Risk of Bias-Assessment

S3-Leitlinie Strategien zur Sicherung rationaler Antibiotika-Anwendung im Krankenhaus

AWMF-Registernummer 092/001 - update 2018

evaluiert wurden folgende Studientypen gemäß den Vorgaben von SIGN und EPOC (Cochrane Review-Arbeitsgruppe)

SECTIONS	REFERENCE Yes or No (notes, if necessary)	Davey et a., 2005	Davey et al., 2006	Davey et al., 2013
INTERNAL VALIDITY (SIGN)	1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes
	1.2 A comprehensive literature search is carried out	yes	yes	yes
	1.3 At least two people should have selected studies.	yes	yes	yes
	1.4 At least two people should have extracted data.	yes	yes	yes
	1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	yes	yes
	1.6 The excluded studies are listed.	yes	yes	yes
	1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes
	1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	yes
	1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	yes
	1.10 Appropriate methods are used to combine the individual study findings	yes	yes	yes
	1.11 The likelihood of publication bias was assessed appropriately.	yes	yes	yes
	1.12 Conflicts of interest are declared.	yes	yes	yes
OVERALL ASSESSMENT OF THE STUDY (SIGN)	**2.1 What is your overall assessment of the methodological quality of this review?**	(++)	(++)	(++)
	2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes
	2.3 notes	Cochrane	Cochrane	Cochrane

REFERENCE Yes or No (notes, if necessary)	Davey et al. 2017	Schuts et al. 2017	Khadem et al., 2012	Rawson et al., 2017
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	no	yes
1.3 At least two people should have selected studies.	yes	yes	no	yes
1.4 At least two people should have extracted data.	yes	yes	no	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	no	no
1.6 The excluded studies are listed.	yes	no	no	no
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	no	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	no	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	no	yes	yes
1.11 The likelihood of publication bias was assessed appropriately.	yes	no	no	no
1.12 Conflicts of interest are declared.	yes	yes	no	yes
2.1 What is your overall assessment of the methodological quality of this review?	(++)	(+)	(-)	(+)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	Cochrane	keine graue Literatur eingeschlossen, Gefahr d. Publikationsbias, Meta-Analyse trotz hoher Heterogenität (I^2=82%), trotzdem (+) da qualitative Synthese gut	nur MEDLINE, keine graue Literatur keine Angaben zu 1.3, 1.4, keine Bewertung der Studienqualität, keine Iks	

REFERENCE Yes or No (notes, if necessary)	Cresswell et al., 2017	Baysari et al., 2016	Ivers et al., 2012	Ranji et al., 2008	Tang et al., 2018
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	no	yes	yes	yes
1.3 At least two people should have selected studies.	yes	yes	yes	yes	yes
1.4 At least two people should have extracted data.	yes	no	yes	yes	no
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	yes	no	no
1.6 The excluded studies are listed.	no	no	yes	no	no
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	no	yes	yes	no	yes
1.9 Was the scientific quality of the included studies used appropriately?	no	no	yes	no	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	no	yes	no	yes
1.11 The likelihood of publication bias was assessed appropriately.	no	no	yes	no	yes
1.12 Conflicts of interest are declared.	yes	yes	yes	yes	no
2.1 What is your overall assessment of the methodological quality of this review?	(+)	(-)	(++)	(-)	(-)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes	yes
2.3 notes	**Scoping Review**, keine Qualiätsbewertung notwendig, da vorläufige Einschätzung von Art und Umfang der Literatur zu einem Thema	Metaanalyse kritisch betrachten! 1.4 keine Angabe 1.8 wird nicht angegeben wie Qualität bewertet wird (nur Aussage wie in anderen Reviews mit Zitat) 1.9 große Gefahr durch Publikationsbias, da nur MEDLINE Suchquelle; Angabe im Bericht dass funnelplots generiert wurden, diese sind aber nicht im Artikel noch imAnhang 1.10 Metaanalysen wurden durchgeführt, trotz hoher Heterogenitätsmaße	Cochrane	1.5 keine Sichtung grauer Literatur 1.8 eigenes Qualitätsbewertungtool, keine indiviudellen nur aggregierte Angaben pro Item, deshalb 1.9 auch nein 1.11 deshalb hohe Gefahr des Publikationsbiases	1.5 keine graue Literatur, Gefahr durch Publikationsbias

REFERENCE Yes or No (notes, if necessary)	Guo et a., 2016	Ohji et al., 2016	Paul et al., 2016	Tabah et al., 2016	Silva et al., 2013
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	yes	yes
1.3 At least two people should have selected studies.	yes	yes	yes	yes	yes
1.4 At least two people should have extracted data.	yes	yes	yes	yes	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	no	no	yes	no	yes
1.6 The excluded studies are listed.	no	no	no	no	yes
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	yes	yes	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	yes	yes	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	yes	yes	yes	yes
1.11 The likelihood of publication bias was assessed appropriately.	yes	yes	no	yes	yes
1.12 Conflicts of interest are declared.	yes	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(+)	(++)	(+)	(+)	(++)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes	yes
2.3 notes	1.11 aufgrund der geringen eingeschlossenen Anzahl an Studien kein funnelplot möglich	1.11 erstellte funnel plots nicht gezeigt		1.5 Kongressbeiträge und andere unpublizierte Forschung wurde explizit ausgeschlossen	leider keine Studien gefunden

REFERENCE Yes or No (notes, if necessary)	Sacco et al., 2017	Wu et al., 2018	Onakpoya et al., 2018	Hanretty et al., 2018
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	no
1.3 At least two people should have selected studies.	yes	yes	yes	yes
1.4 At least two people should have extracted data.	no	yes	yes	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	yes	yes
1.6 The excluded studies are listed.	no	no	yes	no
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	no	yes	no
1.9 Was the scientific quality of the included studies used appropriately?	no	no	yes	no
1.10 Appropriate methods are used to combine the individual study findings	yes	no	yes	no
1.11 The likelihood of publication bias was assessed appropriately.	no	no	yes	no
1.12 Conflicts of interest are declared.	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(-)	0	(++)	(-)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	1.4 nur Erwähnung zum Screening aber nicht zur Datenextrahierung 1.9 keine Beachtung der Studienqualität bei der Analyse (keine Sensitivitätsanalyse) 1.11 keine Angaben, nur im Dikussionsteil Erwähnung, dass negative Ergebnisse nicht einfliesen, da nicht publiziert (ist aber zu allgemein)	1.8 kein RoB!!!!	**Overview of Systematic Reviews** **1.11 nur 6 eingeschlossene Studien (Funnelplot nicht machbar), aber sehr ausführliche Suche**	1.2 lediglich MEDLINE und Leitlinien (unklar welche) 1.8 keine Bewertung des RoB

REFERENCE Yes or No (notes, if necessary)	Schuetz et al., 2018	Gouvea et al., 2015	Pugh et al., 2015	Sallach-Ruma et al., 2013
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	yes
1.3 At least two people should have selected studies.	yes	yes	yes	no
1.4 At least two people should have extracted data.	yes	yes	yes	no
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	yes	yes
1.6 The excluded studies are listed.	no	no	yes	no
1.7 The relevant characteristics of the included studies are provided.	yes	no	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	no	yes	no
1.9 Was the scientific quality of the included studies used appropriately?	yes	no	yes	no
1.10 Appropriate methods are used to combine the individual study findings	yes	no	yes	no
1.11 The likelihood of publication bias was assessed appropriately.	yes	no	yes	no
1.12 Conflicts of interest are declared.	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(++)	0	(++)	0
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes		1.7 Studiencharakteristika sind unvollständig 1.8 Evidenzlevel wurden vergeben ohne Angaben nach welcher Klassifizierung (z.B. Oxford)		wahrscheinlich narratives Review

REFERENCE Yes or No (notes, if necessary)	Athanassa et al., 2008	Rhew et al., 2001	Kouranos et al., 2009	Vouloumanou et al., 2008
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	no	yes
1.3 At least two people should have selected studies.	yes	yes	no	yes
1.4 At least two people should have extracted data.	yes	yes	no	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	no	no	no	no
1.6 The excluded studies are listed.	no	no	no	no
1.7 The relevant characteristics of the included studies are provided.	yes	no	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	no	no	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	no	no	yes
1.10 Appropriate methods are used to combine the individual study findings	no	no	no	yes
1.11 The likelihood of publication bias was assessed appropriately.	no	no	no	no
1.12 Conflicts of interest are declared.	yes	no	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(-)	0	0	(+)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	1.10 Metaanalyse trotz großer Heterogenität durchgeführt (für Outcome Verweildauer) 1.11 Publikationsbias nirgendwo erwähnt, funnel plot aufgrund Anzahl Studien nicht möglich	kein RoB, keine Studiencharakteristika	nur Suche in Pubmed keine Rob, deshalb keine sinnvolle Metaanalyse möglich kein Publikationsbias beachtet	keine graue Literatur keine Angaben zu Publikationsbias, kein funnelplot möglich da nur 8 Studien

REFERENCE Yes or No (notes, if necessary)	Hodson et al., 2007 (2008	Strohmeier et al., 2014	Hao et al., 2016	Smyth et al., 2017
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	yes
1.3 At least two people should have selected studies.	yes	yes	yes	yes
1.4 At least two people should have extracted data.	yes	yes	yes	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	yes	no	yes
1.6 The excluded studies are listed.	yes	yes	yes	yes
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	yes	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	yes	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	yes	yes	yes
1.11 The likelihood of publication bias was assessed appropriately.	yes	yes	yes	yes
1.12 Conflicts of interest are declared.	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(++)	(++)	(++)	(++)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	Cochrane, aktueller Fassung von 2014 verfügbar	Cohrane, aktuellere Fassung von Hodson 2007		Cochrane

REFERENCE Yes or No (notes, if necessary)	Gillaizeau et al., 2013	Sime et al., 2012	Vardakas et al., 2018	Ye et al., 2013
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	no	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	yes
1.3 At least two people should have selected studies.	yes	no	no	yes
1.4 At least two people should have extracted data.	yes	no	yes	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	no	no
1.6 The excluded studies are listed.	yes	no	no	no
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	no	yes	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	no	yes	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	no	yes	yes
1.11 The likelihood of publication bias was assessed appropriately.	yes	no	yes	yes
1.12 Conflicts of interest are declared.	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(++)	0	(+)	(+)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	cochrane	kein RoB keine Angaben zur Auswahl der Literatur	Angabe zur Selektion der Studien fehlt	keine graue Literatur, Pub Bias via funnelplot für nu 6 Studien nicht geeignet

REFERENCE Yes or No (notes, if necessary)	Buehler et al., 2016	Timbrook et al., 2017	Vardakas et al., 2015	Baur et al., 2017
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	yes	yes	yes
1.3 At least two people should have selected studies.	yes	yes	yes	yes
1.4 At least two people should have extracted data.	no	no	yes	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	yes	no	no
1.6 The excluded studies are listed.	no	no	no	yes
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	no	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	no	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	yes	no	yes
1.11 The likelihood of publication bias was assessed appropriately.	yes	yes	no	yes
1.12 Conflicts of interest are declared.	yes	yes	yes	yes
2.1 What is your overall assessment of the methodological quality of this review?	(+)	(+)	(-)	(+)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.3 notes	1.11 kein funnelplot dazu wenige Studien, aber graue Literatur wurde eingeschlossen			1.6 nur die nicht in die Metanaalyse inkludierten Studien aufgelistet

REFERENCE Yes or No (notes, if necessary)	Louh et al., 2017	Wagner et al., 2014	Faezel et al., 2014	Yakob et al., 2014	Hsu et al., 2010
1.1 The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	yes	yes	yes	yes	yes
1.2 A comprehensive literature search is carried out	yes	no	yes	no	yes
1.3 At least two people should have selected studies.	yes	yes	no	no	no
1.4 At least two people should have extracted data.	yes	yes	yes	no	yes
1.5 The status of publication was not used as an inclusion criterion. (graue Literatur)	yes	no	no	no	yes
1.6 The excluded studies are listed.	no	no	yes	no	no
1.7 The relevant characteristics of the included studies are provided.	yes	yes	yes	yes	yes
1.8 The scientific quality of the included studies was assessed and reported.	yes	yes	yes	no	yes
1.9 Was the scientific quality of the included studies used appropriately?	yes	yes	yes	no	yes
1.10 Appropriate methods are used to combine the individual study findings	yes	yes	yes	no	yes
1.11 The likelihood of publication bias was assessed appropriately.	no	no	yes	no	no
1.12 Conflicts of interest are declared.	yes	yes	yes	no	yes
2.1 What is your overall assessment of the methodological quality of this review?	(+)	(+)	(+)	0	(+)
2.2 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	no	yes
2.3 notes	1.4 nur 50% von 2. Reviewer kontrolliert 1.11 kein funnelplot, aber als Limitation angesprochen, dass negative Ergebnisse nicht publiziert wurden	1.2 nur Medline		1.2 nur Suche in MEDLINE; Fokus eher auf Hygienemaßnahmen	hauptsächlich Fokus auf Hygiene, kein Publikationsbias berücksichtigt (Risiko als gering eingeschätzt, da ausführliche Suche)

	Criteria SIGN & EPOC	RCT			
SECTIONS	REFERENCE Yes or No (notes, if necessary)	Camins et al., 2009	Lesprit et al., 2013	Gums et al., 1999	Masia et al., 2008
SIGN (INTERNAL VALIDITY)	1.1 The study addresses an appropriate and clearly focused question.	yes	yes	yes	yes
	1.2 The assignment of subjects to treatment groups is randomised	yes	yes	unclear	yes
	1.3 An adequate concealment method is used.	no	yes	no	yes
	1.7 All relevant outcomes are measured in a standard, valid and reliable way.	unclear	yes	yes	yes
	1.6 The only difference between groups is the treatment under investigation.	yes	yes	yes	yes
	1.4 The design keeps subjects and investigators 'blind' about treatment allocation	no	no	unclear	no
EPOC	5. Were incomplete outcome data adequately addressed?*	yes	yes	yes	yes
	7. Was the study adequately protected against contamination?	no	yes	yes	no
	8. Was the study free from selective outcome reporting?	yes	yes	yes	yes
	9. Was the study free from other risks of bias?	yes	yes	yes	yes
SIGN (INTERNAL VALIDITY)	1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	n.a.	yes	K: 9 von 134 I:11 von 138 da innerhalb von 24h entlassen	yes
	1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	n.a.	yes	yes	yes
	1.10 Where the study is carried out at more than one site, results are comparable for all sites.	n.a.	n.a.	n.a.	n.a.
SIGN (OVERALL ASSESSMENT OF THE STUDY)	2.1 How well was the study done to minimise bias?	(-)	(+)	(-)	(-)
	2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?				
	2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
	2.4 Notes	2. nicht verdeckt 6. keine Verblindung 7. Interventiongruppe-Ärzte waren die gleichen wie Kontrollgruppen-Ärzte, nur ein KH 1.8- und 1.9 es wurde keine Therapie evaluiert sondern die Verordnungspraxis (nicht Patienten, sondern Arzt-Teams wurden randomisiert)		1.2 Methode für Sequenzgeneration unklar 1.3 alle Interventionsteilnehmer erhielten Beratung, aber keiner aus Kontrollgruppe 1.6 Unklar, bis auf primäres Outcome (Verweildauer)	7. an Intervention beteiligte Ärzte und Apotheker hinterlegen Hinweis in Patientenakte wer zur Interventionsgruppe gehört und sind gleichzeitig auch für Kontrollgruppe zuständig

Criteria SIGN & EPOC	RCT			
REFERENCE Yes or No (notes, if necessary)	Farinas et al., 2012	Bouza et al., 2004	Bouza et al., 2007	Kerremans et al., 2008
1.1 The study addresses an appropriate and clearly focused question.	yes	yes	yes	yes
1.2 The assignment of subjects to treatment groups is randomised	yes	yes	yes	yes
1.3 An adequate concealment method is used.	no	unclear	yes	no
1.7 All relevant outcomes are measured in a standard, valid and reliable way.	unclear	unclear	unclear	unclear
1.6 The only difference between groups is the treatment under investigation.	yes	unclear	yes	yes
1.4 The design keeps subjects and investigators 'blind' about treatment allocation	no	no	no	no
5. Were incomplete outcome data adequately addressed?*	yes	unclear	yes	yes
7. Was the study adequately protected against contamination?	yes	no	yes	yes
8. Was the study free from selective outcome reporting?	unclear	unclear	unclear	yes
9. Was the study free from other risks of bias?	no	no	no	yes
1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	yes	unclear	yes	K: 14/ 738 I: 7/739; Patients not registered in a Dutch municipal population register
1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	yes	unclear	yes	yes
1.10 Where the study is carried out at more than one site, results are comparable for all sites.	n.a.	n.a.	n.a.	n.a.
2.1 How well was the study done to minimise bias?	(-)	(-)	(-)	(-)
2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?				
2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes
2.4 Notes	8. primäres Outcome (klinisches Versagen) nicht objektiv und komplex 9. unit of analysis error, keine Adjustierung für intracluster Korrelation	1.4 aufgrund des Studiendesigns nicht möglich 1.7 keine Angaben 9. nicht beachtet, Festlegung von 7 Kriterien, welche klinische Beurteilung erforderten, keine Reliabilitätsprüfung des primären Outcomes erfolgt	6. keine Verblindung 8. kein primäres Outcome wurde angegeben, DDD sind komplett berichtet, aber z.B. nicht %-Anteile adequater AB-Therapie 9. hohes Mibi-Bias-Risiko, keine Falldefinition, keine anderen Infektionspräventionsmaßnahmen untersucht	2. concealment war unmöglich 6. keine Verblindung

	nicht-randomisierte Interventionsstudie	Before-after-Study	Before-after-Study	controlled-before-after-study	before-after-study
Criteria SIGN & EPOC	**nicht-randomisierte Interventionsstudien (mit- und ohne Kontrollgruppe)** (blau markierte Fragen sind nicht zu beantworten)				
REFERENCE Yes or No (notes, if necessary)	Cosgrove et al., 2007	Forrest et al., 2008	Bauer et al., 2010	Landgren et al., 1988	Holtzman et al. 2011
1.1 The study addresses an appropriate and clearly focused question.	yes	yes	yes	yes	yes
1.2 The assignment of subjects to treatment groups is randomised	n.a.	n.a.	n.a.	n.a.	n.a.
1.3 An adequate concealment method is used.	n.a.	n.a.	n.a.	n.a.	n.a.
1.7 All relevant outcomes are measured in a standard, valid and reliable way.	yes	yes	yes	yes	yes
1.6 The only difference between groups is the treatment under investigation.	unclear	yes	yes	unclear	yes
1.4 The design keeps subjects and investigators 'blind' about treatment allocation	n.a.	n.a.	n.a.	n.a.	n.a.
5. Were incomplete outcome data adequately addressed?*	yes	yes	yes	unclear	yes
7. Was the study adequately protected against contamination?	unclear	unclear	unclear	yes	unclear
8. Was the study free from selective outcome reporting?	unclear	yes	yes	yes	unclear
9. Was the study free from other risks of bias?	unclear	yes	yes	yes	no
1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	n.a.	n.a.	n.a.	n.a.	n.a.
1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	n.a.	n.a.	n.a.	n.a.	n.a.
1.10 Where the study is carried out at more than one site, results are comparable for all sites.	n.a.	n.a.	n.a.	n.a.	n.a.
2.1 How well was the study done to minimise bias?	(-)	(+)	(++)	(-)	(-)
2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?					
2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes	yes	yes
2.4 Notes	1.6 keine Angaben zu Charakteristika der Ärzte oder Patienten 1.7 kein vorher veröffentlichtes Studienprotokoll 7. alle Kliniker des KHs waren in Intervention eingebunden 9. zwischen den beiden Interventionsphase lagen 24 Monate, unklar warum	1.7 kein vorher veröffentlichtes Studienprotokoll 7. alle Kliniker des KHs waren in Intervention eingebunden	1.7 kein vorher veröffentlichtes Studienprotokoll	1. Matching der KH unklar 2. nicht angwendet 4. nur KH-Charakteristika, keine Angaben zu Patienten (z.B. case-mix) 6. nicht festgelegt	1.4 mit design nicht möglich, da neuer PNA-FISH-Test für gesamtes KH angewendet wurde und Ergebnis in Patientenakte vermerkt 1.6 keine numerischen Angaben; aber Gefahr für Bias niedrig, da Patienten randomisiert aus dem Prä- und Postinterventionszeitraum retrospektiv ausgewählt wurden 7. unklar ob Patienten gleichzeitig im Prä- und Postzeitraum eingeschlossen oder ausgeschlossen wurden 8. Ergebnisse der Regression sind ungenau berichtet 9. evtl. nicht korrekte stat. Analyse, unklar wie genau die Daten erhoben wurden (evtl. doch Zeitreihenanalyse?)

SECTION	Criteria (EPOC and SIGN) REFERENCE Yes or No (notes, if necessary)	Huh et al., 2016	Elligsen et al., 2012	Hogli et al., 2016
EPOC	1. Was the intervention independent of other changes?	yes	yes	unclear
	If the interrupted time series study has ignored secular (trend) changes and performed a simple t-test of the pre versus post intervention periods without further justification, the study should not be included in the review unless reanalysis is possible. (yes=reanalysis is possible when needed)	yes	yes	yes
	2. Was the shape of the intervention effect pre-specified?	yes	yes	yes
	3. Was the intervention unlikely to affect data collection?	yes	yes	yes
	4. Was knowledge of the allocated interventions adequately prevented during the study?	no	no	no
	5. Were incomplete outcome data adequately addressed?	yes	yes	yes
	6. Was the study free from selective outcome reporting?	yes	yes	yes
	7. Was the study free from other risks of bias?	no	yes	yes
SIGN (OVERALL ASSESSMENT OF THE STUDY)	2.1 How well was the study done to minimise bias?	(+)	(+)	(-)
	2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes
	Notes	4. Intervention für alle gültig, keine Verblindnung (keine Kontrollgruppe) 7. Saisonalität möglich	4. Intervention war offen für alle Teilnehmer und Ärzte, concealment nicht möglich	1. laut Angaben der Authoren nicht auszuschließen ohne Kontrollgruppe 4. Intervention war bekannt, da Schulung erfolgte, unklar wer die Datenerfassung übernommen hat, wahrscheinlich nicht blind nur ein KH(geringe ext. Validität)

Criteria (EPOC and SIGN) REFERENCE Yes or No (notes, if necessary)	Campbell et al., 2017	Tamma et al., 2017	Nault et al., 2017
1. Was the intervention independent of other changes?	no	no	yes
If the interrupted time series study has ignored secular (trend) changes and performed a simple t-test of the pre versus post intervention periods without further justification, the study should not be included in the review unless reanalysis is possible. (yes=reanalysis is possible when needed)	yes	yes	yes
2. Was the shape of the intervention effect pre-specified?	yes	yes	yes
3. Was the intervention unlikely to affect data collection?	no	yes	yes
4. Was knowledge of the allocated interventions adequately prevented during the study?	unclear	no	no
5. Were incomplete outcome data adequately addressed?	yes	yes	yes
6. Was the study free from selective outcome reporting?	yes	yes	yes
7. Was the study free from other risks of bias?	no	no	yes
2.1 How well was the study done to minimise bias?	(-)	(-)	(+)
2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes
Notes	1. nicht abschätzbar da Intervention zu unterschiedlichen Zeitpunkten in den Abteilungen eingeführt wurde 3. unterschiedliche Erhebung des primären Outcomes (zuerst Papierkurve, dann elektronisches System der Apotheke), sekundäres Outcome (AB-Ausgaben) gleich in Prä-als auch Postphase erhoben 7. keine Berücksichtigung für Saisonalität nur ein KH (geringe ext. Validität)	1. unklar, ob die Interventionen sich nicht gegenseitig beeinflussen; vor Studienbeginn war PPA bereits im gesamten KH etabliert, Authoren schreiben selbst, dass sich Personal Wissen durch die 1. Interventionsphase angeeignet hat 4 concealment nicht möglich, da Intervention für alle Patienten der Abteilungen offen war, Hawthorne-Efffekt (auch von Authoren angemerkt), soll durch Vergleich mit Daten aus selben Zeitraum des Vorjahres verglichen werden (Ergebnisse nicht aufgeführt) 5. unwahrscheinlich, da aus gleicher Quelle (standardisiert in elektronischer Patientenakte) 7. keine Adjustierung für Saisonalität, nur ein KH (geringe ext. Validität)	1. ja, weil beide Interventionen in einem ähnlichen Zeitfenster jeweils August bis Juli für 2 Jahre 4. nicht möglich, da Intervention im gesamten KH eingeführt wurde

Criteria (EPOC and SIGN) REFERENCE Yes or No (notes, if necessary)	Tavares et al., 2018	Molina et al., 2017	Fleming et., 2016
1. Was the intervention independent of other changes?	yes	yes	yes
If the interrupted time series study has ignored secular (trend) changes and performed a simple t-test of the pre versus post intervention periods without further justification, the study should not be included in the review unless reanalysis is possible. (yes=reanalysis is possible when needed)	yes	yes	yes
2. Was the shape of the intervention effect pre-specified?	yes	yes	yes
3. Was the intervention unlikely to affect data collection?	yes	unclear	yes
4. Was knowledge of the allocated interventions adequately prevented during the study?	no	no	no
5. Were incomplete outcome data adequately addressed?	yes	unclear	yes
6. Was the study free from selective outcome reporting?	no	unclear	yes
7. Was the study free from other risks of bias?	no	no	no
2.1 How well was the study done to minimise bias?	(-)	(-)	(-)
2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?	yes	yes	yes
Notes	1.Kontrollgruppe vorhanden 3. Datenerfassung retrospektiv aus Akte oder in-house analysis software HVITAL 4. Empfehlungen wurden in die elektronische Patientenakte eingetragen 5. unwahrscheinlich, da alle Daten aus standardisierten elektronischen Quellen 6. Mortaliät und KH-Wiederaufnahme wird im Ergebnisteil berichtet, aber nicht im Methodenteil 7. keine Saisonalität, non-stationary beachtet, Angabe zum ITS-Modell fehlt im Methodenteil	3. keine Angaben zu Datenquellen nur Definitionen der Outcomes 4. durch Intervention nicht mgl. 7. keine Angaben zu Kontrolle/Adjustierung von Saisonalität, Autokorrelation und Non-Stationarity, keine Angabe zu den im Modell verwendeten Variablen	4. Ärzte routierten zwischen den ITSn 7. keine geeignete stat. Analyse, außerdem keine Berücksichtigung der Saisonalität