Online supplementary text S3. Quality assessment of studies that informed the level of evidence in the 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis

Critical appraisal of a meta-analysis

The revised instrument of A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2) was used for a critical appraisal of the methodology of one meta-analysis that determined the level of evidence for the updated recommendations #2, #4, #6 and #8.[1-3]

The 16-item questionnaire is designed to elicit responses of 'Yes', 'Partial Yes', 'No' with seven of the 16 domains regarded as potential critical in relation to the validity of a review: Item 2 (a priori protocol registration), item 4 (adequacy of the literature search), item 7 (justification for excluding individual studies), item 9 (risk of bias from individual studies included), item 11 (appropriateness of meta-analytical methods), item 13 (consideration of risk of bias when interpreting the results of the review) and item 15 (assessment of presence and likely impact of publication bias).[1]

Item by item results for AMSTAR 2 assessment of the meta-analysis by de Thurah et al 2017 are shown in Table 1. The overall confidence in the quality of the meta-analysis was considered as moderate. This decision is in accordance with items in the AMSTAR 2 check-list, which revealed three non-critical weaknesses related to #7 ('partiel yes', because of individual reasons for exclusion, in the list of the excluded studies, are missing), #10 ('No', because the source of funding for the individual included studies are missing) and #15 ('No', because graphical or statistical tests for publication bias are missing). The weaknesses were considered without critical flaw, as it was regarded that the weakness did not have potential impact of an accurate summary of the results of the available studies included in the review.

Bech B, *et al. Ann Rheum Dis* 2019; 79:61–68. doi: 10.1136/annrheumdis-2019-215458

S3 Table 1. Item by item results using the revised instrument of A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2) for critical appraisal of the meta-analysis by de Thurah et al. 2017

AMSTAR 2		YES	Partial YES	NO
Item nr.	QUESTION			
1.	Were components of PICO included in research question and inclusion criteria?	X		
2.	Was an 'a priori' design provided?	X		
3.	Was selection of included study designs explained?	X		
4.	Was a comprehensive literature search performed?	X		
5.	Was there duplicate study selection?	X		
6.	Was there duplicate data extraction?	X		
7.	Was a list of excluded studies provided inclusive justification of the exclusion?		X	
8.	Was included studies described in adequate detail?	X		
9.	Was satisfactory technique used for assessing risk of bias in individual studies?	X		
10.	Was source of funding for included studies reported?			X
11.	Were appropriate methods used for statistical combination of results?	X		
12.	Was the potential impact of risk of bias in individual studies on the results of the meta-analysis assessed?	X		
13.	Was risk of bias in individual studies accounted for when interpreting results?	X		
14.	Was a satisfactory explanation for, and discussion of, any heterogeneity observed being provided?	X		
15.	Was adequate investigation of publication bias performed and likely impact on results discussed?			X
16.	Were potential sources of conflict of interest (including funding received) reported?	X		

PICO: Population, Intervention, Comparator group and Outcome

Quality assessment of Randomized Controlled Trials (RCTs)

The Cochrane Risk of Bias tool was applied of the included primary studies of RCTs.[4-15] The individual domains selection, performance, detection, attrition, reporting and other sources of biases were assessed for each outcome referred in the update as displayed in Figure 1.

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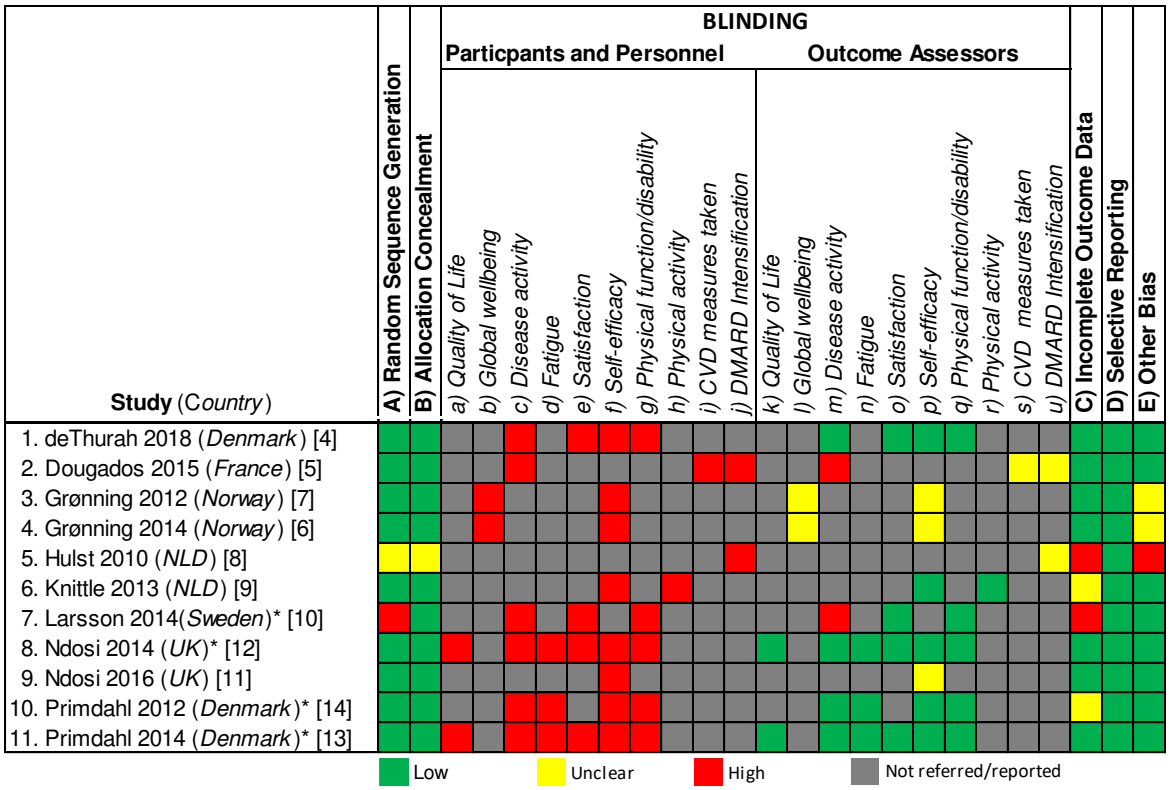
S3 Figure 1. Risk of bias of the included RCTs for each outcome referred to in the 2018 update



Abbreviations: UK: United Kingdom, NLD: The Netherlands. DMARD: Disease Modifying Anti-Rheumatic Drugs, CVD: Cardiovascular disease. Randomized Controlled Trials included in the update: [4-14]. Risk of Bias (RoB), assessed according to the Cochrane Risk of Bias tool.[15]
*Risk of bias was assessed recently in a meta-analysis by De Thurah et al. and was not repeated for this study based on an overall confidence in the quality of the meta-analysis considered as moderate.[3]

Explanatory notes on unclear or high risk of bias for each RCT (by study number in the table above)
The letter A represents random sequence generation, B represents allocation concealment and additional small letters, a through u, represent the different outcomes for each of the RCTs (labled 1-11), which are referred to for an enhanced level of evidence in the updated recommendations. C, D, E represent incomplete outcome data, selective reporting and other bias respectively.

1-11).a-j, m: Due to the nature of the studies, blinding of participants and personnel was not possible. Accordingly, all recieved a high risk of bias for the domain 'Blinding of participants and personnel'. However, attempts to minimize risk of bias for disease activity as an outcome was described in four out of six studies.

2).m: DAS28 at baseline and 6 month follow-up was collected by the nurse who also delivered the intervention. s, t: Does not provide the reader with any details of outcome assessment other than at

baseline (collected after allocation). Apparently, no one was blinded as allocation was entered into the medical file.

3).l, p: The investigator, not blinded to the allocation and who also performed DAS28 assessment, was present when participants responded to baseline questionnaires. Unclear if this could have affected the patients self-reported outcomes. E: Multiple outcomes assessed.

4).l, p, E: Identical comments as to paper 3).

5).A, B: No information about the randomisation process as there was no further elaboration regarding 'the rheumatologists were randomised and stratified by years of experience'. Difference appeared in the number of participants the rheumatologists recruited. u: Only few rheumatologists were randomised (n=7, not blinded to allocation), personal style may have influenced the outcome. C: Decision to change medication likely to be influenced not only by the availability of DAS28 information, but also by many other factors. E: Single centre (pilot)study.

6).C: Likely used appropriate statistical methods, but unknown amount of missing data.

9).p: Potential risk of performance bias (and carry over effect) by the intervention providers (same nurse provided the intervention for the control group and the intervention group). In addition unclear how questionnaires were administered/who collected the data. Likewise for the attempts made to collect missing data by phone.

Quality assessment of observational studies

The risk of bias in two observational studies [16-18], that determined the level of evidence in recommendation #7, was assessed with the QUality In Prognosis Studies tool (QUIPS).[19] The QUIPS evaluates six different areas for potential bias: participation, attrition, prognostic factor measurement, confounding measurement and account, outcome measurement, and analysis. Each area is subdivided in several subdomains, to be rated with 'yes': well described, 'partial': partially described or 'no': not described. Results from the QUIPS evaluation are presented in Table 2.

S3 Table 2. Risk of bias in two observational studies that determined the level of evidence in recommendation #7 in the 2018 update

	Included studies	
	Linker 2011[16], 2012[17]	Cheung 2014[18]
Areas for risk of bias		
1. Study Participation (representative sample)		
Summary	yes	partial
2. Study Attrition (representative sample in follow-up)		
Summary	no	partial

3. Prognostic Factor Measurement		
Summary	partial	yes
4. Outcome Measurement		
Summary	yes	yes
5. Study Confounding		
Summary	no	partial
6. Statistical Analysis and Reporting		
Summary	yes	yes

Rating of subdomains in the risk of bias assessment: 'yes': well described, 'partial': partially described or 'no': not described. The scores represent the lowest score of two reviewers if difference in the independent scoring.

Explanatory notes:
Lineker et al.[16, 17]: Issues for risk of bias: study attrition (almost 50 %, no reasons described), and outcome measurement (measurement of the training, same training and method used, but in different settings, participants were registered by organization).

Cheung et al.[18]: Issues for risk of bias: Study sample (small), however representative, and study attrition (reasons for attrition bias was not described, but also not expected to be relevant).

Quality assessment economic evaluations

Four economic evaluation studies,[12, 20-22] performed alongside clinical trials on the effectiveness of nurse-led care,[5, 10, 12-14] prompted amendment of the additional wording 'this leads to cost-effective care' to recommendation #4.
Methodological quality of the four economic evaluations was assessed using the Consensus on Health Economic Criteria (CHEC) list.[23] The CHEC consists of 19-items comprising specific criteria that have reached consensus as a generic core set of items for the quality assessment of economic evaluations. Each of the 19 items can be scored 'yes': clearly described, or 'no': not described. For this assessment, we scored items 'yes' if the description was in the manuscript.

S3 Table 3. Quality assessment of the included studies regarding economic evaluations

		Included studies							
		Sørensen 2015[22]		Ndosi 2014[12]		Larsson 2015[20]		Mourgues 2017[21]	
	Items in the CHEC-list	yes	no	yes	no	yes	no	yes	no
1.	Is the study population clearly described?	x		x		x		x	
2.	Are competing alternatives clearly described?	x		x		x			x
3.	Is a well-defined research question posed in answerable form?	x		x		x		x	

4.	Is the economic study design appropriate to the stated objective?	x		x		x		x	
5.	Is the chosen time horizon appropriate in order to include relevant costs and consequences?	x		x		x		x	
6.	Is the actual perspective chosen appropriate?	x		x			x		x
7.	Are all important and relevant costs for each alternative identified?	x		x		x			na
8.	Are all costs measured appropriately in physical units?	x		x		x		x	
9.	Are costs valued appropriately?	x		x		x		x	
10.	Are all important and relevant outcomes for each alternative identified?	x		x		x			na
11.	Are all outcomes measured appropriately?	x		x		x		x	
12.	Are outcomes valued appropriately?	x		x		x		x	
13.	Is an incremental analysis of costs and outcomes of alternatives performed?	x		x			na		na
14.	Are all future costs and outcomes discounted appropriately?	x			x		x		x
15.	Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?		x		x		x		x
16.	Do the conclusions follow from the data reported?	x		x		x		x	
17.	Does the study discuss the generalizability of the results to other settings and patient/client groups?		x	x		x			x
18.	Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	x		x		x		x	
19.	Are ethical and distributional issues discussed appropriately?	x			x	x			x

CHEC: Consensus on Health Economic Criteria, na: not applicable

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