that we don't have much evidence to lead to a conclusion for a specific outcome. To prove that there is no effect of anything is a daunting task because you need a great deal of evidence to have precise enough measures of whether there is a risk, and to say that you have excluded reasonable degrees of risk. It is a rare scenario to be in that position.

No further questions for Dr. Samet

Open Discussion with SRC

- Chair Urbina asked the group if they had any questions or comments they wanted to pose.
- Dr. Samet appreciated the comments made by the group thus far and explained that there is some work that needs to be done for question 2 where we follow the methods of question 4.
- Dr. Bero asked the SRC if they were to make recommendations for policy, is the current format of the summary table that is in the appendix helpful when trying to make a decision? Dr. Bero explained that the information is largely pulled from the evidence map. Dr. Bero mentioned that we can try and provide a point estimate, but it is difficult to determine that information with such heterogenous studies which is why we attempted the summary table we presented.
    - Chair Urbina commended the group's effort and the attempt to quantify the amount of evidence for dose, frequency, and the impact it has to suggest harm/ beneficial effects. Chair Urbina rephrased the question asking whether we have strong enough evidence to say that there is definitely harm or an effect based on the research on the studies we have so far and concluded that it is limited. He mentioned that next steps are to see the recommendation posed by the SRC from Cannabis Research & Policy Team.
    - Dr. Greg Kinney asked Dr. Tung for his input on whether this table that Dr. Bero referred to is clear for the general public and legislature to interpret.
        - Dr. Tung weighed in and believes that this table is interpretable to the intended audience with the limitation that were discussed. Dr. Tung discussed long term we could conduct more systematic reviews relating to some of the findings of the analyzed questions.

- Dr. Samet stated that we should recognize the methods used to give a full picture of the evidence through the evidence map and/or the table located in the appendix of this draft report for question 4 that will be replicated for question 2. Dr. Samet referred to Dr. Calcaterra's comment that the literature is diverse with various studies designs that do not all have desired sample sizes where they use one measurement and one drug. Many of the examined studies use various THC products at various THC concentrations and the exposure assessments vary across the studies because the product is not standardized which complicates the conventional systematic review that may be used for a therapeutic agent. It is a useful contrast because the pharmacologic agents is the same but the dosing is inconsistent and complicated. We are trying to find ways to display the extent of the evidence and finding useful ways to summarize as our next step is to draw out what we know that will be useful for policy-based decisions that is evidence based. We are illustrating that there are many limitations, but there are some strengths for specific health outcomes. Through the literature review process, development of evidence map, and the additional analysis conducted over the last several months captured the scope of the evidence in a useful way to support next steps and reach plausible conclusions based on our findings.
- Dr. Calcaterra acknowledged that the available evidence may be limited to make strong or highly supported recommendations to policy makers as stated when we started this project based on the evidence available, but did we discuss how much weight should be placed on the evidence that we found as opposed to expert opinion. How do we see our expert opinion playing a role when making recommendations to policy-makers?
    - Dr. Tung responded that that is up to the SRC. Dr. Tung provided a reminder of the charge presented to the school and SRC which calls for independent reports from the school and the SRC based on the findings of the scoping review. The intent of the SRC is to pull together subject experts and provide their interpretations from the findings by the school.
    - Dr. Bero agrees that it is a question for SRC to have amongst themselves. Dr. Bero also mentioned that consideration of equity, feasibility, regulator status, etc. Can go into the recommendations, not just use of expertise and evidence.
    - Dr. Samet states that with the support of the state, we have developed a valuable and unique resource that we hope others will use when it is complete and publicly available, not just for SRC and review team's use. Dr. Samet hopes that upon the legislature's review that they use this review and use it as a basis for taking one or more steps including some of the factors that Dr. Bero eluded to which will factor into decision making. We see our job to describe the scope of the evidence available and address some of its limitations and collate it into a useful resource for decision makers which is what Policy Question 1-4 are about along with the summaries that illustrate the extent of the evidence and what the balance shows. We are preparing the layout for recommendations to be made. The SRC has the opportunity to provide comments and make their own recommendations.

- Chair Urbina asked when the dashboard will be publicly available and what are the next steps of this draft report? Will the Cannabis Research & Policy Team be making recommendations for the SRC to review?
    - Dr. Samet explained that we have some work that needs to be done for question 2 and our next steps are to add some sections to the report including the summary of findings and concluding recommendations that we would want to be sent to the legislature. We plan to have the dashboard public and for this to be completed before the report is submitted to the legislature. Our priority is to complete the report and ensure the dashboard is able to accept queries from users before making it public.
    - Chair Urbina asked if we should be seeing a report within the next month before it is sent to the legislature?
        - Dr. Samet agreed and states that it is the team's intended plan to complete the report before the legislative session closes.
    - Chair Urbina asked the SRC if they want to see the final draft before the report is submitted or make their own?
        - Dr. Schacht, Heard, Calcaterra, and Kinney all want to see the final draft of the report from the Cannabis Research & Policy Team before making recommendations and prior to the legislative session is closed.

Progress Update on the Educational Campaign:

- Dr. Sheana Bull presented on the progress to date of the educational campaign based on the information discussed with the SRC and using their input to form messages. Moving forward with the end goal in mind to have the messages identified that can be said to our communities, who our audiences should be, and how and where we can share our messages to for maximum reach. This is done through advisory groups who are being created including the intended audience and asking guidance for where and how to disseminate messages. Community advisory groups will start meeting in May 2023 from a variety of age-groups, populations, and geographical areas across the state.
- Dr. Bull's team is proceeding in collaboration with Jean-Pierre and Valerie for two different reviews. One will focus on what works in health communication and campaign strategies while the other will focus on how to use 21st century technology and strategies to reach the wide groups within Colorado. This review should be completed by the end of the month.
- Dr. Bull acknowledged the support from the group and the benefit of having them involved in the group convenings. Dr. Bull states that it would be helpful to have members of the SRC at meetings in the Spring to community advisor meetings to clearly illustrate that the SRC's final approval is needed for implementation and messaging regarding this subject matter. Dr. Bull wants to ensure thorough communication is made among all members involved.
- Chair Urbina explained that we will need the report and recommendation to assist with the campaign and additional meetings to sign off on the educational campaign.

Questions and Answers

- Dr. Heard asked for clarity on the healthy communication search.
    - Dr. Bull explained that we are looking broadly and within the focus of substance use and how messaging is conducted. Dr. Bull is evaluating what methods are effective. Dr. Bull mentioned an example that for some communities, the use of expert opinion is very useful in conveying messages while in other communities, not as much.

No further questions or comments for Dr. Bull.

Next Steps from the Cannabis Research and Policy Team:

- Chair Urbina mentioned the project team will plan to have another meeting next month to follow up on the progress the Cannabis Research & Policy Team has made where they produce their final report and recommendations. In addition to meeting with the educational campaign team.
- Chair Urbina and Dr. Samet commended the Cannabis Research and Policy Team for their work and the SRC for their input.

No further questions or comments for Chair Urbina and Dr. Samet.

Next Meeting Timing and Closing Remarks:

- No final questions or comments.
- Meeting Adjourned 3:30 pm (MT).