

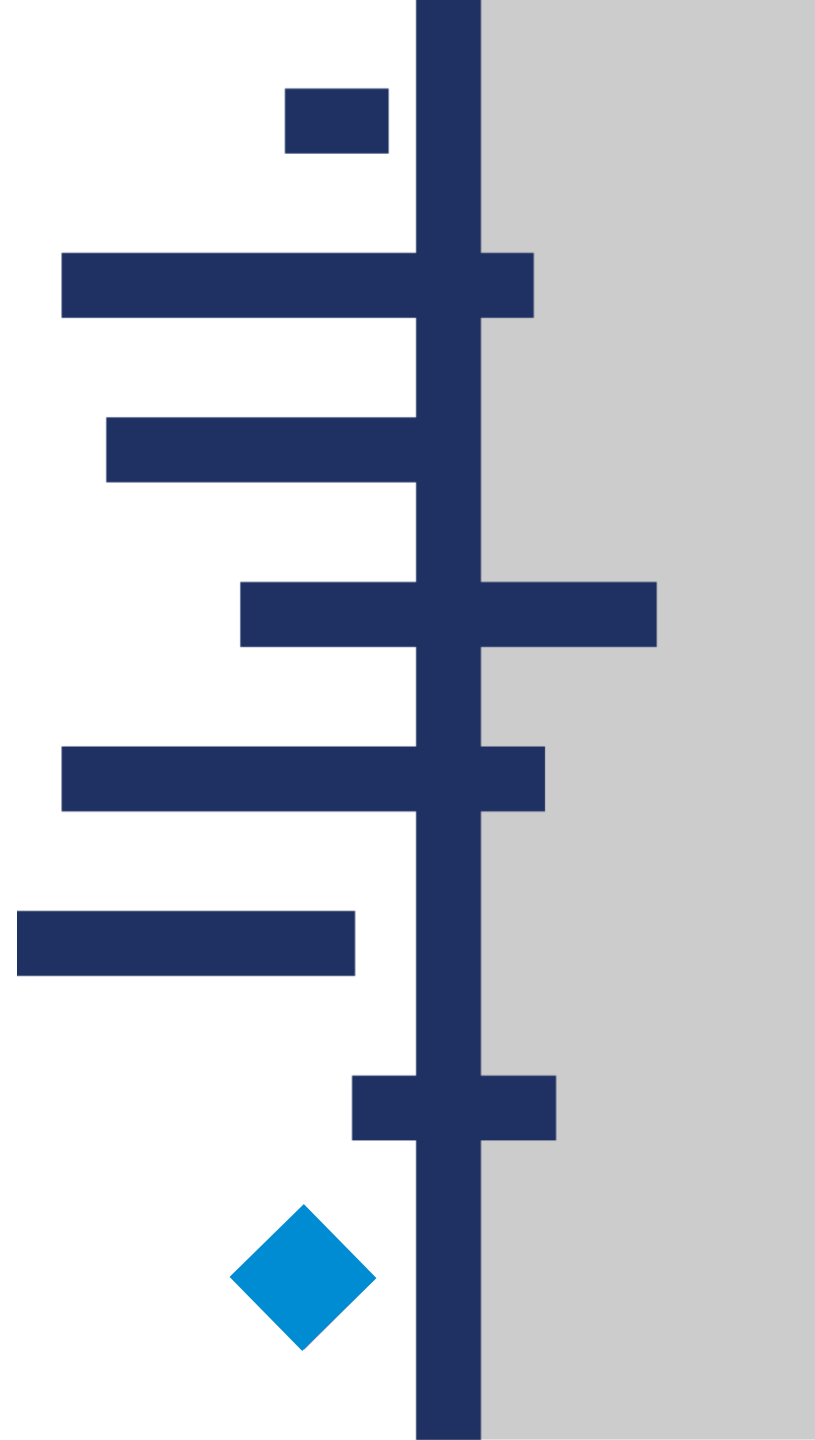


Cochrane
Cancer

How to calculate absolute effects

Nicole Skoetz

Trusted evidence.
Informed decisions.
Better health.



How to calculate absolute effects

- For event-free survival
- For events



Pre-assumption

Pooled hazard ratio (HR) has been correctly calculated



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



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)

Event-free survival



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

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No 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					

Absolute effects for event-free survival

Based on methods described by Tierney et al

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

Example:

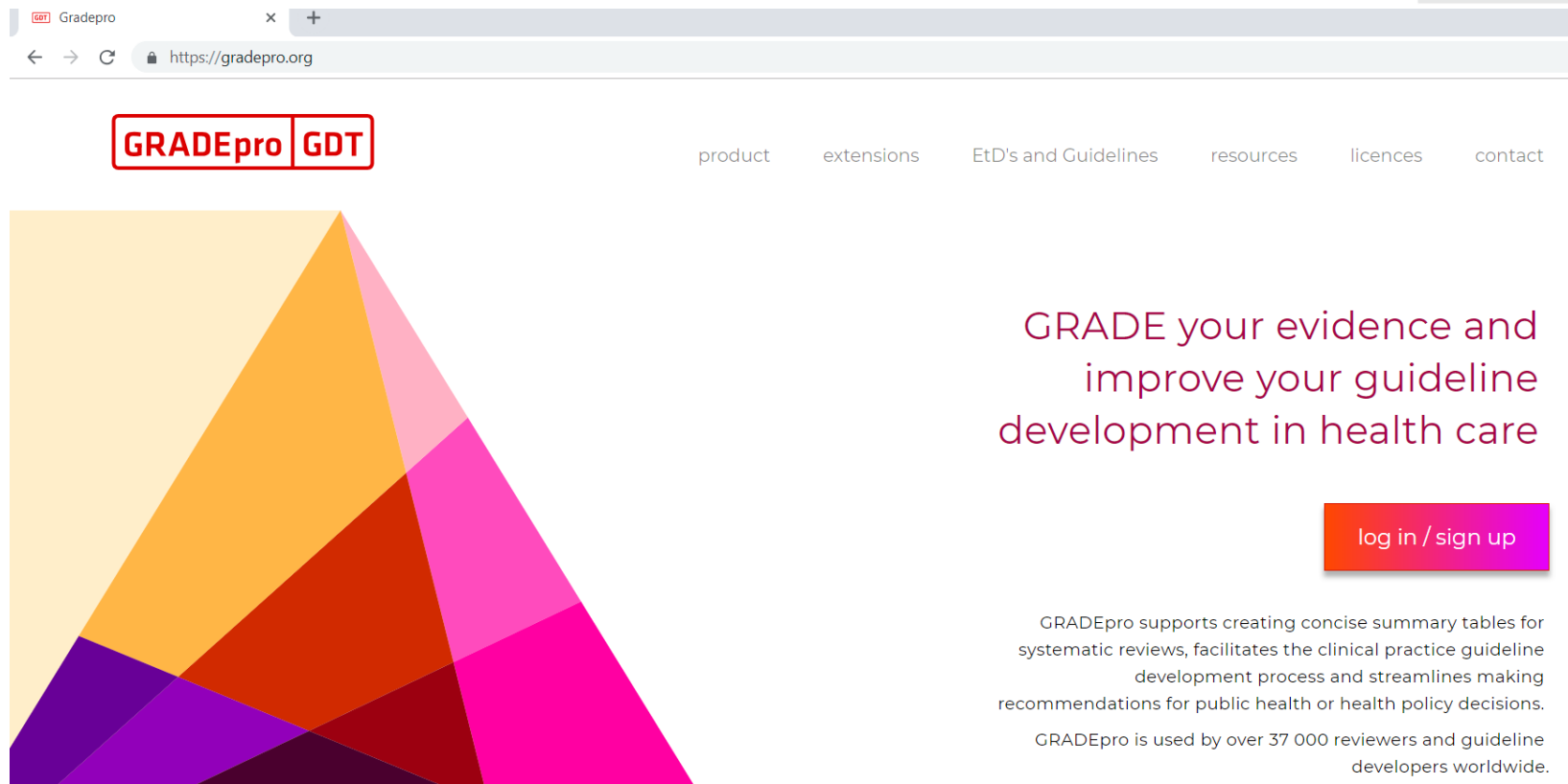
- Pooled HR of **0.42 (95% CI 0.25 to 0.72)**
- Indicating lower risk of death over time in intervention group
- Estimating proportion of patients with event-free survival in control group at **2 years of 900 per 1000:**

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

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

GRADEpro GDT

- <https://gradepro.org/>
- Please use GRADEpro GDT with google chrome



The screenshot shows the GRADEpro GDT website interface. At the top left, there is a navigation menu with the following items: **GRADEpro** (highlighted in a red box), **GDT** (highlighted in a red box), product, extensions, EtD's and Guidelines, resources, licences, and contact. The main content area features a large, colorful geometric graphic on the left side, composed of overlapping triangles in shades of yellow, orange, red, pink, and purple. To the right of this graphic, the text reads: "GRADE your evidence and improve your guideline development in health care". Below this text is a prominent red button with white text that says "log in / sign up". At the bottom of the page, there is a paragraph of text: "GRADEpro supports creating concise summary tables for systematic reviews, facilitates the clinical practice guideline development process and streamlines making recommendations for public health or health policy decisions." followed by another paragraph: "GRADEpro is used by over 37 000 reviewers and guideline developers worldwide."

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**



Guideline Development Tool x +

https://gdt.gradepro.org/app/

GRADEpro GDT Projects

ALL Search

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New project Import project

Welcome!

See what you can do with GDT

- Create Evidence Tables > GRADE Evidence Profile
- Create Guidelines > Summary of Findings (SoF) Table
- Disseminate data > Summary of Findings (SoF) for Cochrane Review
- Evidence to Decision Framework

How can you do that?



Generating a GRADE Evi...

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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

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

Bottom panel Explanations

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

Outcome	Anticipated absolute effects (95% CI) Risk with [comparison]	Risk with [intervention]	Relative effect (95% CI)	No of participants (studies)	Certainty	What happens
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Add outcome

Import outcome(s)

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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)	No of participants (studies)	Certainty
	Risk with [comparison]	Risk with [comparison]			
New outcome	Low				
	0 per 1,000				

Type

 dichotomous time to event narrative pooled not pooled range

Hazard Ratio (HR) is a time event measure of relative effect, estimated in survival analysis. It is calculated for an event (e.g. death) but the absolute effect (e.g. risk difference) has been customarily presented as either reduction/increase of a risk of an event (e.g. Death) or as an improvement/deterioration of non event (e.g. survival).

GRADE HANDBOOK provides [more info](#)

Which category best describes this outcome: "New outcome"

 An event (e.g. death, exacerbation) An non-event (commonly event-free survival)

Cancel

Save

▼ 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)	No of participants (studies)	Certainty
	Risk with [comparison]	Risk with			
New outcome	Low				
	0 per 1.000				

Hazard Ratio (HR) is a time event measure of relative effect, estimated in survival analysis. It is calculated for an event (e.g. death) but the absolute effect (e.g. risk difference) has been customarily presented as either reduction/increase of a risk of an event (e.g. Death) or as an improvement/deterioration of non event (e.g. survival).

GRADE HANDBOOK provides [more info](#)

Which category best describes this outcome: "New outcome"

- An event (e.g. death, exacerbation)
- An non-event (commonly event-free survival)

provide a name of the corresponding event

death

Cancel

Save

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)	No 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

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)	No of participants (studies)	Certainty
	Risk with [comparison]	Risk with [intervention]			
Overall survival follow up: 2 years	Low 0 per 1.000	per 1.000 (0 to 0)	not estimable	(studies)	-

Control risk ✕

Total participants

Denominator per 1.000

Low	<input type="checkbox"/>	Low	%
Moderate	<input checked="" type="checkbox"/>	Moderate	90 %
High	<input type="checkbox"/>	High	0 %

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

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

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

Relative effect ✕

Relative

95% CI from to

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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)	No of participants (studies)	Certainty
	Risk with [comparison]	Risk with [intervention]			
Overall survival follow up: 2 years	Moderate 900 per 1.000	957 per 1.000 (974 to 927)	HR 0.42 (0.25 to 0.72) [death]	(studies)	-

Add outcome

Import outcome(s)

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Events



Reminder: Events: Mortality higher than combined outcome

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No 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					

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

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**



GRADEpro GDT

- <https://gradepro.org/>



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

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

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty
	Risk with [comparison]	Risk with [comparison]			
Overall survival follow up: 2 years	Moderate	900 per 1,000			
New outcome	Low	0 per 1,000			

Type

- dichotomous
- continuous
- time to event
- narrative
- pooled
- not pooled
- range of

Hazard Ratio (HR) is a time event measure of relative effect, estimated in survival analysis. It is calculated for an event (e.g. death) but the absolute effect (e.g. risk difference) has been customarily presented as either reduction/increase of a risk of an event (e.g. Death) or as an improvement/deterioration of non event (e.g. survival).

GRADE HANDBOOK provides [more info](#)

Which category best describes this outcome: "New outcome"

- An event (e.g. death, exacerbation)
- An non-event (commonly event-free survival)

Cancel

Save

Add outcome

Import outcome

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

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

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	Ne 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)			
New outcome	Low		not estimable	(studies)	-
	0 per 1.000	0 per 1.000 (0 to 0)			

Outcome ✕

Outcome name

Short name

Assessed/measured with

Length of follow up years

Import outcome(s)



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

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

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	No 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)			
Mortality follow up: 2 years	Low		not estimable	(studies)	-

Control risk ✕

Total participants

Denominator per ▼

Low Low %

Moderate **Moderate** %

High High %

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)	No 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					

Relative effect

Relative of

95% CI from to

Cancel Apply

Add o

Import outcome(s)

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

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

Outcome	Anticipated absolute effects (95% CI)		Relative effect (95% CI)	No 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)			
Mortality follow up: 2 years	Moderate		HR 0.42 (0.25 to 72.00) [Mortality]	(studies)	-
	100 per 1.000	43 per 1.000 (26 to 999)			

Add outcome

Import outcome(s)

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Any questions?





**Cochrane
Cancer**

**Many thanks for
your attention!**

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