GRADE

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

Afiliaciones

- Medicina interna & Medicina del enfermo en estado critico | OPD Hospitales Civiles de Guadalajara.
- Maestría en métodos de investigación en ciencias de la salud | Universidad de McMaster.
- Profesor de asignatura | CUCS | Universidad de Guadalajara.
- Sistema nacional de investigadores | Conacyt | Nivel I.
- Miembro y autor de la colaboración Cochrane | Cochrane México.
- Miembro del grupo “McMaster GRADE Centre” | Universidad de McMaster.
- Instructor “Core GRADE” | Universidad de McMaster.

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

Conflicto de interés

Financiero

- Ninguno.

Intelectual

- Miembro y autor de la colaboración Cochrane | Cochrane México.
- Miembro del grupo “McMaster GRADE Centre” | Universidad de McMaster
- Instructor “Core GRADE” | Universidad de McMaster

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA SALUD PÚBLICA

Cochrane Iberoamérica

Agenda del día

- Introducción.
- Evaluación de la certeza de la evidencia con el sistema GRADE.
- Transición de la evidencia a las recomendaciones (EtD framework).

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

Agenda del día

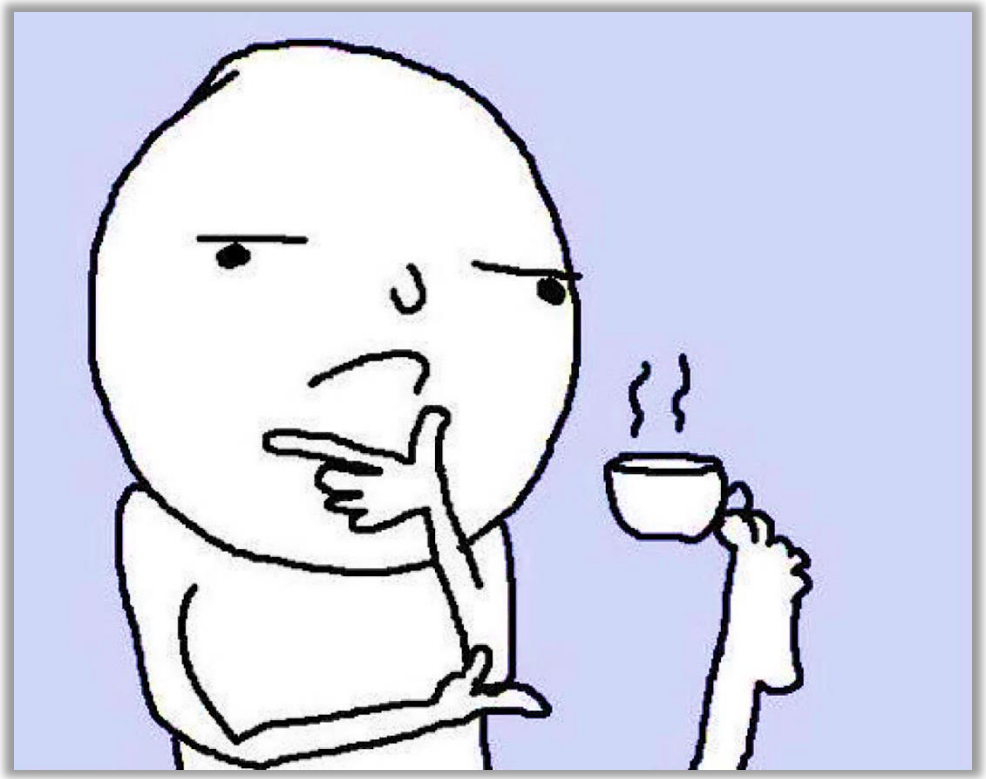
- Introducción.
- Evaluación de la certeza de la evidencia con el sistema GRADE.
- Transición de la evidencia a las recomendaciones (EtD framework).

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

¿De dónde sale GRADE?



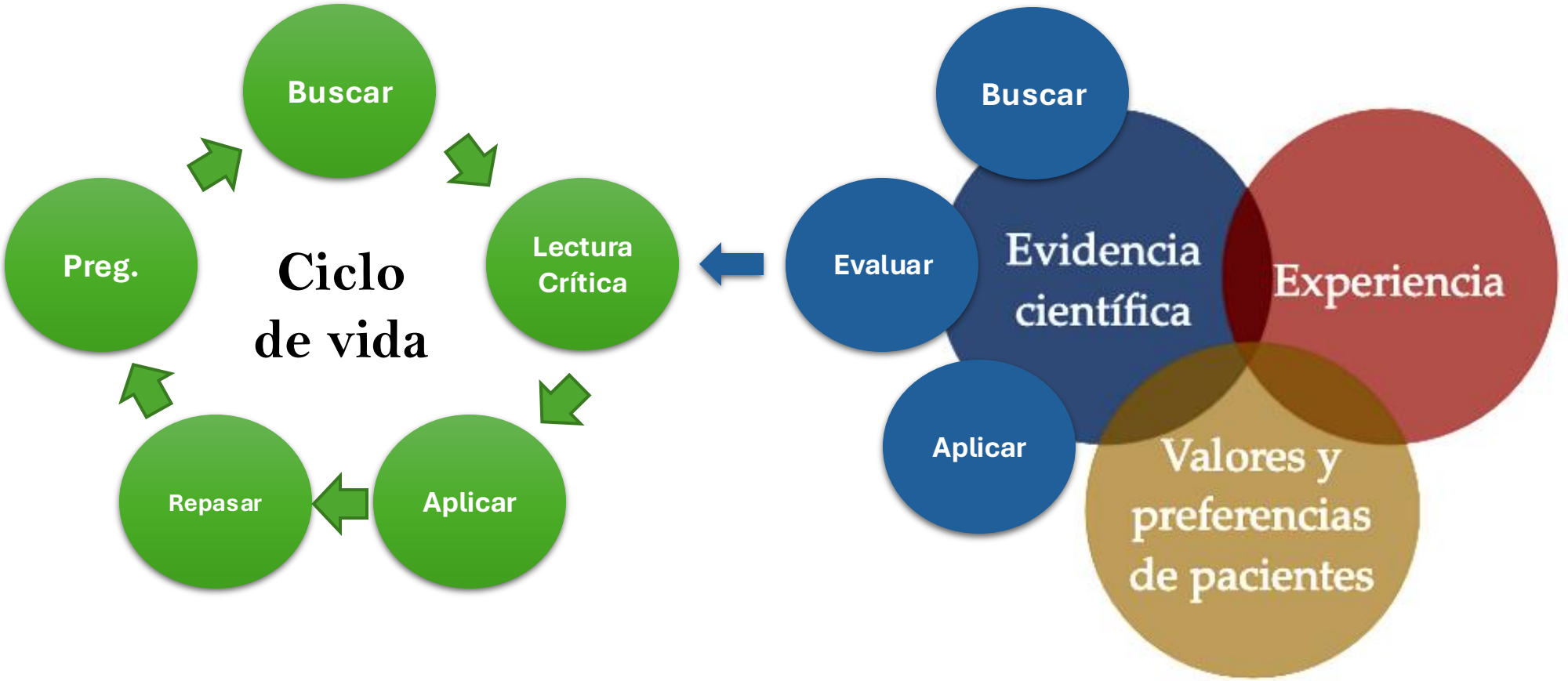
Toma de decisiones

Medicina Basada en Evidencias

Es un enfoque utilizado por los profesionales de la salud, el cual esta dirigido a optimizar la toma de decisiones, a partir de tres constructos: Evidencia científica, experiencia clínica y los valores y preferencias de los pacientes.

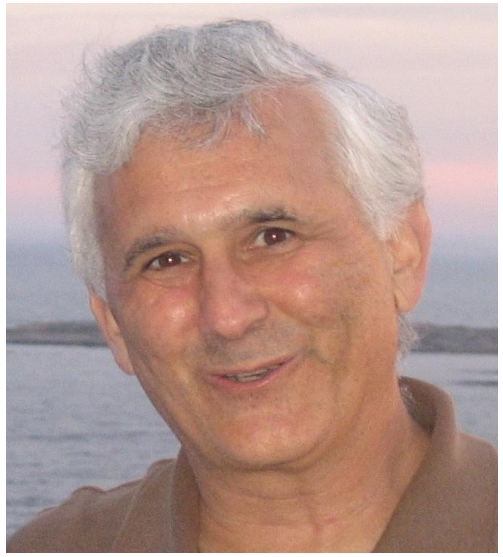
Guyatt, G., Rennie, D., Meade, M., & Cook, D. (3rd Ed). (2015). Users' guides to the medical literature: a manual for evidence-based clinical practice

Medicina Basada en Evidencias



Guyatt, G., Rennie, D., Meade, M., & Cook, D. (3rd Ed). (2015). Users' guides to the medical literature: a manual for evidence-based clinical practice

Evaluación de la credibilidad de la evidencia



Andy Oxman

GRADE

(Grades of recommendation, assessment, development and evaluation)

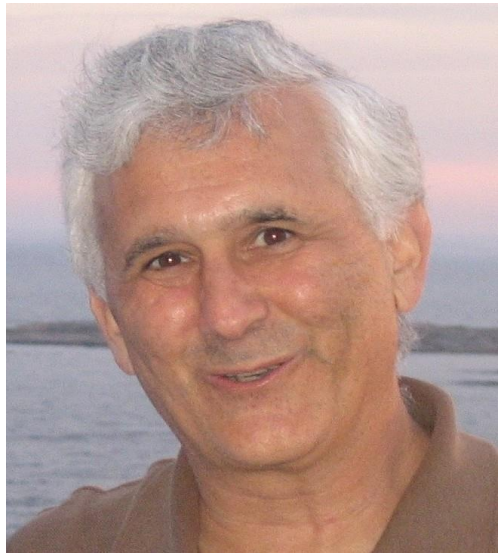
Publicado por primera vez en 2004 en **BMJ.**

2008 Serie de 6 partes en **BMJ.**
Enfocado en clínicos

2011 al presente
Serie de 30 partes (hasta ahora) en **JCE**
Para autores de revisiones sistemáticas y guías

https://www.gradeworkinggroup.org/

Evaluación de la credibilidad de la evidencia



Andy Oxman

>110 organizaciones han implementado

https://www.gradeworkinggroup.org/

GRADE vs Otros sistemas

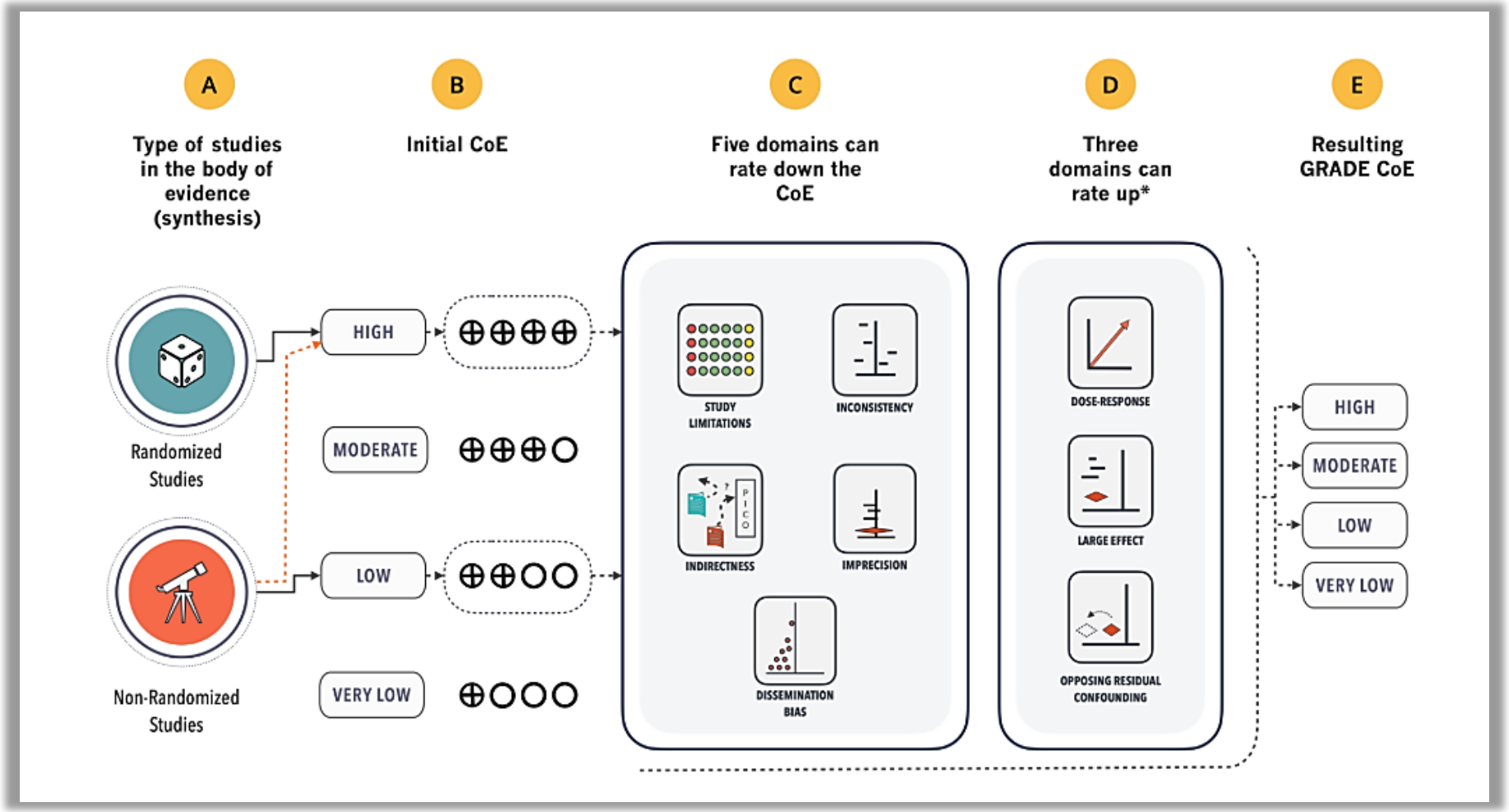
Tabla 1. Ventajas de GRADE en comparación con otros sistemas

1. Separación clara entre la certeza de la evidencia y la fuerza de las recomendaciones.
2. Criterios explícitos y completos para disminuir o aumentar la certeza de la evidencia.
3. Consideración explícita de la importancia relativa de los distintos desenlaces para los pacientes y las personas.
4. Marco estructurado y proceso transparente para pasar de la evidencia a las decisiones.
5. Recomendación explícita de formular recomendaciones incluso cuando solo se dispone de evidencia de certeza muy baja.
6. Interpretación clara y pragmática de las recomendaciones fuertes y condicionales.
7. Equilibrio entre simplicidad, solidez metodológica y exhaustividad.
8. Permite la adaptación y adopción de decisiones y recomendaciones (Adolopment de GRADE).
9. Recursos para aprender sobre GRADE ampliamente disponibles y de acceso libre.
10. Respaldado por una red internacional.
11. Permite la innovación, el perfeccionamiento y el desarrollo continuo.
12. Respaldado por herramientas, por ejemplo, GRADEpro.

GRADEpro GDT

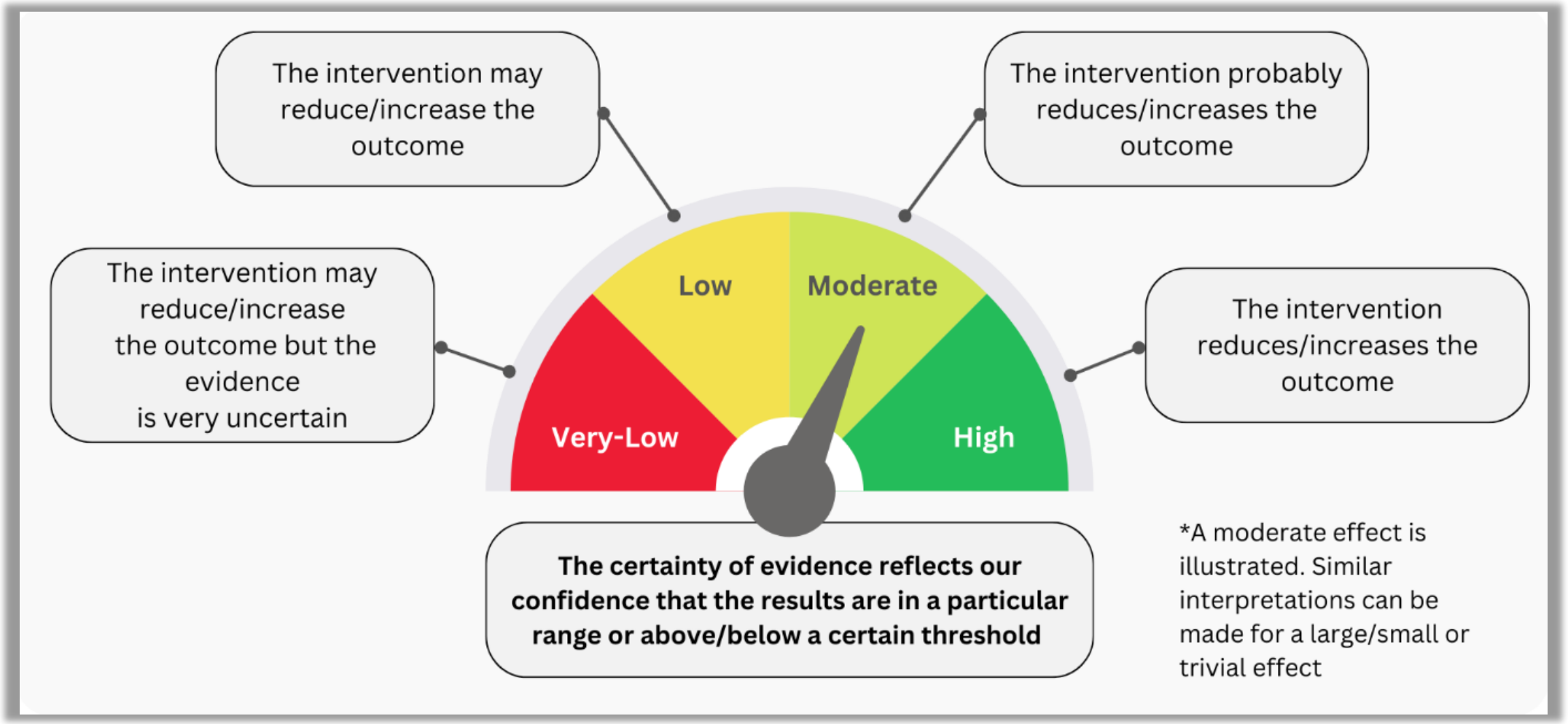
https://book.gradepro.org/guideline/overview-of-the-grade-approach

Abordaje GRADE para la evaluación de la certeza en intervenciones



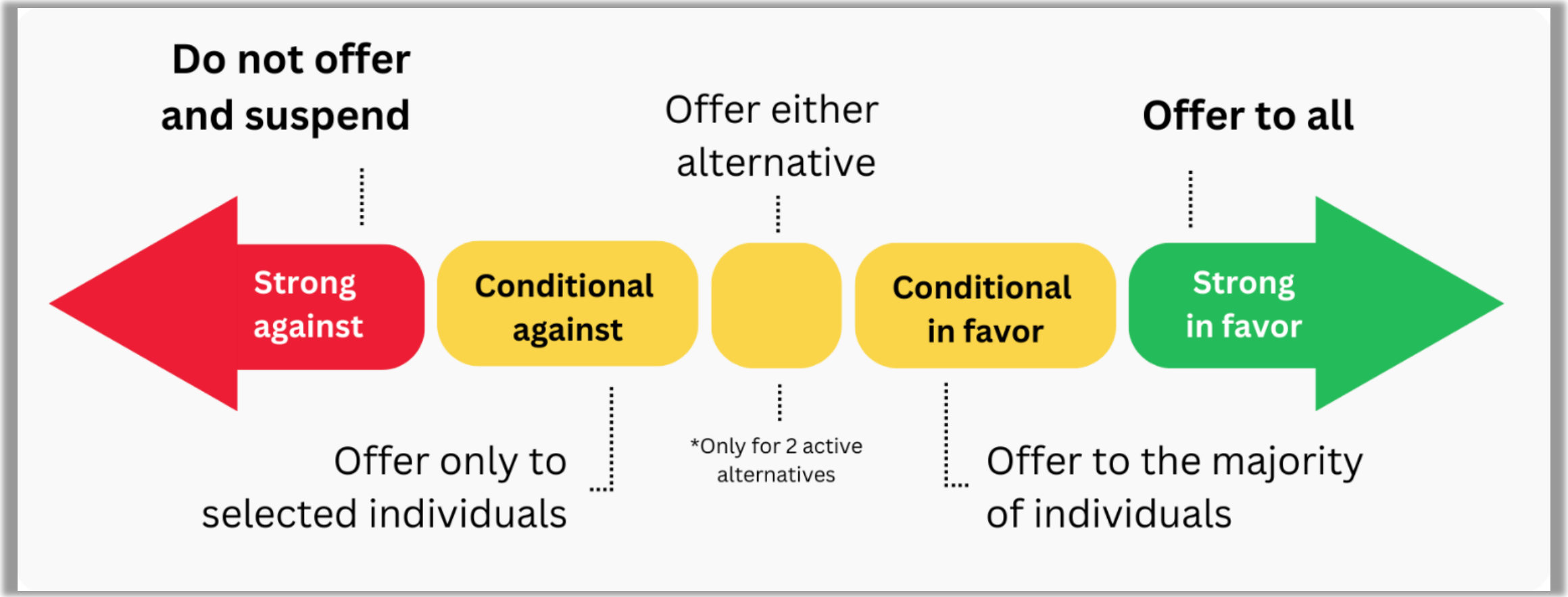
https://book.gradepro.org/guideline/overview-of-the-grade-approach

Interpretación de los niveles de certeza de la evidencia de los efectos de las intervenciones



https://book.gradepro.org/guideline/overview-of-the-grade-approach

Fuerza de las recomendaciones



https://book.gradepro.org/guideline/overview-of-the-grade-approach

Agenda del día

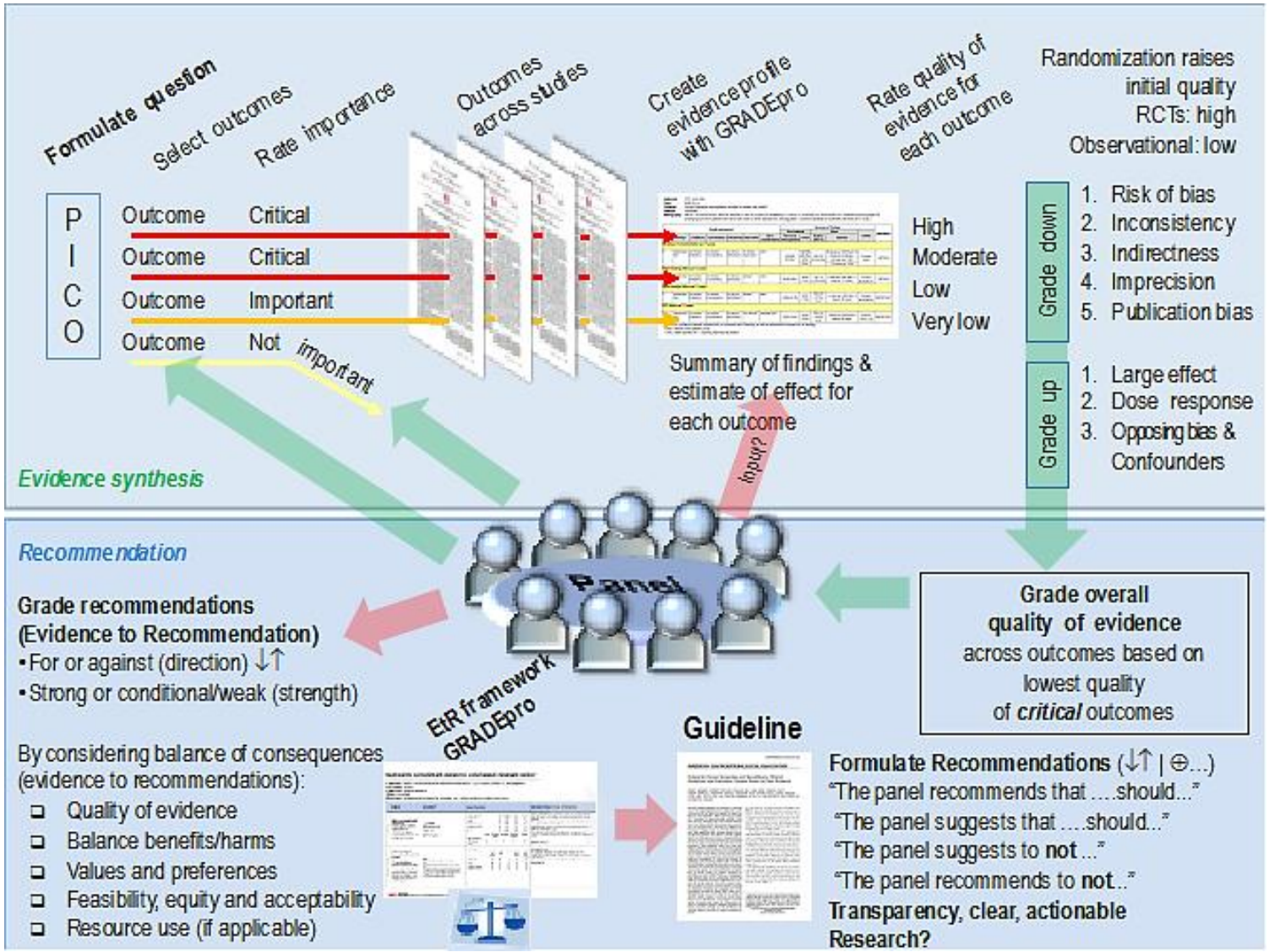
- Introducción.
- **Evaluación de la certeza de la evidencia con el sistema GRADE.**
- Transición de la evidencia a las recomendaciones (EtD framework).

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

Guías de practica clínica

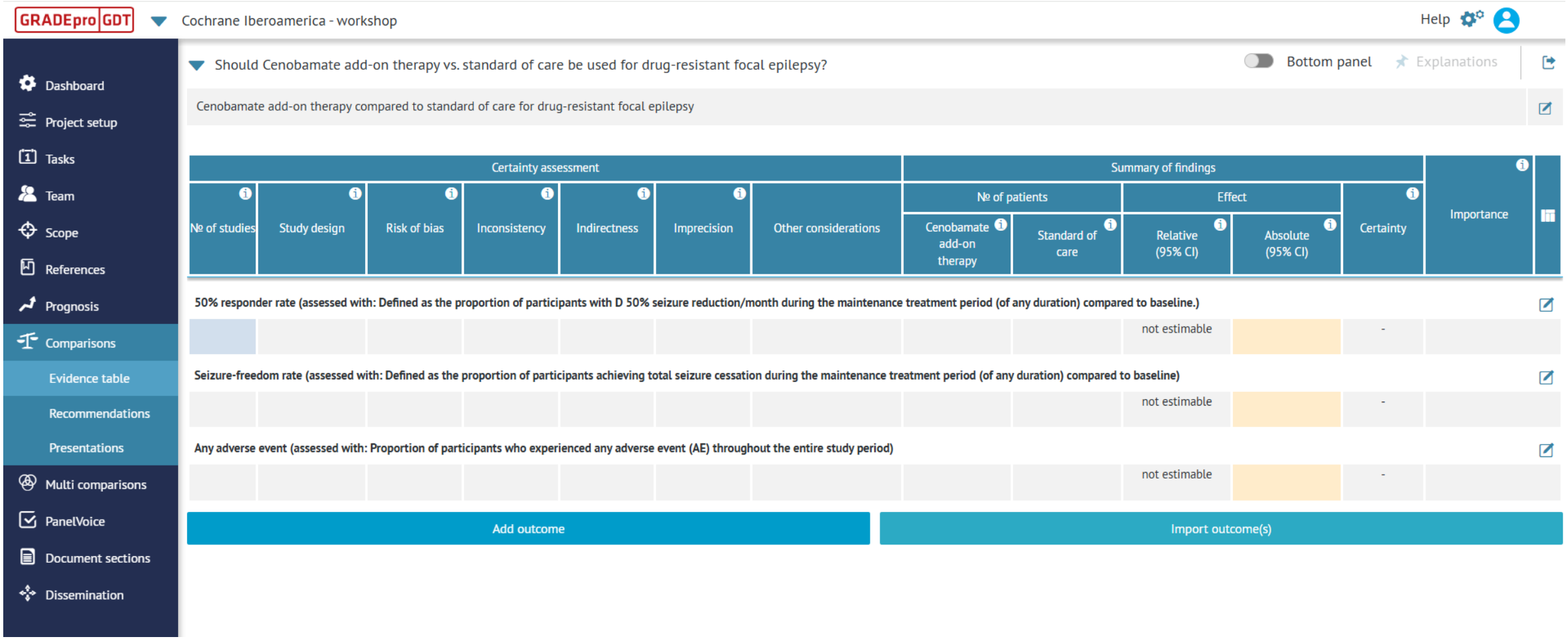


https://www.gradeworkinggroup.org/

Ejercicios en GRADEpro

de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

GRADE evidence profile



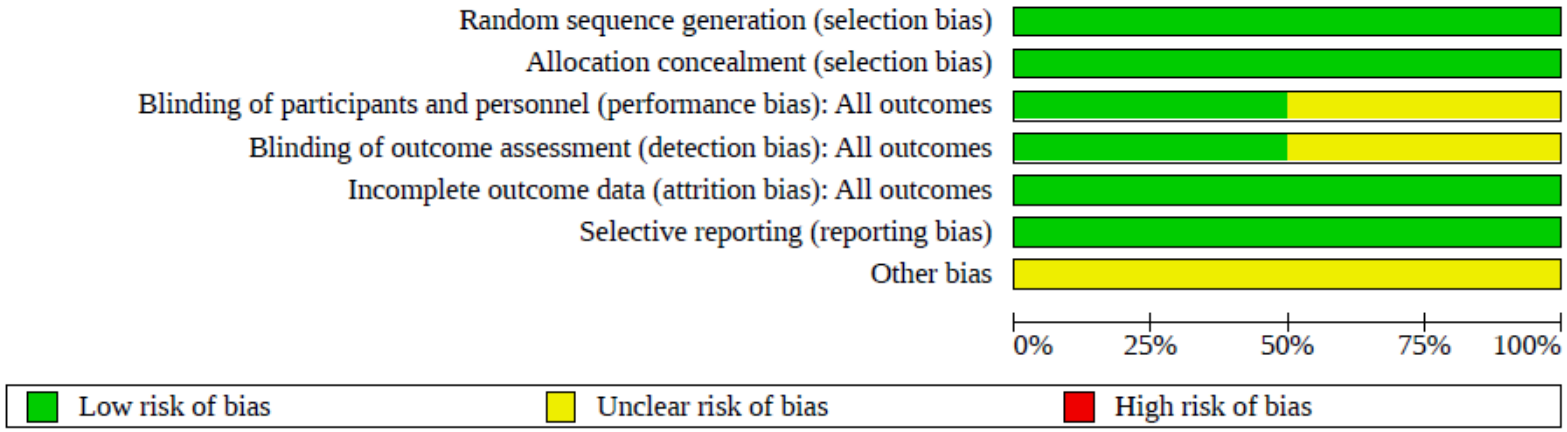
https://www.gradepro.org/

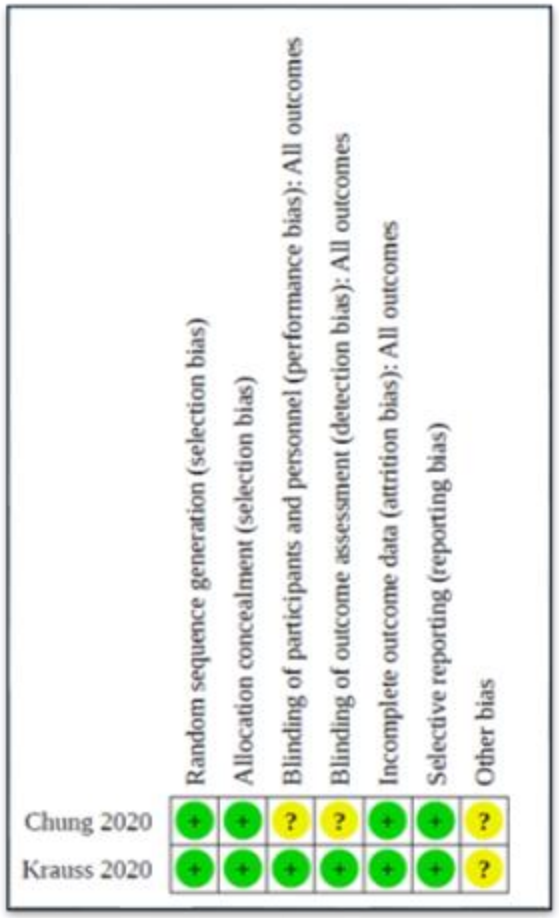
Dominios de penalización
(downgrade)

https://www.gradepro.org/

Riesgo de Sesgo

Figure 2. Risk of bias graph: summary of review authors' judgements about risk of bias for all included studies.





de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Riesgo de Sesgo

Con base a la información proporcionada

¿Hay riesgo de sesgo?

de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Riesgo de Sesgo – GRADE book

Table 1 – Limitations in the design or execution in randomized trials

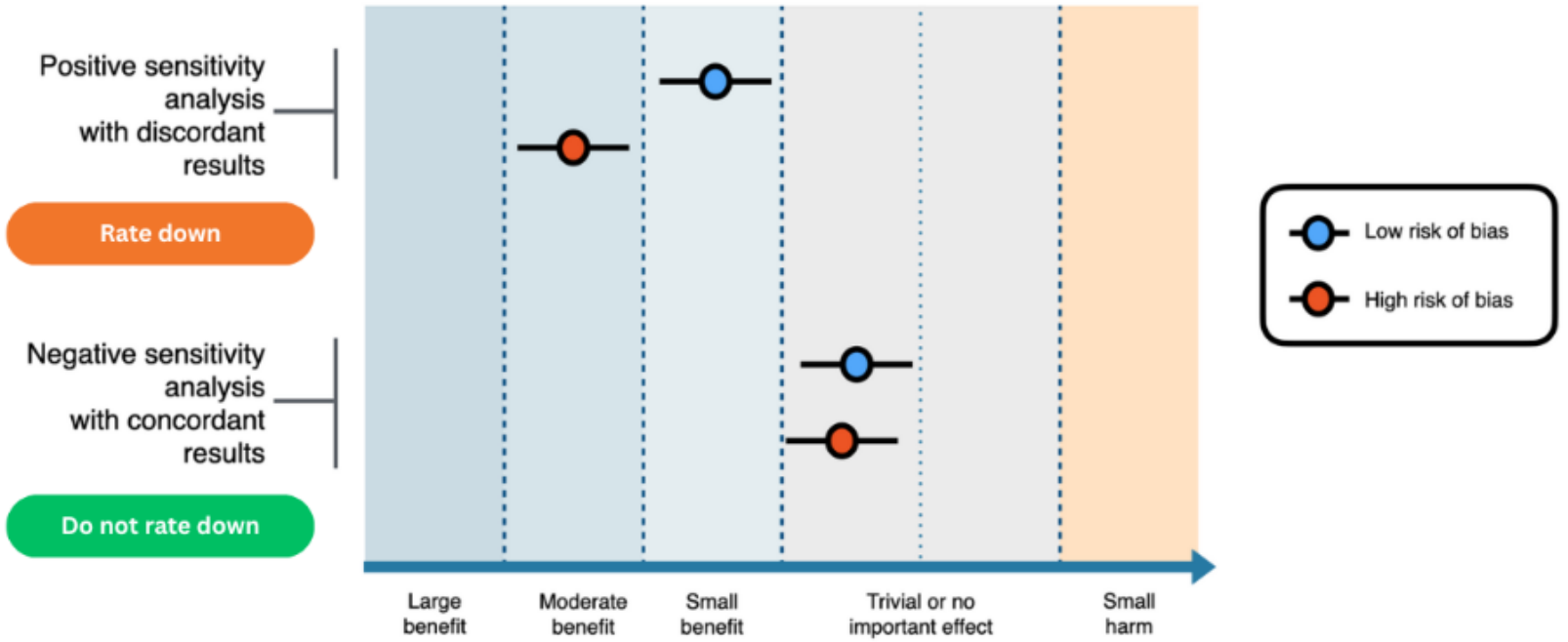
Limitations	Explanation	Ways trialists can reduce bias
Randomization process	Random allocation of participants to the different treatment groups creates groups of similar prognostic profiles and thus, similar probability of experiencing the outcomes of interest	Computer generated sequence with allocation concealment (e.g., central randomization).
Systematic deviations from protocol	Deviations from the intended protocol may change the prognostic similarity between groups established by randomization	Blinding of participants, investigators, and study personnel Intention-to-treat analysis
Missing outcome data	If a substantial proportion of outcome data is missing the prognostic balance between groups established by randomization may be compromised	Strategies to increase follow-up Analytical strategies to deal with missing outcome data
Outcome measurement	Bias in the outcome measurement may arise when the adjudicators are aware of the treatment assignment	Blinding of participants, investigators, study personnel, outcome adjudicators
Selection of the reported result	If different ways to report the same outcome are available, investigators may choose to report the measurement that looks more positive for the treatment group they believe to be superior	Use of core outcomes set Publishing a detailed protocol

https://book.gradepro.org/guideline/risk-of-bias-randomized-trials

Riesgo de Sesgo – GRADE book

Guía para evaluación:

1. Umbrales?
2. Target (objetivo).
3. Comparación de la evidencia
   - (Bajo o Alto RoB).
4. Juicio de valor para disminuir la certeza.



https://book.gradepro.org/guideline/risk-of-bias-randomized-trials

GRADEpro

Should Cenobamate add-on therapy vs. standard of care be used for drug-resistant focal epilepsy?

Bottom panel Explanations

Cenobamate add-on therapy compared to standard of care for drug-resistant focal epilepsy

Certainty assessment							Summary of findings					
							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cenobamate add-on therapy	Standard of care	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
50% responder rate (assessed with: Defined as the proportion of participants with D 50% seizure reduction/month during the maintenance treatment period (of any duration) compared to baseline.)												
2	randomised trials	not serious							not estimable		-	
Seizure-freedom rate (assessed with: Defined as the proportion of participants achieving total seizure cessation during the maintenance treatment period (of any duration) compared to baseline)												
									not estimable		-	
Any adverse event (assessed with: Proportion of participants who experienced any adverse event (AE) throughout the entire study period)												
									not estimable		-	

https://www.gradepro.org/

Inconsistencia

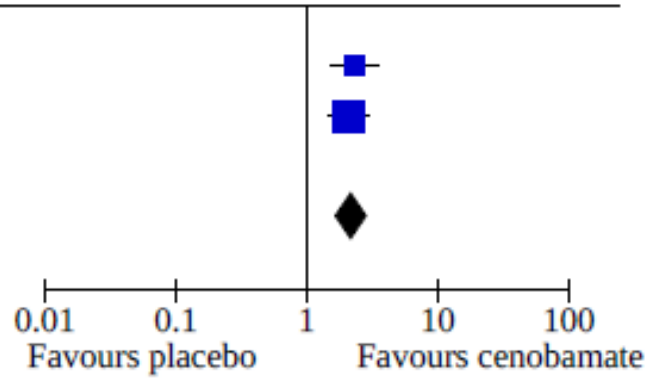
Analysis 1.1. Comparison 1: Cenobamate versus placebo (any dose), Outcome 1: 50% responder rate

Study or Subgroup	Cenobamate Events	Cenobamate Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chung 2020	53	106	22	102	36.7%	2.32 [1.53 , 3.51]
Krauss 2020	157	295	26	102	63.3%	2.09 [1.47 , 2.96]
Total (95% CI)		**401**		**204**	**100.0%**	**2.17 [1.66 , 2.84]**
Total events:	210		48			

Heterogeneity: $Chi^2 = 0.14$, df = 1 (P = 0.70); $I^2 = 0\%$

Test for overall effect: Z = 5.68 (P < 0.00001)

Test for subgroup differences: Not applicable



de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

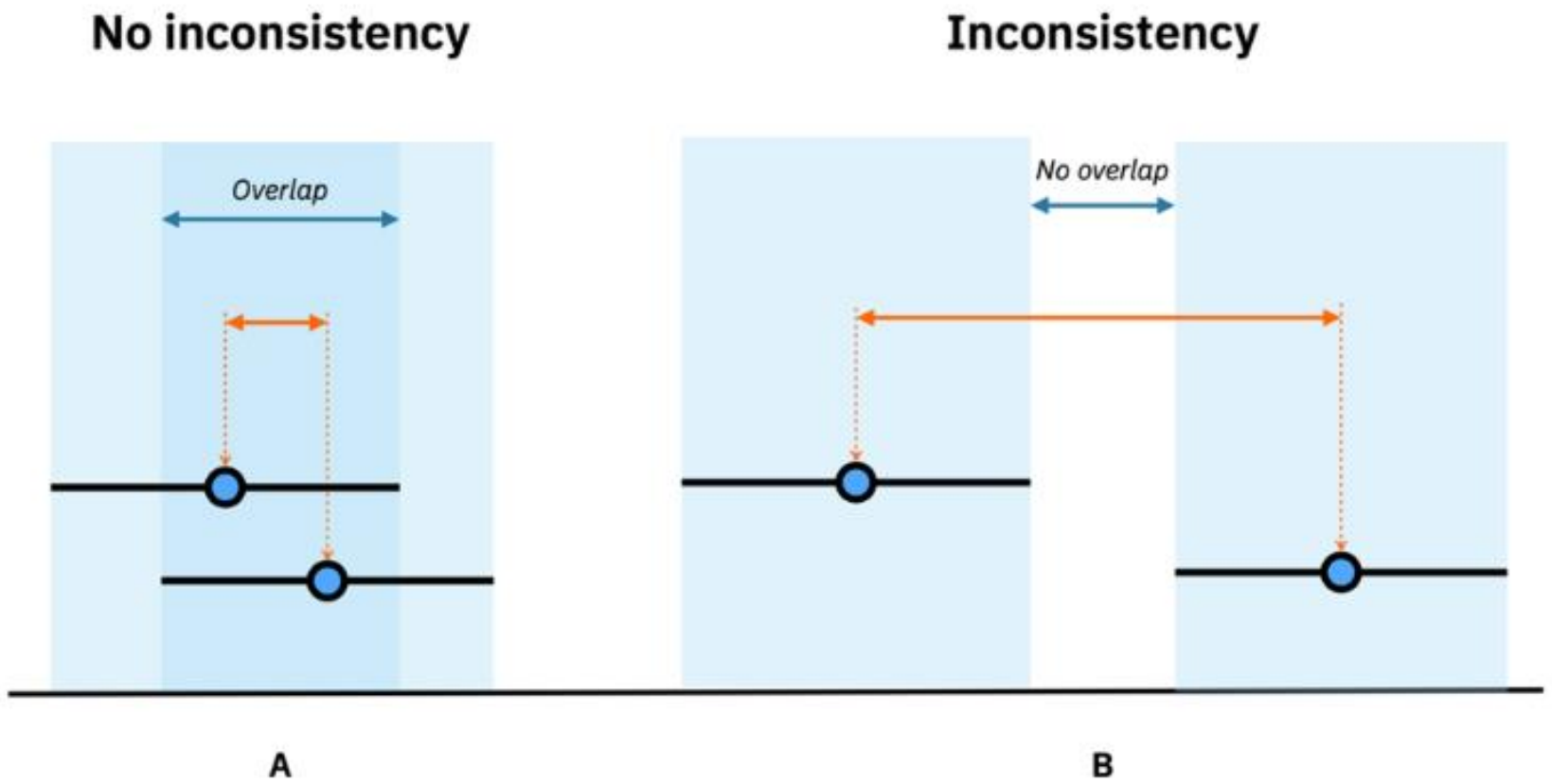
Inconsistencia

Con base a la información proporcionada

¿Hay inconsistencia?

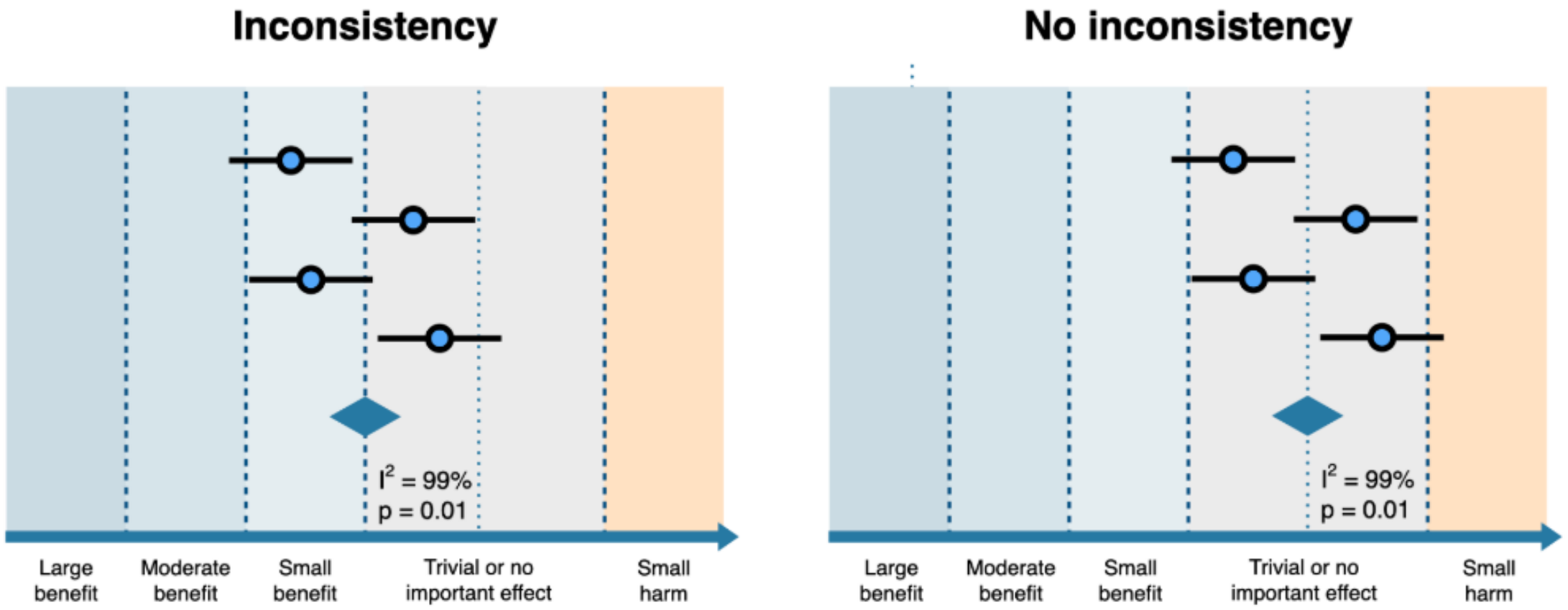
de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Inconsistencia



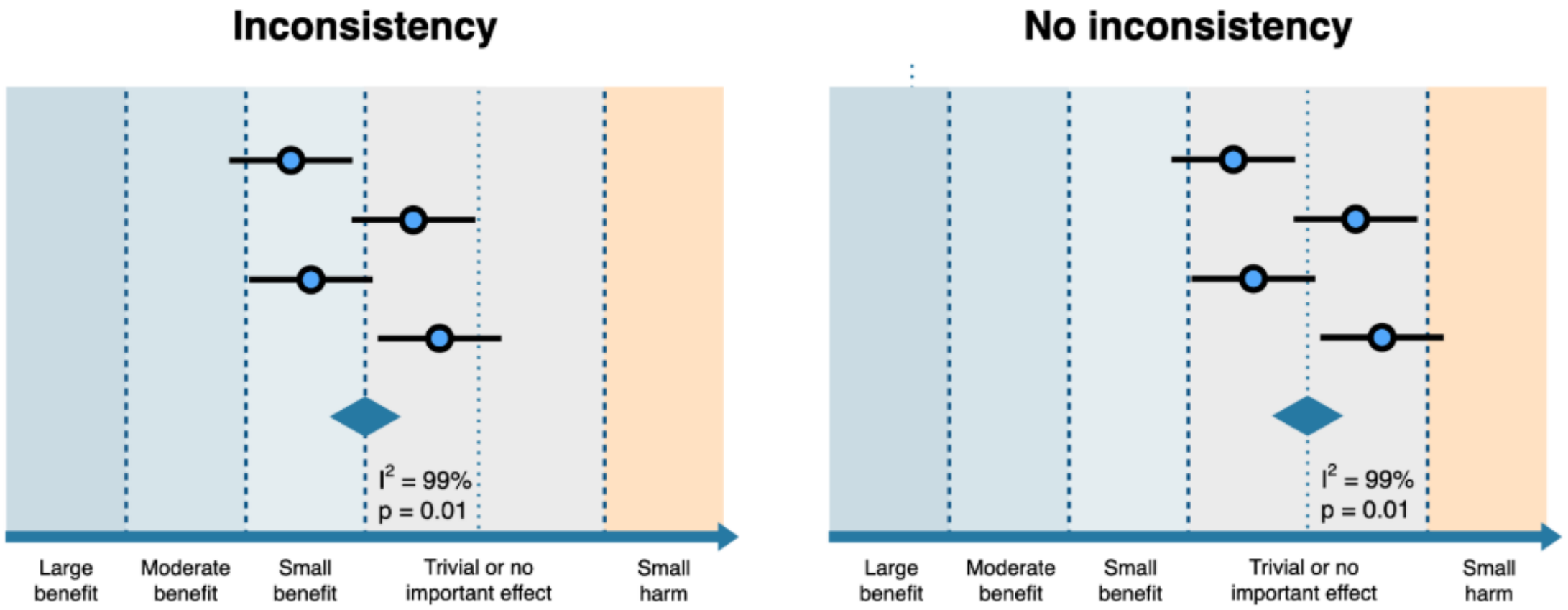
https://book.gradepro.org/guideline/inconsistency

Inconsistencia



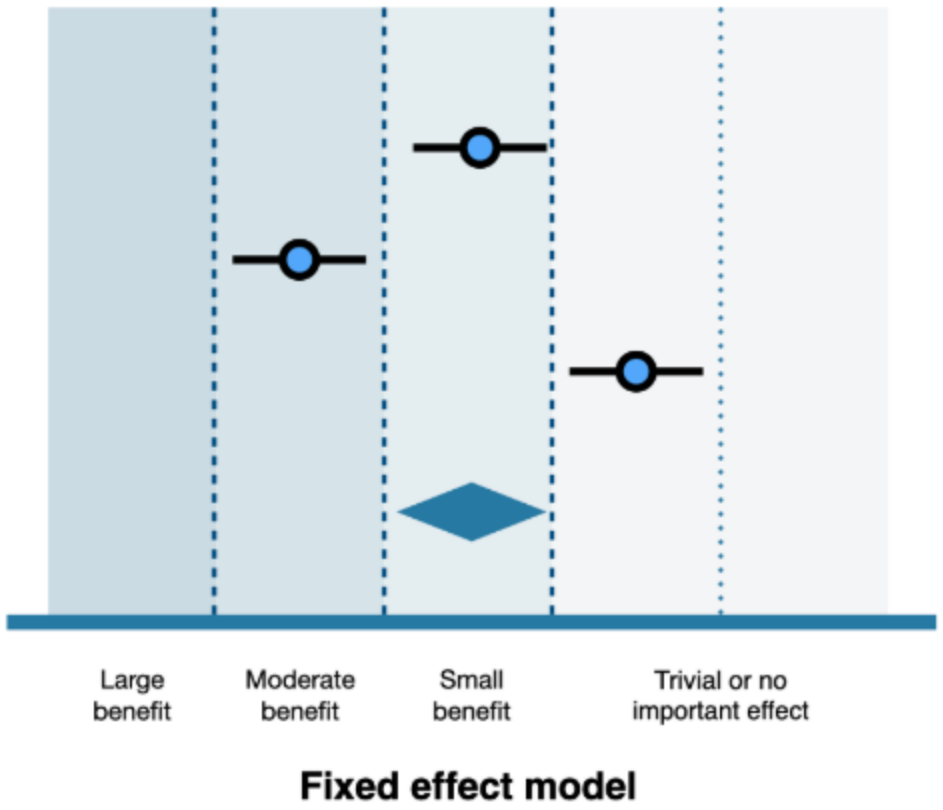
https://book.gradepro.org/guideline/inconsistency

Inconsistencia

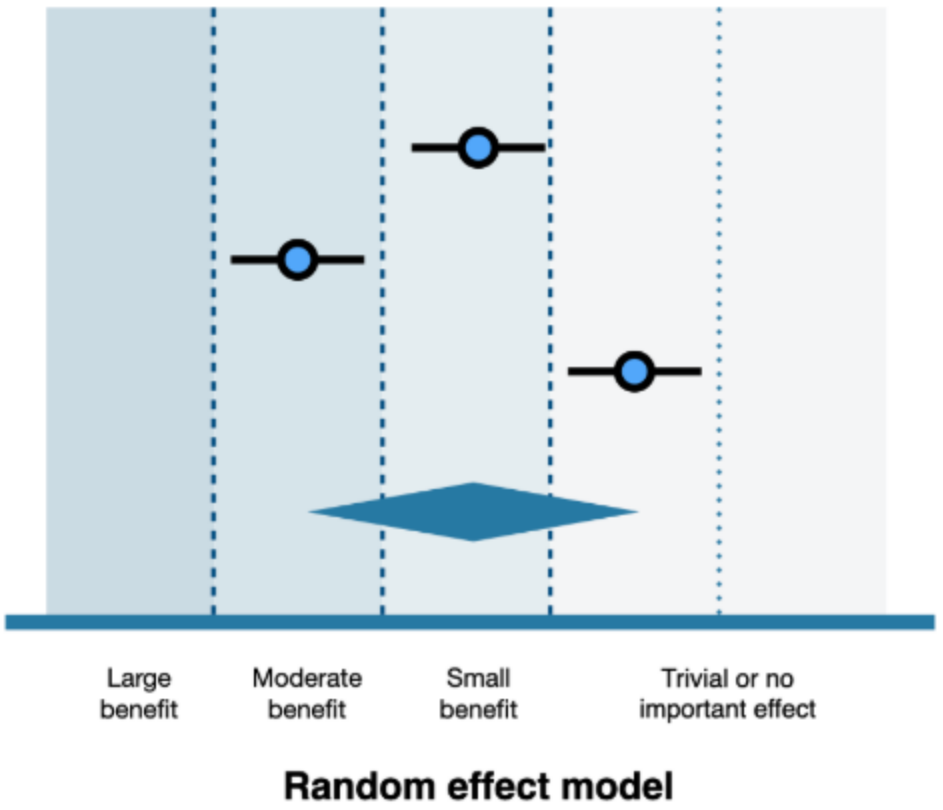


https://book.gradepro.org/guideline/inconsistency

Inconsistencia



Fixed effect model



Random effect model

https://book.gradepro.org/guideline/inconsistency

Inconsistencia – GRADE book

Guía para evaluación:

1. Umbrales?
2. Target (objetivo).
3. Evaluar la evidencia ->
4. Juicio de valor para disminuir la certeza.

¿Cómo evaluamos la consistencia en un cuerpo de evidencia?

Variabilidad del efecto entre los estudios

Superposición de los efectos.

Evaluaciones estadísticas

Prueba de X2 para heterogeneidad

Valor de I2

https://book.gradepro.org/guideline/inconsistency

GRADEpro

Should Cenobamate add-on therapy vs. standard of care be used for drug-resistant focal epilepsy?

Bottom panel Explanations

Cenobamate add-on therapy compared to standard of care for drug-resistant focal epilepsy

Certainty assessment							Summary of findings					
							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cenobamate add-on therapy	Standard of care	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
50% responder rate (assessed with: Defined as the proportion of participants with D 50% seizure reduction/month during the maintenance treatment period (of any duration) compared to baseline.)												
2	randomised trials	not serious	not serious						not estimable		-	
Seizure-freedom rate (assessed with: Defined as the proportion of participants achieving total seizure cessation during the maintenance treatment period (of any duration) compared to baseline)												
									not estimable		-	
Any adverse event (assessed with: Proportion of participants who experienced any adverse event (AE) throughout the entire study period)												
									not estimable		-	

https://www.gradepro.org/

Datos indirectos

Chung 2020	
Study characteristics	
Methods	Phase II, multicentre, parallel-group, placebo-controlled, randomised trial
Participants	***Inclusion criteria*** • Ages eligible for study: 18 to 65 years • Sexes eligible for study: all • Diagnosis of treatment resistant partial epilepsy • History of epilepsy for at least 2 years • Have at least 3 simple partial with motor component, complex partial or secondarily generalised seizures per month with no consecutive 21-day seizure-free period • Currently treated on a stable dose of: 1 to 3 AEDs for at least 12 weeks prior to randomisation • VNS will not be counted as AED; however, the parameters must remain stable for at least 4 weeks prior to baseline • Benzodiazepines taken at least once per week for epilepsy, or for anxiety or sleep disorder, will be counted as 1 AED. Therefore, only a maximum of 2 additional approved AEDs will be allowed.
Interventions	***Intervention*** Oral cenobamate, 200 mg once daily ***Comparator*** Oral placebo, once daily 8-week observational baseline period 6-week double-blind titration 6-week double-blind maintenance phase Open-label extension (optional)

de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Datos indirectos

Krauss 2020 *(Continued)*

Methods	Phase II, multicentre, parallel-group, placebo-controlled, randomised trial
Participants	***Inclusion criteria*** • Ages eligible for study: 18 to 70 years • Sexes eligible for study: all • Weight at least 40 kg • A diagnosis of partial epilepsy according to the International League Against Epilepsy's Classification of Epileptic Seizures. Diagnosis should have been established by clinical history and an electroencephalogram (EEG) that is consistent with localisation-related epilepsy; normal interictal EEGs will be allowed provided that the individual meets the other diagnosis criterion (i.e. clinical history). • Have uncontrolled partial seizures despite having been treated with at least 1 AED within approximately the last 2 years • During the 8-week baseline period, individuals must have at least 8 partial seizures including only simple partial seizures with motor component, complex partial seizures, or secondarily generalised seizures without a seizure-free interval of greater than 25 days any time during the 8-week baseline. Individuals must have at least 3 of these partial seizures during each of the 2 consecutive 4-week segments of the baseline period. • Currently on stable antiepileptic treatment regimen
Interventions	***Intervention*** Oral cenobamate, 100, 200, 400 mg once daily ***Comparator*** Oral placebo, once daily

de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

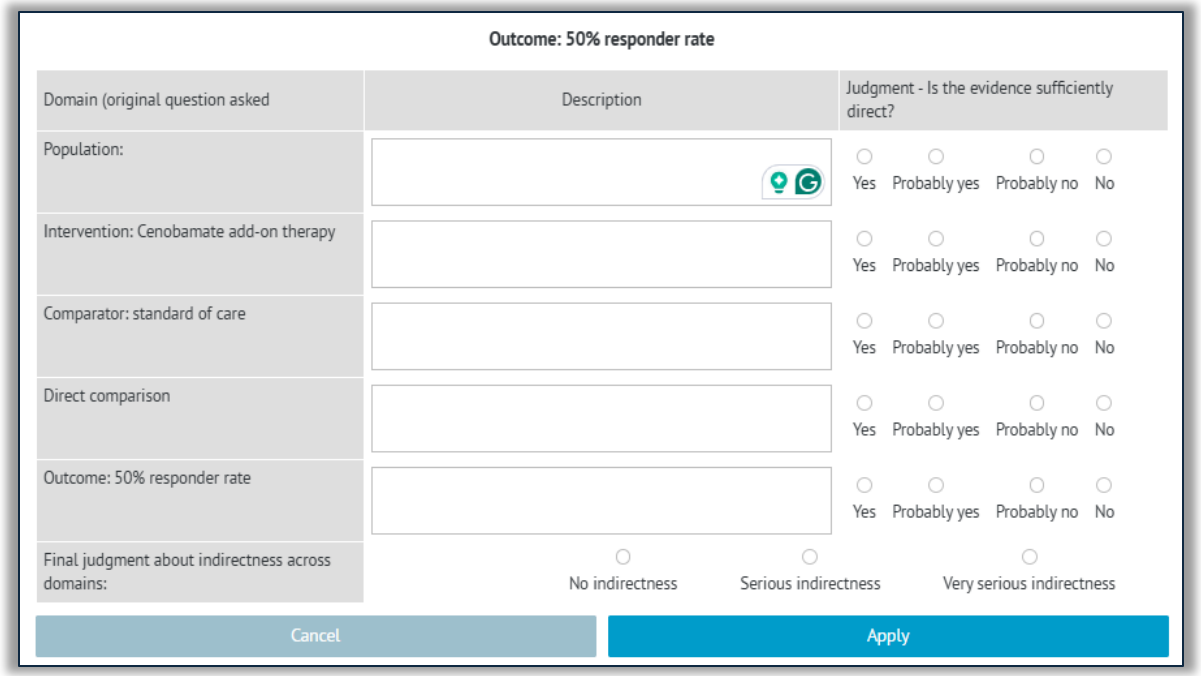
Datos indirectos

Con base a la información proporcionada

¿Hay datos indirectos?

de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Datos indirectos



Outcome: 50% responder rate

Domain (original question asked	Description	Judgment - Is the evidence sufficiently direct?
Population:		○ Yes ○ Probably yes ○ Probably no ○ No
Intervention: Cenobamate add-on therapy		○ Yes ○ Probably yes ○ Probably no ○ No
Comparator: standard of care		○ Yes ○ Probably yes ○ Probably no ○ No
Direct comparison		○ Yes ○ Probably yes ○ Probably no ○ No
Outcome: 50% responder rate		○ Yes ○ Probably yes ○ Probably no ○ No
Final judgment about indirectness across domains:		○ No indirectness ○ Serious indirectness ○ Very serious indirectness

Cancel | Apply

Subdomains	Items and sub-items
POPULATION **Interaction between population and intervention**: when the effect of the intervention may differ across subpopulations **Uncertainty about baseline risk**: when the relative estimates of an intervention effect are applied or generalized to a population of interest for which the baseline risk is not well known.	• **Disease and co-morbidities:** Primary condition of interest, secondary conditions of interest (co-morbidities). • **Non-modifiable person or population characteristics:** Age, gender, genetics, ethnicity. • **Modifiable person or population characteristics:** Anthropometric (weight), type of community or organization. • **Environmental and geographic characteristics:** Urban on non-urban, exposure to toxins. • **Setting:** Health care system and provision (tertiary care, secondary, primary care), regulatory environment.
INTERVENTION **Interaction between intervention and how is delivered:** when the effect of the intervention may differ depending on how, where, or by whom it is delivered.	• **Type of intervention:** Drugs/medications, behavioural, policy change. • **Components of the intervention:** Provider of the intervention, intensity and duration • **Naturally occurring intervention:** Type of exposure
COMPARISON **Interaction between intervention and comparator**: when the effect of the intervention may vary depending on the specific comparator used.	• **No active comparison:** Use of placebo or sham intervention, usual care (may include different interventions), no intervention at all. • **Active comparison:** same considerations that with the intervention.
OUTCOMES **Interaction between intervention and outcomes**: when the effect of the intervention may vary depending on which outcomes are measured, how they are defined, and the timing of their assessment.	• **Health and well being outcomes:** How is the outcome measured, when is measured. • **Burden:** from the intervention and the comparison • **Health systems outcomes:** Resources and societal outcomes

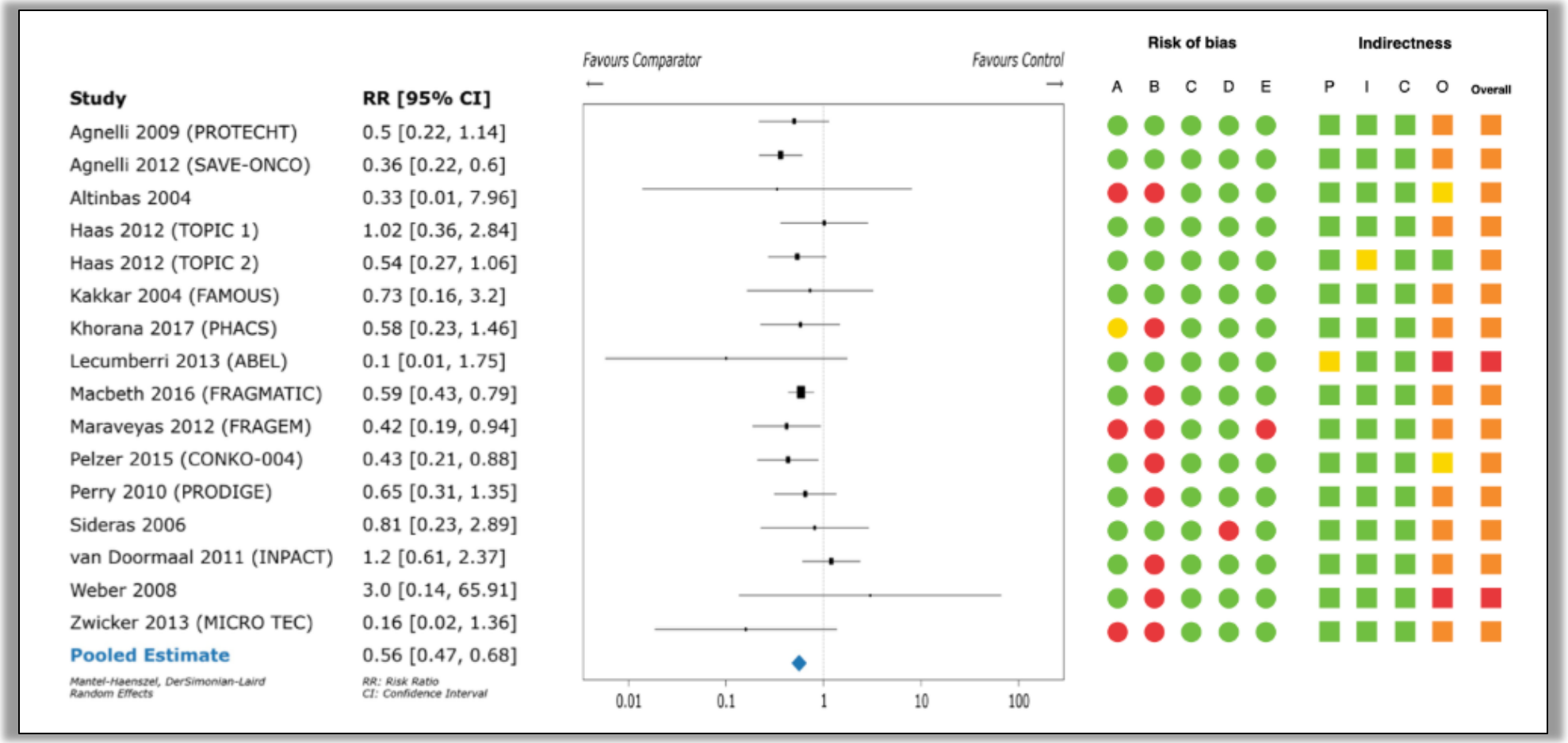
https://book.gradepro.org/guideline/indirectness

Datos indirectos

Subdomain Target question	Description Evidence found	Judgment Is the evidence is sufficiently direct?			
Population: All patients with advanced cancer	The trial included patients with advanced small cell lung cancer. The study population was representative of patients seen in practice	Yes ■	Probably Yes ☐	Probably No ☐	No ☐
Intervention: Heparins (any type)	The trial assessed the effect of Low Molecular Weight Heparin (LMWH)	Yes ■	Probably Yes ☐	Probably No ☐	No ☐
Comparison: No aticoagulation	The trial used placebo injections similar to LMWH	Yes ■	Probably Yes ☐	Probably No ☐	No ☐
Outcome: Symptomatic venous thromboembolism	The trial reported symptomatic and asymptomatic venous thromboembolism determined by screening	Yes ☐	Probably Yes ☐	Probably No ■	No ☐
Judgment across subdomains	The trial is relevant, but there are concerns about indirectness due to the use of surrogate outcomes	**Serious Indirectness**			

https://book.gradepro.org/guideline/indirectness

Datos indirectos



https://book.gradepro.org/guideline/indirectness

Datos indirectos – GRADE book

Guía para evaluación:

1. Umbrales?
2. Target (objetivo).
3. Evaluar la evidencia.
4. Juicio de valor para disminuir la certeza.

Table 1. Subdomains (PICO components), common source of indirectness and strategies to mitigate their impact

Subdomain	Common sources of indirectness	Ways to mitigate it
Population indirectness (sub group effect)	Most of the evidence—based on the weight of included studies—comes from a population that differs from the population of interest, and there are differences in relative effects due to interaction	Prioritize studies that directly include the population of interest. Conduct subgroup analyses for the relevant population to assess whether effect estimates are concordant
Population indirectness (uncertainty on baseline risk)	Concerns that the baseline risk in the included studies does not represent the baseline risk of the target population	Calculate absolute effect estimates using baseline risk data from observational studies Test plausible baseline risks and assess whether the corresponding absolute effect estimates are concordant.
Intervention indirectness	Most of the evidence relates to interventions that differ from the intervention of interest, and relative effects are likely to differ between the intervention of interest and those evaluated in the studies.	Prioritize studies that evaluate the intervention of interest. Use additional evidence (e.g., observational studies) to test for differences in relative effects.
Comparator indirectness	Interventions are compared with a comparator that differs from the one specified in the review or guideline question and relative effects are likely to differ due to the different comparison	Prioritize the most direct comparison Conduct sensitivity analyses using different comparators and assess whether absolute estimates are concordant
Outcome indirectness	Outcomes most important to people are not directly measured, requiring reliance on surrogate outcomes, outcomes measured sub-optimally, or follow-up periods that are too short.	Focus on studies that measure the outcome of interest Use additional evidence (e.g., observational studies) to model outcomes with more accurate measurement.

https://book.gradepro.org/guideline/indirectness

GRADEpro

Certainty assessment							Summary of findings					
							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cenobamate add-on therapy	Standard of care	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
50% responder rate (assessed with: Defined as the proportion of participants with D 50% seizure reduction/month during the maintenance treatment period (of any duration) compared to baseline.)												
2	randomised trials	not serious	not serious	not serious					not estimable		-	
Seizure-freedom rate (assessed with: Defined as the proportion of participants achieving total seizure cessation during the maintenance treatment period (of any duration) compared to baseline)												
									not estimable		-	
Any adverse event (assessed with: Proportion of participants who experienced any adverse event (AE) throughout the entire study period)												
									not estimable		-	

Add outcome | Import outcome(s)

https://www.gradepro.org/

Imprecisión

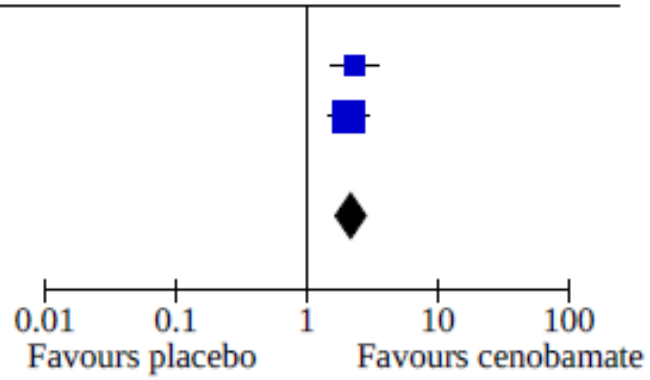
Analysis 1.1. Comparison 1: Cenobamate versus placebo (any dose), Outcome 1: 50% responder rate

Study or Subgroup	Cenobamate Events	Cenobamate Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chung 2020	53	106	22	102	36.7%	2.32 [1.53 , 3.51]
Krauss 2020	157	295	26	102	63.3%	2.09 [1.47 , 2.96]
Total (95% CI)		**401**		**204**	**100.0%**	**2.17 [1.66 , 2.84]**
Total events:	210		48			

Heterogeneity: $Chi^2 = 0.14$, df = 1 (P = 0.70); $I^2 = 0\%$

Test for overall effect: Z = 5.68 (P < 0.00001)

Test for subgroup differences: Not applicable



de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

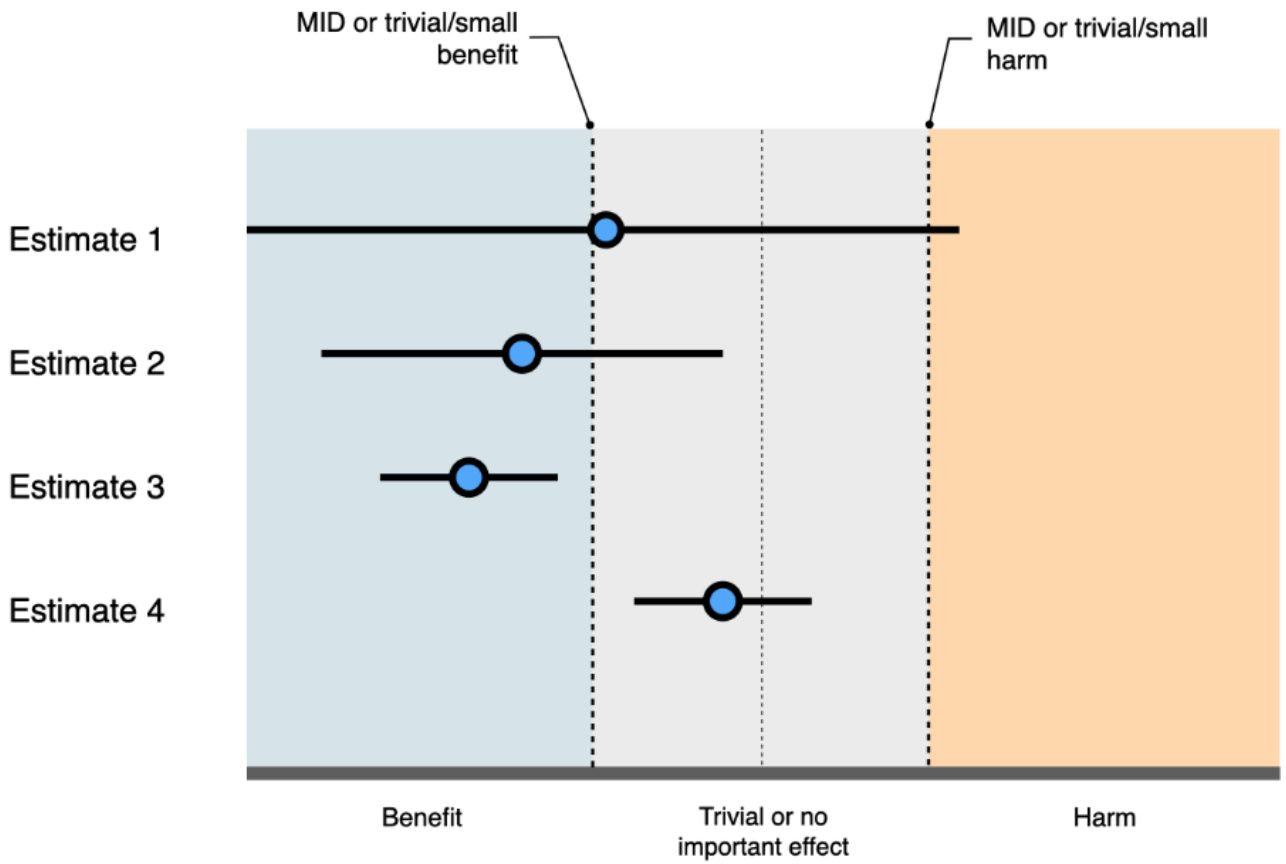
Imprecisión

Con base a la información proporcionada

¿Hay datos imprecisión?

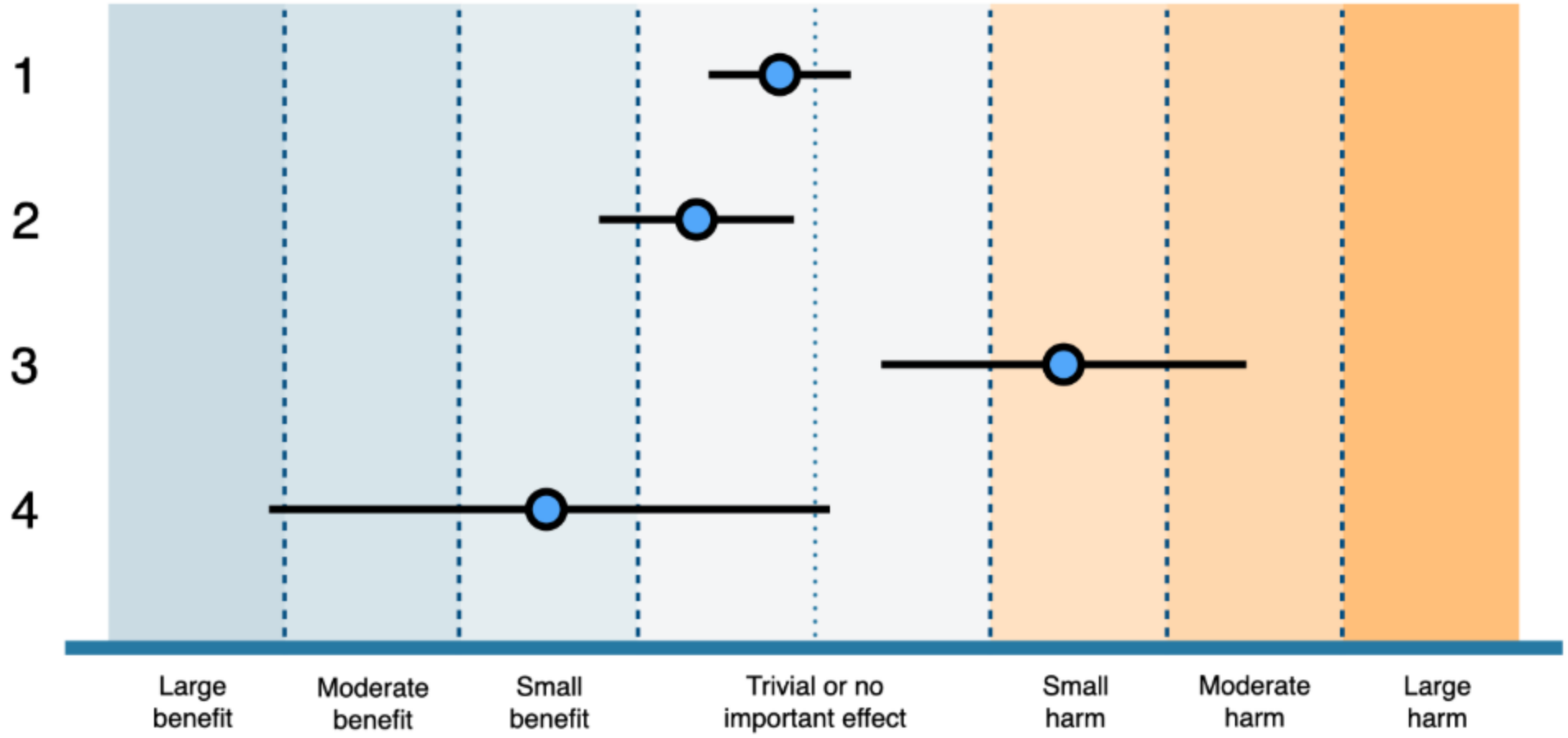
de Paiva FA, Menegaz de Almeida A, Lima AAFR, Tozzo TJ, Tanimoto LE, de Oliveira Carriço HRM, Ribeiro DM. Cenobamate add-on therapy for drug-resistant focal seizures: a systematic review and meta-analysis. Expert Rev Neurother. 2025 May;25(5):591-597. doi: 10.1080/14737175.2025.2484439. Epub 2025 Mar 25. PMID: 40131227.

Imprecisión



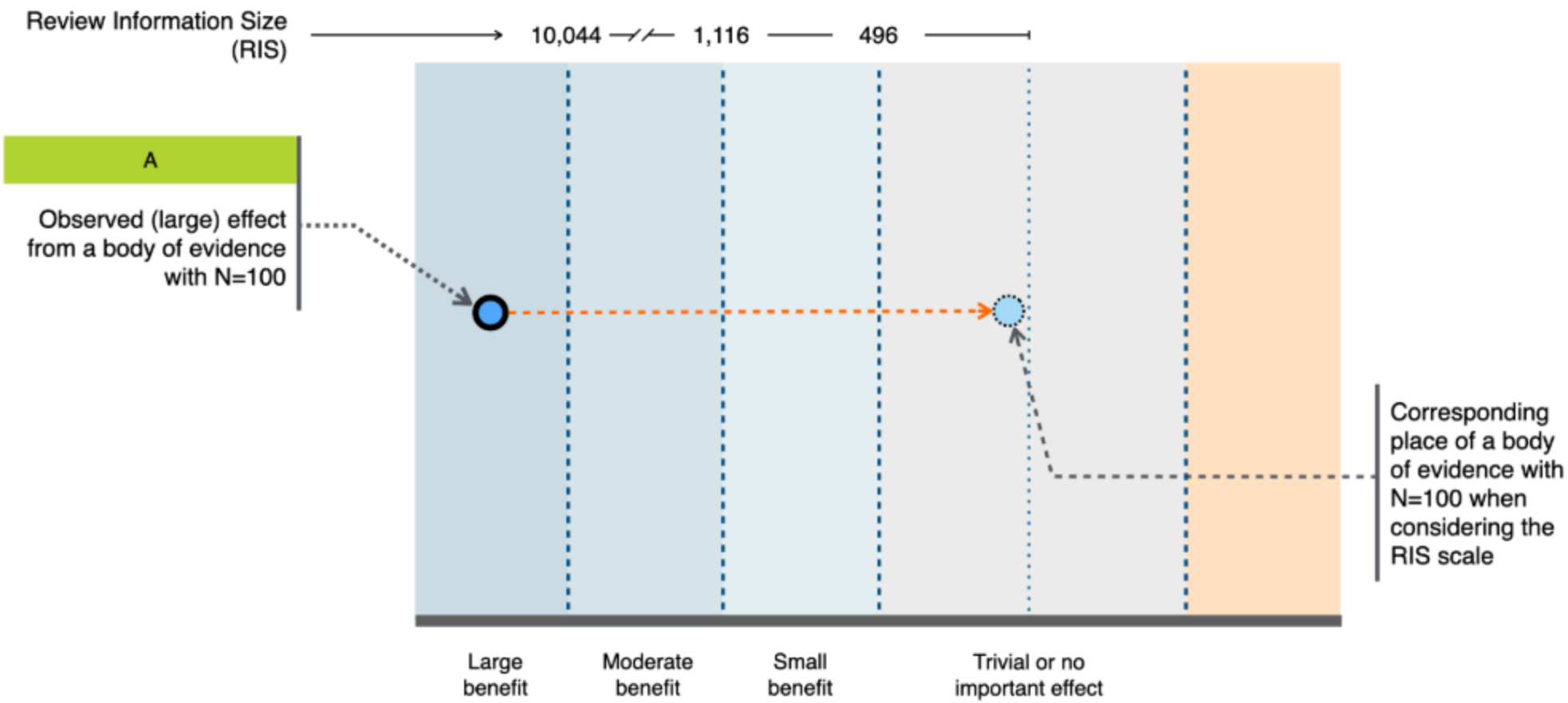
https://book.gradepro.org/guideline/imprecision

Imprecisión



https://book.gradepro.org/guideline/imprecision

Imprecisión



https://book.gradepro.org/guideline/imprecision

Imprecisión

4.1. When systematic review and guideline authors should check optimal information size

Considering OIS refers to considering whether the total number of participants or events in the meta-analysis is more than the number of participants or events generated by a conventional sample size calculation for a single adequately powered trial [1,2]. When the CI overlaps with threshold(s) of interest, authors would rate down for imprecision and do not need to consider the OIS.

When the CI does not overlap with the threshold(s) of interest and the effect is sufficiently large and [e.g., relative risk (RR) reduction or an RR increase over 30%] that the authors consider the results implausible, authors should consider implementing the OIS [1,2,12]. If the OIS is met, authors do not need to rate down for imprecision; otherwise, authors should rate down. It is important to notice that because the calculation of OIS is based on relative estimates of effect [1], all assessments and steps in OIS approach focus on the relative estimate of effect (as opposed to the CI approach, which is done based on absolute estimates of effect).

ELSEVIER

Journal of Clinical Epidemiology 150 (2022) 216–224

Journal of Clinical Epidemiology

GRADE GUIDANCE SERIES

GRADE Guidance 34: update on rating imprecision using a minimally contextualized approach

Linan Zeng[a,b,*], Romina Brignardello-Petersen[b], Monica Hultcrantz[c], Reem A. Mustafa[d], Mohammad H. Murad[e], Alfonso Iorio[b,f], Gregory Traversy[g], Elie A. Akl[h], Martin Mayer[i,j,k], Holger J. Schünemann[b,f], Gordon H. Guyatt[b,f]

Zeng, L., Brignardello-Petersen, R., Hultcrantz, M., Mustafa, R. A., Murad, M. H., Iorio, A., ... & Guyatt, G. H. (2022). GRADE Guidance 34: update on rating imprecision using a minimally contextualized approach. *Journal of clinical epidemiology*, *150*, 216-224.

Imprecisión

ELSEVIER

Journal of Clinical Epidemiology 150 (2022) 216–224

Journal of Clinical Epidemiology

GRADE GUIDANCE SERIES

GRADE Guidance 34: update on rating imprecision using a minimally contextualized approach

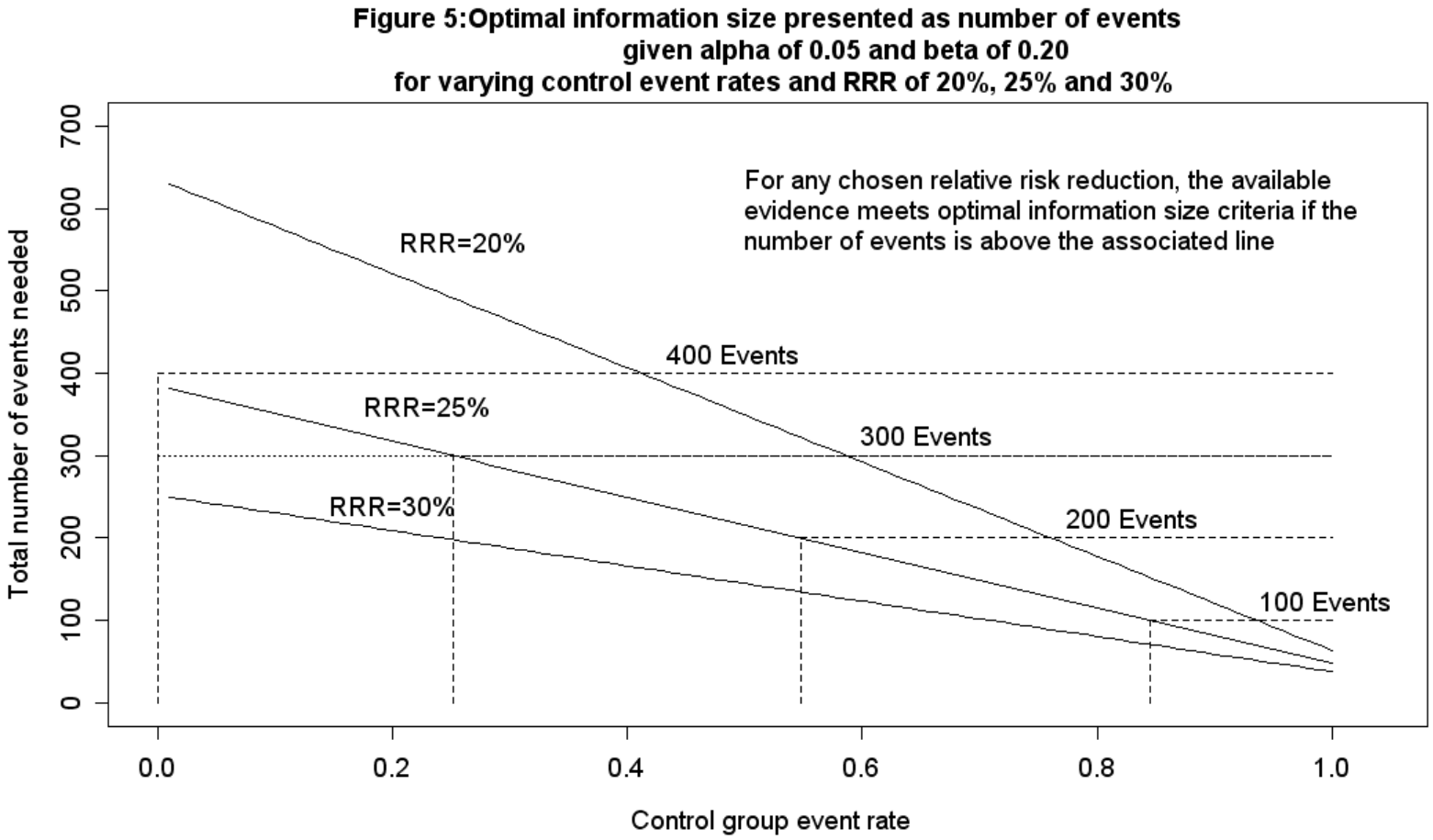
Linan Zeng[a,b,*], Romina Brignardello-Petersen[b], Monica Hultcrantz[c], Reem A. Mustafa[d], Mohammad H. Murad[e], Alfonso Iorio[b,f], Gregory Traversy[g], Elie A. Akl[h], Martin Mayer[i,j,k], Holger J. Schünemann[b,f], Gordon H. Guyatt[b,f]

Box 5 Circumstances when one should consider rating down two levels for imprecision based on optimal information size calculation using a minimally contextualized approach

1. For dichotomous outcomes, when the ratio of the upper to the lower boundary of the CI is more than 2.5 for odds ratio or three for risk ratioR (Appendix A, Example 1).
2. For continuous outcomes, when the total sample size of a meta-analysis is smaller than 30–50% of the OIS (Appendix A, Example 2).

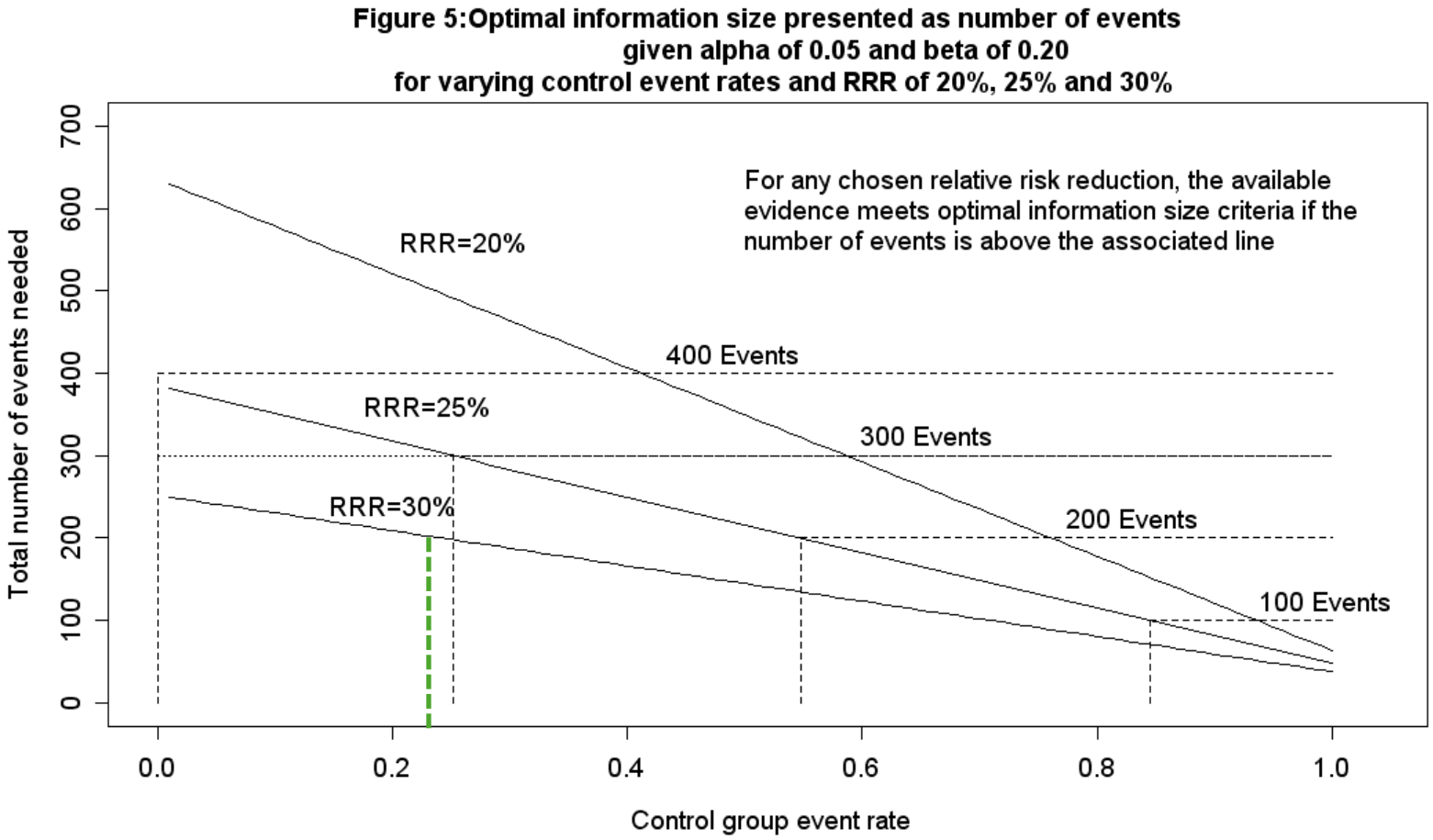
Zeng, L., Brignardello-Petersen, R., Hultcrantz, M., Mustafa, R. A., Murad, M. H., Iorio, A., ... & Guyatt, G. H. (2022). GRADE Guidance 34: update on rating imprecision using a minimally contextualized approach. *Journal of clinical epidemiology*, *150*, 216-224.

Imprecisión



https://www.gradeworkinggroup.org/

Imprecisión



https://www.gradeworkinggroup.org/

Imprecisión – GRADE book

Guía para evaluación:

1. Umbrales?
2. Target (objetivo).
3. Evaluar la evidencia.
4. Juicio de valor para disminuir la certeza.
5. OIS o RIS.

Considera disminuir la certeza por imprecisión:

- Tamaño de muestra pequeño, IC amplio.
  - Observa los límites superior e inferior del IC.
- Si cruza el umbral, es probable que se deba disminuir la calificación.
- Si cruza los umbrales de beneficio importante o daño, actúa en consecuencia.
  - Considera un resumen en lenguaje claro.
- Si el efecto es grande (RRR > 30%), revisa nuevamente.
  - Está bien si se cumple el OIS (revisa la figura o al menos 300 eventos).

https://book.gradepro.org/guideline/imprecision

GRADEpro

Should Cenobamate add-on therapy vs. standard of care be used for drug-resistant focal epilepsy?

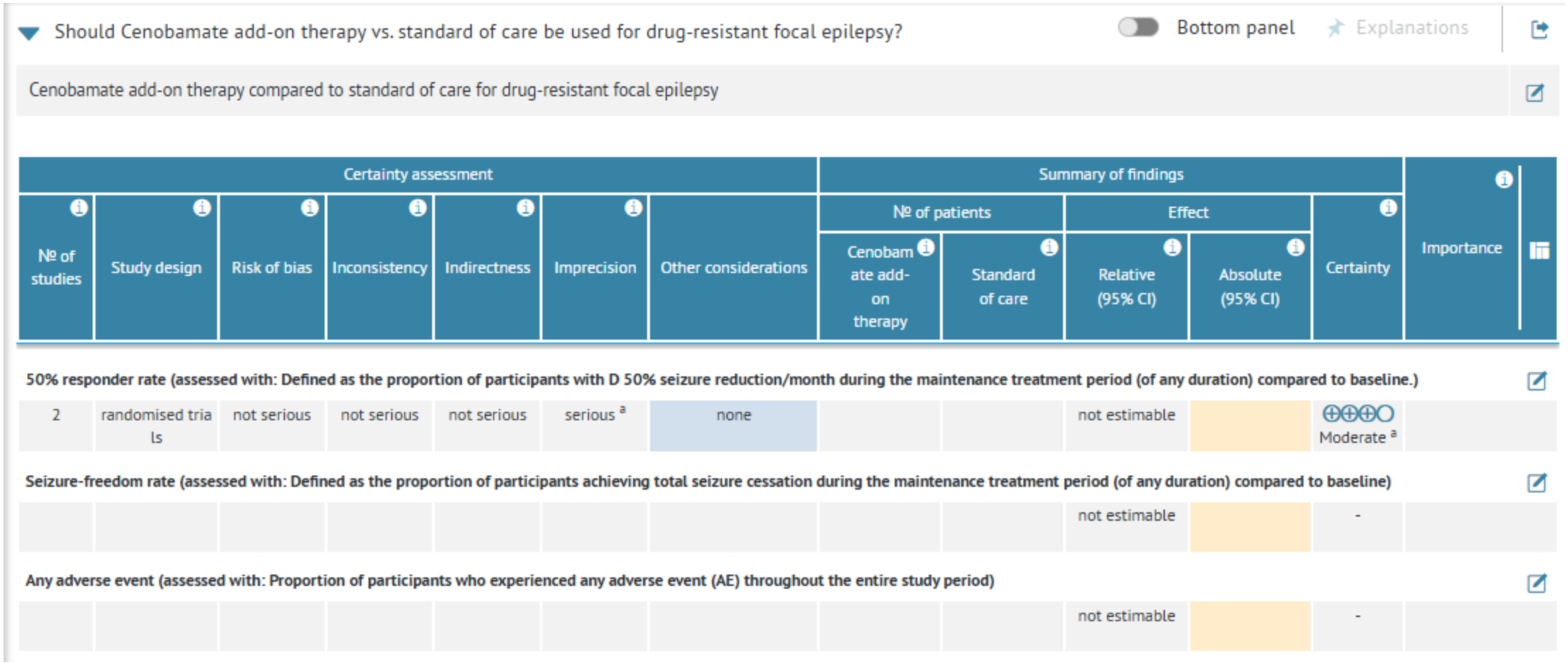
Bottom panel Explanations

Cenobamate add-on therapy compared to standard of care for drug-resistant focal epilepsy

Certainty assessment							Summary of findings					
							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cenobamate add-on therapy	Standard of care	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
50% responder rate (assessed with: Defined as the proportion of participants with D 50% seizure reduction/month during the maintenance treatment period (of any duration) compared to baseline.)												
2	randomised trials	not serious	not serious	not serious	serious [a]				not estimable		- [a]	
Seizure-freedom rate (assessed with: Defined as the proportion of participants achieving total seizure cessation during the maintenance treatment period (of any duration) compared to baseline)												
									not estimable		-	
Any adverse event (assessed with: Proportion of participants who experienced any adverse event (AE) throughout the entire study period)												
									not estimable		-	

https://www.gradepro.org/

Sesgo de publicación - GRADEpro



Should Cenobamate add-on therapy vs. standard of care be used for drug-resistant focal epilepsy?

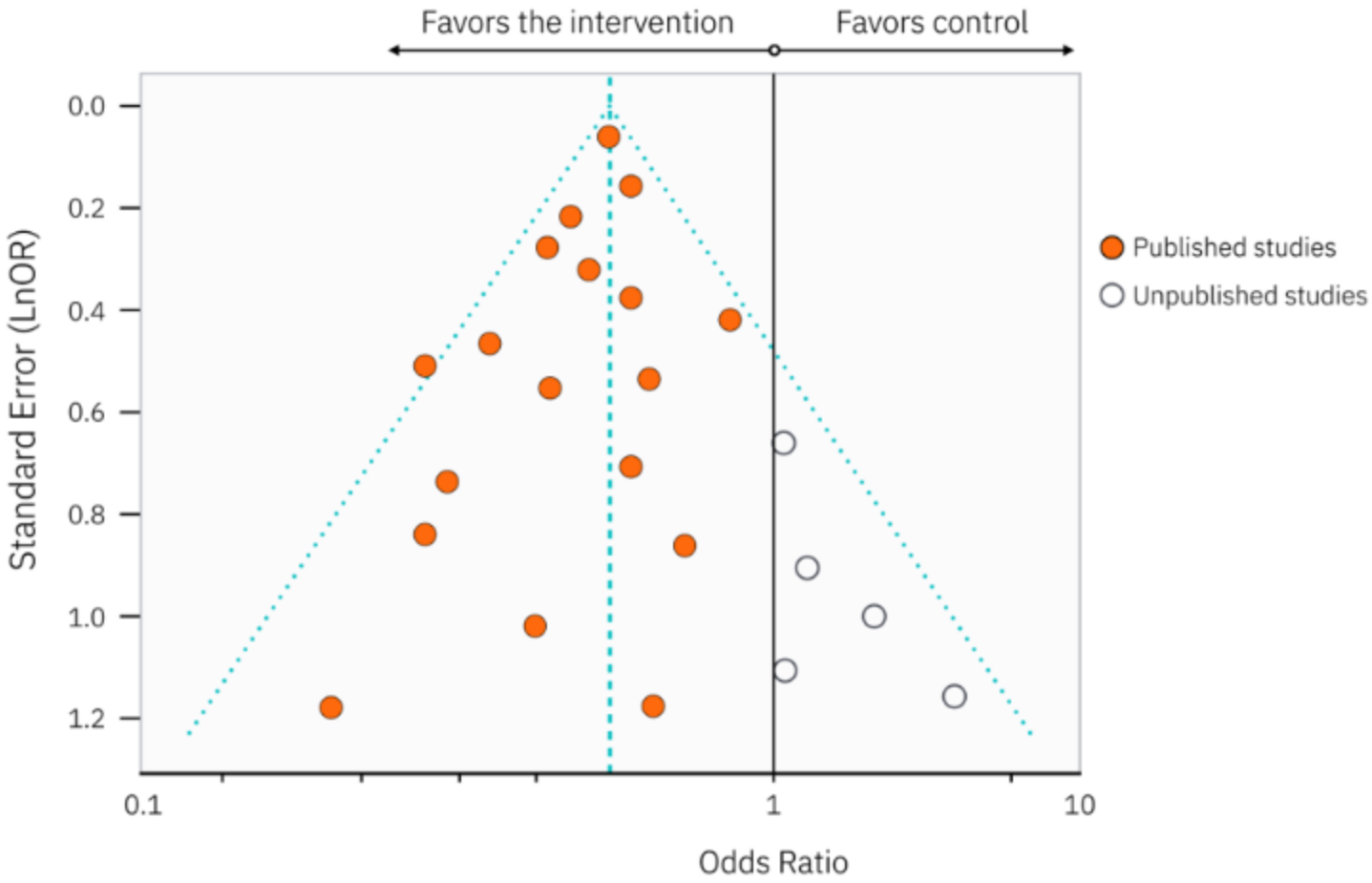
Bottom panel Explanations

Cenobamate add-on therapy compared to standard of care for drug-resistant focal epilepsy

Certainty assessment							Summary of findings					
							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cenobamate add-on therapy	Standard of care	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
50% responder rate (assessed with: Defined as the proportion of participants with D 50% seizure reduction/month during the maintenance treatment period (of any duration) compared to baseline.)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none			not estimable		⨁⨁⨁◯ Moderate [a]	
Seizure-freedom rate (assessed with: Defined as the proportion of participants achieving total seizure cessation during the maintenance treatment period (of any duration) compared to baseline)												
									not estimable		-	
Any adverse event (assessed with: Proportion of participants who experienced any adverse event (AE) throughout the entire study period)												
									not estimable		-	

https://www.gradepro.org/

Sesgo de publicación



https://book.gradepro.org/guideline/dissemination-bias

Sesgo de publicación

- Estudios negativos son menos probables a ser publicados
- Existe una alta probabilidad de que el sesgo de publicación afecte la calidad de la información
  - Pocos estudios en el cuerpo de la evidencia
  - Estudios realizados por la industria.

https://www.gradeworkinggroup.org/

Dominios de mejora
(upgrade)

https://www.gradepro.org/

GRADE book

- Tamaño del efecto
- Dosis respuesta
- Variables de confusión

Efecto
+1 grande
+2 muy grande
Dosis-respuesta
+1 gradiente evidente
Todos los factores de confusión:
+1 reducirían el efecto observado
+1 sugerirían un efecto espurio si no hay efecto observado

https://book.gradepro.org/

Agenda del día

- Introducción.
- Evaluación de la certeza de la evidencia con el sistema GRADE.
- Transición de la evidencia a las recomendaciones (EtD framework).

Cochrane República Dominicana

GOBIERNO DE LA REPÚBLICA DOMINICANA
SALUD PÚBLICA

Cochrane Iberoamérica

Transición de la evidencia a las recomendaciones

(EtD framework)

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction

Pablo Alonso-Coello,[1,2] Holger J Schünemann,[2,3] Jenny Moberg,[4] Romina Brignardello-Petersen,[2,5] Elie A Akl,[2,6] Marina Davoli,[7] Shaun Treweek,[8] Reem A Mustafa,[2,9] Gabriel Rada,[10,11,12] Sarah Rosenbaum,[4] Angela Morelli,[4] Gordon H Guyatt,[2,3] Andrew D Oxman[4] the GRADE Working Group

Journal of Clinical Epidemiology

Journal of Clinical Epidemiology 162 (2023) 38–46

GRADE RELATED SERIES

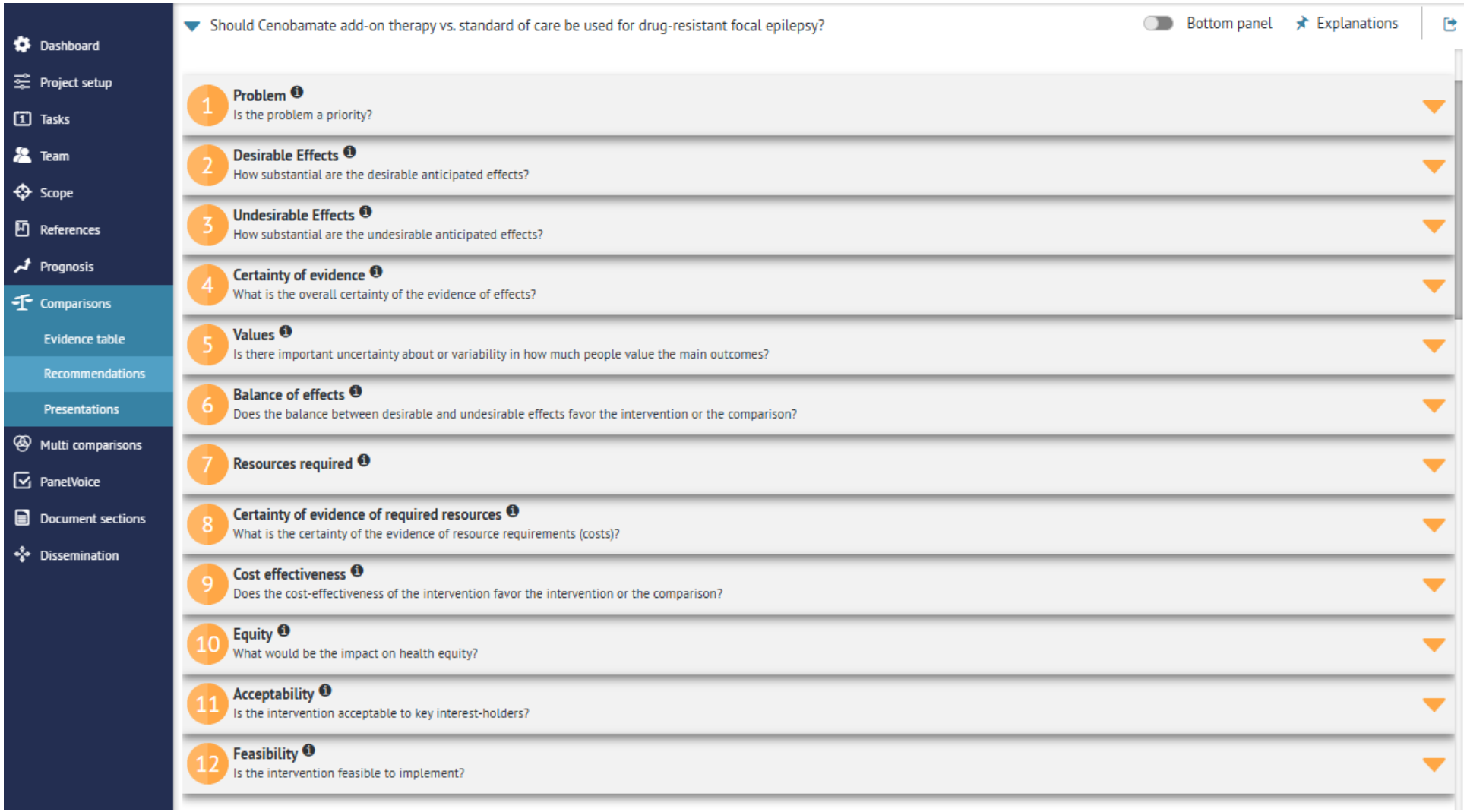
Using evidence to decision frameworks led to guidelines of better quality and more credible and transparent recommendations

Jose F. Meneses-Echavez[a,b,*], Julia Bidonde[a,c], Camila Montesinos-Guevara[d], Yasser S. Amer[e], Andres Felipe Loaiza-Betancur[f,g], Luis Andres Tellez Tinjaca[g], David Fraile Navarro[h,i], Tina Poklepović Peričić[j], Ružica Tokalić[j], Malgorzata M. Bala[k], Dawid Storman[l], Mateusz Swierz[k], Joanna Zając[k], Ivan D. Flórez[m,n,o], Holger Schünemann[p], Signe Flottorp[a,q], Pablo Alonso-Coello[r]

GRADEpro

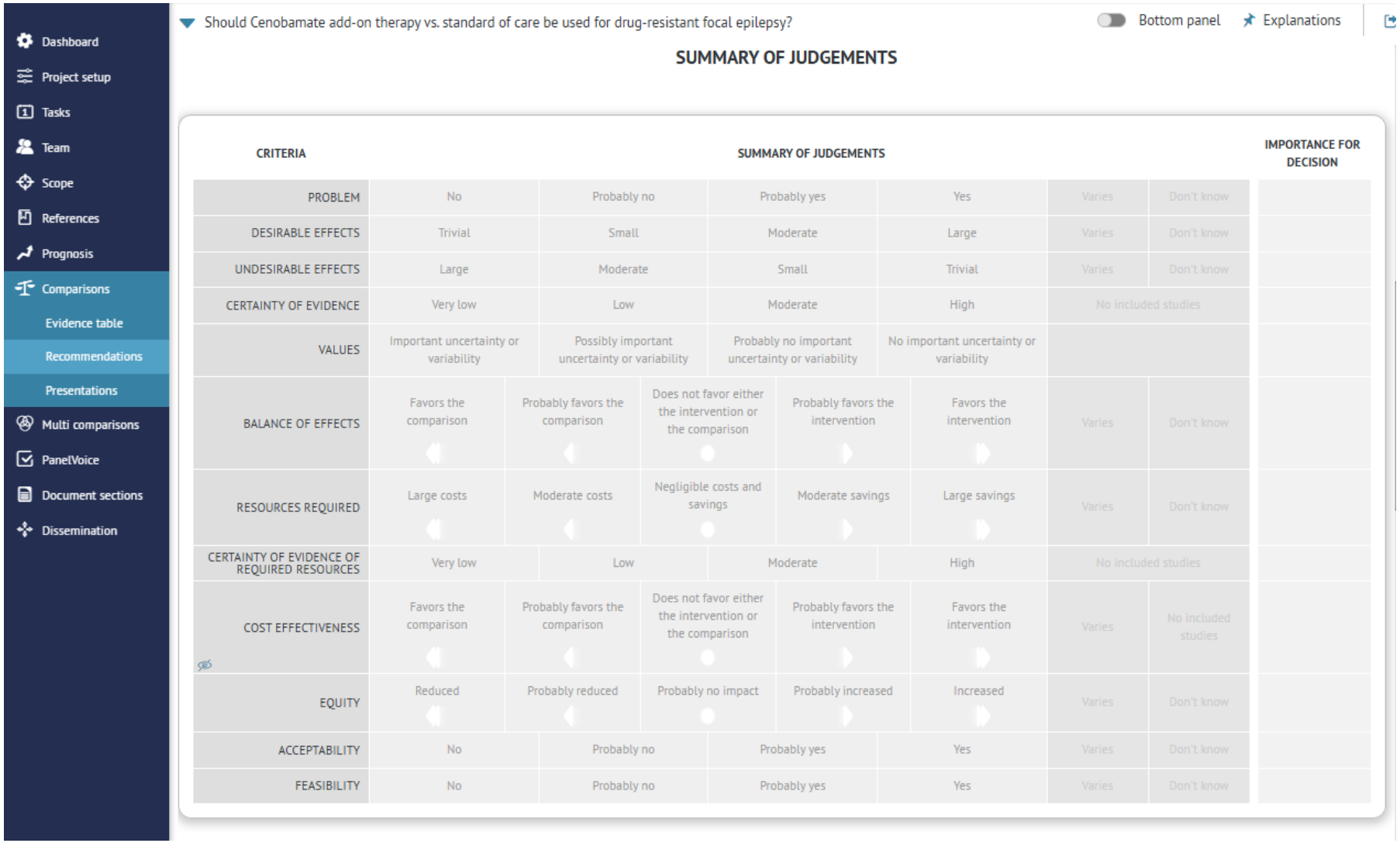
https://www.gradepro.org/

Evidence to Decision Framework



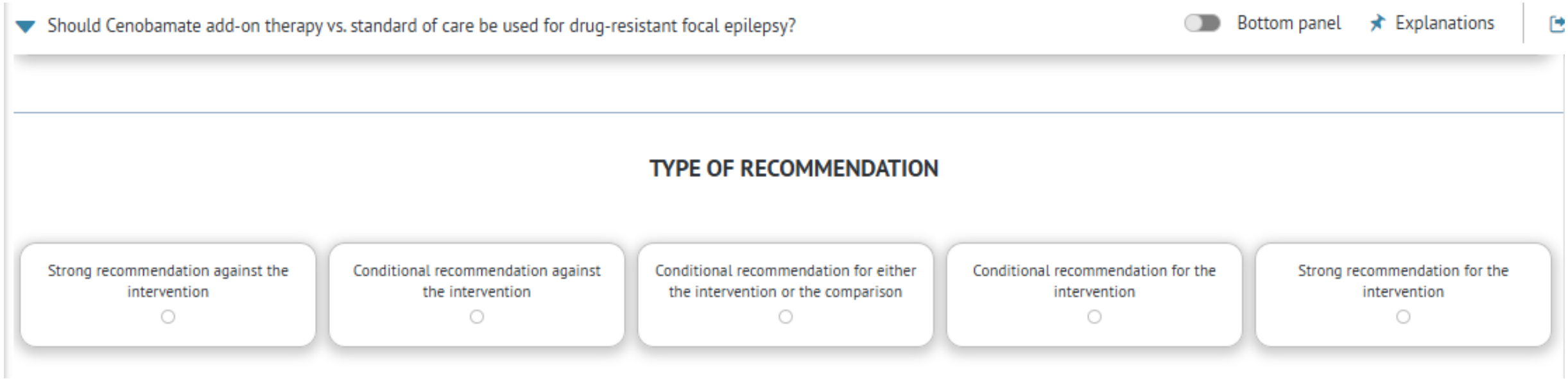
https://www.gradepro.org/

Evidence to Decision Framework



https://www.gradepro.org/

Evidence to Decision Framework



https://www.gradepro.org/

Gracias por su atención