



Input gleich Output – über die Qualität der Cochrane Reviews – Wie erkenne ich Unterschiede?

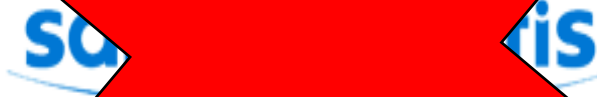
PD Dr. med Nicole Skeotz

Cochrane

- Internationale, unabhängige Non-profit Organisation
- Erstellung, Publikation, Verbreitung von systematischen Übersichtsarbeiten
- 52 Reviewgruppen weltweit



Cochrane gefördert durch



Cochrane Library

- Datenbank von Cochrane
- Kostenfreier Zugang teilweise über Bibliotheken/ Ärztekammern
- ...und über ADKA
 - Cochrane Reviews
 - Randomisiert kontrollierte Studien
 - HTA

Wie erkenne ich Unterschiede?

- Aktualität
- Art des Reviews
- GRADE/ Summary of Findings Tabelle

Wie erkenne ich Unterschiede?

- Aktualität
- Art des Reviews
- GRADE/ Summary of Findings Tabelle

Cochrane Reviews letzte 5 Jahre

The screenshot shows the Cochrane Library website interface. At the top, there is a navigation bar with the Cochrane Library logo and the tagline "Trusted evidence. Informed decisions. Better health." The search bar contains the text "All Text" and an asterisk "*". The main navigation menu includes "Cochrane Reviews", "Trials", "Clinical Answers", "About", and "Help".

Below the navigation menu, there are several filters and a search result summary:

- Cochrane Reviews** 7892
- Cochrane Protocols** 2439
- Trials 1300023
- Editorials 126
- Special collections 25
- Clinical Ans 1898

The search results are filtered by date, with a custom date range of "01/01/2014" to "28/01/2019". The search results show 3844 matching reviews. The first result is:

1 **Topiramate for juvenile myoclonic epilepsy**
Jia Liu, Lu-Ning Wang, Yu-Ping Wang
[Show Preview](#) Intervention Review 28 January 2019 [New search](#)

The second result is partially visible:

2 **Pharmacotherapies for cannabis dependence**

Cochrane MECIR checklist

Methodological Expectations of Cochrane Intervention Reviews

C37	<i>Rerunning searches</i>		Mandatory
	Rerun or update searches for all relevant databases within 12 months before publication of the review or review update, and screen the results for potentially eligible studies.	The published review should be as up to date as possible. The search must be rerun close to publication, if the initial search date is more than 12 months (preferably six months) from the intended publication date, and the results screened for potentially eligible studies. Ideally the studies should be incorporated fully in the review. If not, then the potentially eligible studies will need to be reported, at a minimum as a reference under 'Studies awaiting classification' (or 'Ongoing studies' if they have not yet completed).	

Wie erkenne ich Unterschiede?

- Aktualität
- Art des Reviews
- GRADE/ Summary of Findings Tabelle

Systematische Übersichtsarbeit

- Klar formulierte Fragestellung (PICO)
- Umfassende Literaturrecherche (mehrere Datenbanken)
- Unverzerrte Auswahl und Auswertung der gefundenen Studien
- Kritische Bewertung der Qualität der einzelnen Studien (garbage in – garbage out) (Risk of Bias)
- Beschreibende und ev. quantitative Zusammenfassung der Einzelergebnisse (Meta-analyse)
- Regelmäßige Aktualisierung

Besonderheiten Cochrane Review

- Titelregistrierung mit der entsprechenden Cochrane Gruppe
- Vorab Protokoll erstellt und publiziert

Arten an Cochrane Reviews: letzte 5 Jahre

Intervention	3681
Diagnostic	101
Overview	42
Methodology	15
Qualitative	3
Prognosis	2

Intervention Review (3681 letzte 5 Jahre)

- Meistens basierend auf RCTs
- Zur Beurteilung von Interventionen (z.B. medikamentöse Therapie, Sport, Operation bei bestimmter Erkrankung)
- Neuerdings: Wenn keine vorhanden: non-RCTs
- Mit oder ohne Meta-analyse

Zentrale Annahmen für Meta-analyse

- Studien hinsichtlich möglicher Effektmodifikatoren ähnlich (Ähnlichkeitsannahme)
 - Alter
 - Dosis
 - Stadium
 - ...

Diagnostische Reviews (101 letzte 5 Jahre)

- Diagnostic Test Accuracy Review
 - Sensitivität
 - Spezifität
 - Positiver/negativer Vorhersagewert

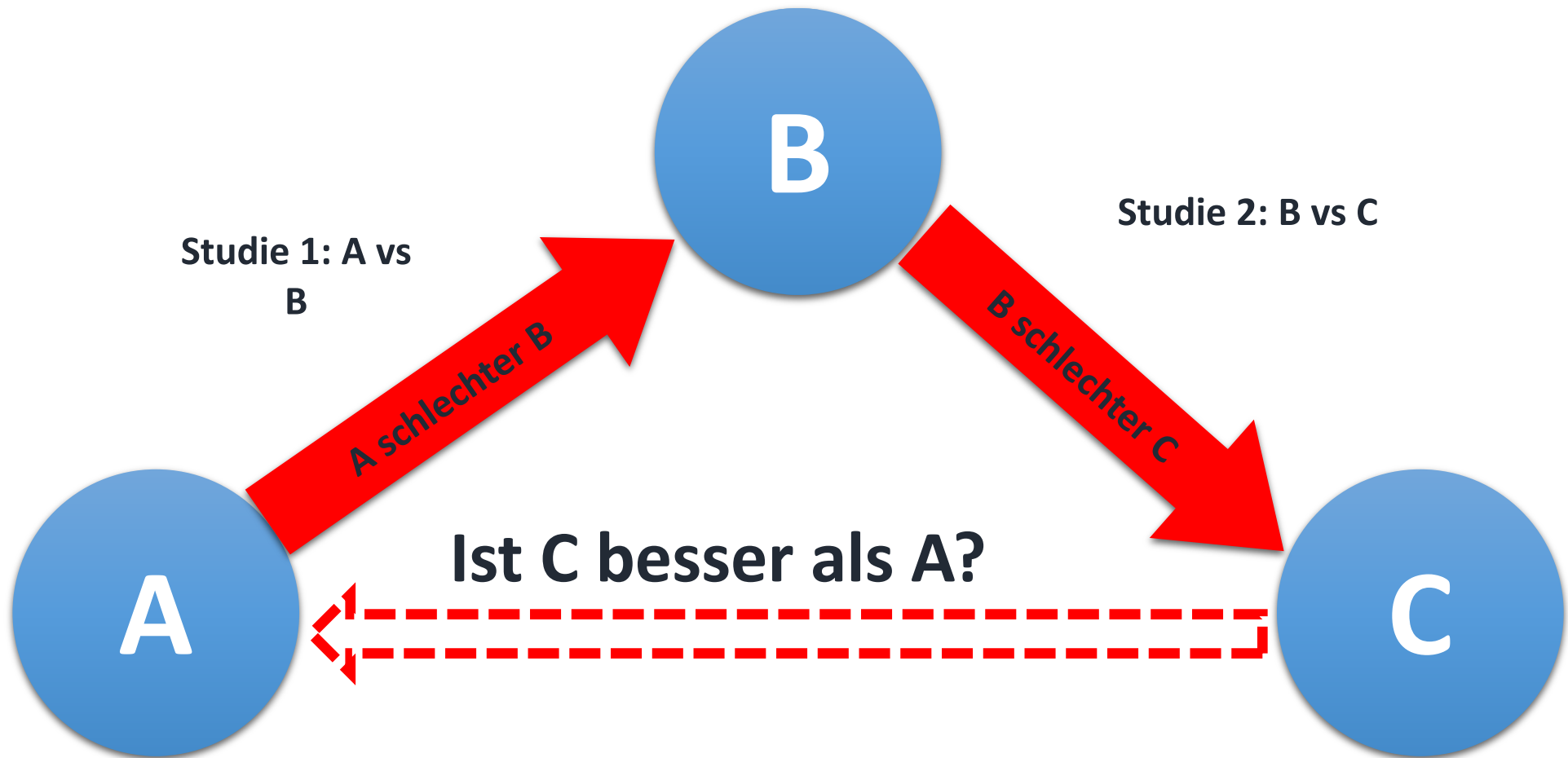
Overview Review (letzte 5 Jahre: 42) Welche Therapie ist die beste?



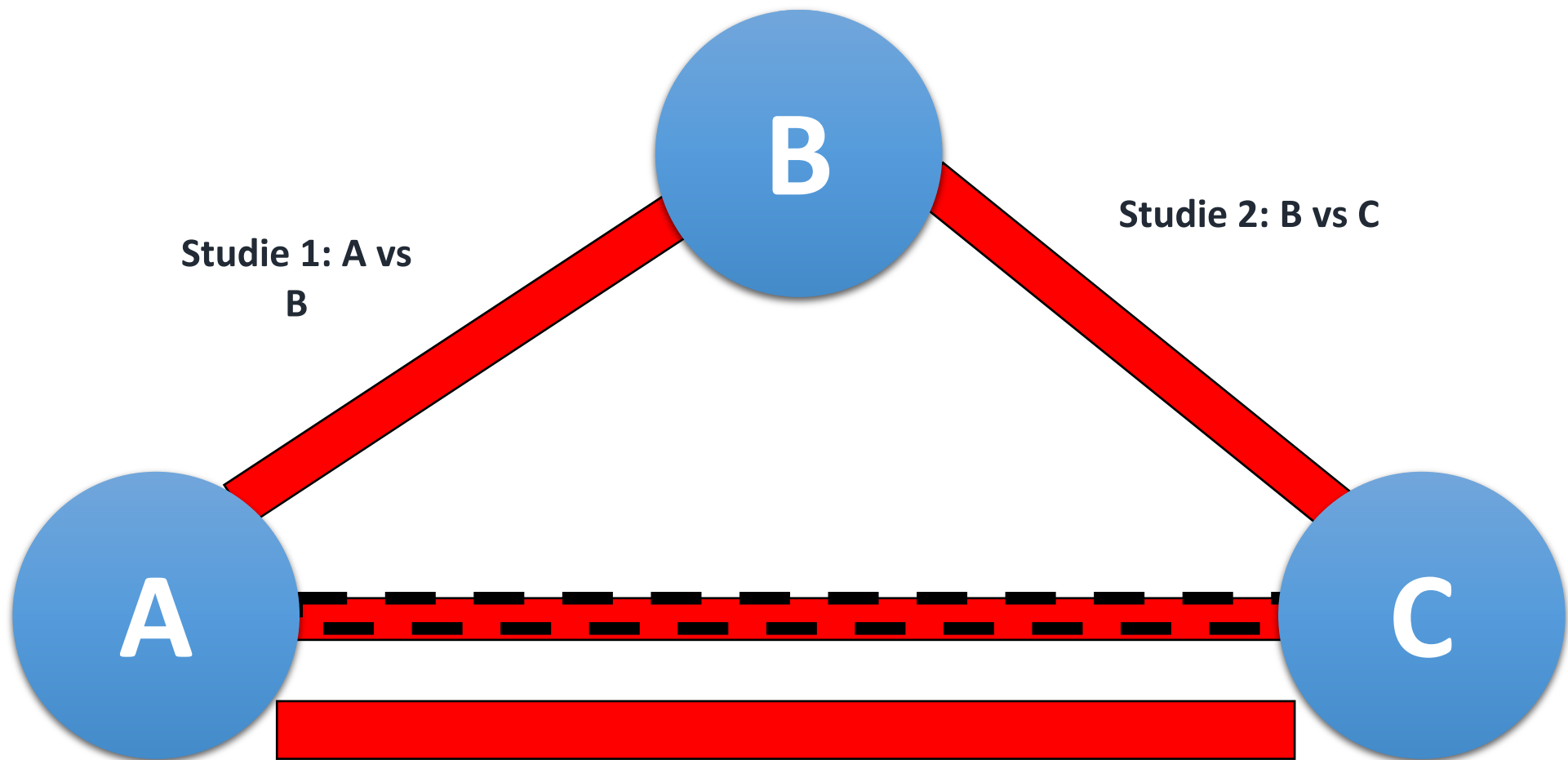
Indirekter Vergleich



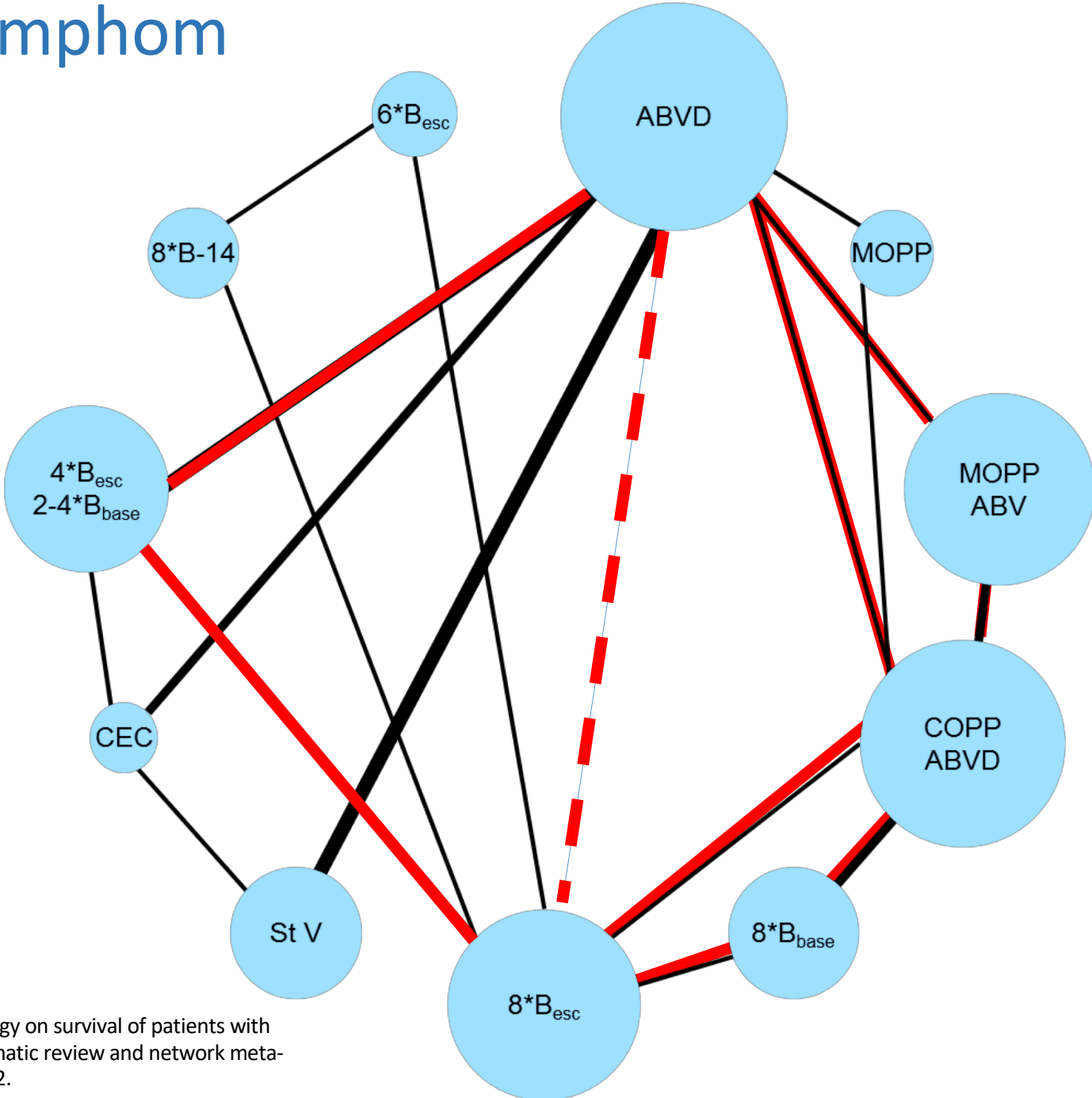
Indirekter Vergleich



Indirekter Vergleich + direkter Vergleich Netzwerk Meta-analyse



Hodgkin Lymphom Netzwerk



Skoetz N et al. Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin's lymphoma: a systematic review and network meta-analysis. Lancet Oncol. 2013 Sep;14(10):943-52.

Zentrale Annahmen für Netzwerk Meta-analyse

- Studien hinsichtlich möglicher Effektmodifikatoren ähnlich (Ähnlichkeitsannahme)
- Zwischen direkter und indirekter Evidenz keine bedeutsame Diskrepanz (Konsistenzannahme)

Wie erkenne ich Unterschiede?

- Aktualität
- Art des Reviews
- GRADE/ Summary of Findings Tabelle

Cochrane Reviews 4019 Cochrane Protocols 1212 Trials 57 Editorials 8 Special collections 0 Clinical Answers 1436 Other Reviews

Filter your results

Date

Publication date

- The last 3 months
- The last 6 months
- The last 9 months
- The last year
- The last 2 years

Custom Range:

to

Status

New search 982
Conclusions changed 330

Language

Español 1853
[Show 13 more ▾](#)

Type

Intervention 2993
Diagnostic 101

Date: Custom date range ✕

3133 Cochrane Reviews matching on "'summary of findings" in All Text'

Cochrane Database of Systematic Reviews

Issue 1 of 12, January 2019

Select all (3133) [Export selected citation\(s\)](#) [Show all previews](#)

Order by:

Results per page

- Pharmacotherapies for cannabis dependence**
Suzanne Nielsen, Linda Gowing, Pamela Sabioni, Bernard Le Foll
[Show Preview ▾](#) [Intervention](#) [Review](#) 28 January 2019 [New search](#)
- School-based self-management interventions for asthma in children and adolescents: a mixed methods systematic review**
Katherine Harris, Dylan Kneale, Toby J Lasserson, Vanessa M McDonald, Jonathan Grigg, James Thomas
[Show Preview ▾](#) [Intervention](#) [Review](#) 28 January 2019
- Topiramate for juvenile myoclonic epilepsy**
Jia Liu, Lu-Ning Wang, Yu-Ping Wang
[Show Preview ▾](#) [Intervention](#) [Review](#) 28 January 2019 [New search](#)
- Drug-eluting balloon angioplasty versus uncoated balloon angioplasty for the treatment of in-stent restenosis of the femoropopliteal arteries**
Ahmed Kayssi, Wissam Al-Jundi, Giuseppe Papia, Daryl S Kucey, Thomas Forbes, Dheeraj K Rajan, Richard Neville, Andrew D Dueck
[Show Preview ▾](#) [Intervention](#) [Review](#) 26 January 2019
- Antibiotics for treating urogenital *Chlamydia trachomatis* infection in men and non-pregnant women**

Grading of Recommendations Assessment, Development and Evaluation

GRADE

GRADEpro GDT (gradepro.org)

The screenshot displays the GRADEpro GDT software interface. At the top left, there is a logo for "GRADEpro GDT". To the right, a navigation menu includes links for "HOME", "GRADEpro GDT OVERVIEW", "GUIDELINE RESOURCES", "CALENDAR OF EVENTS", "GRADE HANDBOOK", "CONTACT SUPPORT", and a "LOG IN" button. The main content area shows a "Summary of Findings" table with columns for "CRITERIA", "JUDGEMENTS", "RESEARCH EVIDENCE", and "ADDITIONAL CONSIDERATIONS". The "CRITERIA" column lists questions like "Is there a problem priority?" and "What is the overall certainty of this evidence?". The "JUDGEMENTS" column shows radio button options for "No", "Probably no", "Uncertain", "Probably yes", "Yes", and "Varies". The "RESEARCH EVIDENCE" column contains text describing the prevalence of allergic rhinitis (AR) in children and adolescents. The "ADDITIONAL CONSIDERATIONS" column includes a "V&P:" section with text about a cross-sectional study of 170 patients with allergic rhinitis. A red circle highlights the text "Summary of Findings" in the table header. At the bottom center, there is a "LOG IN / SIGN UP" button.

GRADE's software for Summary of Findings tables, Health Technology Assessment and Guidelines

[LOG IN / SIGN UP](#)

GRADE

Endpunkte
priorisieren

Strukturierte Frage (PICO)

- Patienten
- Intervention
- Vergleichsintervention
- Endpunkte: **patientenrelevant**

Endpunkte für PICO Frage priorisieren

• **Mortalität** **Spätschäden**

Hospitalisierung

Lebensqualität

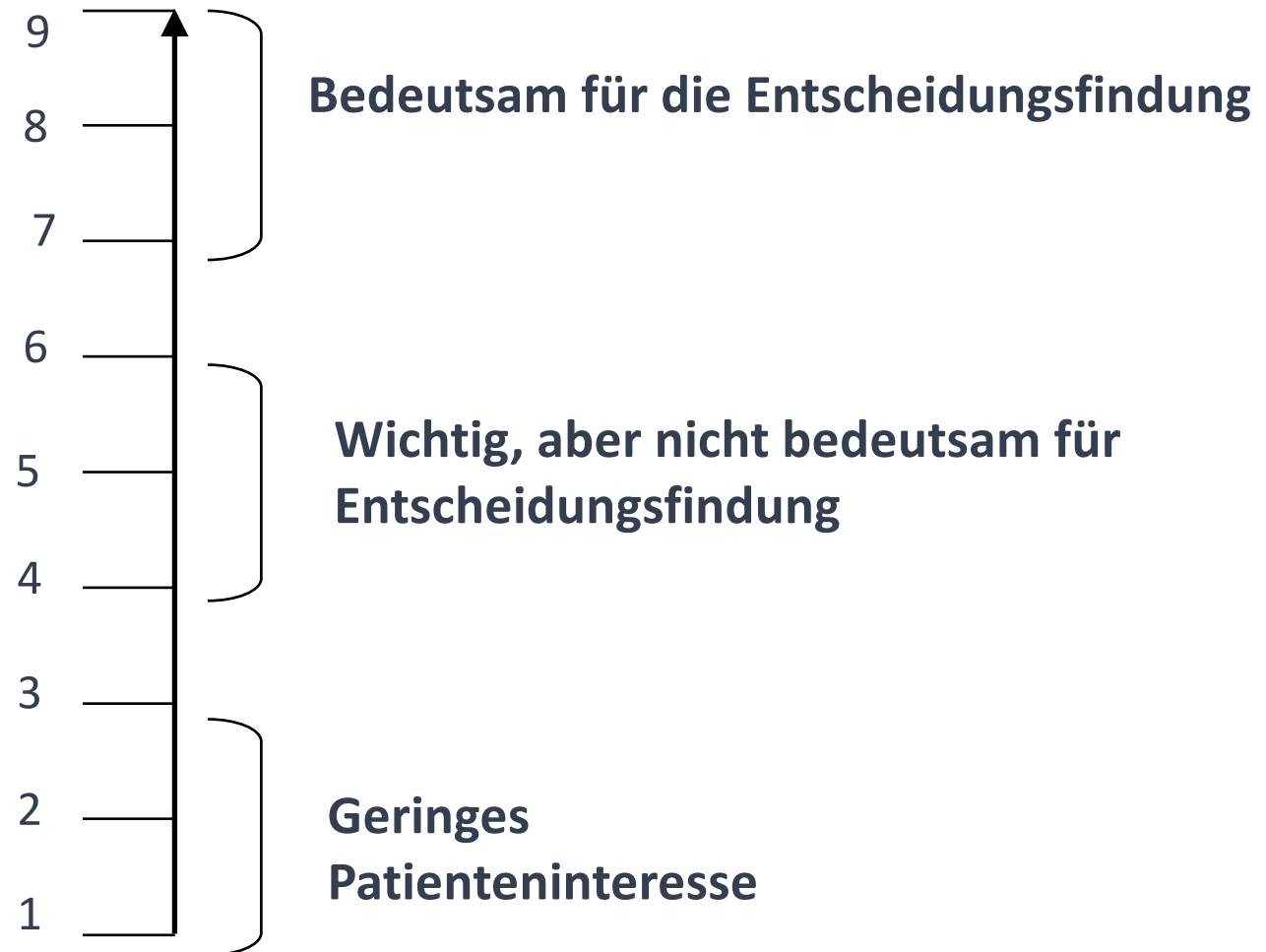
Nebenwirkungen

Schmerzen

Laborwerte

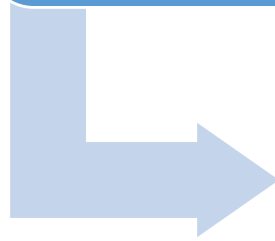
Krankheitsverlauf

Wichtigkeit des Endpunktes



GRADE

Endpunkte
priorisieren



Vertrauen je
Endpunkt
bewerten

Ziel der Bewertung des Vertrauens in Evidenz

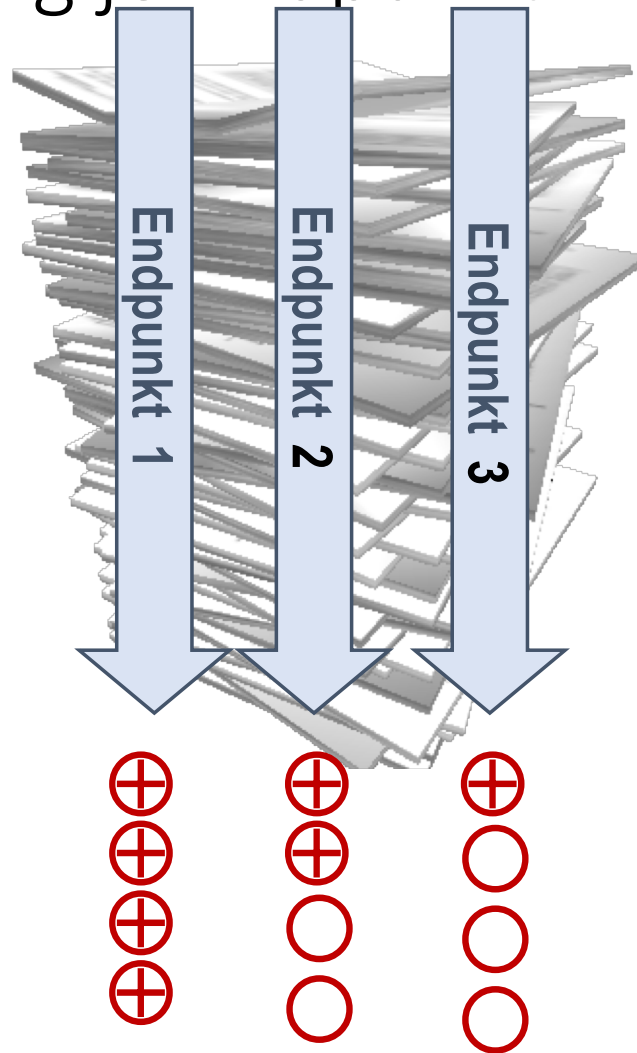
- Starkes Vertrauen in Ergebnisse
 - Keine weiteren Studien notwendig
 - Wohlergehen der Patienten
 - Einsparung von Kosten
- Niedriges Vertrauen in Ergebnisse
 - Weitere klinische Studien notwendig

GRADE: Vertrauensbewertung Evidenz

- Hohes Vertrauen
- Moderates Vertrauen
- Niedriges Vertrauen
- Sehr niedriges Vertrauen



GRADE: Bewertung je Endpunkt



GRADE-Bewertung des Vertrauens

Qualität		Studiendesign
Hoch	⊕⊕⊕⊕	Randomisierte Studie
Moderat	⊕⊕⊕○	
Niedrig	⊕⊕○○	Beobachtungsstudie
Sehr niedrig	⊕○○○	

Vertrauen herabstufen

- 5 Kriterien
 - Je Kriterium bis zu 2 Punkte herabstufen
 - Transparent dokumentieren

2. Heterogenität – klinisch

- Patienten
- Interventionen
- Endpunktdefinitionen

Guyatt et al. GRADE guidelines: 7. Rating the quality of evidence—inconsistency. J Clin Epidemiol 2011; 64(12): 1294-1302.

2. Heterogenität – statistisch

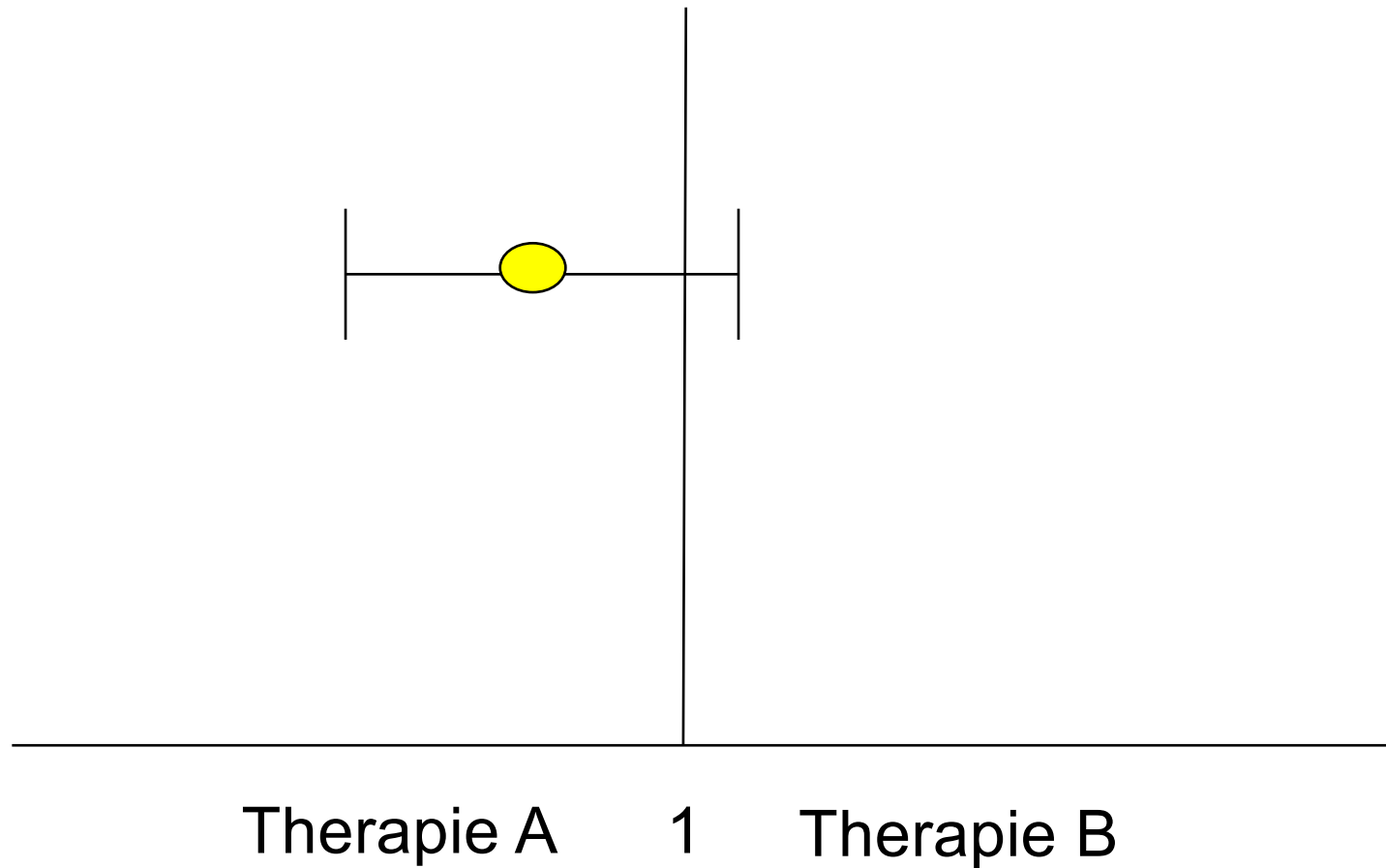
- Keine überlappenden Konfidenzintervalle
- Hohes I^2 (> 60%)
- Variation in der Richtung des Effektes

3. Indirekte Evidenz

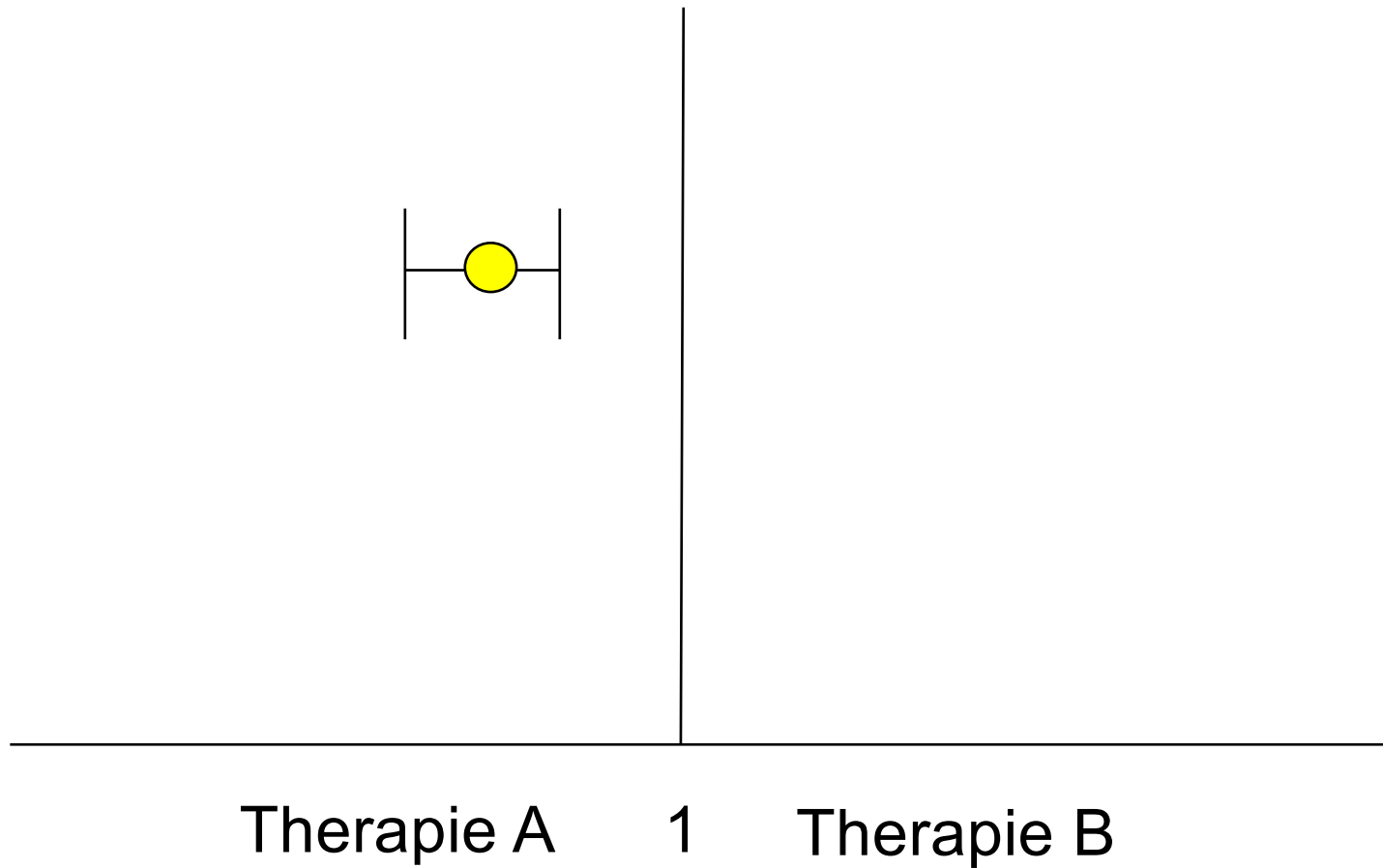
- Patienten
 - Kinder vs. Erwachsene
- Interventionen
 - Dosierung
- Endpunkte
 - Patientenrelevant vs. Surrogatparameter

Guyatt et al. GRADE guidelines: 8. Rating the quality of evidence—indirectness. J Clin Epidemiol 2011; 64(12): 1303-1310.

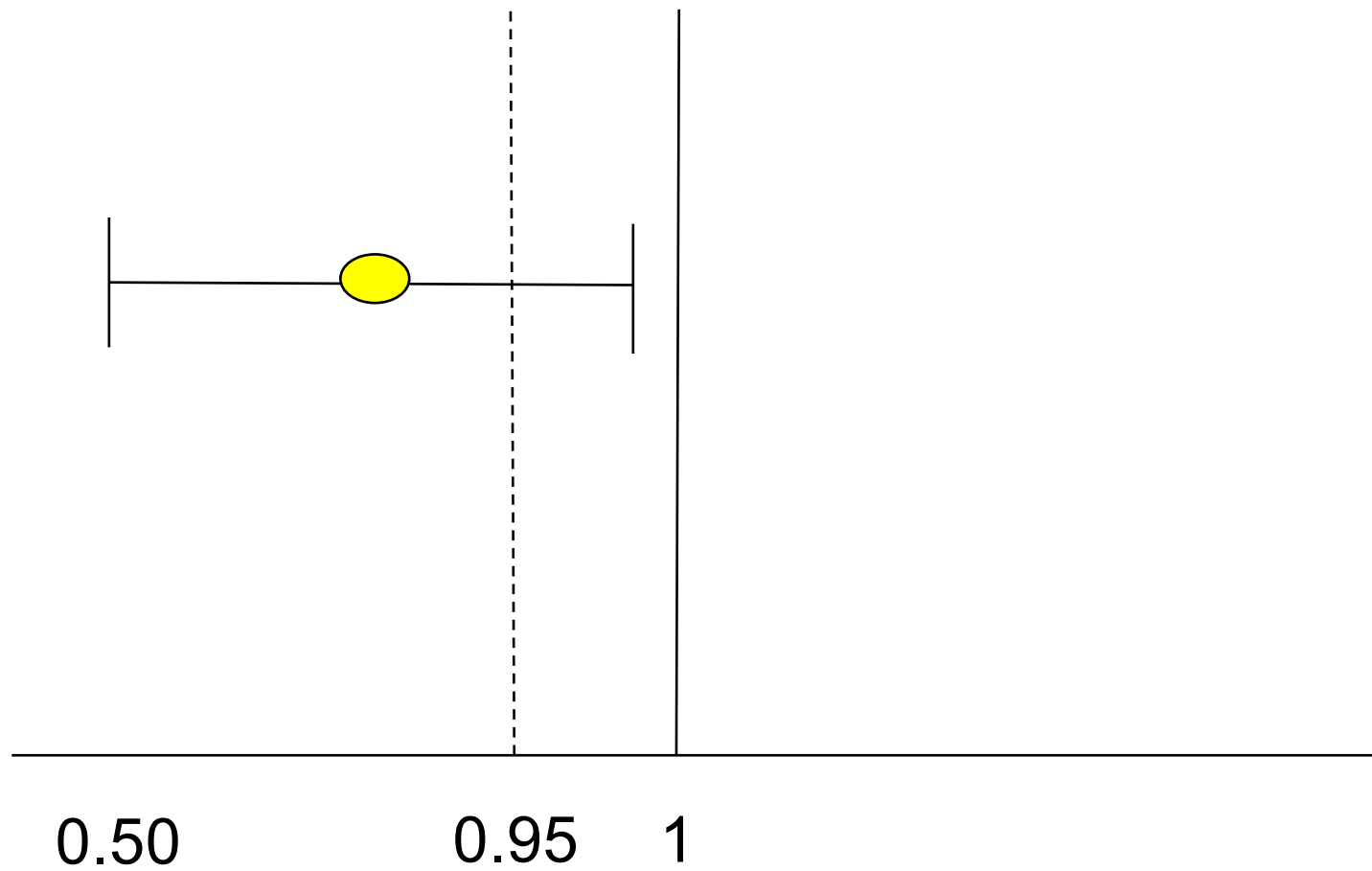
4. Fehlende Präzision



4. Fehlende Präzision



4. Fehlende Präzision



5. Publikationsbias

- Studien mit negativem Ergebnis werden seltener publiziert

Publikationsbias abschätzen

- Studienregister durchsuchen!
 - Beendete aber nicht publizierte Daten?
- Kongressberichte durchsuchen
- Ggf Funnel Plot (≥ 10 Studien)

Vertrauensbewertung heraufstufen

- Wenn bisher nicht herabgestuft wurde

1. Großer Effekt



Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Smith et al. Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. *BMJ*. 2003 Dec 20;327(7429):1459-61.

2. Dosis-Wirkungsbeziehung

Zusammenfassung GRADE

- Randomisierte Studie



- Beobachtungsstudie



- Vertrauen herabstufen

- Risk of Bias
- Heterogenität
- Indirekte Evidenz
- Fehlende Präzision
- Publikationsbias

- Vertrauen heraufstufen

- Großer Effekt
- Dosis-Wirkungs-Beziehung
- Residuelles Confounding

Summary of Findings Beispiel

Summary of findings for the main comparison. Group 1 Pulmonary arterial hypertension - PDE5i compared to placebo [Open in table viewer](#)

Group 1 Pulmonary arterial hypertension - PDE5i compared to placebo

Patient or population: people with pulmonary arterial hypertension

Setting: outpatients

Intervention: PDE5 inhibitors

Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with PDE5i				
Improvement in WHO functional class	61 per 1000	358 per 1000 (204 to 549)	OR 8.59 (3.95 to 18.72)	262 (4 RCTs)	⊕⊕⊕⊕ HIGH	-
Six-minute walk distance	Ranges from 170 - 319 m ^a	MD 48 metres higher (40 higher to 56 higher)	-	880 (8 RCTs)	⊕⊕⊕⊖ ^b MODERATE	6MWD in PAH MCID is 41 metres
Mortality	41 per 1000	9 per 1000 (3 to 28)	OR 0.22 (0.07 to 0.68)	1119 (8 RCTs)	⊕⊕⊕⊕ HIGH	-
Quality of life SF-36: (scores 1 to 100, higher scores	Galiè 2005a found a statistically significant improvement in all SF-36 domains for sildenafil-treated participants, and when compared to placebo in physical functioning (P < 0.001), general health (P < 0.001), and vitality (P < 0.05). There was also a statistically significant improvement in placebo-treated participants in the physical functioning domain			163 (2 RCTs)	-	Data considered too heterogeneous to meta-analyse

Summary of Findings Beispiel

Summary of findings for the main comparison. Group 1 Pulmonary arterial hypertension - PDE5i compared to placebo [Open in table viewer](#)

Group 1 Pulmonary arterial hypertension - PDE5i compared to placebo

Patient or population: people with pulmonary arterial hypertension

Setting: outpatients

Intervention: PDE5 inhibitors

Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with PDE5i				
Improvement in WHO functional class	61 per 1000	358 per 1000 (204 to 549)	OR 8.59 (3.95 to 18.72)	282 (4 RCTs)	⊕⊕⊕⊕ HIGH	-
Six-minute walk distance	Ranges from 170 - 319 m ^a	MD 48 metres higher (40 higher to 56 higher)	-	880 (8 RCTs)	⊕⊕⊕⊖ ^b MODERATE	6MWD in PAH MCID is 41 metres
Mortality	41 per 1000	9 per 1000 (3 to 28)	OR 0.22 (0.07 to 0.68)	1119 (8 RCTs)	⊕⊕⊕⊕ HIGH	-
Quality of life SF-36: (scores 1 to 100, higher scores	Galiè 2005a found a statistically significant improvement in all SF-36 domains for sildenafil-treated participants, and when compared to placebo in physical functioning (P < 0.001), general health (P < 0.001), and vitality (P < 0.05). There was also a statistically significant improvement in placebo-treated participants in the physical functioning domain			163 (2 RCTs)	-	Data considered too heterogeneous to meta-analyse



Vielen Dank!



UNIKLINIK
KÖLN