

# ANHANG (151 Seiten)

Bewertung der Studienqualität von 15 Studien mit Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

# Inhalt

deprexis Studie 1	2
Risk of bias assessment	
deprexis Studie 2	
Risk of bias assessment	
deprexis Studie 3	
Risk of bias assessment	
deprexis Studie 4	
Risk of bias assessment	
deprexis Studie 5	
Risk of bias assessment	
deprexis Studie 6	
Risk of bias assessment	
deprexis Studie 7	62
Risk of bias assessment	
deprexis Studie 8	
Risk of bias assessment	75
deprexis Studie 9	82
Risk of bias assessment	85
deprexis Studie 10	92
Risk of bias assessment	95
deprexis Studie 11	102
Risk of bias assessment	105
elevida Studie 1	112
Risk of bias assessment	115
somnio Studie 1	122
Risk of bias assessment	125
velibra Studie 1	132
Risk of bias assessment	135
vorvida Studie 1	142
Risk of bias assessment	145

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 1

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study o	letails		
Refere		Bücker L, Bierbrodt J, Hand I, Wittekind C, Moritz S. Effects of a depression-focused internet intervention in slot machine gamblers: A randomized controlled trial. PLoS One. 2018 Jun 8;13(6):e0198859. doi: 10.1371/journal.pone.0198859. Erratum in: PLoS One. 2018 Aug 23;13(8):e0203145. PMID: 29883479; PMCID: PMC5993308.	
	Individua Cluster-r Individua purposes	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial of this assessment, the interventions being compared are	
Experi	imental:	Deprexis Comparator: Wartelist	e / Care as usual (CAU)
Specif	y which o	utcome is being assessed for risk of bias	Patient Health Questionnaire - 9 (PHQ-9)
analys 0.83 to	ses being p o 2.77) and	nerical result being assessed. In case of multiple alternative presented, specify the numeric result (e.g. RR = 1.52 (95% Cod/or a reference (e.g. to a table, figure or paragraph) that is the result being assessed.	
		m's aim for this result?	
X □		s the effect of <i>assignment to intervention</i> (the 'intention-to- s the effect of <i>adhering to intervention</i> (the 'per-protocol' e	•
	e checked) occurrenc failures in		etions from intended intervention that should be addressed (at least one

2021-07-22\_ANHANG\_\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

© 2021 ProHTA Advisors in Healthcare Copyright:

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		PY
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		PY
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / <u>PN / N</u> / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / Y / PY / PN / N / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

# Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PY
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		PY
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	High
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 2

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study d	letails		
Refere		Zwerenz R, Becker J, Knickenberg RJ, Siepmann M, Hagen K, Beutel ME. Online Self-Help as an Add-On to Inpatient Psychotherapy: Efficacy of a New Blended Treatment Approach. Psychother Psychosom. 2017;86(6):341-350. doi: 10.1159/000481177. Epub 2017 Nov 3. PMID: 29131090.	
Study d  X    For the	Individua Cluster-ra Individua	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial of this assessment, the interventions being compared are	e defined as
		Deprexis Comparator: Wartelist	
Specif	y the num	utcome is being assessed for risk of bias nerical result being assessed. In case of multiple alternative	
0.83 to	o 2.77) and	oresented, specify the numeric result (e.g. RR = 1.52 (95% Cd/or a reference (e.g. to a table, figure or paragraph) that sthe result being assessed.	
Is the re	to assess	m's aim for this result?  Is the effect of assignment to intervention (the 'intention-to the effect of adhering to intervention (the 'per-protocol' estimates).	·
must be	e checked) occurrenc failures in		ations from intended intervention that should be addressed (at least one ne outcome

Vorstand der Kassenärztlichen Vereinigung Bayern (KVB) © 2021 ProHTA Advisors in Healthcare

Datei: Verfasser: Empfänger:

Copyright:

Which	of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
Χ	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		Ϋ́
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		<u>PN</u>
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

# Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		N
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		<u>Y</u>
analysed in accordance with a pre-specified		
analysis plan that was finalized before unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions, time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the data?		N
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



Datei:

Verfasser:

This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 3

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

Study details

Referenc	ce	Krieger T, Meyer B, Sude K, Urech A, Maercker A, Berger T. Evaluating an e-mental health program ("deprexis") as adjunctive treatment tool in psychotherapy for depression: design of a pragmatic randomized controlled trial. BMC Psychiatry. 2014;14:285. Published 2014 Oct 8. doi:10.1186/s12888-014-0285-9	
	ndividua Cluster-ra	ally-randomized parallel-group trial andomized parallel-group trial ally randomized cross-over (or other matched) trial	
_		of this assessment, the interventions being compared are define	
Experim	ental: [	Psychotherapie plus deprexis Comparator: Reguläre Psych	otherapie
Specify v	which ou	utcome is being assessed for risk of bias	Beck Depression Inventory (BDI-II)
analyses 0.83 to 2	being pr 2.77) and	erical result being assessed. In case of multiple alternative resented, specify the numeric result (e.g. RR = 1.52 (95% Cl d/or a reference (e.g. to a table, figure or paragraph) that the result being assessed.	
Is the rev	iew tean	n's aim for this result?	
X t	o assess	the effect of assignment to intervention (the 'intention-to-treat' the effect of adhering to intervention (the 'per-protocol' effect)	effect)
If the aim		<del>-</del>	from intended intervention that should be addressed (at least one
		nce of non-protocol interventions	
		implementing the intervention that could have affected the outcomes to their assigned intervention by trial participants.	ome
□ N(	on-auner	rence to their assigned intervention by trial participants	
Which of	the follo	owing sources were obtained to help inform the risk-of-bias asse	essment? (tick as many as annly)

2021-07-22\_ANHANG\_\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Χ	Journal article(s) with results of the trial
Χ	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare Seite 24 von 151

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		N
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

# Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		PN
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		N
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		<u>Y</u>
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		<u>N</u>
data?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 4

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study d	etails		
Beevers CG, Pearson R, Hoffman JS, Foulser AA, Shumake J, Meyer B. Effectiver depression in a united states adult sample: A parallel-group pragmatic random Apr;85(4):367-380. doi: 10.1037/ccp0000171. Epub 2017 Feb 23. PMID: 282303		depression in a united states adult sample: A parallel-grou	p pragmatic randomized controlled trial. J Consult Clin Psychol. 2017
Study d	Individua Cluster-ra Individua	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
		of this assessment, the interventions being compared are  Deprexis  Comparator: Wartelist	
Specify	y which o	utcome is being assessed for risk of bias	Quick Inventory of Depression Symptoms (QIDS-SR)
analys 0.83 to	es being p o 2.77) and	nerical result being assessed. In case of multiple alternative presented, specify the numeric result (e.g. RR = 1.52 (95% CI d/or a reference (e.g. to a table, figure or paragraph) that is the result being assessed.	
Is the re	to assess	m's aim for this result? The effect of assignment to intervention (the 'intention-to- to the effect of adhering to intervention (the 'per-protocol' ef	·
must be	checked) occurrence failures in		tions from intended intervention that should be addressed (at least one e outcome

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	Which of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)	
Χ	Journal article(s) with results of the trial	
	Trial protocol	
	Statistical analysis plan (SAP)	
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)	
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)	
	"Grey literature" (e.g. unpublished thesis)	
	Conference abstract(s) about the trial	
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)	
	Research ethics application	
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)	
	Personal communication with trialist	
	Personal communication with the sponsor	

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare Seite 34 von 151

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		<u>Y</u>
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		N
Risk-of-bias judgement		Low
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		PY
interventions aware of participants'		
assigned intervention during the trial?		
2.3. <u>If Y/PY/NI to 2.1 or 2.2</u> : Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		PN
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		NI
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 5

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study details

Reference	Klein JP, Berger T, Schröder J, Späth C, Meyer B, Caspar F, Lutz W, Arndt A, Greiner W, Gräfe V, Hautzinger M, Fuhr K, Rose M, Nolte S, Löwe B, Anderssoni G, Vettorazzi E, Moritz S, Hohagen F. Effects of a Psychological Internet Intervention in the Treatment of Mild to Moderate Depressive Symptoms: Results of the EVIDENT Study, a Randomized Controlled Trial. Psychother Psychosom. 2016;85(4):218-28. doi: 10.1159/000445355. Epub 2016 May 27. PMID: 27230863; PMCID: PMC8117387.
☐ Cluster-	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial
1	of this assessment, the interventions being compared are defined as
Experimental:	Deprexis Comparator: Care as usual (CAU)
Specify which o	utcome is being assessed for risk of bias  Patient Health Questionnaire (PHQ 9)
analyses being p 0.83 to 2.77) an	presented, specify the numeric result (e.g. RR = 1.52 (95% CI d/or a reference (e.g. to a table, figure or paragraph) that is the result being assessed.
Is the review tea	m's aim for this result?
X to asses	s the effect of assignment to intervention (the 'intention-to-treat' effect)
☐ to asses	s the effect of adhering to intervention (the 'per-protocol' effect)
must be checked  ☐ occurren  ☐ failures in	ssess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one ):  ce of non-protocol interventions in implementing the intervention that could have affected the outcome erence to their assigned intervention by trial participants
	owing sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)

 Datei:
 2021-07-22\_ANHANG\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

© 2021 ProHTA Advisors in Healthcare

Copyright:

Χ	Journal article(s) with results of the trial
Χ	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare Seite 44 von 151

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

#### Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		N
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		PY
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		<u>N</u>
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		<u>Y</u>
analysed in accordance with a pre-specified		
analysis plan that was finalized before unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions, time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the data?		N
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

#### Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 6

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

© 2021 ProHTA Advisors in Healthcare

Study d	letails			
•	Fischer A, Schröder J, Vettorazzi E, Wolf OT, Pöttgen J, Lau		Lau S, Heesen C, Moritz S, Gold SM. An online programme to reduce mised controlled trial. Lancet Psychiatry. 2015 Mar;2(3):217-23. doi: PMID: 26359900.	
Study of X	Individua Cluster-r Individua	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial of this assessment, the interventions being compared a	are defined as	
Experi	mental:	Deprexis Comparator: Warte	eliste / Care as usual (CAU)	
Specif	Specify which outcome is being assessed for risk of bias  Beck Depression Inventory (BDI)			
analys 0.83 to	ses being p o 2.77) and	nerical result being assessed. In case of multiple alternatoresented, specify the numeric result (e.g. RR = 1.52 (95% d/or a reference (e.g. to a table, figure or paragraph) that see the result being assessed.	6 CI	
Is the review team's aim for this result?  X to assess the effect of assignment to intervention (the 'intention-to-treat' effect)  to assess the effect of adhering to intervention (the 'per-protocol' effect)				
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):  ccurrence of non-protocol interventions failures in implementing the intervention that could have affected the outcome non-adherence to their assigned intervention by trial participants				

Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)
© 2021 ProHTA Advisors in Healthcare

Datei: Verfasser: Empfänger:

Copyright:

Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: Vorstand der Kassenarztlichen Vereinigung Bayern (KVB

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

#### Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		Ĭ
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		<u>PN</u>
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 7

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

© 2021 ProHTA Advisors in Healthcare

Study d	letails			
·	Schröder J, Brückner K, Fischer A, Lindenau M, Köther U, Ve		/ettorazzi E, Moritz S. Efficacy of a psychological online intervention for ed trial. Epilepsia. 2014 Dec;55(12):2069-76. doi: 10.1111/epi.12833.	
Study d  X    For the	Individua Cluster-ra Individua	ally-randomized parallel-group trial andomized parallel-group trial ally randomized cross-over (or other matched) trial of this assessment, the interventions being compared are	defined as	
Experi	mental:	Deprexis Comparator: Wartelist	e / Care as usual (CAU)	
Specif	Specify which outcome is being assessed for risk of bias  Depression – Beck Depression Inventory I (BDI-I)			
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.				
Is the review team's aim for this result?  X to assess the effect of assignment to intervention (the 'intention-to-treat' effect)				
	$\square$ to assess the effect of <i>adhering to intervention</i> (the 'per-protocol' effect)			
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):  coccurrence of non-protocol interventions failures in implementing the intervention that could have affected the outcome non-adherence to their assigned intervention by trial participants				

2021-07-22\_ANHANG\_\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)		
Χ	Journal article(s) with results of the trial		
	Trial protocol		
	Statistical analysis plan (SAP)		
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)		
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)		
	"Grey literature" (e.g. unpublished thesis)		
	Conference abstract(s) about the trial		
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)		
	Research ethics application		
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)		
	Personal communication with trialist		
	Personal communication with the sponsor		

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Copyright: © 2021 ProHTA Advisors in Healthcare

Datei:

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

#### Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		NI
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		N
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / <mark>Y / PY / PN / N</mark> / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		PN
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>PN</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 n 00 n 00 n 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

## Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 8

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study details					
Reference		Meyer B. Bierbrodt J, Schröder J, Berger T, Beevers CG, Weiss M, Jacob G, Späth C, Andersson G, Lutz W, Hautzinger M, Löwe B, Rose M, Hohagen F, Caspar F, Greiner W, Moritz S, Klein JP. Effects of an Internet intervention (Deprexis) on severe depression symptoms: Randomized controlled trial. Internet Interventions. 2015;2(1): 48-59. http://dx.doi.org/10.1016/j.invent.2014.12.003			
<b>x</b>	☐ Cluster-randomized parallel-group trial				
		of this assessment, the interventions being compared and Deprexis  Comparator: Warte	eliste / Care as usual (CAU)		
Specify	Specify which outcome is being assessed for risk of bias  Depression – Patient Health Questionnaire - 9 items (PHQ-9)  Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI				
0.83 to	0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.				
Is the review team's aim for this result?  X to assess the effect of assignment to intervention (the 'intention-to-treat' effect)  U to assess the effect of adhering to intervention (the 'per-protocol' effect)					
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):  occurrence of non-protocol interventions failures in implementing the intervention that could have affected the outcome non-adherence to their assigned intervention by trial participants					

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)				
Χ	Journal article(s) with results of the trial				
	Trial protocol				
	Statistical analysis plan (SAP)				
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)				
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)				
	"Grey literature" (e.g. unpublished thesis)				
	Conference abstract(s) about the trial				
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)				
	Research ethics application				
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)				
	Personal communication with trialist				
	Personal communication with the sponsor				

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare Seite 74 von 151

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		PN (nur Alter)
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Y
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. <u>If Y/PY/NI to 2.1 or 2.2</u> : Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / <u>PN / N</u> / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / Y / PY / PN / N / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		N
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Ontional: What is the overall predicted	NA / Favours
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

© 2021 ProHTA Advisors in Healthcare

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 9

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

© 2021 ProHTA Advisors in Healthcare

Study detail	<u> </u>				
Reference	Moritz S, Schilling L, Hauschildt M, Schröder J, Treszl A. A randomized controlled trial of internet-based therapy in depression. Behav Res Ther. 2012 Aug;50(7-8):513-21. doi: 10.1016/j.brat.2012.04.006. Epub 2012 May 3. PMID: 22677231.				
X Indi	☐ Cluster-randomized parallel-group trial				
Experiment		of this assessment, the intervent Deprexis	1 F	ned as Care as usual (CAU)	
Specify the	Specify which outcome is being assessed for risk of bias  Depression - Beck Depression Inventory (BDI)  Specify the numerical result being assessed. In case of multiple alternative				
0.83 to 2.7	analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.				
		's aim for this result?			
If the aim is to assess the effect of <i>adhering to intervention</i> , select the deviations from intended intervention that should be addressed (at least one must be checked):					
☐ failu	$\Box$ failures in implementing the intervention that could have affected the outcome				

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)				
Χ	Journal article(s) with results of the trial				
	Trial protocol				
	Statistical analysis plan (SAP)				
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)				
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)				
	"Grey literature" (e.g. unpublished thesis)				
	Conference abstract(s) about the trial				
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)				
	Research ethics application				
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)				
	Personal communication with trialist				
	Personal communication with the sponsor				

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>NI</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		N
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / <u>PN / N</u> / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / Y / PY / PN / N / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>PN</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Ontional: What is the overall predicted	NA / Favours
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 10

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study d	Study details				
Refere	Berger T, Hämmerli K, Gubser N, Andersson G, Caspar F. Internet-based treatment of depression: a randomized controlled tr comparing guided with unguided self-help. Cogn Behav Ther. 2011;40(4):251-66. doi: 10.1080/16506073.2011.616531. PMIE 22060248.		·		
X	☐ Cluster-randomized parallel-group trial				
Specify	y which ou	atcome is being assessed for risk of bias	Depression – Beck Depression Inventory (BDI-II)		
analyse 0.83 to	es being po 2.77) and	rescal result being assessed. In case of multiple alternative resented, specify the numeric result (e.g. RR = 1.52 (95% CI I/or a reference (e.g. to a table, figure or paragraph) that the result being assessed.			
Is the re		n's aim for this result?			
X □					
must be	failures in implementing the intervention that could have affected the outcome				

2021-07-22\_ANHANG\_\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare Seite 94 von 151

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		PY
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		<u>N</u>
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PN
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		NI
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diels of his a independent		Comp. 00 00 00 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

#### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

deprexis Studie 11

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study d	etails		
Refere	Meyer B, Berger T, Caspar F, Beevers CG, Andersson G, Weiss M. Effectiveness of a novel integrative online treatment for depression (Deprexis): randomized controlled trial. J Med Internet Res. 2009 May 11;11(2):e15. doi: 10.2196/jmir.1151. PMID: 19632969; PMCID: PMC2762808.		
Study d X —	Individua Cluster-ra Individua	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial	
		Deprexis Comparator: Warts	are defined as eliste / Care as usual (CAU)
Specif	y which o	utcome is being assessed for risk of bias	Beck Depression Inventory (BDI)
analys 0.83 to	es being p o 2.77) and	nerical result being assessed. In case of multiple alterna oresented, specify the numeric result (e.g. RR = 1.52 (950 d/or a reference (e.g. to a table, figure or paragraph) the sthe result being assessed.	% CI
Is the re	to assess	m's aim for this result?  Is the effect of assignment to intervention (the 'intention of the effect of adhering to intervention (the 'per-protoco	·
must be	e checked) occurrenc failures in		

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	of the following sources were <u>obtained</u> to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare

#### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>PY</u>
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		N
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. <u>If Y/PY/NI to 2.1 or 2.2</u> : Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / <u>PN / N / NI</u>
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

© 2021 ProHTA Advisors in Healthcare

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		N
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		NI
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		PY
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Υ
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>N</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 n 00 n 00 n 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	High
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

elevida Studie 1

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study de	tails		
Referer	Pöttgen J, Moss-Morris R, Wendebourg JM, Feddersen L, Lau S, Köpke S, Meyer B, Friede T, Penner IK, Heesen C, Gold SM.		
For the p	Individua Cluster-ra Individua <b>purposes</b>	ally-randomized parallel-group trial randomized parallel-group trial ally randomized cross-over (or other matched) trial of this assessment, the interventions being compared are	
Specify analyse 0.83 to	which ou the num s being p 2.77) and	Elevida Comparator: Warteliste  utcome is being assessed for risk of bias  perical result being assessed. In case of multiple alternative presented, specify the numeric result (e.g. RR = 1.52 (95% CI d/or a reference (e.g. to a table, figure or paragraph) that is the result being assessed.	Fatigue - Chalder Fatigue Scale (Müdigkeit)
Χ	to assess	m's aim for this result? the effect of assignment to intervention (the 'intention-to-to-to-to-to-to-to-to-to-to-to-to-to-	·
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):  occurrence of non-protocol interventions failures in implementing the intervention that could have affected the outcome non-adherence to their assigned intervention by trial participants			

 Verfasser:
 Prof. Dr. med. Peter Kolominsky-Rabas, MBA

 Empfänger:
 Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

 Copyright:
 © 2021 ProHTA Advisors in Healthcare

Datei:

Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

## Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		<u>PN</u>
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Y
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. <u>If Y/PY/NI to 2.1 or 2.2</u> : Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

# Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Y / PY / <u>PN / N</u> / NI
interventions aware of participants'		
assigned intervention during the trial?		
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:		NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions		
balanced across intervention groups?		
2.4. [If applicable:] Were there failures in		NA / <mark>Y / PY / <u>PN / N</u> / NI</mark>
implementing the intervention that could		
have affected the outcome?		
2.5. [If applicable:] Was there non-		NA / <mark>Y / PY</mark> / <u>PN / N</u> / NI
adherence to the assigned intervention		
regimen that could have affected		
participants' outcomes?		
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or		NA / <u>Y / PY</u> / <mark>PN / N</mark> / NI
2.5: Was an appropriate analysis used to		
estimate the effect of adhering to the		
intervention?		
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		PN
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		<u>PY</u>
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		NI
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>PN</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Disk of hiss indoment		Sama concorns
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

somnio Studie 1

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study details					
Reference		Lorenz N, Heim E, Roetger A, Birrer E, Maercker A. Randomized Controlled Trial to Test the Efficacy of an Unguided Online Intervention with Automated Feedback for the Treatment of Insomnia. Behav Cogn Psychother. 2019 May;47(3):287-302. doi: 10.1017/S1352465818000486. Epub 2018 Sep 6. PMID: 30185239.			
x	☐ Cluster-randomized parallel-group trial				
	imental:	Somnium Comparator: Warteliste			
Specif	Specify which outcome is being assessed for risk of bias  Insomnia - Insomnia Severity Index (ISI)				
analys 0.83 to	Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.				
Is the review team's aim for this result?  X to assess the effect of assignment to intervention (the 'intention-to-treat' effect)  to assess the effect of adhering to intervention (the 'per-protocol' effect)					
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):  occurrence of non-protocol interventions failures in implementing the intervention that could have affected the outcome non-adherence to their assigned intervention by trial participants					

Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei: Verfasser: Empfänger:

Copyright:

Which	Which of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)		
Χ	Journal article(s) with results of the trial		
	Trial protocol		
	Statistical analysis plan (SAP)		
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)		
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)		
	"Grey literature" (e.g. unpublished thesis)		
	Conference abstract(s) about the trial		
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)		
	Research ethics application		
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)		
	Personal communication with trialist		
	Personal communication with the sponsor		

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright: © 2021 ProHTA Advisors in Healthcare

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		Ĭ
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		PY
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Y
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. <u>If Y/PY/NI to 2.1 or 2.2</u> : Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		NI
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		NI
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / <u>PN / N</u> / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / Y / PY / PN / N / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		<u>Y</u>
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		<u>PN</u>
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

# Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before		
unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>PN</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Diele of his a independent		Comp. 00 n 00 n 00 n 00
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

© 2021 ProHTA Advisors in Healthcare

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

velibra Studie 1

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study details						
Reference		ncent A, Moser CT, Moritz S, Meyer B. Effects of a transdiagnostic unguided ders in primary care: results of a randomized controlled trial. Psychol Med. 2017 270. Epub 2016 Sep 22. PMID: 27655039.				
☐ Cluster-☐ Individu	X Individually-randomized parallel-group trial  Cluster-randomized parallel-group trial					
	s of this assessment, the interventions being comp					
Experimental:	Velibra Comparator:	Warteliste / Care as usual (CAU)				
Specify which o	Anxiety Disorders - Depression Anxiety Stress Scales – Short Form (DASS-21); Beck Anxiety Inventory (BAI); Beck Depression Inventory-II (BDI-II); Brief Symptom Inventory (BSI); Short-Form Health Survey-12 (SF-12)					
Specify the numerical result being assessed. In case of multiple alternative analyses being presented, specify the numeric result (e.g. RR = 1.52 (95% CI 0.83 to 2.77) and/or a reference (e.g. to a table, figure or paragraph) that uniquely defines the result being assessed.						
Is the review team's aim for this result?						
X to assess the effect of assignment to intervention (the 'intention-to-treat' effect)						
□ to asses						
If the aim is to assess the effect of adhering to intervention, select the deviations from intended intervention that should be addressed (at least one must be checked):   — occurrence of non-protocol interventions						

Vorstand der Kassenärztlichen Vereinigung Bayern (KVB) © 2021 ProHTA Advisors in Healthcare

	failures in implementing the intervention that could have affected the outcome
	non-adherence to their assigned intervention by trial participants
Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Χ	Journal article(s) with results of the trial
	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB) © 2021 ProHTA Advisors in Healthcare

Datei: Verfasser:

Copyright:

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

### Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		N
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		NI
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Some concerns
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / PN / N / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / Y / PY / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / <mark>Y / PY / PN / N</mark> / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / Y / PY / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		<u>PY</u>
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>N</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Y
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		Υ
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		NI
analysed in accordance with a pre-specified		
analysis plan that was finalized before unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from		
5.2 multiple eligible outcome		<u>PN</u>
measurements (e.g. scales, definitions,		
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		NI
data?		
Risk-of-bias judgement		Some concerns
Ontional: What is the predicted direction of		NA / Favours experimental /
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator /
bias due to selection of the reported result!		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Some concerns
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.

© 2021 ProHTA Advisors in Healthcare

Datei:

# Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) TEMPLATE FOR COMPLETION

Edited by Julian PT Higgins, Jelena Savović, Matthew J Page, Jonathan AC Sterne on behalf of the RoB2 Development Group

Version of 22 August 2019

vorvida Studie 1

The development of the RoB 2 tool was supported by the MRC Network of Hubs for Trials Methodology Research (MR/L004933/2- N61), with the support of the host MRC ConDuCT-II Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1), by MRC research grant MR/M025209/1, and by a grant from The Cochrane Collaboration.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Study details			
Reference	Zill JM, Christalle E, Meyer B, Härter M, Dirmaier J: The effectiveness of an internet intervention aimed at reducing alcohol consumption in adults: results of a randomized controlled trial (Vorvida). Dtsch Arztebl Int 2019; 116: 127–33. DOI: 10.3238/arztebl.2019.0127		
Study design			
	ually-randomized parallel-gro	oup trial	
☐ Cluste	r-randomized parallel-group t	rial	
☐ Individ	ually randomized cross-over	(or other matched) trial	
Ear the nurnes	os of this assassment the int	erventions being compared are de	ofined as
Experimental:		Comparator: Warteliste /	
Experimental.	VOIVIGU	variensie /	Care as asaar (erro)
Specify which	outcome is being assessed for	or risk of bias	Quantity-Frequency-Index (QFI) und "Time-line Follow-Back"- Methode (TFB)
analyses being 0.83 to 2.77) a	g presented, specify the nume	d. In case of multiple alternative eric result (e.g. RR = 1.52 (95% Clable, figure or paragraph) that	
Is the review to	eam's aim for this result?		
X to asse	ess the effect of assignment to	o intervention (the 'intention-to-tre	at' effect)
□ to asse	ess the effect of adhering to in	ntervention (the 'per-protocol' effe	ct)
must be checke	ed):		ons from intended intervention that should be addressed (at least one
	nce of non-protocol interven		
	,	ntion that could have affected the c	outcome
⊥ l non-ad	nerence to their assigned into	ervention by trial participants	

2021-07-22\_ANHANG\_\_KVB\_GUTACHTEN\_Bewertung von DIGAS auf Evidenz-basierter Grundlage.docx Prof. Dr. med. Peter Kolominsky-Rabas, MBA

Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei: Verfasser: Empfänger:

Copyright:

Which	of the following sources were obtained to help inform the risk-of-bias assessment? (tick as many as apply)
Х	Journal article(s) with results of the trial
Х	Trial protocol
	Statistical analysis plan (SAP)
	Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
	Company-owned trial registry record (e.g. GSK Clinical Study Register record)
	"Grey literature" (e.g. unpublished thesis)
	Conference abstract(s) about the trial
	Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
	Research ethics application
	Grant database summary (e.g. NIH RePORTER or Research Councils UK Gateway to Research)
	Personal communication with trialist
	Personal communication with the sponsor

Verfasser: Prof. Dr. med. Peter Kolominsky-Rabas, MBA
Empfänger: Vorstand der Kassenärztlichen Vereinigung Bayern (KVB)

Datei:

Copyright:

### Risk of bias assessment

Responses <u>underlined in green</u> are potential markers for low risk of bias, and responses in <u>red</u> are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

### Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		<u>Y</u>
1.2 Was the allocation sequence concealed		<u>Y</u>
until participants were enrolled and		
assigned to interventions?		
1.3 Did baseline differences between		<u>N</u>
intervention groups suggest a problem with		
the randomization process?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias arising from the randomization process?		Favours comparator / Towards
		null /Away from null /
		Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Signalling questions	Comments	Response options
2.1. Were participants aware of their		Υ
assigned intervention during the trial?		
2.2. Were carers and people delivering the		Υ
interventions aware of participants'		
assigned intervention during the trial?		
2.3. If Y/PY/NI to 2.1 or 2.2: Were there		<u>PN</u>
deviations from the intended intervention		
that arose because of the trial context?		
2.4 If Y/PY to 2.3: Were these deviations		
likely to have affected the outcome?		
2.5. If Y/PY/NI to 2.4: Were these		
deviations from intended intervention		
balanced between groups?		
2.6 Was an appropriate analysis used to		<u>Y</u>
estimate the effect of assignment to		
intervention?		
2.7 If N/PN/NI to 2.6: Was there potential		
for a substantial impact (on the result) of		
the failure to analyse participants in the		
group to which they were randomized?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to deviations from intended		Favours comparator /
interventions?		Towards null /Away from
		null / Unpredictable

## Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signalling questions	Comments Response options
2.1. Were participants aware of their	Y / PY / <u>PN / N</u> / NI
assigned intervention during the trial?	
2.2. Were carers and people delivering the	Y / PY / <u>PN / N</u> / NI
interventions aware of participants'	
assigned intervention during the trial?	
2.3. [If applicable:] If Y/PY/NI to 2.1 or 2.2:	NA / <u>Y / PY</u> / PN / N / NI
Were important non-protocol interventions	
balanced across intervention groups?	
2.4. [If applicable:] Were there failures in	NA / Y / PY / PN / N / NI
implementing the intervention that could	
have affected the outcome?	
2.5. [If applicable:] Was there non-	NA / Y / PY / PN / N / NI
adherence to the assigned intervention	
regimen that could have affected	
participants' outcomes?	
2.6. If N/PN/NI to 2.3, or Y/PY/NI to 2.4 or	NA / <u>Y / PY</u> / PN / N / NI
2.5: Was an appropriate analysis used to	
estimate the effect of adhering to the	
intervention?	
Risk-of-bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of	NA / Favours experimental /
bias due to deviations from intended	Favours comparator /
interventions?	Towards null /Away from
	null / Unpredictable

## Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available		N
for all, or nearly all, participants		
randomized?		
3.2 If N/PN/NI to 3.1: Is there evidence that		PY
the result was not biased by missing		
outcome data?		
3.3 If N/PN to 3.2: Could missingness in the		
outcome depend on its true value?		
3.4 If Y/PY/NI to 3.3: Is it likely that		
missingness in the outcome depended on		
its true value?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to missing outcome data?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

### Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the		<u>PN</u>
outcome inappropriate?		
4.2 Could measurement or ascertainment		<u>N</u>
of the outcome have differed between		
intervention groups?		
4.3 If N/PN/NI to 4.1 and 4.2: Were		Υ
outcome assessors aware of the		
intervention received by study		
participants?		
4.4 If Y/PY/NI to 4.3: Could assessment of		PY
the outcome have been influenced by		
knowledge of intervention received?		
4.5 If Y/PY/NI to 4.4: Is it likely that		NI
assessment of the outcome was influenced		
by knowledge of intervention received?		
Risk-of-bias judgement		High
Optional: What is the predicted direction of		NA / Favours experimental /
bias in measurement of the outcome?		Favours comparator /
		Towards null /Away from
		null / Unpredictable

## Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result		<u>PY</u>
analysed in accordance with a pre-specified		
analysis plan that was finalized before unblinded outcome data were available for		
analysis?		
Is the numerical result being assessed likely		
to have been selected, on the basis of the		
results, from 5.2 multiple eligible outcome		N
measurements (e.g. scales, definitions,		<u>1V</u>
time points) within the outcome		
domain?		
5.3 multiple eligible analyses of the		<u>N</u>
data?		
Risk-of-bias judgement		Low
Optional: What is the predicted direction of		NA / Favours experimental /
bias due to selection of the reported result?		Favours comparator /
size the to detection of the reported result.		Towards null /Away from
		null / Unpredictable

### Overall risk of bias

Risk-of-bias judgement	Low
Optional: What is the overall predicted	NA / Favours
direction of bias for this outcome?	experimental / Favours
	comparator / Towards
	null /Away from null /
	Unpredictable



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License</u>.