
12 Steps to EAST Practice Management Guideline (PMG) Development, 2nd Edition



Eastern Association for the Surgery of Trauma
Advancing Science, Fostering Relationships, and Building Careers

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January 2022

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12 Steps to EAST PMG Development



1. DECIDE ON PRACTICE MANAGEMENT GUIDELINE (PMG) TOPIC

- Select a topic for the Guideline in an area of enthusiastic interest where you feel you can contribute something meaningful to current clinical practice.
- Ensure that no other societies already have a Guideline in place for the exact same topic (survey Western Trauma, AAST, other non-surgical societies that may be relevant to the topic, etc).
- Do a quick literature search to ensure there are enough data available on the topic. The importance of this step cannot be overstated! Time and effort spent on developing PICO questions for a topic with little or no available literature is not time well spent.
- During this brief literature review, note what questions are commonly being asked, what comparisons made, and what outcomes considered. These will prove very helpful in informing the PIC stems and outcomes to be considered. Trying to develop a guideline with questions no one else has asked and outcomes no other investigator has considered can be a frustrating exercise in futility. Thankfully, this is avoidable with a quick, early literature search. GRADE methodology adheres to a priori development of PICO questions, so ensure that your formal literature search is not conducted until after your PICO questions are finalized.
- **Duration: 2-3 weeks**

2. SUBMIT YOUR PROPOSAL & BUILD YOUR TEAM

- Use your EAST network to identify peers who share your excitement about the topic you have selected and recruit them to participate!
- Visit <https://www.east.org/education/practice-management-guidelines/guidelines-under-development/proposal> to submit and provide details for your PMG proposal. If/when approved, it will be posted on the EAST website which will likely prompt more volunteers to sign up!
- Estimate how many members you would need on your team in total. The EAST Guidelines Committee maintains a list of volunteers, that can be proactively approached to join your team, based on interest and availability. Notify Rachel Dixon (rdixon@east.org) with the number of additional members you anticipate you will need, and we can enlist them for you!
- While topic experts are desirable in the team, ensure that opinions held by team members among the team are well-balanced, and there are no conflicts of interest.
- All team members need to be EAST members! Exceptions can be made when required expertise is unavailable within the EAST community (e.g. an orthopedic surgeon may be involved in orthopedic injury PMGs) and for trainees (medical students, residents, and fellows).
- As your team is assembled, contact your Task Force leader (Rachel Dixon can direct you to the appropriate person, depending on whether your PMG falls under the umbrella of Critical Care, Emergency General Surgery, Injury Prevention or Trauma) for the first 1-on-1 guidance call. During this call, the first steps towards PMG development (group assembly, literature search, Covidence access, abstract and full text review) will be reviewed in detail.
- Set up a conference call among group members (Rachel can also help you with this) to start getting to know each other, exchange contact information, inquire about each other's practice patterns on the topic of interest, and start identifying potential questions and outcomes that could/should be addressed. Review the notes you gathered from your brief literature search in the previous step, so everyone has realistic expectations about the available literature.
- It is a good idea to keep notes of what is discussed during each conference call, and share afterwards with everyone on the team, including those who were unable to participate. Good communication helps bring everyone up to speed!
- **Duration: 2-3 weeks**

3. FORMULATE PIC STEMS, VOTE ON OUTCOMES, FINALIZE PICO QUESTIONS

- Once you have decided on specific topics/questions to be addressed, based on team preferences and what literature already exists, start framing these questions in the **PICO** format: Decide on a specific patient population (**P**) (e.g. patients with high grade blunt splenic injury), and pick two methods that can be used to address the problem at hand, the Intervention (**I**) and the Comparator (**C**). (e.g. angioembolization vs splenectomy). '**O**' refers to the outcomes, which are discussed below.
- These are best and most efficiently decided via email discussions, although a conference call may be helpful if there are differing ideas about how best to frame the PIC stems. Ensure you include everyone in the group!
- Whenever you ask for feedback on PIC stems, outcomes, or other considerations, set a deadline to respond (around a week), and set expectation that you will consider non-responding group members to be in agreement with the proposed questions/outcomes/results. If you are not receiving feedback/responses from a few members repeatedly, contact them individually to ensure they are still interested in the project.
- Avoid addressing topics that have very obvious answers and have been the standard of care for decades (e.g. In patients with gunshot wounds to the abdomen presenting with hemodynamic instability and peritonitis, should immediate operative intervention vs observation be considered), but areas where management is still reasonably controversial and variable (e.g. In patients with persistent neck pain after blunt trauma and negative CT imaging, should MRI imaging be obtained vs prolonged c-spine immobilization), or topics where new technology and interventions have recently become available (e.g. In patients with hemorrhagic shock after penetrating trauma, should thromboelastography be used to guide resuscitation vs low-ratio component therapy)
- Remember that each outcome requires its own literature search, abstract & manuscript review, data extraction and analysis, so choose wisely the number of questions / outcomes you want to address. 2-3 PICO Questions with 1-4 outcomes each is a good number for a PMG.
- With the PIC stems available, it is time to decide on the Outcomes (O). Come up with a broad list of potential outcomes for each PIC stem, both specific to the studied topic, plus some broad commonly measured outcomes (e.g. mortality, ICU LOS, hospital LOS, duration of mechanical ventilation, etc). Consider outcomes commonly seen in reviewed literature from Step 1 to help formulate this list. Aiming to do a review and meta-analysis on outcomes that have not been previously studied will be fruitless. Share with the group and ask for suggested outcomes . Best done via email, not conference call.
- The outcomes are specific to and tailored to each PIC stem, and different PICO questions covering the same topic may cover different outcomes.

- When the final list of potential outcomes for each PIC stem is available, send again to the group, and ask everyone to rate each outcome on a scale from 1-9, with 9 being very important, and 1 of very little importance. Stress that each rating should be specific for the PICO question asked: e.g. although survival is obviously the most important outcome overall, it should not be rated as the most important when the intervention studied is a form of analgesia. Pain control should be the most critical outcome for such a question as it is the most relevant outcome.
- Stress that each member has to respond to you privately (so they do not influence one another). Set a small internal deadline, as discussed earlier. Send individual emails to those who have not responded . You need a rating for each outcome for each PICO from every member of the group!
- Calculate the means of the ratings for each outcome for each question - there can only be up to 7 per PICO question. Even that is too many usually, as each outcome requires its own analysis. You may have to typically limit to just the critical ones (those with a rounded mean of 7-9), and perhaps the important ones (those with a rounded mean of 4-6). The outcomes of limited importance (rounded means of <4) are typically not studied.
- Keep track of the list of outcomes and their ratings for each PICO question, as this process is commonly included in the manuscript!
- When the PICOs are final, please share with your Task Force leader, Committee chair and vice-chair - they will need to approve the final PICO questions. Minor edits are not uncommon.
- **Duration: 4-6 weeks**

4. REGISTER WITH PROSPERO

- Register your project with PROSPERO (<http://www.crd.york.ac.uk/PROSPERO>) – ideally before the literature search, and definitely before data extraction! Takes approximately 30 minutes! You describe the project in a few words, and state what questions you will be addressing. The purpose of this registration is so that questions do not change after the results of the review, and to show other potentially interested investigators around the world that a team is already working on the topic.
- Remember to visit again at the end of the project and update your registration with your findings / recommendations.
- For a step-by-step guide on how to complete this registration, please view **Appendix A**.
- **Duration: 30 minutes**

5. SYSTEMATIC LITERATURE SEARCH & REVIEW

- Use your institution's librarian for your literature search if they have experience conducting systematic literature searches. Please ensure that at least 3 different search engines are queried. The most commonly used ones are PubMed, Cochrane, Embase, and Web of Science. If you do not have access to a librarian, please contact your Task Force leader to get you in contact with one of five academic libraries available to our Committee to help you with the search. (Duke University, Yale University, Tufts University, Washington University and Texas Christian University).
- The librarian will ask for some input to build the search strategy. Try to use broad search terminology, especially if you are aiming to do just one literature search for all PICO's combined (have librarian use Boolean terms). Keep track of the exact terms / methodology used, as this will be included in the manuscript submission as an e-supplement.
- The librarian will provide you with a file in appropriate file format to upload to Covidence.org. References can be imported in the EndNote XML format, the PubMed format, or the RIS text format. Ensure your librarian provides you with the results of the literature search in one of these.
- Rachel will give you and your team members access to Covidence.org, a service that enables management of your systematic review online, and will be provided to you through EAST free of charge. A blank systematic review will already be created, to which the literature search results will have to be uploaded.
- Once the literature search results are online, invite your team members to start reviewing them. Every abstract is reviewed by two independent reviewers, and conflicts are adjudicated by a third. Options for each abstract include 'Yes', 'No' and 'Maybe', on whether they should be considered for inclusion in the final analysis. Every abstract is reviewed by two independent reviewers, and conflicts are adjudicated by a third. The whole process is organized and tracked by Covidence, so you can easily see the amount of work contributed by each team member, and automatically create the Prisma flow diagram for your project.
- Stress that the abstract review is best done on mobile devices. The majority of abstracts may be easily screened out by merely looking at the title alone, and one can easily screen hundreds of abstracts in a short period of time. The reason for exclusion does not need to be recorded at this step.
- For abstracts to be included in the next step (full manuscript review), they need to include a patient population similar to the one you are studying, and must include groups with the two interventions being compared (or a single group before and after the intervention) in your PICO. Commentaries, reviews, case reports/series, animal studies and studies published in languages other than English are typically excluded. Although meta-analyses on the same topic are also excluded, they can be useful to help identify literature that should be included in your PMG.

- In rare instances when there is not enough literature comparing the intervention against the comparator, case studies and case series may be analyzed, based on principles included in the guide at this [link](#). This essentially describes how to conduct a qualitative and quantitative synthesis from case reports and/or series, provided they meet certain objectivity criteria, and there are similarities and obvious trends across patients who were managed with the same intervention, and that led to similar outcomes.
- Cheerleading emails to the entire group, providing a progress tracker and emphasizing the work of the 2-3 most productive members (easily found in Covidence) every 1-2 weeks are recommended, as a way to keep the entire team energized and engaged.
- When this step is complete, communicate with your librarian, who can upload full PDFs of the selected manuscripts on Covidence for full text review. Ask your team members for PDFs that may not be available in the literature search-conducting library. They may be uploaded directly to Covidence.
- Invite your team members to conduct the full text review at the next step. Again, every manuscript is reviewed by two independent reviewers, and conflicts are adjudicated by a third. The inclusion / exclusion criteria are still the same, but this time the reason for the exclusion should be noted. The most common ones are: not in English; commentary; review/meta-analysis; case report/series; animal study; dissimilar patient population; dissimilar intervention/comparator; etc.
- Of note, retrospective studies should include similar patients in their comparisons, or have used some kind of matching algorithm to be considered for inclusion. For example, assessing the efficacy of hemostatic interventions for isolated splenic injury, similar proportions of splenic injury grades should be included in both groups. If a paper demonstrates that one intervention (e.g. observation) is clustered around low grade splenic injuries, and another (e.g. angioembolization) around high-grade injuries, it should not be considered for inclusion.
- Full text review typically requires a larger screen (e.g. desktop, laptop, tablet), as the full text PDFs need to be reviewed.
- At this stage, as a team lead, consider quickly reviewing all full manuscripts marked for final inclusion as the first reviewer, so you have a broad idea of the available literature.
- Cheerleading emails to the entire group, providing a progress tracker and emphasizing the work of the 2-3 most productive members (easily tracked on Covidence) every so often are again recommended, as a way to keep the entire team energized and involved.
- When this step is also complete, contact your Task Force leader to set up the second 1-on-1 guidance call. During this call, the remaining steps towards PMG development (data extraction, meta-analysis, evidence grading, manuscript drafting and submission) will be

reviewed in detail, and templates will be shared for data extraction, manuscript and figure/table drafts.

- **Duration 8-12 weeks**

6. DATA EXTRACTION

- Edit the data extraction templates (shared to you from the previous step) to include your project's patient populations and outcomes (separate ones available for continuous and binary outcomes) and share with your team members. Ask team members to start populating the template with data from the manuscripts marked for analysis.
- This step again needs to be conducted by two independent reviewers/data extractors, and any conflicts adjudicated by a third.
- It is a good idea to do the data extraction from all included manuscripts as the first reviewer/data extractor, as you will be the only team member with a good grasp of all data available, if the volume is manageable.
- **Duration: 4-6 weeks**

7. META-ANALYSIS

- To conduct the meta-analysis and generate the Forest Plots, you will need to create an account with RevMan.
- For a Step-by-Step guide of how to register and use RevMan, please refer to **Appendix B**. Links to YouTube tutorials are also available there.
- Separate the prospective randomized clinical data (if available) from the retrospective cohort data in the meta-analyses (separate Forest Plots for each).

- **Duration: 2 weeks**

8. ASSESS QUALITY OF EVIDENCE, GENERATE GRADEPRO TABLES

- To grade the quality of available evidence, you will need to register with GradePro.
- For a Step-by-Step guide of how to register and use GradePro, please refer to **Appendix C**. Links to YouTube tutorials are also available there.

- **Duration: 2 weeks**

9. CREATE RECOMMENDATIONS, VOTE ON STRENGTH

- When the Forest Plots and the GradePro tables are available, set up a second team conference call through Rachel, to discuss results and formulate recommendations.
- The results of the Forest Plots essentially guide the Recommendations. If there are multiple outcomes that go in different directions with implementation of the studied intervention (improvement, no change, deterioration), then the primary outcome (for which the intervention should be considered) guides the overall recommendation. For example, in a comparison between two different analgesia techniques, the one that improves pain the most should be recommended. Similarly, in a comparison of hemostatic interventions, the one that leads to less blood loss or fewer transfusions should be recommended. Differences in secondary outcomes (survival, length of stay, thromboembolic events) should be considered in creating the recommendation, but should not be the primary drivers .
- If there are enough prospective randomized data (typically at least 3 studies) that tackle the same PICO question, they can help formulate a recommendation with confidence. If the retrospective data corroborate those from the prospective studies, the confidence in the recommendation is greater. If the retrospective data contradict evidence from the prospective randomized studies, follow the direction of the prospective data.
- In formulating the recommendations, follow the highest quality data for the most benefit in the critical primary outcome, and follow the lowest quality data for the harmful critical outcomes. The Quality of Evidence for the harmful critical outcomes outweighs the Quality of Evidence for the beneficial critical outcomes. (Important outcomes can be ignored in making recommendations, if the risk for harm is considerable).
- Decide on the strength of the recommendation for each PICO: **Strong** (should be the new standard of care) vs **Conditional** (intervention should be employed in the majority of applicable cases). To decide on strength, consider:
 - The quality of the evidence;
 - The risk-to-benefit ratio of implementing the recommendation and potential side effects that may arise;
 - Patients' values / wishes;
 - Cost and resources needed to implement the recommendation;
 - Acceptability among physicians and patients;
 - Feasibility.
- For a recommendation to be strong, at least 70% of the group has to approve a strong recommendation.
- The final recommendations need to be approved by the entire team. If there are differences in opinion, those can be addressed with a second conference call, or series of emails, where each party can express their opinion and the reasons for their voted recommendation.

- When consensus is achieved, word your recommendations as if they were a direct answer to your PICO question. (e.g. In adult penetrating trauma patients who present with hemodynamic instability and peritonitis, we recommend immediate operative intervention)

- **Duration: 2-3 weeks**

10. DRAFT MANUSCRIPT

- Time for manuscript writing! A manuscript draft is available, and should have been made available to you during the 2nd 1-on-1 guidance call with your Task Force leader.
- This template includes information and guidance on what to include in each segment of the manuscript.
- Once the manuscript and related Figures, Tables & Supplementary Material are drafted, circulate within your team, and allow 1-2 weeks for feedback and edits. The entire team needs to approve the manuscript before the next step.
- **Duration: 3-4 weeks**

11. SUBMIT TO EAST FOR INTERNAL BLIND REVIEW

- When the entire team has approved the manuscript draft, submit to the Guidelines Committee chair for blind review, indicating clearly that it has been approved by the entire team, and is being submitted for the blind review.
- Once all reviews are in, the Committee Chair will respond with a structured review that includes critiques, comments, and suggested edits. Edit your manuscript based on this feedback, as if you were responding to a journal's reviewer comments, and send back to the Committee Chair.
- Once reviewers are satisfied with the edits, you are cleared to submit to the Journal of Trauma (or other target journal).
- **Duration: 4-6 weeks**

12. SUBMISSION TO TARGET JOURNAL

- Good luck!
- Don't forget to sign up to help with other PMGs in development!
- **Duration: 1 afternoon**

APPENDIX A

PROSPERO Instructions for Registering Systematic Reviews

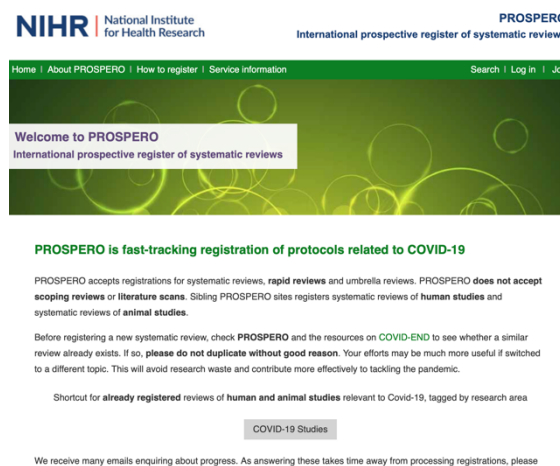
Jennifer Freeman, MD FACS

Aim:

These instructions will cover using the PROSPERO website for registering systematic reviews.

Instructions:

1. Visit <https://www.crd.york.ac.uk/prospero/>
 - a. Access is free.
 - b. Click "Join" in the top right corner if you do not yet have an account.
 - c. Sign up with your name, address, email, password, phone number, organization, and country. The other check boxes are optional.
 - d. Click "Save Details"
 - e. Enter username and password to login



2. Scroll down to "Search PROSPERO" and verify that there is not already a registered study which matches your current project. If there is, PROSPERO will likely not accept your study. If not, proceed with registration.
3. Go back to the home page. Scroll down to "Register you review now" and click.

COVID-19 Studies

We receive many emails enquiring about progress. As answering these takes time away from processing registrations, please email only if absolutely necessary. We are working hard to process registration requests as quickly as possible. **If your enquiry is related to a COVID-19 registration please add #COVID-19 to your subject line.**

If you do not already have a PROSPERO account, you will need to create one to register a review

Register a review

Registering a review is quick and easy. Just follow these simple steps to register your review in PROSPERO

[Register your review now](#)

Accessing and completing the registration form

Search PROSPERO

Search for PROSPERO registrations by entering words in the record or the registration number below

[Go](#)

Important notice

To allow the PROSPERO team to focus on COVID-19 and to avoid further delay, during the pandemic all submissions that have been waiting for registration for more than 30 days and which pass a basic automated check will be published automatically. The PROSPERO team will not check these submissions; this will be stated clearly on the published record. Records will be published exactly as submitted; therefore extra care should be taken to ensure that submitted information is accurate. Submissions which do not pass the basic

4. Click the purple human studies button.

NIHR | National Institute
for Health Research

PROSPERO
International prospective register of systematic reviews

Home | About PROSPERO | How to register | Service information
Search | My PROSPERO | Logout: Jennifer Freeman

Registering a review is easy. Please read the guidance notes for registering a **systematic review of human studies** or a **systematic review of animal studies relevant to human health**, then just follow the five step process below.

- Step 1** Check the inclusion criteria to make sure that your review is eligible for inclusion in PROSPERO
- Step 2** Ensure that your review protocol is in its (near) final form and that no major changes are anticipated at this stage - e.g. if your protocol will be peer reviewed it will usually be sensible to wait until this is complete before registering.
- Step 3** Search PROSPERO to ensure that your review has not already been registered by another member of your team
- Step 4** Search PROSPERO to ensure that you are not unnecessarily duplicating a review that is being done by another team or has been registered previously
- Step 5** Start registering your review

Register a systematic review of health research studies (study participants are people)

Register a systematic review of animal research studies (study subjects are animals) that is of direct relevance to human health

5. Next is a series of questions to be answered as below:
- a. “Yes” for English submission.
 - b. “No” for scoping, literature or mapping review.
 - c. “Yes” for outcome related to human health
 - d. “No” for Cochrane review
 - e. “No” for training course
 - f. “Yes” for searched for similar reviews
 - g. Select the appropriate selection.
 - h. “Yes” for protocol
 - i. “Yes” for more than one person involved
 - j. “Yes” for you intend to publish
 - k. “Started” for preliminary searches
 - l. “Not started” for the remainder of the selections.
6. Click “register your review” to open the next section

7. This is the body of the application where you will enter all of the information detailing your project. At this point, you can save your submission in order to come and go as needed.
 - a. Review title – enter the title of your project
 - b. Original language title – skip
 - c. Anticipated or actual start date – estimate when you think your library search will be done
 - d. Anticipate completion date – estimate when you think the project will complete
 - e. Stage of review at time of submission – should copy from your previous screen
 - f. Named contact – should prefill
 - g. Named contact email – should prefill
 - h. Named contact address – should prefill
 - i. Named contact phone number – should prefill
 - j. Organizational affiliation – should prefill
 - k. Review team members – do not need to add entire team
 - l. Funding sources – add any funding that needs to be disclosed
 - m. Conflicts of interest – fill out as appropriate
 - n. Collaborators – usually skip
 - o. Review question – enter your PICO
 - p. Searches – Enter MEDLINE, EMBASE, Cochrane, and Web of Science for sources. Provide your inclusion and exclusion criteria.
 - q. URL to search strategy – skip
 - r. Condition or domain being studied – briefly describe the condition your project will be studying
 - s. Participants – Describe your study population from your PICO
 - t. Intervention – from your PICO
 - u. Comparator – from your PICO
 - v. Types of study to be included – describe your inclusion and exclusion criteria
 - i. Ex: Prospective trials and retrospective cohort/case-control studies that compared embolization to control patients are eligible for inclusion and will be retrieved. Case reports, commentaries, reviews, editorials, and animal studies will be excluded.
 - w. Context – skip
 - x. Main outcomes – from your PICO
 - y. Measures of effect – usually odds ratio
 - z. Additional outcomes – enter “none”
 - aa. Data extraction – list inclusion criteria and data points which will be extracted
 - i. Ex: Data extraction from each included study will be performed using a standardized data collection sheet and performed in duplicate. Data extracted included authors, journal, publication year, study design, number of patients in embolization, splenectomy and control arms, and the critical outcomes previously outlined.
 - bb. Risk of bias assessment – describe how studies will be assessed for bias

- i. Ex: Publication bias will be evaluated using the Egger test, and the GRADE framework will be applied to all quantified outcomes for assessment of bias, publication bias, inconsistency, imprecision, and indirectness. Evidence profiles will be created for the PICO question using GRADEpro GDT software (GRADEpro Guideline Development Tool. McMaster University, 2015).
 - cc. Strategy for data synthesis – describe your meta-analysis plan
 - i. Ex: Meta-analysis will be performed in Review Manager (RevMan, 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) with random-effects modeling to generate forest plots. Treatment effects will be calculated with each study weight being proportional to the number of subjects it contributes to each outcome analysis. For continuous outcomes, differences in mean will be calculated, while for the binary variables, odds ratios will be calculated for the intervention against the comparator groups. Heterogeneity will be calculated and quantified with I^2 . High heterogeneity was considered present for I^2 values >75%, moderate for I^2 values of 50-74%, and low if I^2 <50%.
 - dd. Analysis of subgroups – none
 - ee. Type and method of review
 - i. Click “Meta-analysis”
 - ff. Health area of review
 - i. Click “Wounds, injuries, and accidents”
 - gg. Language – English is already selected
 - hh. Country – should prefill
 - ii. Other registration details – skip
 - jj. Reference for protocol – skip
 - kk. Dissemination plan – Click “Yes” for intend to publish. In the box, type “Work will be presented at Eastern Association for the Surgery of Trauma annual meeting and published in the Journal of Trauma.”
 - ll. Keywords – Enter your keywords
 - mm. Details of existing review of same topic – skip unless you are performing an update
 - nn. Current review status – should prefill
 - oo. Any additional information – skip unless you feel something needs clarification
 - pp. Details of final report – skip
- 8. Click “Submit” once you have filled everything out.

APPENDIX B

Review Manager (RevMan) Web Instructions for Creating Forest Plots

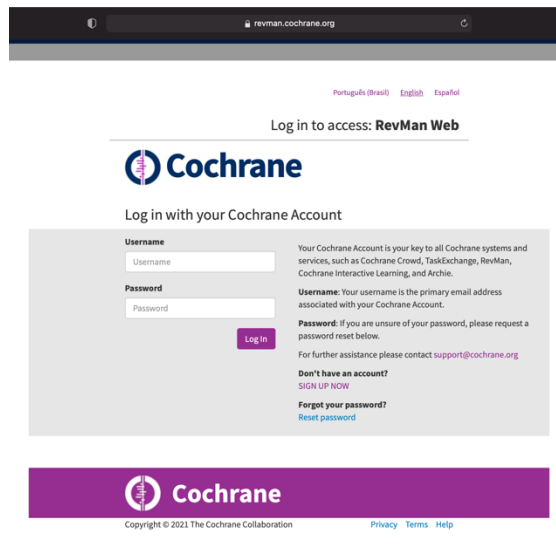
Jennifer Freeman, MD

Aim:

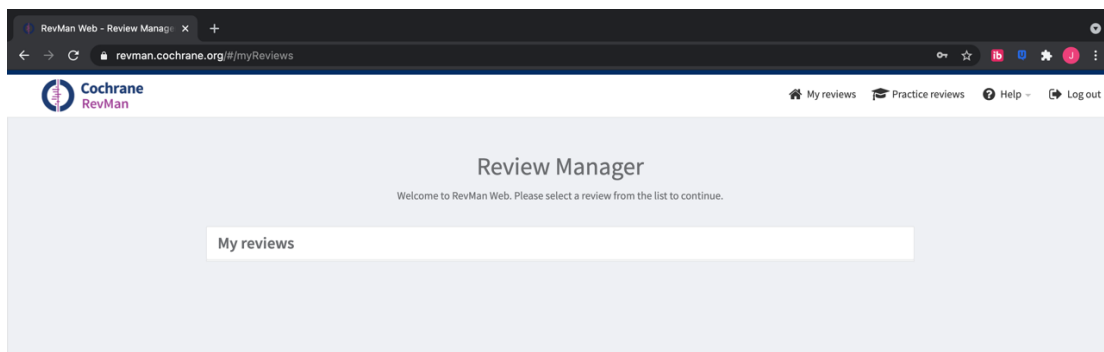
These instructions will cover using the RevMan Web software to create forest plots. The software has other team management functions that are outside the scope of this document.

Instructions:

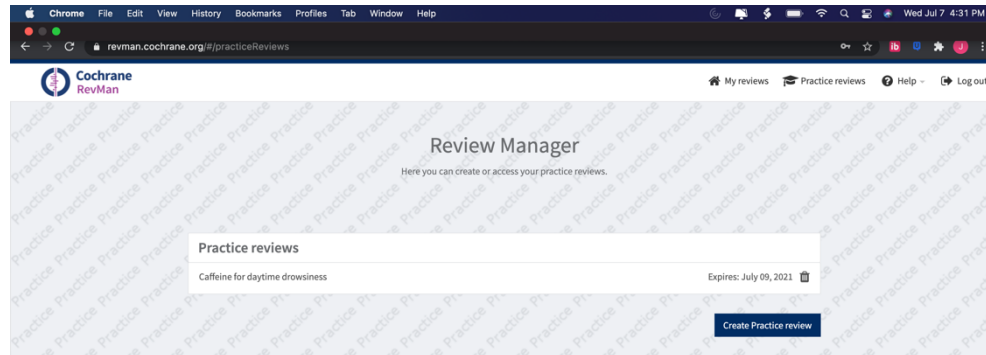
1. Visit <https://revman.cochrane.org>
 - a. RevMan suggests using Google Chrome for best functionality.
 - b. Access is free.
 - c. Sign up with your name, email, password, and agree to the terms.
 - d. Enter username and password to login



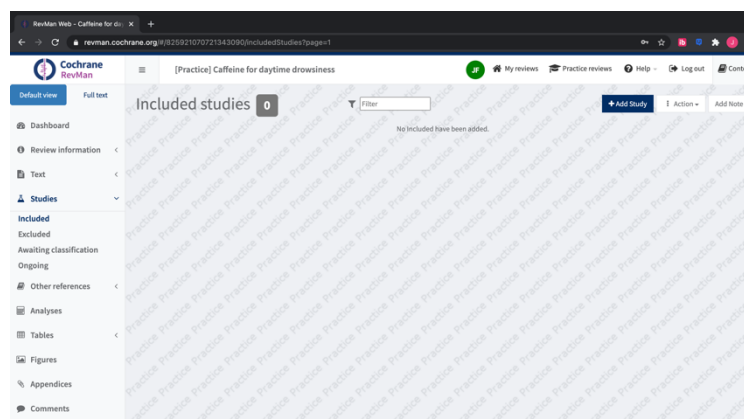
2. Click "Practice Reviews" in the top right corner



3. Click “Create Practice Review” to start working with your data. Select “Use Template Review” to open all features.

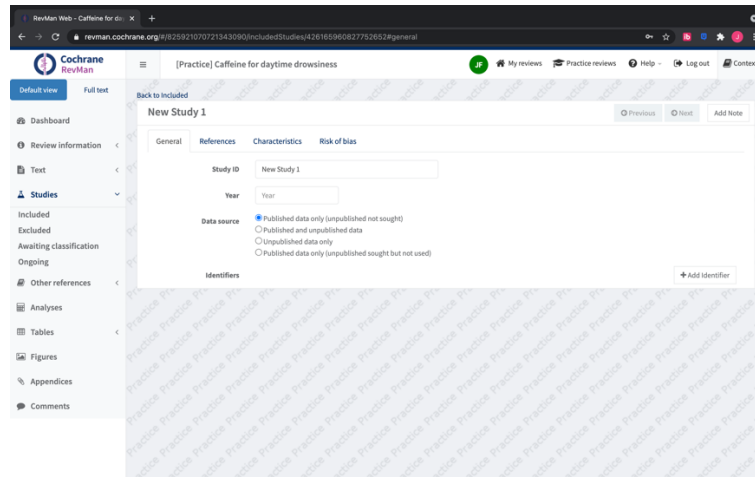


4. Click "Studies" from the toolbar on the left. Select "Included". You will need to delete all the preloaded studies by clicking the trash can by each one. You are ready to start adding your studies when the screen looks as below.

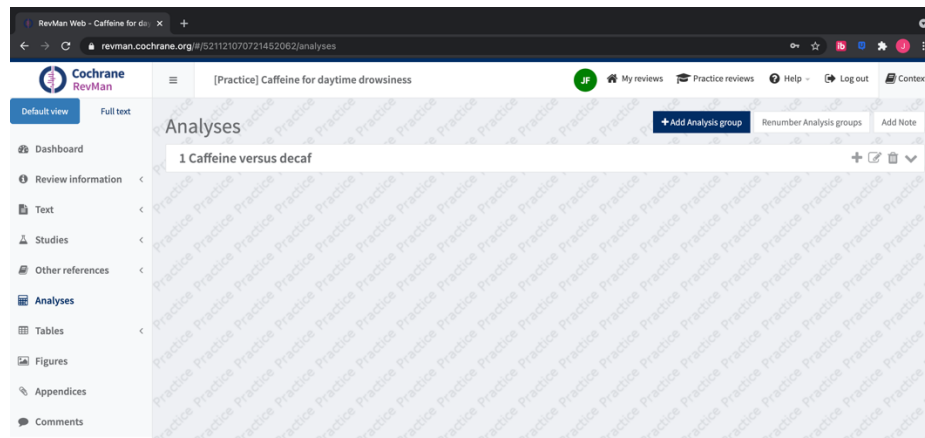


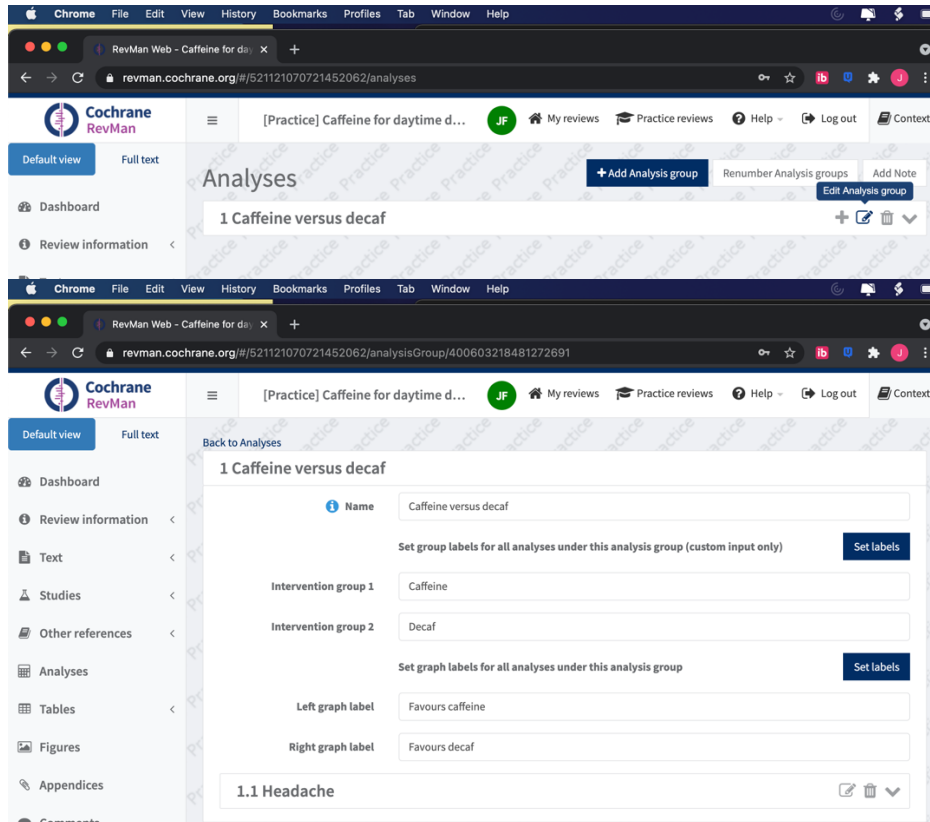
5. Click “Add Study” and fill out the form for each of the studies you are analyzing. Repeat until each study is listed separately.
 - a. On the “General” tab, for the “Study ID” enter the last name of the first author and year of publication; add the year of publication in “Year”. “Data Source” should remain “Published data only”. You may leave the “Identifiers” blank.
 - b. You may leave the “Characteristics” tab blank.
 - c. On the “Risk of Bias” tab, for randomized control trials, you will have to assess each category based on the individual study design. For retrospective reviews (which are most of our articles), you may select the following:
 - i. “Random sequence generation” -> “High Risk of Bias”
 - ii. “Allocation concealment” -> “High Risk of Bias”
 - iii. “Blinding of participants” -> “High Risk of Bias”

- iv. “Blinding of outcome assessment, Self-reported outcomes” -> “Unclear risk of bias”
- v. “Blinding of outcome assessment, Objective measures” -> “Low Risk of Bias”
- vi. “Incomplete outcome data” -> “Unclear risk of bias”
- vii. “Selective reporting” -> “Unclear risk of bias”
- viii. “Other Bias” -> “High Risk of Bias”



6. Click “Analyses” from the toolbar on the left. This will open the preloaded analysis. Click the ‘Edit Analysis group’ icon (second icon on the analysis title bar) to edit the details. Change the Name, Intervention and Comparator groups and graph labels as appropriate for your study.





7. Click “Back to Analyses” on the top left when you are finished editing. Click “Add Analysis” and fill out the three tabs of the form.
 - a. On the “Data” tab, click “Add Data Row”. Your included studies will be listed in a drop-down box. Select the appropriate study one at a time and enter the data. Create separate Forest plots for prospective randomized and for retrospective studies. Continue until all the included studies that have data for this outcome are listed.
 - b. On the “Options” tab, select “Dichotomous” if your outcome is binary (e.g. mortality, infection, presence of complication, etc), or “Continuous” as appropriate (e.g. length of stay, etc). Fill out the names of the intervention and comparator groups in the Intervention Group 1 & 2 boxes.
 - i. For **dichotomous** data:
 1. For the “Statistical Method” select “Mantel-Haenszel”
 2. For “Effect Measure” select “Odds Ratio”
 3. For the “Analysis model” select “Random Effects”
 4. For “Totals” select “Totals and Subtotals”
 5. Leave all Confidence Intervals at 95%.
 - ii. For **continuous** data:
 1. For the “Statistical Method” select “Inverse Variance”
 2. For “Effect Measure” select “Mean Difference”
 3. For the “Analysis model” select “Random Effects”
 4. For “Totals” select “Totals and Subtotals”

5. Leave all Confidence Intervals at 95%.

Back to Analyses

1 Caffeine versus decaf

1.2 New Analysis

Data Options Graphs

+ Add Data row + Add Subgroup Add Note

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M-H, Fixed, 95% CI	Action
Amore-Coffea 2000	0	0	0	0	0	Not estimable	Action
Total (95% CI)	0	0	0	0		Not estimable	

Footnote

Back to Analyses

1 Caffeine versus decaf

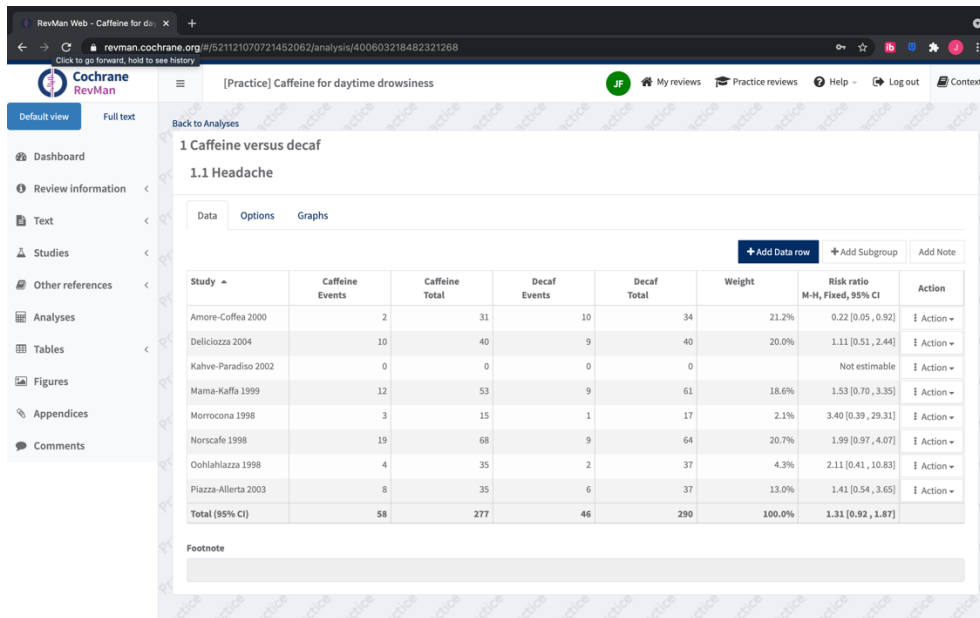
1.2 New Analysis

Data Options Graphs

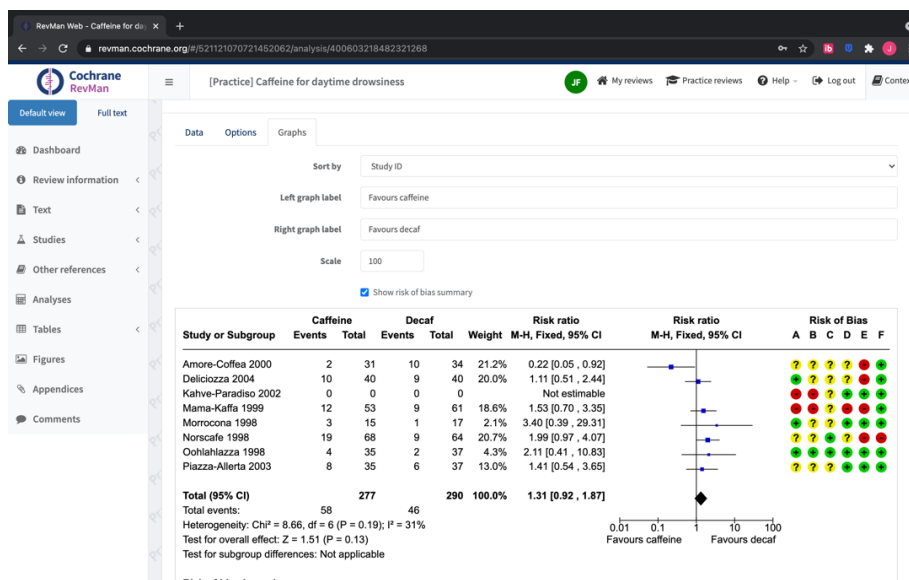
+ Add Data row + Add Subgroup Add Note

Study	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds ratio M-H, Fixed, 95% CI	Action
Amore-Coffea 2000	0	0	0	0	0	Not estimable	Action
Delicchioza 2004	0	0	0	0	0	Not estimable	
Kahwe-Paradiso 2002	0	0	0	0	0	Not estimable	
Mama-Kaffa 1999							
Morroccna 1998							
Norscafe 1998							
Oohlahiazza 1998							
Piazza-Allerta 2003							

8. When you are done entering all the data for the outcome, the screen should look as below:

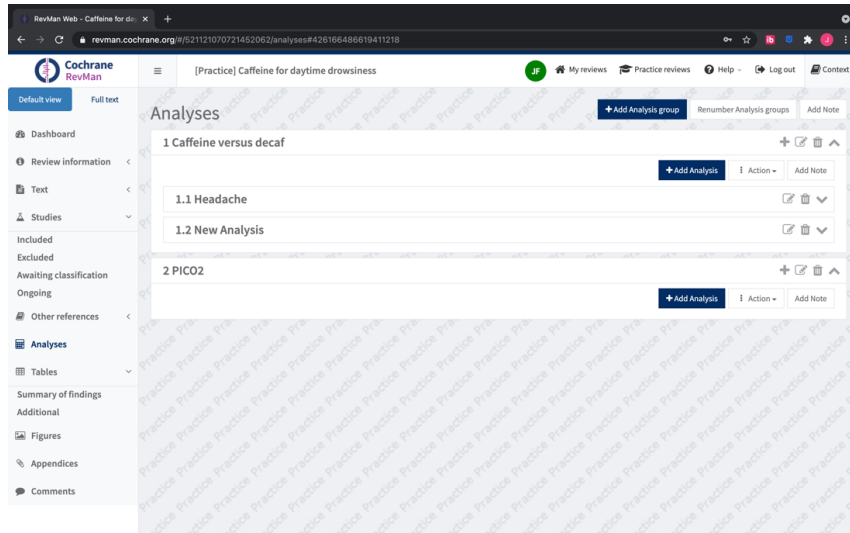


9. Click the “Graph” tab, and the Forest Plot, along the Risk of Bias tool will be generated. The I^2 (or heterogeneity test) will also be given under the plot, as well as the z-test for overall effect (this will be >0.05 if the overall effect crosses the midline).

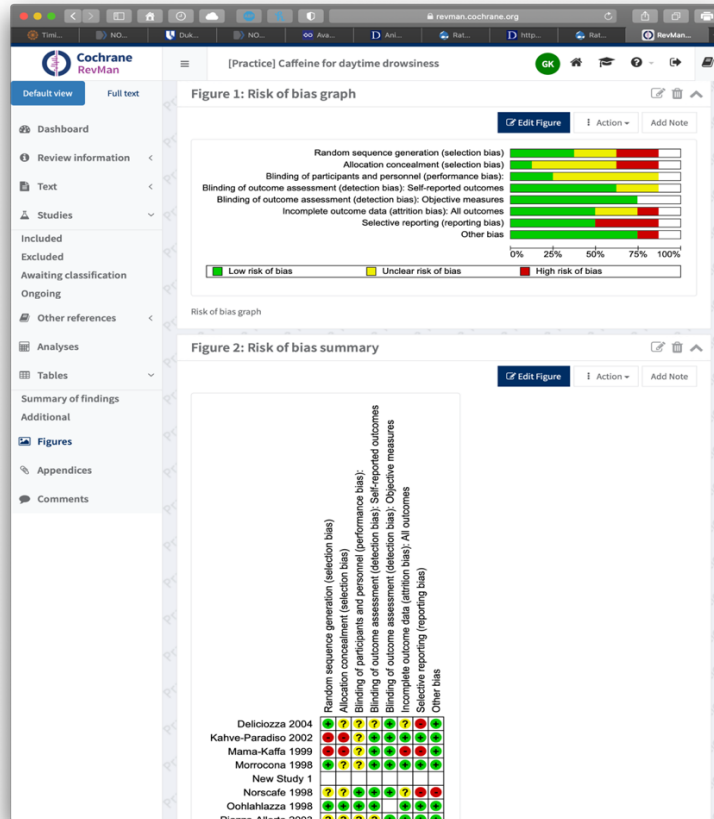


10. Repeat the process for each outcome.

- When you are ready for the next PIC stem/question, return to the “Analyses” section from the left toolbar. Click “Add Analysis group” in the top right, and fill out the form for your next PIC stem. Click “Back to Analyses” when done. In the end, each PIC stem should be numbered (1, 2, etc.) and each outcome listed under its respectful stem (1.1, 1.2, 1.3, etc.).



- Under the “Figures” option on the left-hand toolbar, you will also find the “Risk of Bias graph” and the “Risk of bias summary”.



13. The Forest Plots, and the above graphs can be exported for use in the manuscript.

Other RevMan Resources:

- A Quickstart User Guide: <https://documentation.cochrane.org/revman-kb/get-started>
- The RevMan Web Knowledge Base: <https://documentation.cochrane.org/revman-kb/>
- Training Videos: <https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/rmw-training-videos>

APPENDIX C

GRADEpro Instructions for Creating Evidence Tables

Jordan M. Kirsch, DO

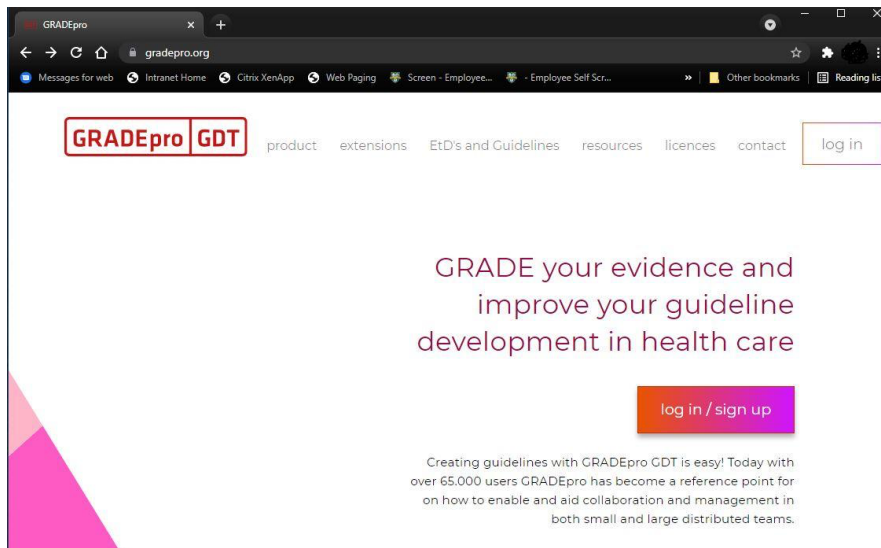
Julius Cheng, MD MPH

Aim:

These instructions will cover using the GradePro software to create evidence tables. The software has other team management functions that are outside the scope of this document.

Instructions:

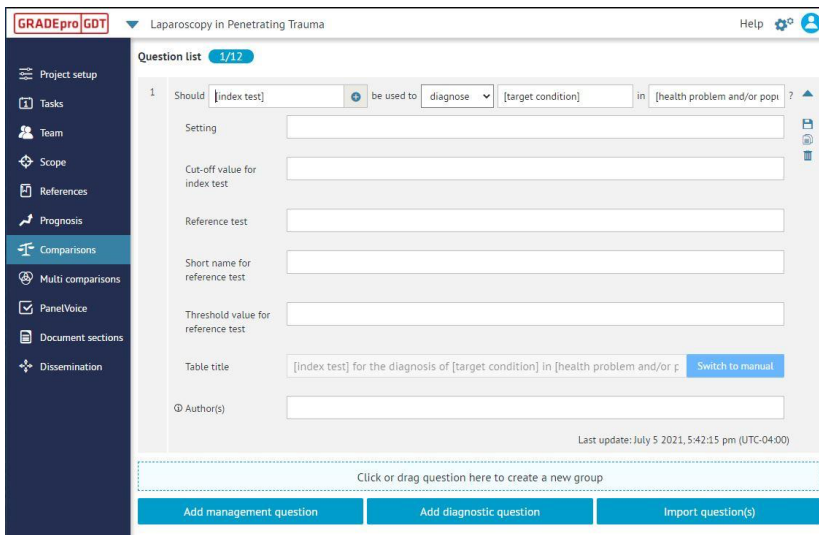
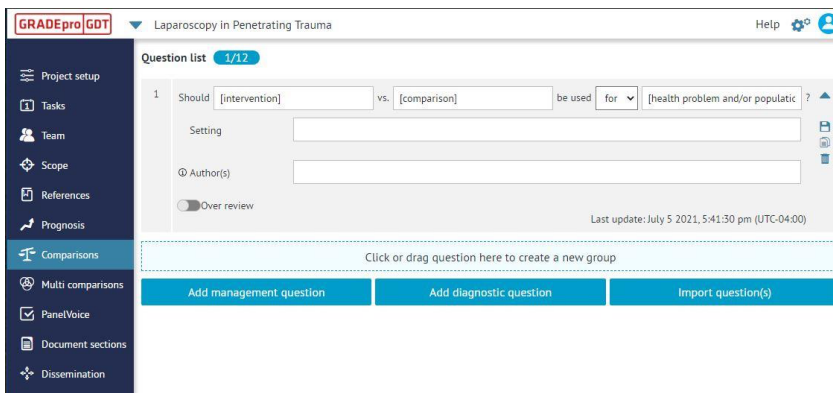
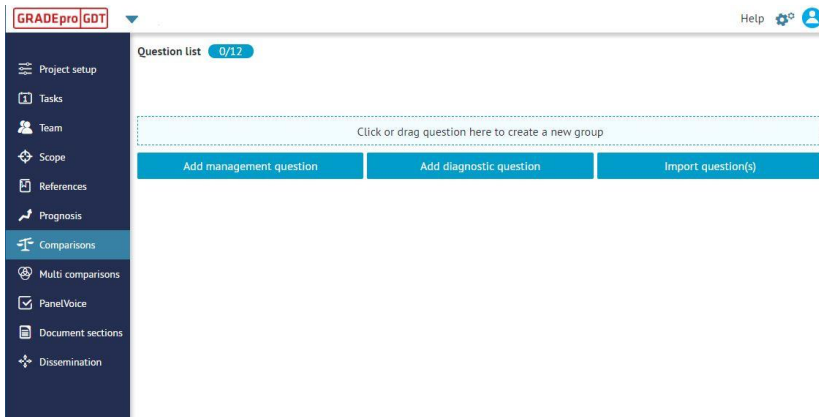
1. Visit <https://gdt.gradepro.org/app/>
 - a. Access is free.
 - b. Sign up with your name, email, password, and agree to the terms.
 - c. Enter username and password to login



2. Click "New project" in the top right corner and enter the project name in the box and hit "Create Project"



3. Click the on the title of the newly created project to open it
4. Click "Comparisons" from the toolbar on the left then select "add management question" (or "add diagnostic question") and fill in the form



5. Click on the name of the newly created question then select "add outcomes" or "import outcome(s)" and fill out the form (Most outcomes will be "di-chotomous" or "continuous", and "pooled" – select the appropriate buttons)
 - a. Import outcomes can be used to upload reviews from RevMan
 - i. This will be the most common method for populating the evidence table for EAST Guideline development purposes

- ii. A separate set of instructions is available for RevMan on the EAST website
- b. Continue the process until every PIC stem and outcome are added
- c. The outcomes will be added to the evidence table for each respective question. Create separate tables for prospective randomized and for retrospective studies. Click on the gray edit boxes on the right of each outcome to fill in any data from the pertinent studies. Certain responses will require an explanation. This can be entered now by following the prompt, or you can return to it later.
 - i. Enter the **'No of Studies'** in the first box
 - ii. Enter the **'Study Design'** in the second. These will overwhelmingly be 'Observational Studies'. (If there are more than a couple of randomized trials, you may want to create a separate table for the same outcome for those, and ensure that data from the two different study types point to the same direction of outcome)
 - iii. Enter the **'Risk of Bias'** in the next. In the vast majority of cases where most studies are observational, the option to select here would be 'Very serious'. (May select 'serious' in cases of prospective trials with lack of blinding/randomization)
 - iv. Fill out the **'Inconsistency'** box. If different studies show different results, and Confidence Intervals are all over the map on the Forest plot, or heterogeneity is high ($I^2 > 70$) consider 'Very Serious'. If confidence intervals are mostly clustered around the same area on the forest plot, consider choosing 'Serious'
 - v. Fill out the **'Indirectness'** box. Unless the studies you have reviewed used exactly the same patient population, intervention, comparator and outcomes, and with the same inclusion/exclusion criteria, select 'Very serious'. May select 'serious' if inclusion/exclusion criteria or comparator were slightly different.
 - vi. Fill out the **'Imprecision'** box. Select 'Very Serious' if there are fewer than 5 studies, if the pooled Confidence intervals are wide, or if there is uncertainty about the magnitude of the intervention effect on the studied outcome.
 - vii. Fill out the **'Other Considerations'** box. In **'Publication Bias'** select 'strongly suspected' if there are fewer than 5 studies, if the majority of studies show a positive intervention-outcome association. In **'Large effect'** select the magnitude of the intervention effect on the outcome – to select anything but 'no', the pooled Confidence Interval on the forest plot needs to be narrow and not cross the y-axis. If >50% change, consider 'very large', otherwise 'large'. In **'Plausible Confounding'** consider one of the options if there is plausible residual confounding that could weaken support for the intervention (e.g. the intervention increases survival in less sick patients, and the severity of illness has not been accounted for in the analysis). In **'Dose Response Gradient'** select

- 'yes' if outcome increases proportionally with intervention dose, e.g. higher risk of bleeding with higher INR, greater survival in sepsis with earlier administration of ABx and achievement of source control, etc.
- viii. Enter the **No of patients** that received the **Intervention** and the **Comparison**.
 - ix. **'Relative effects'** are typically reported as Odds Ratios and 95% confidence intervals. The 'Absolute Effect' is autocalculated as a 95% confidence interval.
 - x. In the **'Importance'** box, select the rating for that outcome, as it was voted early in the PICO question generation step.
 - xi. All the above boxes, provide additional, detailed explanations to guide your selections by clicking the little 'i' sign in each.
 - xii. Once all the options are selected under the certainty tool, the classification of certainty (+ to +++) will automatically be generated
 - xiii. Do the same for each outcome.
 - xiv. Finally select the box-like button all the way to the right of the top bold column for each PICO, and select 'Grade Profile v2', then the top right page corner export button, to Export your tables in word or PDF format.
 - xv. Clicking on the "what happens" tab will allow selection of several automatically generated options for "size of effect" and "narrative statements"
 1. Click "insert" to use the automatically generated option
 2. Manual entries can be typed into the "what happens" free text box.

Other GRADEpro Resources:

GRADEpro user guide https://gdt.gradepro.org/app/help/user_guide/index.html

A handbook is available under the help menu located in the top right corner. This handbook serves as a reference for guideline development using GRADE methodology.

An EAST instructional video is available at the following link: [GRADE - Ch. 5 Using GRADEPro](#)