NKR 40: PICO 8 *Bør patienter med nyopståede lænderygsmerter tilbydes paracetamol i tillæg til vanlig behandling*?

Review information

Authors

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Citation example: [Empty name]. NKR 40: PICO 8 *Bør patienter med nyopståede lænderygsmerter tilbydes paracetamol i tillæg til vanlig behandling*? Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Abstract

Background

Objectives

Search methods

Selection criteria

Data collection and analysis

Main results

Authors' conclusions

Characteristics of studies

Characteristics of included studies

Bacon 2002

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** Paracetamol (regular= sustained release - SR) paracetamol (immediate release - SR) **Included criteria:** OA ofthe knee, and experienced mild to moderate pain suitablefor treatment with a simple analgesic. This diagnosis wasconfirmed by X-ray (antero-posterior view of the knee)prior to entry into the study. Patients were required toexperience pain from OA of the knee on at least half ofthe days in the 3 months prior to the screening visit atthe start of the study. The pain was to be exacerbated bymovement or weight-bearing **Excluded criteria:** received intra-articular corticosteroids within14 days prior to screening, or if systemic steroids, NSAIDsor other analgesics were required for any medicalcondition. **Pretreatment:** Demographic characteristics were comparablebetween groups in the intention to treat population(Table 1) as was also the case for the per protocolpopulation (results not shown)
Interventions	**Intervention Characteristics** Paracetamol (regular= sustained release - SR) ● *SR paracetamol (2r665 mg tablets, three times daily), 7 days*: ● *IR paracetamol (2r500 mg tablets, four times daily) for 7 days*:

	● *placebo tablets in the regular box and 500 mg paracetamol immediate-release tablets in the as-needed box.*: ● *placebo tablets in both boxes*: ● *The treating clinician provided eligible patients with guideline recommended advice3 to remain active and avoid bed rest, and reassurance of the favourable prognosis of acute low-back pain*: paracetamol (immediate release - SR) ● *SR paracetamol (2r665 mg tablets, three times daily), 7 days*: ● *IR paracetamol (2r500 mg tablets, four times daily) for 7 days*: ● *placebo tablets in the regular box and 500 mg paracetamol immediate-release tablets in the as-needed box.*: ● *placebo tablets in both boxes*: ● *The treating clinician provided eligible patients with guideline recommended advice3 to remain active and avoid bed rest, and reassurance of the favourable prognosis of acute low-back pain*:
Outcomes	*Serious Adverse event* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** We thank all the investigators* and also Carolyn Adnitt and AnneDarby-Dowman from GlaxoSmithKline for their contribution tothis study. **Country:** UK **Setting:** Primary care **Comments:** **Authors name:** T. H. Bacon,1 J. G. Hole,2 M. North1 & I. Burnett1 **Institution:** GlaxoSmithKline, St George's Avenue, Weybridge, Surrey KT13 0DE, UK, 2Adcroft Surgery, Prospect Place, Trowbridge, Wiltshire BA14 8QA, UK, and also on behalf of Profiad Ltd, Reading, Berkshire RG1 1NY, UK **Email:** teresa.h.bacon@gsk.com **Address:** GlaxoSmithKline, St George's Avenue,Weybridge, Surrey KT13 0DE, UK
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Sequence Generation	Unclear risk	
Allocation concealment	Unclear risk	
Blinding of participants and personnel	Unclear risk	
Blinding of outcome assessors	High risk	
Incomplete outcome data	Low risk	
Selective outcome reporting	Low risk	
Other sources of bias	Unclear risk	

Bradley 1991

Methods	**Study design:** **Study grouping:** **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** Paracetamol 4000 mg/day Ibuprofen 1200 mg/day Ibuprofen 2400 mg/day **Included criteria:** **Excluded criteria:** **Pretreatment:**
Interventions	**Intervention Characteristics** Paracetamol 4000 mg/day Ibuprofen 1200 mg/day Ibuprofen 2400 mg/day

Outcomes	*Frafald, bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Range**: 0-1 ● **Direction**: Lower is better ● **Data value**: Change from baseline
Identification	**Sponsorship source:** Supported by grant from the National Institute of arthritis and musculoskeletal and skin disorders **Country:** USA **Setting:** general practice, rheumatology and orthopedic surgery dept. at Indiana School of medicine and surrounding community **Comments:** **Authors name:** Bradley, Brandt, Katz et al. **Institution:** Rheumatology department, Indiana School of medicine, Indiana, USA **Email:** not reported **Address:**
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Sequence Generation	Low risk	
Allocation concealment	High risk	
Blinding of participants and personnel	Low risk	
Blinding of outcome assessors	Low risk	
Incomplete outcome data	Low risk	
Selective outcome reporting	Low risk	
Other sources of bias	Unclear risk	

Pincus 2001

Methods	**Study design:** Randomized controlled trial **Study grouping:** Crossover **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** All exposed to Acetaminophen All exposed to Diclophenac+misoprostol **Included criteria:** Patients with osteoarthritis ofthe hip or knee.The major inclusion criteria were age .40 years,Kellgren/Lawrence radiographic grade 2–4 osteoarthritis ofthe hip or knee (16), and a visual analog pain scale (17–19)score of $30 mm (range 0–100 mm). **Excluded criteria:** Exclusion criteria wererestricted to severe comorbidities and hypersensitivity to acetaminophen,diclofenac, or misoprostol. **Pretreatment:** II. Patientswho were randomized to group I or group II weresimilar in demographic measures of age, sex, maritalstatus, and formal education level; in osteoarthritismeasures of radiographic grade, severity of joint spacenarrowing and osteophytes, and mean global severity ofosteoarthritis at the time of screening; and (other thanfor SF-36 bodily pain, which is likely explained bymultiple comparisons) in measures to assess clinicalstatus from the WOMAC, MDHAQ, and SF-36 questionnairesat screening (
Interventions	**Intervention Characteristics** All exposed to Acetaminophen ● *75 mg diclofenac 1 200 mg misoprostol (to be taken twice daily) and acetaminophen placebo (2 pills to be taken 4 times daily) for 45 days*: ● *500-mg acetaminophen tablets (2 pills to be taken 4 times daily) and diclofenac 1 misoprostol placebo (to be taken twice daily) for 45 days*: x All exposed to Diclophenac+misoprostol ● *75 mg diclofenac 1 200 mg misoprostol (to be taken twice daily) and acetaminophen placebo (2 pills to be taken 4 times daily) for 45 days*: x ● *500-mg acetaminophen tablets (2 pills to be taken 4 times daily) and diclofenac 1 misoprostol placebo (to be taken twice daily) for 45 days*:

Outcomes	*Serious Adverse event* ● **Outcome type**: DichotomousOutcome *Frafald, bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Scale**: nej/ja ● **Range**: 0-1 ● **Unit of measure**: none ● **Direction**: Lower is better ● **Data value**: Change from baseline ● **Notes**: All exposed to acetaminophen is now group 1, which got acetaminophen i period 1 (6 weeks)All exposed to diclophenac is now group 2, which got diclophenac i period 1
Identification	**Sponsorship source:** The sponsor provided funds anddrugs, labeled the randomized drug, and had the only copy ofthe randomization code. The study was reviewed and approvedby the Food and Drug Administration and was approved by theInstitutional Review Board for the Protection of HumanSubjects at Vanderbilt University and by the other 11 individ-ual study sites **Country:** USA **Setting:** not reported **Comments:** **Authors name:** T. Pincus,1G. G. Koch,2T. Sokka, et al. **Institution:** Division of Rheumatology and Immunology, Vanderbilt Univer-sity School of Medicine, USA **Email:** not reported **Address:** . Pincus,MD, Division of Rheumatology and Immunology, Vanderbilt Univer-sity School of Medicine, 203 Oxford House, Box 5, Nashville, TN37232-450; USA
Notes	*Fagkonsulent Nkr40* on 06/02/2016 05:41 **Outcomes** NB - i serious adverse events er alle der har fået Acetaminophen (dvs. event i gr. 1 og 2 kombineret)I frafald, er det kun de første 6 uger svarende til 1. periode, der af rapporteret

Risk of bias table

Bias	Authors' judgement	Support for judgement
Sequence Generation	Low risk	
Allocation concealment	Unclear risk	Quote: "patients was concealed from personnel at the study sites and data center."
Blinding of participants and personnel	Low risk	Quote: "double-blind," Judgement Comment: No specification of how double-blinding was achieved
Blinding of outcome assessors	Unclear risk	Judgement Comment: not reported
Incomplete outcome data	Unclear risk	Judgement Comment: Correction - follow rates are provided in figure - however, high droop out rate
Selective outcome reporting	Low risk	Quote: "The study was reviewed and approved by the Food and Drug Administration and was approved by the Institutional Review Board for the Protection of Human Subjects at Vanderbilt University and by the other 11 individ- ual study sites." Judgement Comment: no protocol available, but unlikely
Other sources of bias	Unclear risk	Judgement Comment: General lack of reporting of methodology

Williams 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** Paracetamol (regular group) paracetamol (as-needed) Placebo **Included criteria:** a new episode of acute low-backpain (defi ned as pain between the 12th rib and buttockcrease that was shorter than 6 weeks' duration andpreceded by 1 month of no pain) with or without leg pain,and at least moderate-intensity pain (measured by anadaptation of item 7 of the Short Form [36] HealthSurvey **Excluded criteria:** Exclusion criteria were suspected serious spinalpathology (eg, spinal cancer, infection, fracture);

	currentuse of full, regular recommended doses of an analgesic;spinal surgery in the preceding 6 months; contraindicationto paracetamol; use of psychotropic drugs for a disorderjudged to prevent reliable recording of study information;or pregnant or planning pregnancy. **Pretreatment:** similar across groups
Interventions	**Intervention Characteristics** Paracetamol (regular group) ● *Two types of tablets for up to 4 weeks: 2 tablets from the regular box every 6–8 h (6 tablets/day), and 1 or two tablets from the as-needed box when needed for pain relief (4–6 h apart, to a maximum of 8 tablets/day).*: x ● *665 mg modified-release paracetamol tablets in the regular box and placebo tablets in the as-needed box*: x ● *placebo tablets in the regular box and 500 mg paracetamol immediate-release tablets in the as-needed box.*: ● *placebo tablets in both boxes*: ● *The treating clinician provided eligible patients with guideline recommended advice3 to remain active and avoid bed rest, and reassurance of the favourable prognosis of acute low-back pain*: x paracetamol (as-needed) ● *Two types of tablets for up to 4 weeks: 2 tablets from the regular box every 6–8 h (6 tablets/day), and 1 or two tablets from the as-needed box when needed for pain relief (4–6 h apart, to a maximum of 8 tablets/day).*: x ● *665 mg modified-release paracetamol tablets in the regular box and placebo tablets in the as-needed box*: ● *placebo tablets in the regular box and 500 mg paracetamol immediate-release tablets in the as-needed box.*: x ● *placebo tablets in both boxes*: ● *The treating clinician provided eligible patients with guideline recommended advice3 to remain active and avoid bed rest, and reassurance of the favourable prognosis of acute low-back pain*: x Placebo ● *Two types of tablets for up to 4 weeks: 2 tablets from the regular box every 6–8 h (6 tablets/day), and 1 or two tablets from the as-needed box when needed for pain relief (4–6 h apart, to a maximum of 8 tablets/day).*: x ● *665 mg modified-release paracetamol tablets in the regular box and placebo tablets in the as-needed box*: ● *placebo tablets in the regular box and 500 mg paracetamol immediate-release tablets in the as-needed box.*: ● *placebo tablets in both boxes*: x ● *The treating clinician provided eligible patients with guideline recommended advice3 to remain active and avoid bed rest, and reassurance of the favourable prognosis of acute low-back pain*: x

Outcomes	*pain* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: NRS ● **Range**: 0-10 ● **Unit of measure**: none ● **Direction**: Lower is better ● **Data value**: Endpoint *Disability* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: Roland Morris ● **Range**: 0-24 ● **Unit of measure**: none ● **Direction**: Lower is better ● **Data value**: Endpoint *Serious Adverse event* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Scale**: ja/no ● **Range**: 0-1 ● **Unit of measure**: none ● **Direction**: Lower is better ● **Data value**: Change from baseline *Frafald, generelt* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Scale**: frafald ja/nej ● **Range**: 0-1 ● **Unit of measure**: none ● **Direction**: Lower is better

	● **Data value**: Endpoint
Identification	**Sponsorship source:** AJM has received funding for a postgraduate research scholarshipfrom GlaxoSmithKline. CGM has received funding to review teachingmaterials prepared by GlaxoSmithKline. The other authors declare nocompeting interests. **Country:** Australia **Setting:** primary care **Comments:** **Authors name:** Christopher M Williams, Christopher G Maher, Jane Latimer, Andrew J McLachlan, Mark J Hancock, Richard O Day, Chung-Wei Christine Lin **Institution:** The George Institute for Global Health, Sydney Medical School, University of Sydney, Camperdown, NSW, Australia **Email:** cwilliams@georgeinstitute. org.au **Address:** Hunter Medical ResearchInstitute, Longworth Avenue,Wallsend, NSW 2287, Australia
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Sequence Generation	Low risk	Judgement Comment: RoB fra Machado (2015) SR
Allocation concealment	Low risk	
Blinding of participants and personnel	Low risk	
Blinding of outcome assessors	Low risk	
Incomplete outcome data	Low risk	
Selective outcome reporting	Low risk	
Other sources of bias	Low risk	

Footnotes

References to studies

Included studies

Bacon 2002

Bacon, T. H.; Hole, J. G.; North, M.; Burnett, I.. Analgesic efficacy of sustained release paracetamol in patients with osteoarthritis of the knee. British Journal of Clinical Pharmacology 2002;53:629-636. [DOI: 10.1046/j.1365-2125.2002.01603.x]

Bradley 1991

Bradley,J. D.; Brandt,K. D.; Katz,B. P.; Kalasinski,L. A.; Ryan,S. I.. Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. The New England journal of medicine 1991;325(2):87-91. [DOI: 10.1056/NEJM199107113250203 [doi]]

Pincus 2001

Pincus,T.; Koch,G. G.; Sokka,T.; Lefkowith,J.; Wolfe,F.; Jordan,J. M.; Luta,G.; Callahan,L. F.; Wang,X.; Schwartz,T.; Abramson,S. B.; Caldwell,J. R.; Harrell,R. A.; Kremer,J. M.; Lautzenheiser,R. L.; Markenson,J. A.; Schnitzer,T. J.; Weaver,A.; Cummins,P.; Wilson,A.; Morant,S.; Fort,J.. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. Arthritis and Rheumatism 2001;44(7):1587-1598. [DOI: 10.1002/1529-0131(200107)44:7<1587::AID-ART282>3.0.CO;2-X [doi]]

Williams 2014

Williams CM.; Maher CG.; Latimer J.; McLachlan AJ.; Hancock MJ.; Day RO.; Lin CW.. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial.. Lancet 2014;384(9954):1586-96. [DOI: 10.1016/S0140-6736(14)60805-9]

Data and analyses

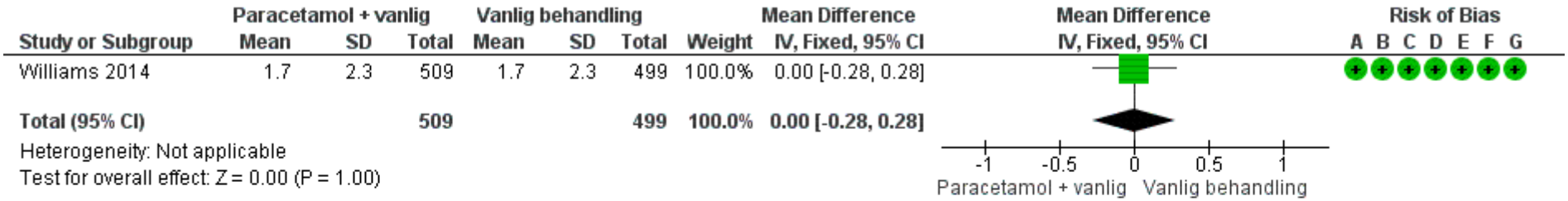
1 Paracetamol i tillæg til vanlig behandling vs vanlig behandling

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Smerteniveau 0-12 uger	1	1008	Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.28, 0.28]

1.2 Funktionsniveau 0-12 uger	1	1001	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.74, 0.54]
1.3 Alvorlige Bivirkninger 0-12 uger	1	1097	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.29, 3.42]
1.4 Livskvalitet 6-18 måneder	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.5 Recidiv af smerter 6-18 måneder	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
1.6 Sygefravær - antal sygedage 6-18 måneder	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.7 Sygefravær - tid tilbage-til-arbejde 6-18 måneder	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.8 Sygefravær - proportion i arbejde 6-18 måneder	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.9 Frafald - generelt EOT	1	1103	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [0.25, 8.99]
1.10 Frafald - på grund af bivirkninger EOT	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable

Figures

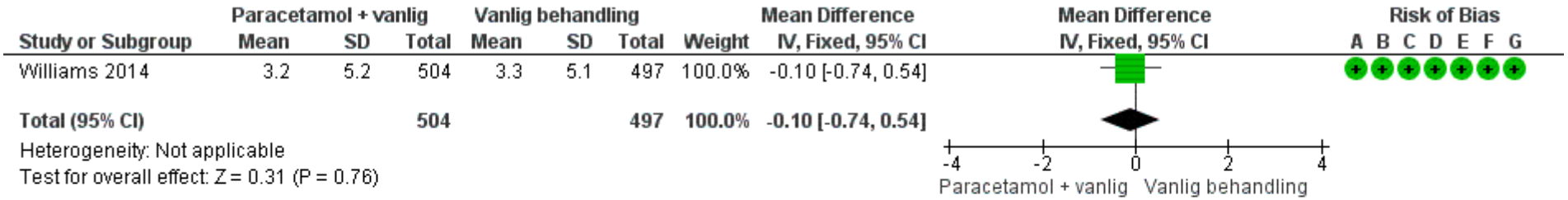
Figure 1 (Analysis 1.1)



Risk of bias legend
(A) Sequence Generation
(B) Allocation concealment
(C) Blinding of participants and personnel
(D) Blinding of outcome assessors
(E) Incomplete outcome data
(F) Selective outcome reporting
(G) Other sources of bias

Forest plot of comparison: 1 Paracetamol i tillæg til vanlig behandling vs vanlig behandling, outcome: 1.1 Smerteniveau 0-12 uger.

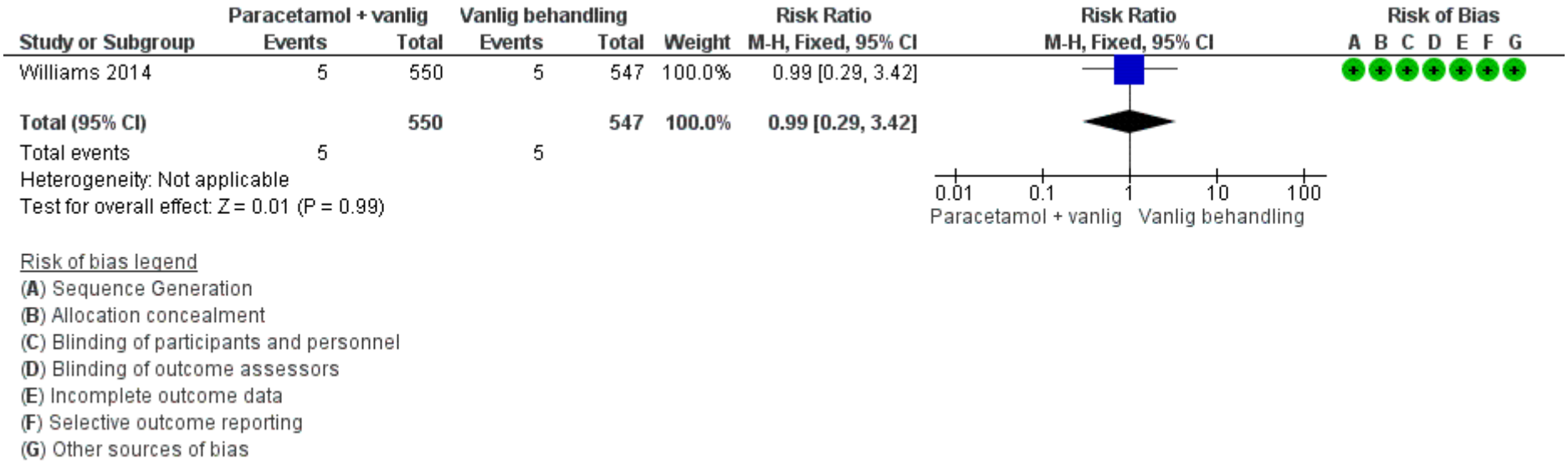
Figure 2 (Analysis 1.2)



Risk of bias legend
(A) Sequence Generation
(B) Allocation concealment
(C) Blinding of participants and personnel
(D) Blinding of outcome assessors
(E) Incomplete outcome data
(F) Selective outcome reporting
(G) Other sources of bias

Forest plot of comparison: 1 Paracetamol i tillæg til vanlig behandling vs vanlig behandling, outcome: 1.2 Funktionsniveau 0-12 uger.

Figure 3 (Analysis 1.3)

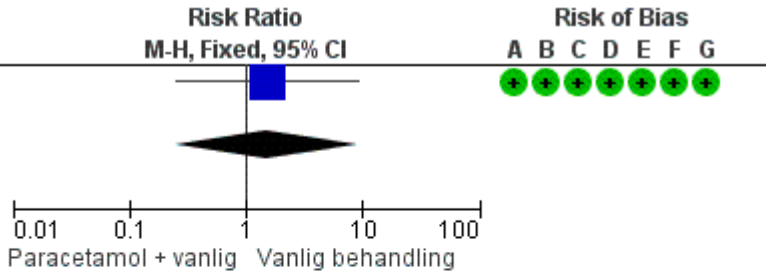


Forest plot of comparison: 1 Paracetamol i tillæg til vanlig behandling vs vanlig behandling, outcome: 1.3 Alvorlige Bivirkninger 0-12 uger.

Figure 4 (Analysis 1.9)

Study or Subgroup	Paracetamol + vanlig Events	Total	Vanlig behandling Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Williams 2014	3	550	2	553	100.0%	1.51 [0.25, 8.99]
Total (95% CI)		**550**		**553**	**100.0%**	**1.51 [0.25, 8.99]**
Total events	3		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.45 (P = 0.65)



Risk of bias legend
(**A**) Sequence Generation
(**B**) Allocation concealment
(**C**) Blinding of participants and personnel
(**D**) Blinding of outcome assessors
(**E**) Incomplete outcome data
(**F**) Selective outcome reporting
(**G**) Other sources of bias

Forest plot of comparison: 1 Paracetamol i tillæg til vanlig behandling vs vanlig behandling, outcome: 1.9 Frafald - generelt EOT.