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How to calculate absolute effects

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How to calculate absolute effects

- For event-free survival
- For events

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Pre-assumption

Pooled hazard ratio (HR) has been correctly calculated

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How to estimate baseline risk

- Baseline risk should be representative of type of individuals it is intended to be applied to
- Ideally from appropriate observational studies with representative patients
- Clearly describe in footnotes where baseline risk comes from and which specific time point has been chosen

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How to estimate baseline risk from Kaplan-Meier curves

- Included trials evaluating patient groups being at different risks could be grouped according to risks
- Representative trials for each risk group could be used to estimate baseline risk

- Time point chosen should not be extrapolated from Kaplan-Meier curves (e.g. Kaplan-Meier curve for 2 years provided: can't estimate risk for 5 years!)

- Uncertainty of baseline risk is not included in confidence interval of absolute effect
- Uncertainty of baseline risk is not considered in GRADEing (certainty of evidence refers to pooled effect estimate only)

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Event-free survival

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Reminder: Event-free survival: OS higher than PFS (same time point)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with chemotherapy only	Risk with intervention in addition to chemotherapy				
Overall survival follow up: 24 months	Moderate 900 per 1,000					
Progression-free survival follow up: 24 months	Moderate 800 per 1,000					

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Absolute effects for event-free survival

Based on methods described by Tierney et al

$$p1 = \exp(\log(p0) \times HR)$$

Example:

- Pooled HR of **0.42 (95% CI 0.25 to 0.72)**
- Indicating lower risk of death over time in intervention group
- Estimating proportion of patients with event-free survival in control group at **2 years** of **900 per 1000**:

$$p1 = \exp(\log(0.9) \times 0.42) = 0.956$$

956 per 1000 people will be alive with experimental intervention **at 2 years**

Tierney et al: Practical methods for incorporating summary time-to-event data into meta-analysis. Trials. 2007

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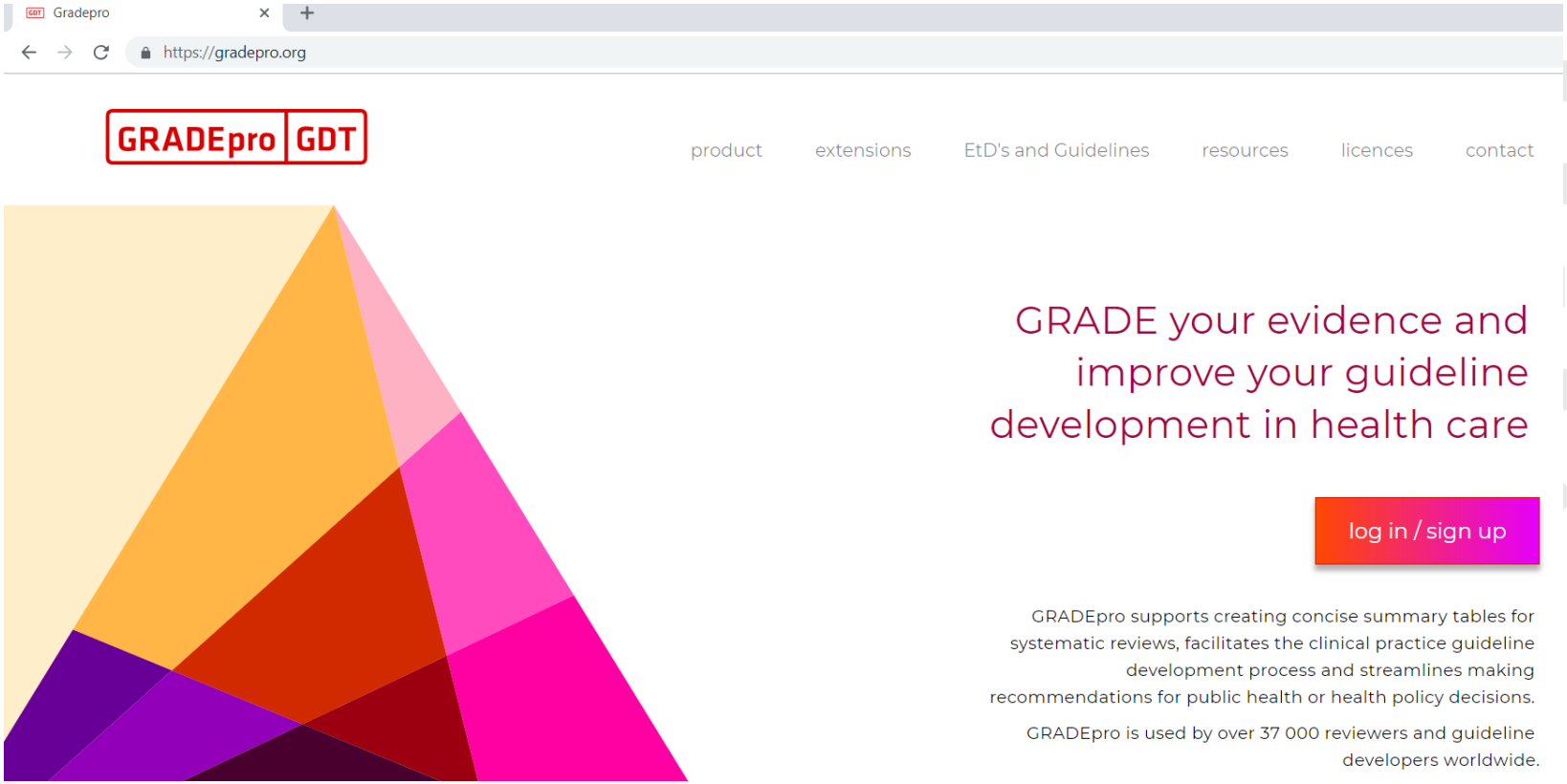
- Please use GRADEpro GDT with google chrome



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Example 1: event-free survival: overall survival

Pooled **HR of 0.42 (95% CI 0.25 to 0.72**)

Indicating a lower risk of death over time in intervention group

Estimating a proportion of patients with event-free survival in control group at **time point 2 years of 900 per 1000**

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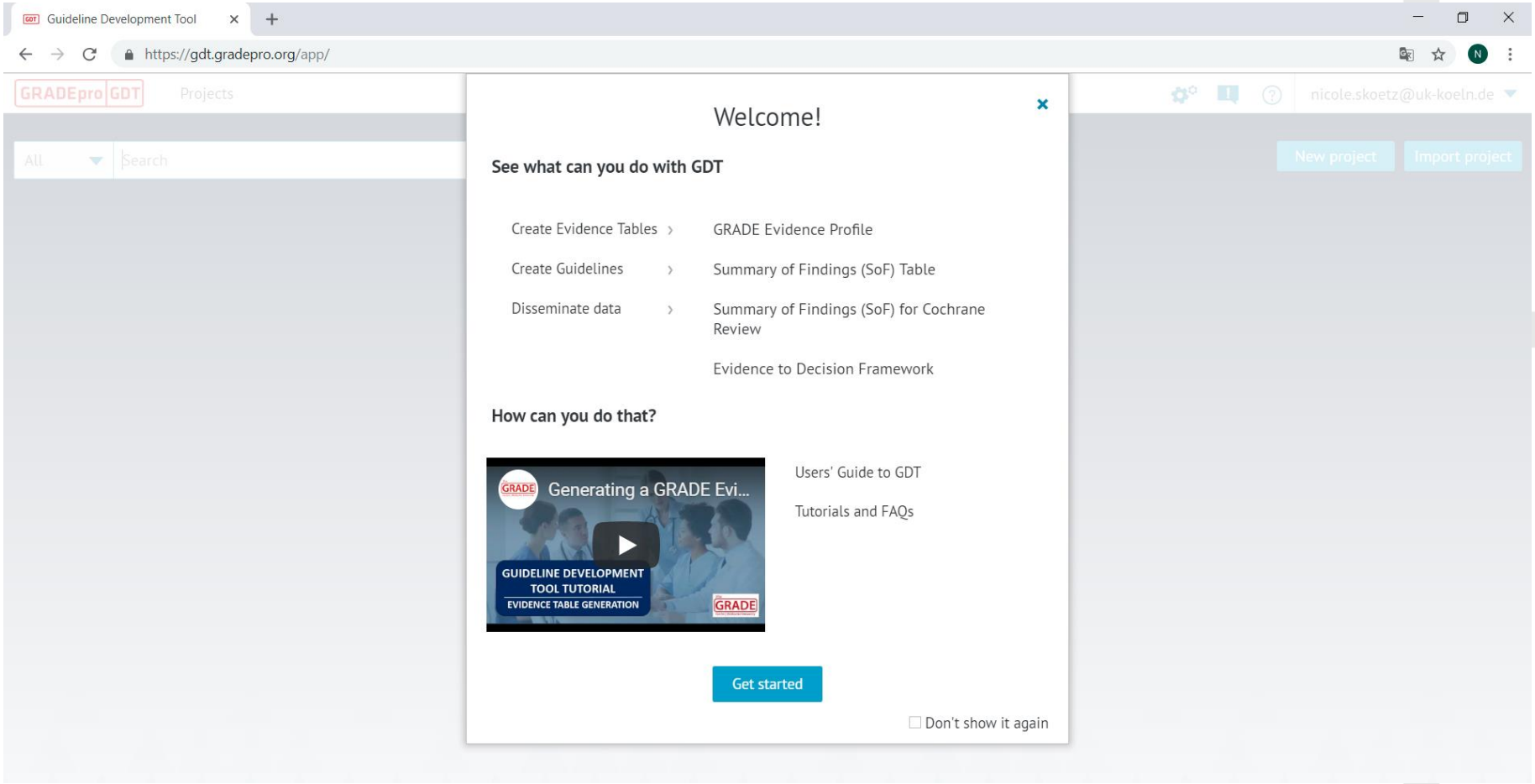

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New group

1	Should [intervention] vs. [comparison] be used for [health problem and/or population]?

Click or drag question here to create a new group

Add management question

Add diagnostic question

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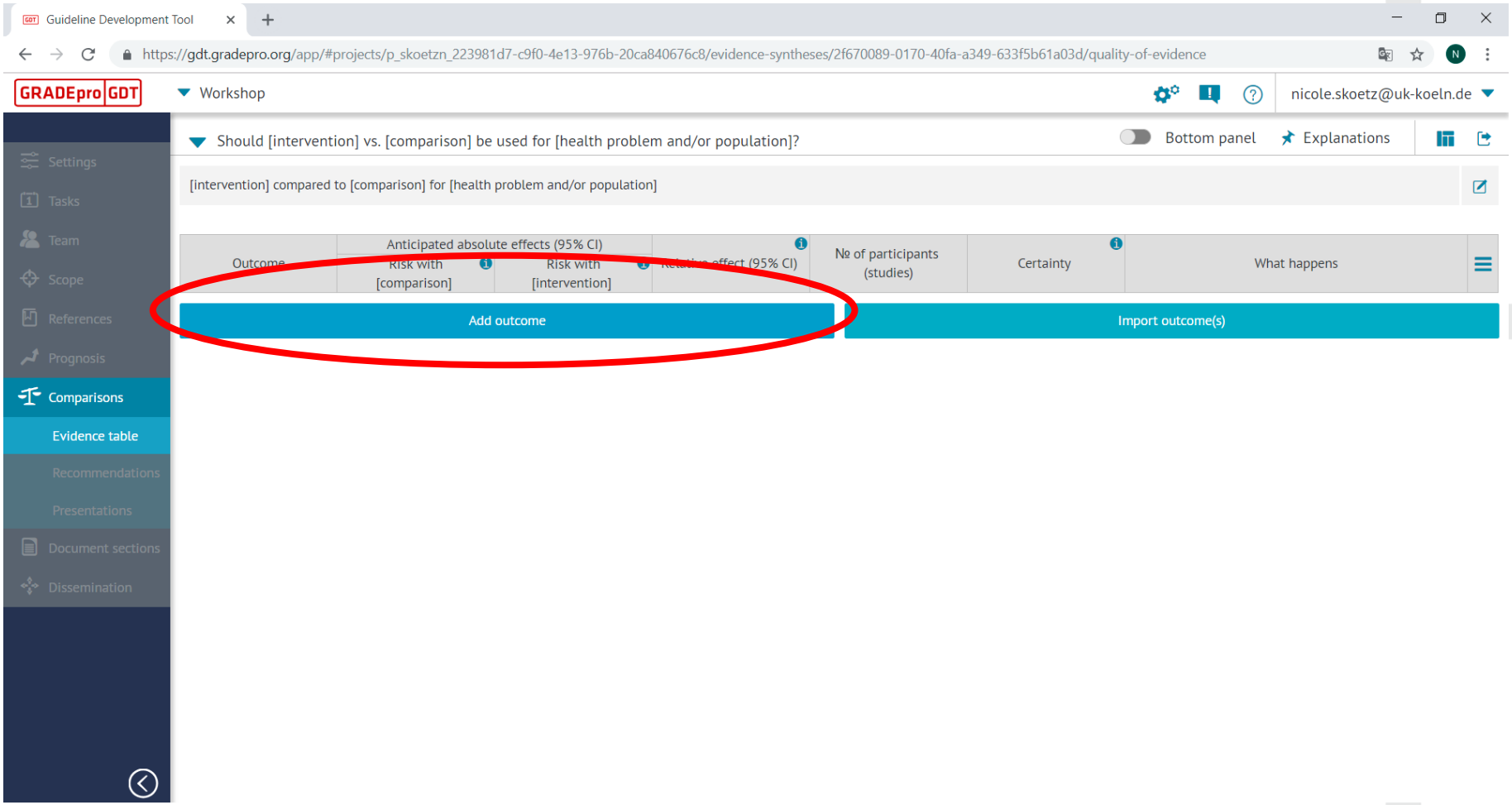

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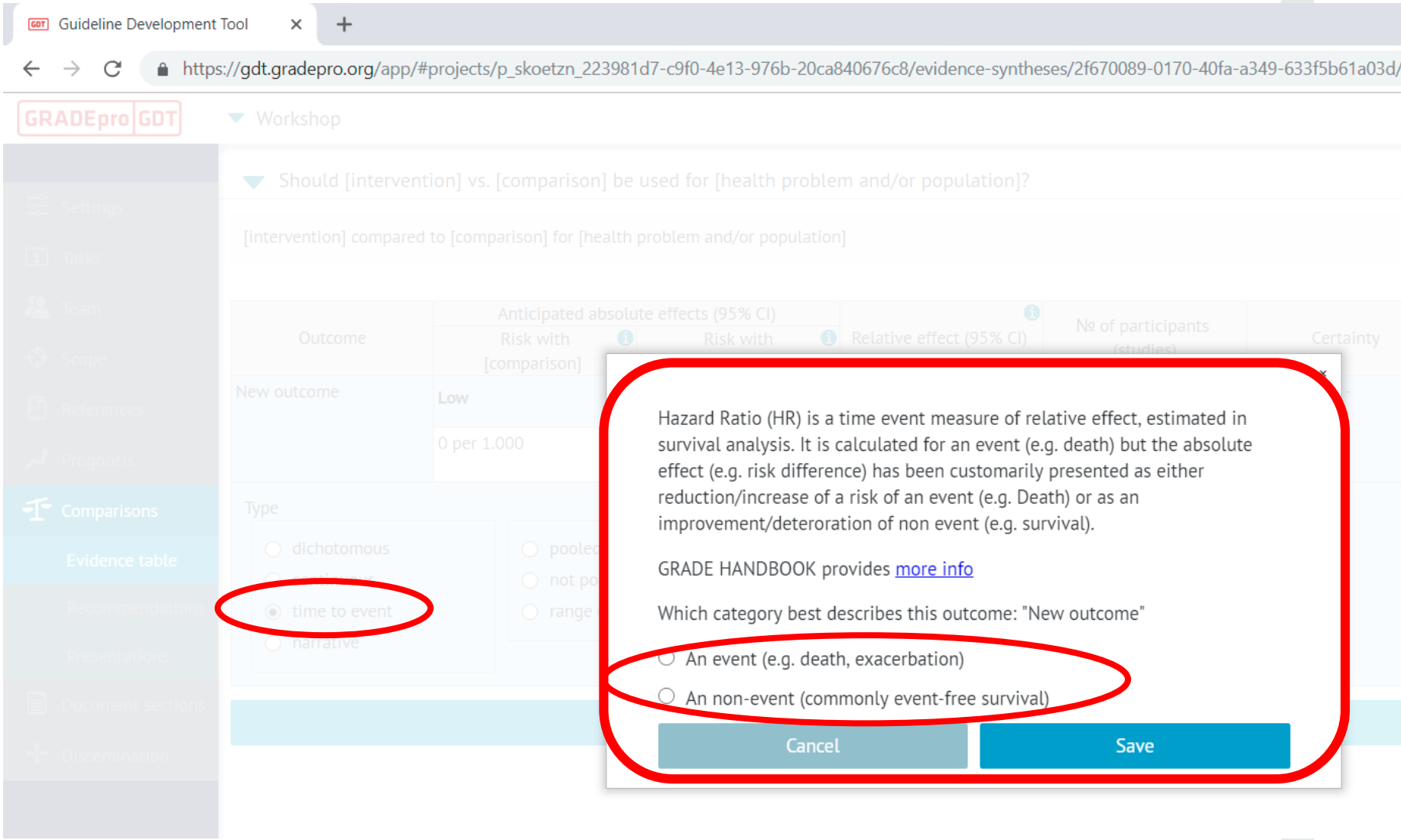

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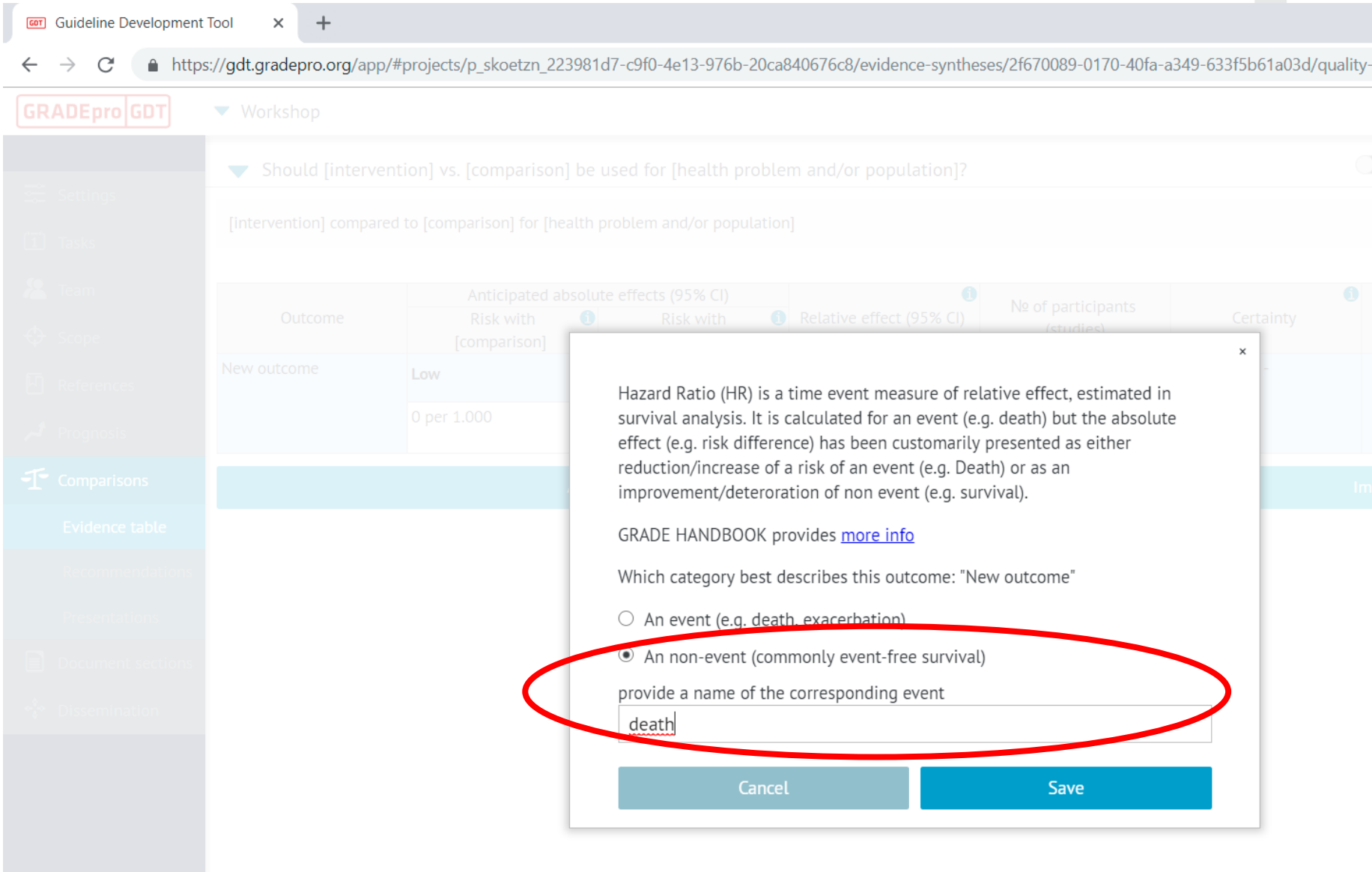

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Should [intervention] vs. [comparison] be used for [health problem and/or population]?

[intervention] compared to [comparison] for [health problem and/or population]

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	№ of participants (studies)
	Risk with [comparison]	Risk with [intervention]		
New outcome	**Low**		not estimable	(studies)
	0 per 1.000	**0 per 1.000**		

Outcome

Outcome name: Overall survival

Short name:

Assessed/measured with:

Length of follow up: 2 years

Cancel | Apply

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[intervention] compared to [comparison] for [health problem and/or population]

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty
	Risk with [comparison]	Risk with [intervention]			
Overall survival follow up: 2 years	**Low**		not estimable	(studies)	-
	0 per 1.000	**0 per 1.000** (0 to 0)			

Import

Control risk

Total participants

Denominator per 1.000

Low	☐	Low	%
Moderate	☑	Moderate	90 %
High	☐	High	0 %

Cancel Apply

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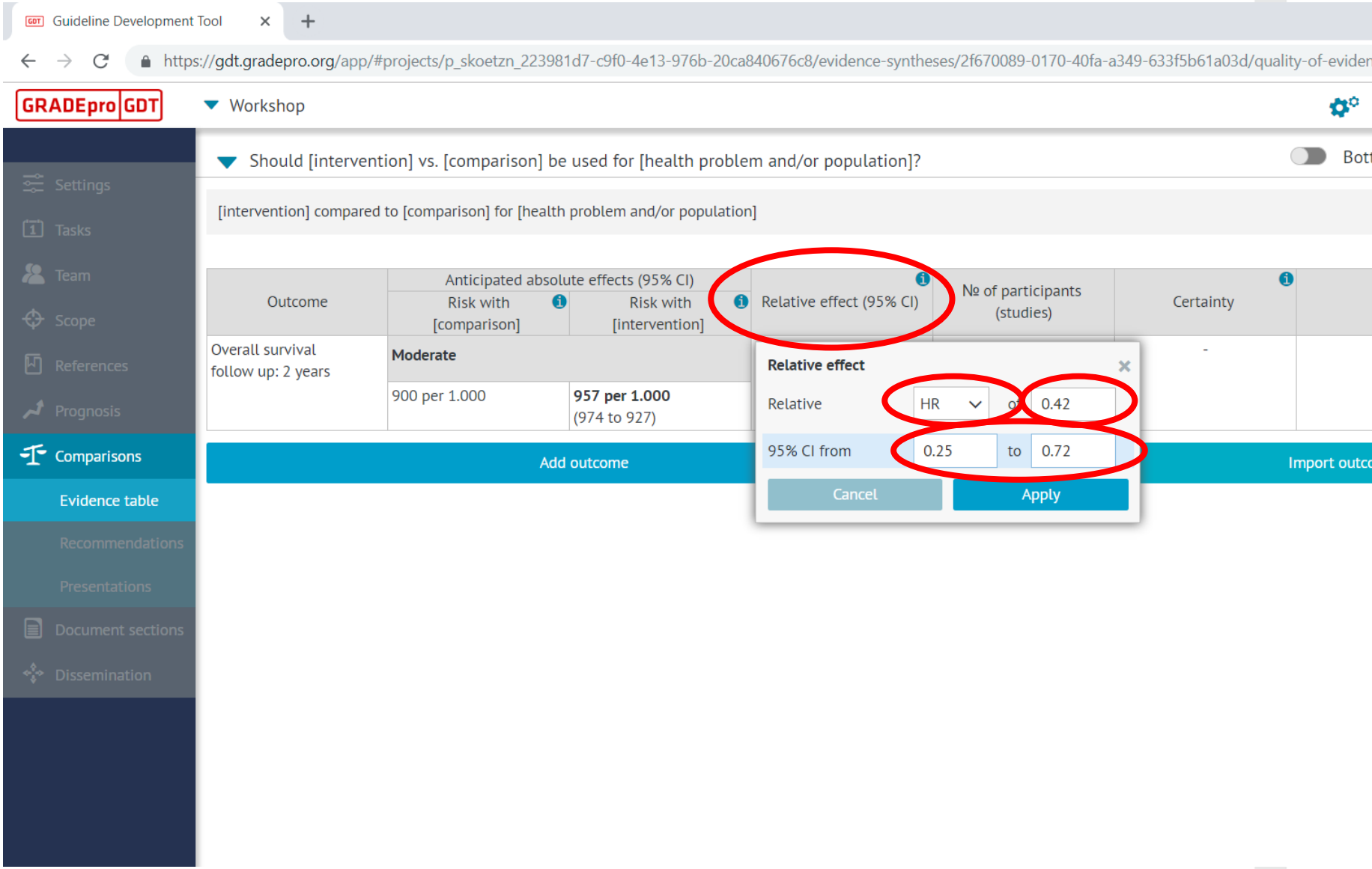

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Should [intervention] vs. [comparison] be used for [health problem and/or population]?

Bottom p

[intervention] compared to [comparison] for [health problem and/or population]

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty	
	Risk with [comparison]	Risk with [intervention]				
Overall survival follow up: 2 years	**Moderate**		**HR 0.42** (0.25 to 0.72) [death]	(studies)	-	
	900 per 1.000	**957 per 1.000** (974 to 927)				

Add outcome

Import outcome(s)

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Events

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Reminder: Events: Mortality higher than combined outcome

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with chemotherapy only	Risk with intervention in addition to chemotherapy				
Mortality (instead of overall survival) follow up: 24 months	Moderate					
	100 per 1,000					
Mortality, relapse and progress (instead of progression-free survival) follow up: 24 months	Moderate					
	200 per 1,000					

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Absolute effects for events

- Similar formula can be used

$$r1 = 1 - \exp(\log(1-r0) \times HR)$$

- **Hazard ratio = 0.42 (95% CI 0.25 to 0.72**), assuming control risk of events (e.g. for mortality, people being dead) **at 2 years = 100 per 1000**

$$r1 = 1 - \exp(\log(1-0.1) \times 0.42) = 0.044$$

- **44 per 1000** people will be dead with the experimental intervention at 2 years

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Example 2: events: mortality

Pooled **HR of 0.42 (95% CI 0.25 to 0.72**) indicating a lower risk of death over time in intervention group

Estimating a proportion of patients with events in the control group at the **time point 2 years of 0.1**

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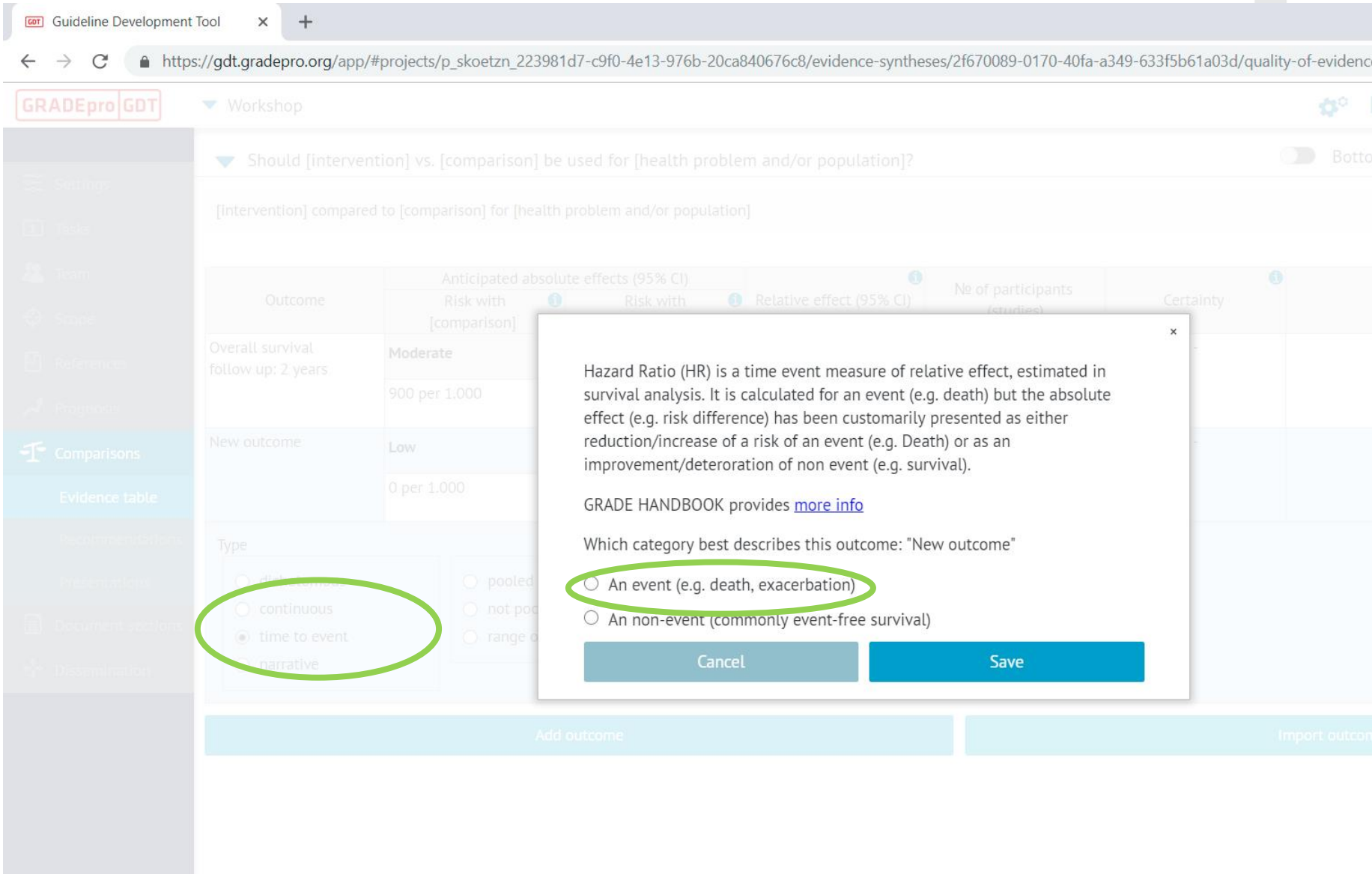

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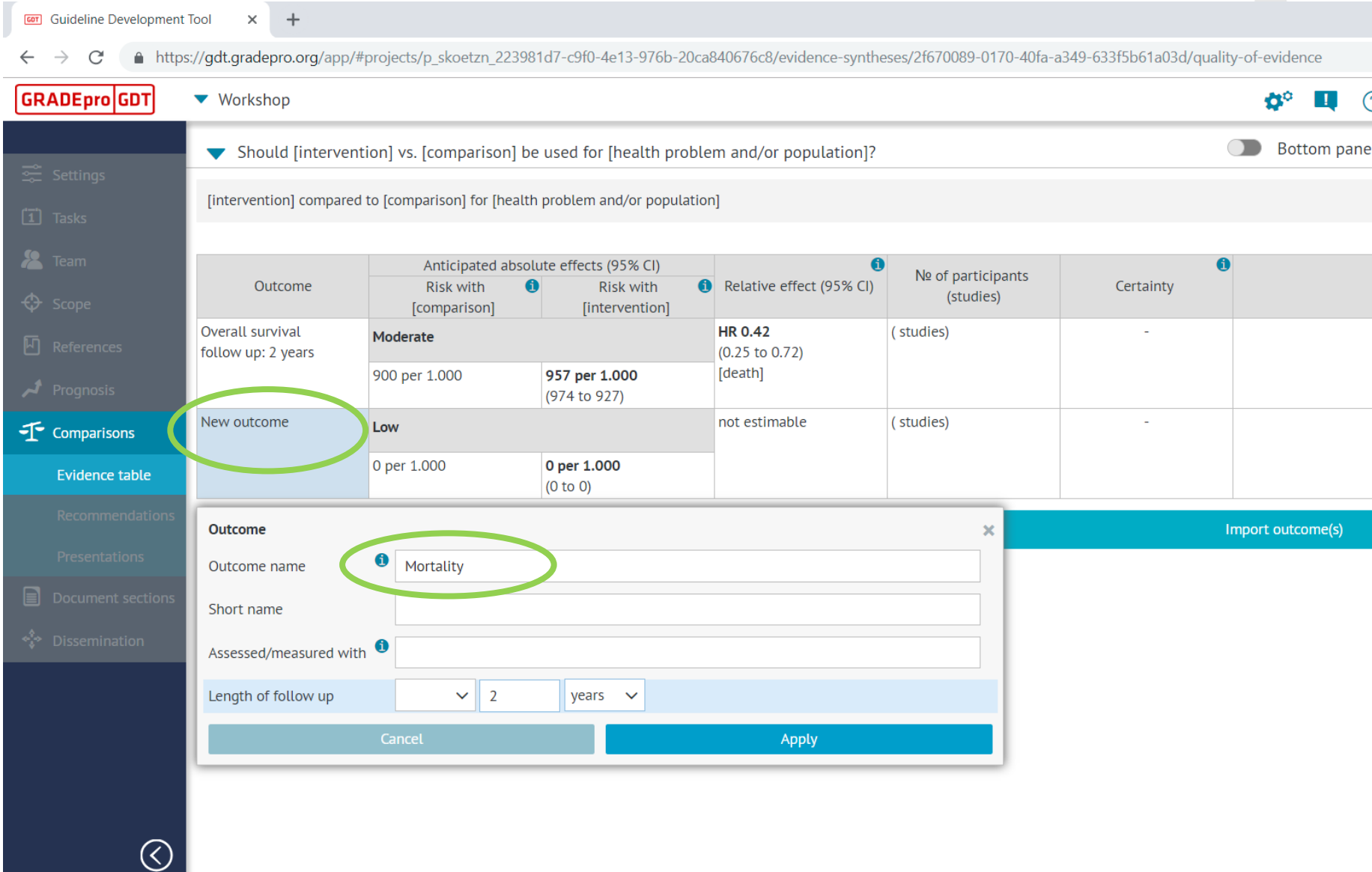

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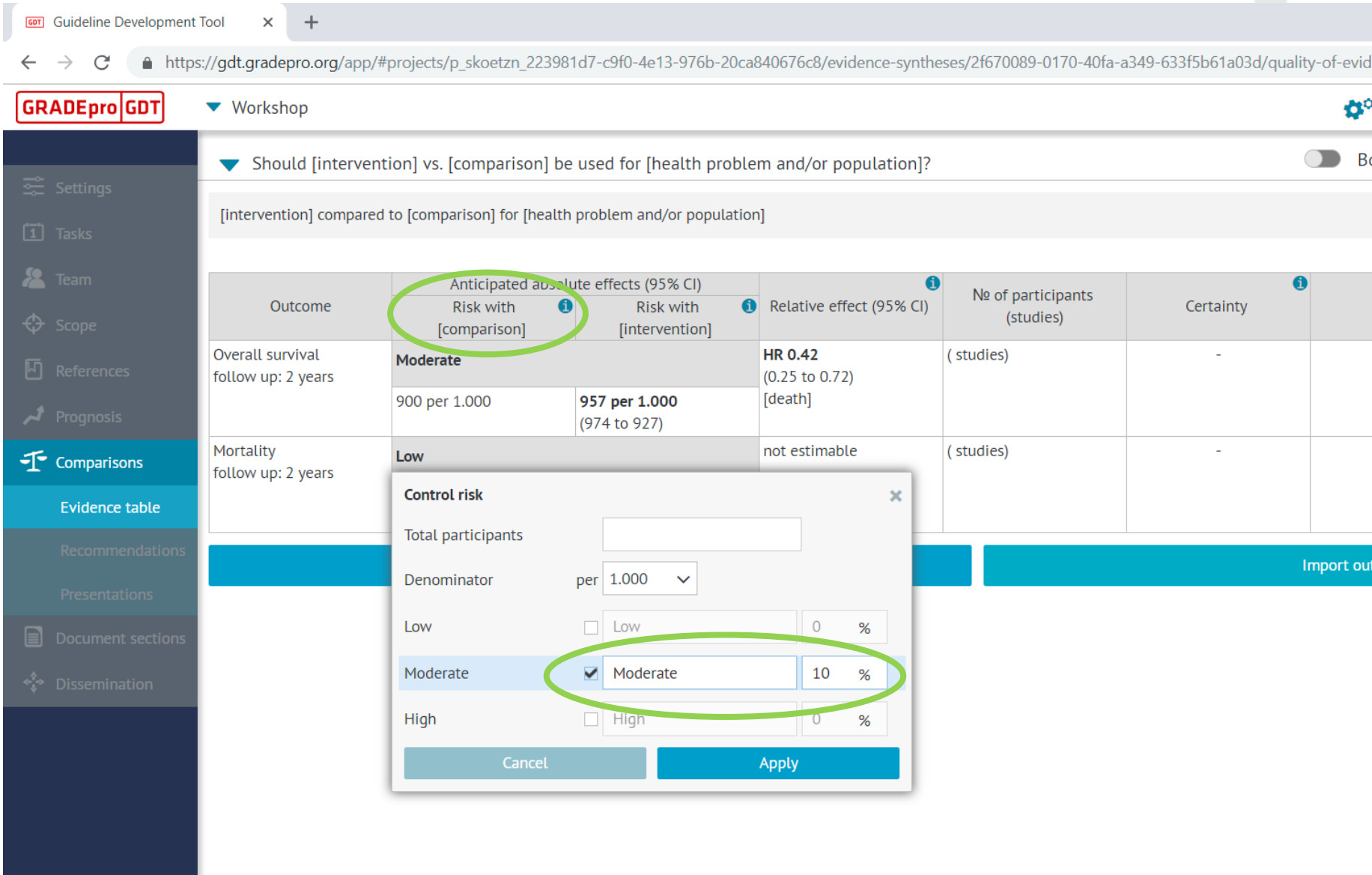

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Bottom panel

[intervention] compared to [comparison] for [health problem and/or population]

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty	What h
	Risk with [comparison]	Risk with [intervention]				
Overall survival follow up: 2 years	**Moderate**		**HR 0.42** (0.25 to 0.72) [death]	(studies)	-	
	900 per 1.000	**957 per 1.000** (974 to 927)				
Mortality follow up: 2 years	**Moderate**			udies)	-	
	100 per 1.000					

Add

Import outcome(s)

Relative effect

Relative: HR of 0.42

95% CI from 0.25 to 72

Cancel | Apply

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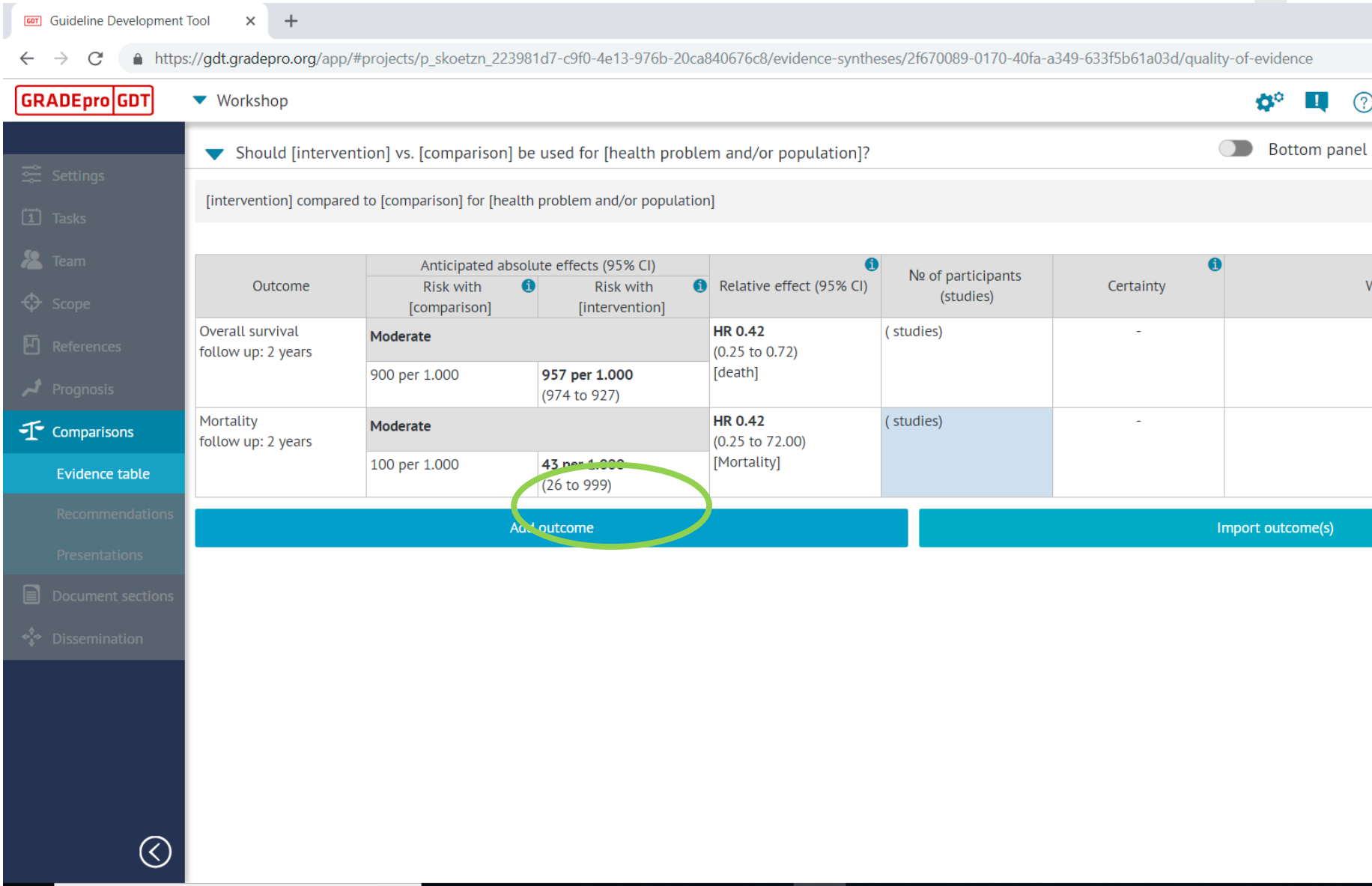

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Any questions?

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Many thanks for your attention!

Contact:

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