Meeting Minutes

HB 21-1317 Tenth Meeting of the Scientific Review Council

December 21, 2022; 12:00 pm – 2:00 pm MT

General Remarks and Welcome:

- Dr. Chris Urbina, Chair of the Scientific Review Council (SRC), called to order the Tenth meeting of the SRC on December 21, 2022, at 12:00 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
    - Kennon Heard
    - Archana Shrestha
    - Erica Wymore
    - Paula Riggs
    - Susan Calcaterra
    - Lesley Brooks
- The following Council members were absent:
    - David Brumbaugh, with advanced notice and apologies
    - Joseph Schacht, with advanced notice and apologies
    - Kent Hutchison, with advanced notice and apologies
- The following SPH team members were present and introduced:
    - Jonathan Samet
    - Lisa Bero
    - Tianjing Li
    - Valerie Yim
    - Neeloo Soleimanpour
    - Sam Wang
    - Jean-Pierre Oberste
    - Meghan Buran
    - Sheana Bull
    - Bobbi Ortega
- The following SPH team members were absent:
    - Christi Piper, with advanced notice and apologies
    - Thanitsara Rittiphairoj, with advanced notice and apologies
    - Greg Tung, with advanced notice and apologies
    - Rosa Lawrence, with advanced notice and apologies
    - Louis Leslie, with advanced notice and apologies
    - Ashley Brooks-Russell, 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.

General Approach to the Evidence Map from the Cannabis Research & Policy Project:

- Drs. Jonathan Samet and Lisa Bero presented on the progress to date of the scoping review. They discussed how to move from the completed evidence map to the approaches of synthesis using a top-down approach where the project team has specific a priori questions that are directly relevant to policy and they query the evidence map seeking studies to address the questions. Additionally, they discussed the bottom-up approach that is centered around examining the studies on specific topics (e.g., respiratory health outcomes) and how they are clustered for possible future systematic reviews to answer specific questions.
- Dr. Samet discussed the progress of the preliminary draft of the interim report that was sent to the SRC to review, which included three of the four policy-motivated questions discussed in the last SRC meeting and the dissection of the respiratory health outcomes and mental health outcomes, which focused on psychosis and schizophrenia. Dr. Samet acknowledged the question the team received from Dr. Wymore at the last SRC meeting and offered to the group the opportunity to pose additional questions for the Cannabis Research & Policy team to investigate using the findings from the evidence map. Additionally, Dr. Samet stated that given the 566 studies on broad topics, how do we determine the priority for the bottom-up approach that keeps policy-relevance and high-concentration THC products in mind.
- Dr. Bero discussed the methodologic approaches and the move from the evidence map to those approaches after extracting the data. Starting from the evidence map is a great advantage; Dr. Bero walked through Figure 1 of the interim report, which outlined steps from the protocol, and how the Cannabis Research & Policy Team progressed with the top-down and bottom-up approaches from the evidence map. Comparing both approaches with a traditional systematic review, in these two approaches, we do not conduct a risk of bias assessment for each included individual study. The project team is dealing with a body of evidence that is quite heterogeneous. Consequently, they cannot proceed with a quantitative summary with either of the approaches. Instead, for summarization they are proceeding with a qualitative summary that adheres to the SWiM guidelines (synthesis without meta-analysis) since they cannot yet conduct a formal meta-analysis. The project team provides in this report a narrative summary with counts, where their next step may be formal systematic reviews, but this method allows them to narrow down the pool of evidence we are able to examine. This was largely outlined in the initial protocol and methods are further detailed in the upcoming report.

- Dr. Samet commented for the group to keep in mind that utility for key policy questions is central in using the evidence map. the idea of the risk of bias assessments in these approaches is considered when screening the studies. Dr. Samet provided an example of the first paper published regarding respiratory health—in 1971. That paper and other early papers would not be relevant to the charge from the General Assembly.

No questions for Drs. Samet or Bero.

Discussion of the Top-Down Approach:

Policy Motivated Question 1

- Jean-Pierre Oberste explained the question-driven or "top down" approach. It involves a priori, policy-relevant questions developed to identify those strata of the evidence map that are sufficiently robust for carrying out systematic reviews of policy relevance.
- Jean-Pierre Oberste detailed the findings for three of the policy-motivated questions and how the exclusion criteria were utilized. Jean-Pierre and his team used a relevancy criteria to determine which studies best supported evidence for the question at hand. Studies that had all the components of dose-response exhibited potency, frequency, and duration. Those that did not mention all three were categorized in a lower relevancy group. The evidence was limited for the first question, which focused on adolescents and young adults being more susceptible to harmful physical or mental health outcomes with the use of high-concentration THC products. 15 studies showed some association, but only 2 studies had a relation to the study question. Both studies showed some relationship between potency and health outcomes, but the evidence base was quite limited.

Questions and Answers

- Dr. Paula Riggs expressed concern with how the question and response will be interpreted by the public. She worries that the outcomes of the report may be misconstrued in relation to the harmful effects if the project team says the evidence is limited for the focused policy questions.
    - Dr. Tianjing Li discussed how high-concentration THC was defined, but if the policy question is important to the SRC, the project team can make it broader and as a result, there could potentially be more studies selected that may be relevant to answer the broader question.
    - Dr. Riggs is concerned with how this will be understood by the public given the data and the project team can consider making it broader. However, as the question stands, the conclusion is valid. However, we should consider how these and other THC products affect adolescent brain development.
    - Chair Urbina asked if the project team can add a disclaimer or additional reference that illustrates THC effect on cognitive development generally.
    - Dr. Li explained that the pool of studies includes 13 studies, but the project team can go back and broaden the pool of studies. Regardless, the evidence is scarce on the certainty of evidence.

    - Dr. Samet asked to come back to this in general after a complete review of the report as the project team continues to explain how they evaluated the vast number of studies.
- Dr. Erica Wymore supports Dr. Riggs' comments that the project team has a paucity of data for this question, but the focus is on a narrowly described high-concentration cannabis product and therefore several studies were excluded because of the definition. Dr. Wymore also has concerns with how high-concentration THC is defined, and the interpretation of high-concentration THC may be too low of a threshold.
    - Dr. Samet asked for Dr. Sam Wang to chime in and explained that the project team can pick out studies with whatever concentrations may be specified because the data extraction team captured those amounts. However, the larger concern is that the higher the team-established threshold for high-concentration THC amounts, the fewer studies available for further analysis.
    - Dr. Wang acknowledged the comments made by Dr. Riggs and Dr. Wymore as conversations the project team had leading up to the development of this report. The project team is determining how to solve this while keeping in mind the charge of HB 1317 where they look at specific evidence on high-concentration products on various outcomes, not necessarily looking at the overall literature. There is a paucity of literature as these products are all relatively new and there is not a robust literature. The project team does not want to exclude or shrug off any of the existing literature on cannabis health effects. Dr. Wang mentions that moving forward the project team has to establish how to take the findings that are likely limited on many medical and mental health outcomes--specifically relating to linking high-concentration THC products to the literature as a whole and how to use them together. Dr. Wang emphasized that these are conversations that the project team is having; it is not being overlooked.
    - Dr. Wang explained the definition of high-concentration THC limits and the literature is limited on specific dose-response or dose outcome measures on today's cannabis where in Colorado flower averages 20% and concentrates average in the 60s%. Consequently, the higher the limit set, the already limited evidence becomes even less. So, the project team can set these limits as a starting point and can discuss down the line what happens to the evidence with varying criteria. The definition was based on the CDPHE report in 2014 which showed serving size limitation and what has the least amount of reported adverse effects. The literature at the time showed less than 5-10 mg was the "safest," but can be further discussed.
    - Dr. Bero reminded the group that the project team did not define what high concentration was in the initial protocol and had a broad search, but any cut-offs or definitions now are based on the data that was found in the literature. As a result, this makes the project team confident that we did not miss anything by setting a cut-off a priori.

Policy Motivated Question 2

- Jean-Pierre Oberste discussed policy-motivated question #2 which focused on individuals with pre-existing mental health conditions and whether they were more susceptible to a negative mental health outcome or therapeutic benefits. Jean-Pierre noted that the evidence was limited to 18 studies where 7 studies focused on harm and 11 studies focused on therapeutic evidence.

Six of the seven harm studies were case-control trials involving first episode psychosis patients and all 6 found a relation between high-concentration cannabis use and first episode psychosis as well as high frequency use and first episode psychosis. The seventh study looked at symptoms associated with cannabis use in psychiatric patients in general with similar findings. Jean-Pierre elaborated on the findings by condition and therapeutic applications, and the similar evidence that was found between them. The project team was unable to reach conclusions on these studies that discuss therapeutic effects, but could proceed with a systematic review focusing on the psychosis outcome

Questions and Answers

- Chair Urbina asked if the same methodology was used to evaluate policy-motivated question 2.
    - Jean-Pierre responded that the same method was used where studies were ranked by priority, and they underwent the exclusion criteria hierarchy.
- Dr. Paula Riggs clarified the question of interest and asked if having a pre-existing mental health condition and initial onset of psychosis may be causally related. Is the project team completely focusing on pre-existing conditions and excluding any onset of conditions?
    - Jean-Pierre responded that the project team was able to capture the first episode psychosis due to the study design being case-controls and are only focusing on pre-existing conditions for this question.
    - Chair Urbina explained that the project team can modify the questions if desired.
    - Jean-Pierre and Dr. Li confirmed that the project team can modify the questions. Dr. Li also discussed the additional findings found in both approaches relating to psychosis. A risk of bias assessment would need to be completed as these are case-control studies which may adjust our certainty of evidence. Dr. Li offered two potential systematic reviews that can be carried out but will follow up after the latter approach is discussed.
    - Chair Urbina asked Dr. Riggs if she agrees with the available literature that is relevant to the broader use of THC, not limited to concentration.
        - Dr. Riggs is comfortable with the question framework, and it being limited to pre-existing conditions, since they are discussing a broader literature of psychosis being an outcome.
        - Chair Urbina clarified that this question is limited to high-concentration THC products. Is the same issue relevant to the broader outcome of interest?
        - Dr. Riggs agreed. There is a sparse literature distinguishing the effects between high and low concentration products to address this question. There is a broader body of literature that would address the relationship of pre-existing mental health conditions and cannabis use regardless of concentration used. The project team has to address these limitations in the report.
    - Dr. Greg Kinney commented that he agrees with Dr. Riggs. The legislature asks specific questions, and we may want to provide feedback on the specific questions asked. The team should state the context that we see rather than the context that they came with. Dr. Riggs agrees.

Policy Motivated Question 4

- Jean-Pierre Oberste explained that the project team has skipped question 3 regarding potency thresholds due to the expansive data that will requrie more time. He proceeds to review question 4 regarding pregnant and nursing women being more susceptible to harmful health outcomes and are infant and children with prenatal and postnatal exposure to high-concentration cannabis products more susceptible to harmful health effects. The data is not well captured, 9 studies addressed an association between the use of high-concentration products and health outcomes, but none showed a direct association to answer the question. There is no evidence to answer this question from the evidence map.
- Dr. Li added that this question was posed by the SRC during the last meeting and no studies meet the relevancy criteria.

Question and Answers

- Dr. Wymore explained that she is concerned with the wording of the question and how it may be interpreted in relation to safety. The limitations are how the project team structured the data query and she suggested a disclaimer. Otherwise the interpretation will be misconstrued with the understanding that there are no deleterious effects, which is incorrect.
    - Dr. Riggs agrees completely.
    - Dr. Samet commented that if the project team were dealing with tobacco, they would cite the Surgeon General's reports, outlining what is known and what has been looked at by authoritative sources. However, the project team has a mandate from the legislature, and it would be overwhelming to conduct a systematic review for each area of interest. It is important to be communicative and pose information about what is known generally and what is known in the limited literature about high-concentration THC products. Are there sources that have the weight of a Surgeon General's report, up front to illustrate where the literature stands. And note that in this report, we are answering more limited questions posed in the eye of future policy measures.
        - Dr. Riggs asked in relation to tobacco, what is the state of the evidence of high-nicotine products associated with negative outcomes? If we found 2-3 studies associated with these claims, wouldn't there be concern that it would not obscure the substantive data that there is no safe level to smoke the product at.
        - Dr. Samet clarified responding that the project team can begin with a broader context and then focus. The project team is trying to sort out the methodologies to use and what are the right policy questions to ask, especially in relation to high-concentration THC products. How do they communicate the narrower set of questions in the context of what might be known generally about THC containing products; is there any good starting point that they should look at?
        - Chair Urbina asked can the project team add a disclaimer or links to additional systematic reviews that are available and talk about marijuana in general or low-dose marijuana use in these same policy question that they are raising so that people can go to the literature and see the associations and their concerns to avoid making a blanket statement that there is no evidence to support adverse effects with high-concentration. He agrees that someone may interpret this incorrectly.

- Dr. Wymore said that the interpretation is not that limiting evidence means safety in use. She suggests adding a couple of bullets that summarize the findings, that the project team was limited and limited their scope, therefore when they only address those questions mentioned then they are not accounting for lower concentration use. The project team must be clear from the beginning that this is evolving literature. The limitation of the literature is that it does not specifically quantify dose-response relationships. It must be highlighted as some may interpret this as there is no effect and safe to use in pregnancy and lactation, which Dr. Wymore feels strongly that that is not true.
- Dr. Bero emphasized the importance of this discussion and that we need to have the context and framing of the questions. This would not be a limitation of the review because a limitation would be an unfocused and not answerable question, but the reviews are strong with adequate context and framing in place. If the project team was producing clinical guidelines, they would provide indirect evidence that does not directly answer the policy question but that gives us context of THC generally or with certain disorders. This is where the project team could use the SRC's help. The project team could cite upfront the indirect evidence and what they generally know about THC, but they have been asked to answer these focused questions and, as a result, do not find much. Dr. Bero believes it would be beneficial to add the disclaimer in the context of no evidence is not evidence of no effect. Dr. Bero asked for key references to build up the context.
    - Dr. Riggs is on board and explained that when evaluating high-concentration products and these questions there was not significant evidence, that is not to say that there is not any boarder literature that shows any evidence. The project team must cite what the broader literature shows.
    - Dr. Wymore appreciated the response and thinks it is something the project team can include and/or focus on in the report.
    - Dr. Bero states that they do not have an equivalent reference like the Surgeon General's report to cite. It would be beneficial for the group if some citations could be sent over to be included in the background section.
- Dr. Wymore asked for a call to action to encourage investigators to use or state a standard dose or concentration of product used. The current literature lacks standardization and the project team is grappling with exposures that are variably described.
- Dr. Samet agreed that it is a gap and broad limitations need to be addressed.
- Dr. Wymore said she will send over a piece of literature regarding a call to action to researchers to be more robust in their definition of exposure.

Discussion of the Bottom-Up Approach:

Respiratory Health Outcomes

- The “bottom-up” approach was described, involving interrogation of the evidence map to identify those strata of the evidence map that are sufficiently robust for carrying out systematic reviews of policy relevance.
- Dr. Samet explained the findings for respiratory outcomes. The project team had 55 studies addressing respiratory outcomes, two researchers reviewed the findings and different measures into broad categories. Neeloo Soleimanpour and Dr. Samet explained how the conclusion tables were developed that were placed in the appendix of the report. Dr. Samet and Neeloo discussed how they tried to organize the findings of these studies that related to respiratory outcomes. Dr. Samet walked through the evidence description they found when reviewing the studies included for this outcome of interest.

Questions and Answers

- Chair Urbina asked for an example from one of the studies in the appendix table to be described further.
    - Neeloo explained how the data was extracted including population, exposure, study type, outcome, symptoms, and key results. These items were used to identify commonalities between the vast number of studies included.
    - Dr. Samet also expanded on the purpose of the tables and how they tried to organize these wide range of studies and determine and overlapping conclusions. He emphasized the amount of time it takes to complete the bottom-up approach.
- Dr. Riggs asked how nicotine and vaping and mixed groups were being addressed and controlled for.
    - Dr. Samet acknowledged that this is an area being covered in youth and their use of combustible products. Some studies are being addressed in California.
    - Chair Urbina believes this is an important question and if it is being asked then the project team should address how to distinguish studies addressing THC alone from those addressing THC and tobacco use together.
    - Dr. Kinney asked if there were any studies that met the criteria for exposure that have CT outcomes.
        - Dr. Samet responded that no studies illustrated that.
    - Dr. Bero commented on co-exposures and if the project team proceeds to the point where they conduct formal systematic reviews on any groups of these studies then one of the tools for assessing the risk of bias would account for the co-exposures in a particular study were being accounted for and how. This would have to be done for each individual study.
- Dr. Wang explained the common knowledge that excessive use of THC can depress respiratory and provided additional literature to support these findings.

Select Mental Health Outcomes

- Dr. Wang explained the bottom-up approach for psychosis and schizophrenia outcome of focus where Neeloo and Dr. Wang followed a similar approach to how Dr. Samet and Neeloo evaluated the respiratory health outcomes. Dr. Wang highlighted some findings from this pool of studies that met the inclusion criteria. Most studies were conducted recently except for one study before 2005, but most were after 2010. Dr. Wang outlined the findings after the studies

were filtered and categorized with the outcome of interest. Papers were explained by study type and exposure product type following high-concentration THC use. There was no standardized way to report the symptoms of psychosis and schizophrenia.

Question and Answers

- Chair Urbina asked if these conditions were general or pre-existing.
    - Dr. Wang clarified that there was a combination, an effect of heterogeneity of these studies.
- Dr. Samet commented on the time and effort it takes to review this literature.
- Dr. Riggs encouraged distinguishing between the diagnoses of psychosis and schizophrenia despite the interchanged terminology in the studies..
    - Dr. Wang agreed and addressed why the project team included both conditions.
    - Dr. Riggs said that the project team needs to be clearer between the conditions and if there is no clear diagnosis of schizophrenia, then the classification is not schizophrenia.

Discussion:

- Dr. Samet asked if the group had any additional policy motivated questions after looking at the report further.
    - Chair Urbina asked where to send questions to and if there are any policy or research questions to be made.
    - Dr. Samet advised remarks to be sent to Meghan Buran to collect and send to the Cannabis Research & Policy Team, hopefully by first week of January.
- Chair Urbina asked if this research will be ongoing and will the evidence map be continually updated.
    - Dr. Samet responded that ideally, the project team would have funding to sustain the evidence map as they had about ~12,000 included in the updated analysis. The project team will have to discuss what will be made publicly available and what can be made publicly accessible.

No further questions or remarks from the group.

Progress Update on the Educational Campaign:

- Dr. Sheana Bull presented on the progress to date of the educational campaign. 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. This is done through advisory groups who are being created including the intended audience and asking guidance for where and how to disseminate messages. Groups will start to convene in January and identify liaisons to establish diversity amongst each group.
- 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.
- Dr. Kinney, Riggs, Brooks, and Wymore are willing to help with the advisory groups.

Questions and Answers

- Chair Urbina and Dr. Wymore explained that there is increased cannabis use in reproductive aged women, perinatal, pregnancy, and post-partum use and advised this is dramatically needed to be addressed in our campaign.
    - Dr. Bull explained that her team must proceed with caution in who is included in the advisory groups.
- Dr. Lesley Brooks asked that they focus on those who have been, are and after being pregnant as well.
- Dr. Kinney asked if an elderly population (+70) is being included in the advisory groups.
    - Dr. Bull responded that they are currently in the process of identifying who should be participating in these groups. Those who have used it for a long period of time have different viewpoints, but a wide range of users will be included.
- Dr. Brooks asked if there will be a rural focus.
    - Dr. Bull said "yes", and countered is there a particular region in Colorado to target, rural, urban, mountain, etc. (e.g., does one area have more hospital visits as a result of use than another?)
    - Dr. Brooks thinks it would be one rural population to make a conclusion about all rural regions may be of concern. Also, a group that may be of assistance is an agricultural population and asking them to weigh in, especially chronic pain in this population.
- Dr. Wymore asked if the team can expand the education campaign to dispensaries, industries, and healthcare providers.
    - Dr. Bull stated that her interpretation of the campaign charge is rather broad. They cannot use one campaign, rather targeted campaigns for each population.
- Dr. Samet acknowledged the complexity of this campaign.
- Dr. Brooks discussed intersectionality with a variety of multiple institutions and the need to educate all involved in this field. Not all understand medical guidance especially in the criminal justice field.
    - Dr. Bull responded that one liaison that is helping form the community advisory group does work with juvenile justice care providers, which is one part of the team's focus and attention. Dr. Bull wants to populate advisory groups with those who have directly or indirectly been affected by the juvenile or adult justice system pre-legalization to speak to messaging and stigma. Dr. Bull will keep in mind how to address prescription use and pain management.
    - Dr. Brooks emphasized those who are supervising these individuals and the consequences if populations are misinformed or undereducated on this matter.
- Dr. Kinney mentioned the idea of word medicine and asked if the team has a pharmacologist available on this as the team does not have instructions for OTC medicine dosing and self-titrating.
    - Chair Urbina mentioned that this discussion will continue in the next meeting.
- Dr. Samet concluded that the campaign must be framed in the scope of our mandate and it may be done in a broader context.

No further questions or comments for Dr. Bull.

Next Steps from the Cannabis Research and Policy Team:

- Dr. Samet provided a review of the next steps for the Cannabis Research and Policy Team and the overall tentative timeline. They hope to have a report submitted by the end of February that addresses key policy questions and highest priority bottom-up approach questions with help of priorities from the SRC which may include recommendations for the future and a request for ongoing funding.
- Chair Urbina mentioned the project team will plan to have another meeting in late January/ early February, to follow up on the progress the Cannabis Research & Policy Team has made.
- Chair Urbina commended the Cannabis Research and Policy Team for their work.

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

Next Meeting Timing and Closing Remarks:

- No final questions or comments.
- Meeting Adjourned 1:56 pm (MT).