NKR 33 Urininkontinens, PICO 9: Bør postmenopausale kvinder med urgency urininkontinens behandles med vaginal østrogentilskud som add-on til antimuskarinergika/beta-3 agonist?

Review information

Authors

Sundhedsstyrelsen [1,a]

[1] [Empty affiliation]

[a] The Danish Health and Medicines Authority, Denmark

Citation example: S. NKR 33 Urininkontinens, PICO 9: Bør postmenopausale kvinder med urgency urininkontinens behandles med vaginal østrogentilskud som add-on til antimuskarinergika/beta-3 agonist? Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Serati 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** Intervention ● *Age*: 61 (40-81) ● *BMI*: 26 (19-37) ● *DO following provocative manoeuvres* : 18/100 ● *No of partcicpants*: 100

	Control ● *Age*: 61 (40-81) ● *BMI*: 26 (19-37) ● *DO following provocative manoeuvres* : 18/100 ● *No of partcicpants*: 100 **Included criteria:** All postmenopausal women referred to the urogynaecologyunit of King's College Hospital (London, UK) from January 2004to September 2007 for symptoms of OAB and urodynamicallyproven pure DO (ie, without concomitant urodynamic stressincontinence) were included in this prospective study. **Excluded criteria:** We excluded women with documented recurrent urinary tractinfections, previous antimuscarinic treatment, previous pelvicsurgery, concomitant systemic hormone replacement therapy(HRT), history of breast cancer or endometrial cancer,neurological disease, clinical contraindications to treatmentwith oestrogen or antimuscarinics, and patients included inother ongoing clinical trials during the same study period.
Interventions	**Intervention Characteristics** Intervention ● *Treatment*: tolterodine ER 4 mg and concomitant oestriol cream application once daily to be taken at night for at least 12 wk ● *Duration of treatment*: 12 wk ● *Follow-up*: End of treatment (12 wk) Control ● *Treatment*: tolterodine ER 4 mg once daily to be taken at night for atleast 12 wk ● *Duration of treatment*: 12 wk ● *Follow-up*: End of treatment (12 wk)
Outcomes	*Patientoplevet effekt (patientreported effect) - End of treatment* ● **Outcome type**: DichotomousOutcome ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Data value**: Endpoint ● **Notes**: Cured+improved

Identification	**Sponsorship source:** None **Country:** England **Setting:** Urogynaecology unit of King´s College Hospital **Comments:** **Authors name:** Serati M **Institution:** Department of Urogynaecology, King´s College Hospital, University of London **Email:** **Address:**
Notes	*Herdis Bohn Olesen BrøDbæK* on 24/08/2015 05:12 **Continuous Outcomes** jeg kan kun finde odsratios *Herdis Bohn Olesen BrøDbæK* on 24/08/2015 05:12 **Dichotomous Outcomes** der er ikke angivet patientoplevet effekt *Herdis Bohn Olesen BrøDbæK* on 24/08/2015 05:12 **Adverse Outcomes** der er ikke angivet bivirkninger *Herdis Bohn Olesen BrøDbæK* on 24/08/2015 05:13 **Pretreatment** Characteristic Group 1 (tolterodine)(n= 129)Group 2 (tolterodine + localoestrogens) (n= 100)pvalueAge (yr) 61 (42–85) 61 (40–81) 0.19aParity 2 (0–5) 2 (0–9) 0.08cBody mass index 26.5 (20–41) 26 (19–37) 0.34aDelivery of a foetus>4000 g 32/129 (24.8%) 33/100 (33%) 0.19bVacuum delivery 18/129 (14%) 19/100 (19%) 0.36bDO following provocative manoeuvres 24/129 (18.6%) 18/100 (18%) 1.00bGenital prolapse2 30/129 (23.2%) 28/100 (28%) 0.23bCoital urinary incontinence at orgasm 4 (3.1%) 2(2%) 0.69bAbbreviation: DO, detrusor overactivity.aStudentttest.bFisher exact test.cMann-WhitneyUtest

Risk of bias table

Bias	Authors' judgement	Support for judgement
Other sources of bias	Low risk	
Selective outcome reporting	Low risk	
Blinding of outcome assessors	High risk	Judgement Comment: Deltageren angiver til en blindet personale ved end-of-treatment om patientoplevet effekt = deltager er outcome assessor
Blinding of participants and personnel	High risk	Judgement Comment: Patienter og personale ikke blindet for intervention.
Allocation concealment	High risk	Judgement Comment: Each of the two urogynaecologists always prescribed the same treatment to all patients; the assignation of the therapeutic regimen to each urogynaecologist was made randomly before the beginning of the study; the date of the visit was assigned by the booking centre of the King's College Hospital, which has no direct relation to the urogynaecology unit; both the patients in this study and the employees working at the booking centre did not know which of the two urogynaecologists was present
Sequence Generation	Low risk	Quote: "Each of the two urogynaecologists always prescribed the same treatment to all patients; the assignation of the therapeutic regimen to each urogynaecologist was made randomly before the beginning of the study; the date of the visit was assigned by the booking centre of the King's College Hospital, which has no direct relation to the urogynaecology unit; both the patients in this study and the employees working at the booking centre did not know which of the two urogynaecologists was present the day of the visit."
Incomplete outcome data	Low risk	

Tseng 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group **Open Label:** **Cluster RCT:**
Participants	**Baseline Characteristics** Intervention ● *Age*: 66.2 (6.8) ● *BMI*: 25.3 (3.8) ● *DO following provocative manoeuvres* : ● *No of partcicpants*: 40 ● *UUI/24 h*: 2.2 (1.1) ● *UDI-6 score*: 8.6 (3.8) ● *IIQ-7 score*: 9.4 (3.6) Control ● *Age*: 66.2 (6.8) ● *BMI*: 25.3 (3.8) ● *DO following provocative manoeuvres* : ● *No of partcicpants*: 40 ● *UUI/24 h*: 2.2 (1.1) ● *UDI-6 score*: 8.6 (3.8) ● *IIQ-7 score*: 9.4 (3.6) **Included criteria:** OABPostmenopausal women de according to ICS terminology.Menopause was defined by 12 months of amenorrheaafter thefinal menstrual period or an elevated serum folliclestimulating hormone concentration (over 30–40 mIU/ml)for women had undergone hysterectomy. OAB is defined asa condition characterized by urgency, with or without urgeincontinence, usually with frequency and nocturia, if there isno proven infection or obvious pathology. **Excluded criteria:** Women with both storage andvoiding symptoms and unable to tell the priority. (2) Womenwith advanced pelvic prolapse, severe constipation, elevatedpost-void residual, or neurological deficit. Advanced pelvicorgan prolapse was defined as the prolapse greater thanstage II of the pelvic organ prolapse quantitation system(POP-Q).17Women with above conditions were at risk forelevated post-void residual urine and might further attenuatethe efficacy of antimuscarinic agents.18(3) Women who hadmedical illness and contraindication for using tolterodineincluded: significant hepatic and renal disease; abnormalcardiac conduction, rate or rhythm; narrow-angle

	glaucoma;myasthenia gravis; obstructive uropathy; decreased gastro-intestinal motility. Additional concerns for using estrogenincluded: a history of cerebrovascular disease; thromboem-bolic disorders; gallbladder disease; known or suspectedbreast carcinoma; estrogen-dependent neoplasm or undiag-nosed abnormal genital bleeding. Women who were on HRTwithin 3 months were also excluded from the study.
Interventions	**Intervention Characteristics** Intervention ● *Treatment*: 2 mg tolterodine twice per day/vaginal conjugated equine estrogen (CEE) 0.625 mg twiceaweek ● *Duration of treatment*: 12 wk ● *Follow-up*: End of treatment (12 wk) Control ● *Treatment*: 2 mg tolterodine twice per day ● *Duration of treatment*: 12 wk ● *Follow-up*: End of treatment (12 wk)
Outcomes	*Patientoplevet effekt (patientreported effect) - End of treatment* ● **Outcome type**: DichotomousOutcome ● **Measure names**: ["End of treatment"] *Serious adverse events* ● **Outcome type**: AdverseEvent ● **Measure names**: ["End of treatment"] ● **Data value**: Endpoint *Frafald* ● **Outcome type**: DichotomousOutcome ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Data value**: Endpoint *Patientoplevet effekt* ● **Outcome type**: UDI-6 ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Scale**: UDI-6 score 0-100

	● **Direction**: Lower is better ● **Data value**: Endpoint *Inkontinensrelateret livskvalitet* ● **Outcome type**: IIQ-7 ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Scale**: IIQ-7 score 0-100 ● **Direction**: Lower is better ● **Data value**: Endpoint *Antal vandladninger per døgn* ● **Outcome type**: ContinuousOutcome ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Scale**: Day time frequence/day ● **Direction**: Lower is better ● **Data value**: Endpoint *Antal tilfælde af urgency inkontinens per døgn* ● **Outcome type**: ContinuousOutcome ● **Measure names**: ["End of treatment"] ● **Reporting**: Fully reported ● **Scale**: Urge incontinence/24 h ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Unclear **Country:** Taiwan **Setting:** **Comments:** **Authors name:** Tseng LH **Institution:** Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital and University of Chang Gung School of Medicine, Tao-Yuan, Taiwan **Email:**

	Address:
Notes	*Herdis Bohn Olesen BrøDbæK* on 26/08/2015 05:12 **Baseline Characteristics** hvad er UUI og DO? *Herdis Bohn Olesen BrøDbæK* on 26/08/2015 05:24 **Continuous Outcomes** i antall vandladninger pr døgn har jeg lagt daytime frequency sammen med nocturia - men jeg kan vel ikke bare lægge SD sammen - og jeg kan ikke huske om jeg kan lægge det sammen og dele med to. *Herdis Bohn Olesen BrøDbæK* on 26/08/2015 05:29 **Dichotomous Outcomes** jeg kan ikke finde et antal, der har effekt

Risk of bias table

Bias	Authors' judgement	Support for judgement
Other sources of bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias
Selective outcome reporting	Low risk	Judgement Comment: The study protocol is available and all pre-specified outcomes have been reported
Blinding of outcome assessors	High risk	Judgement Comment: Patients = outcome assessors on most outcomes
Blinding of participants and personnel	High risk	Judgement Comment: No blinding
Allocation concealment	Low risk	
Sequence Generation	Low risk	Quote: "After enrolment, the patient was randomly allocated, via permuted block method with a block of 4, into two groups."
Incomplete outcome data	Low risk	Judgement Comment: No incomplete data

Footnotes

References to studies

Included studies

Serati 2009

Serati M; Salvatore S; Uccella S; Cardozo L; Bolis P. Is there a synergistic effect of topical oestrogens when administered with antimuscarinics in the treatment of symptomatic detrusor overactivity?.. European urology 2009;55(3):713-719. [DOI: http://dx.doi.org/10.1016/j.eururo.2008.06.051]

Tseng 2009

Tseng,L. H.; Wang,A. C.; Chang,Y. L.; Soong,Y. K.; Lloyd,L. K.; Ko,Y. J.. Randomized comparison of tolterodine with vaginal estrogen cream versus tolterodine alone for the treatment of postmenopausal women with overactive bladder syndrome. Neurourology and urodynamics 2009;28(1):47-51. [DOI: 10.1002/nau.20583 [doi]]

Excluded studies

Tseng 2007

Tseng,L. H.; Liang,C. C.; Chang,Y. L.; Lin,Y. H.; Soong,Y. K.; Wang,A.. A randomized comparative study of vaginal estrogen cream in postmenopausal women with overactive bladder syndrome (Abstract number 27). International urogynecology journal and pelvic floor dysfunction 2007;18 Suppl 1(Journal Article):S15-S16. [DOI:]

Data and analyses

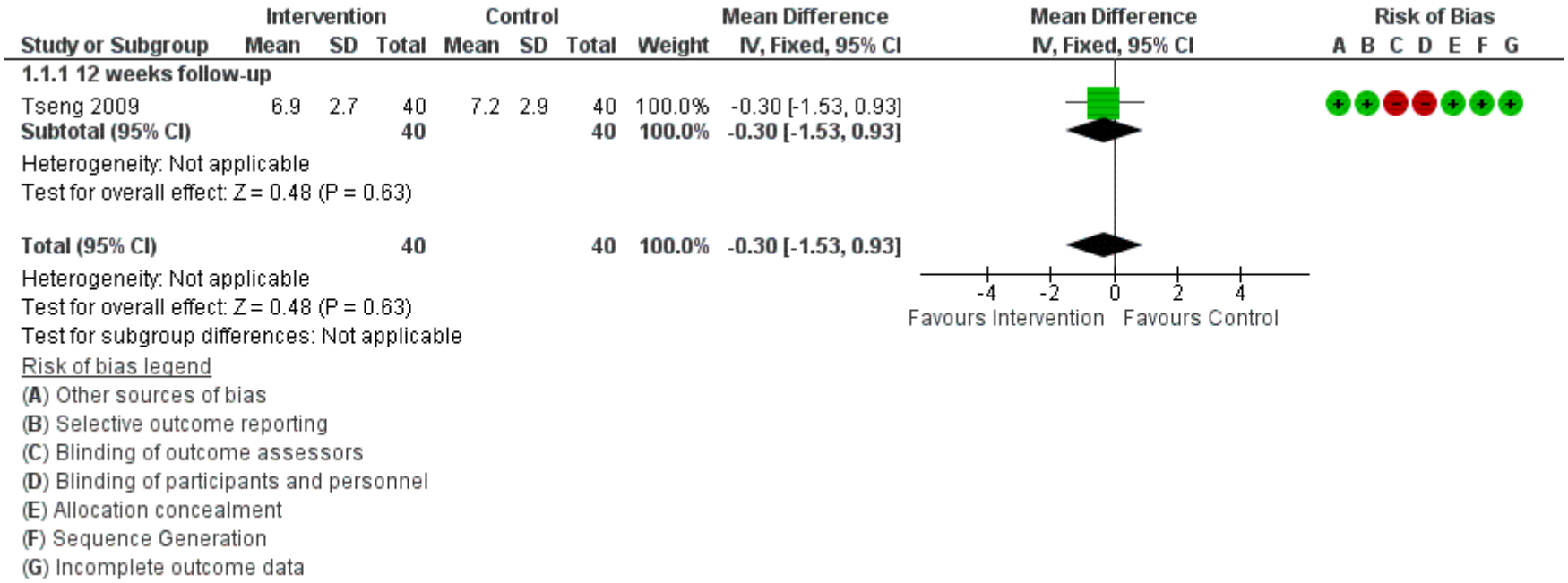
1 Intervention vs Control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Patientoplevet effekt	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.53, 0.93]
1.1.1 12 weeks follow-up	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.53, 0.93]

1.2 Patientoplevet effekt (patientreported effect) - End of treatment	1	229	Risk Ratio (Non-event) (IV, Fixed, 95% CI)	0.93 [0.54, 1.60]
1.2.1 12 weeks follow-up	1	229	Risk Ratio (Non-event) (IV, Fixed, 95% CI)	0.93 [0.54, 1.60]
1.3 Antal vandladninger per døgn	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.25, 0.05]
1.3.1 12 weeks follow-up	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.25, 0.05]
1.4 Antal tilfælde af urgency inkontinens per døgn	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.44, 0.04]
1.4.1 12 weeks follow-up	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.44, 0.04]
1.5 Inkontinensrelateret livskvalitet	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-1.54, 0.74]
1.5.1 12 weeks follow-up	1	80	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-1.54, 0.74]
1.6 Frafald	1		Risk Ratio (IV, Fixed, 95% CI)	No totals
1.6.1 End of treatment (12 weeks)	1		Risk Ratio (IV, Fixed, 95% CI)	No totals

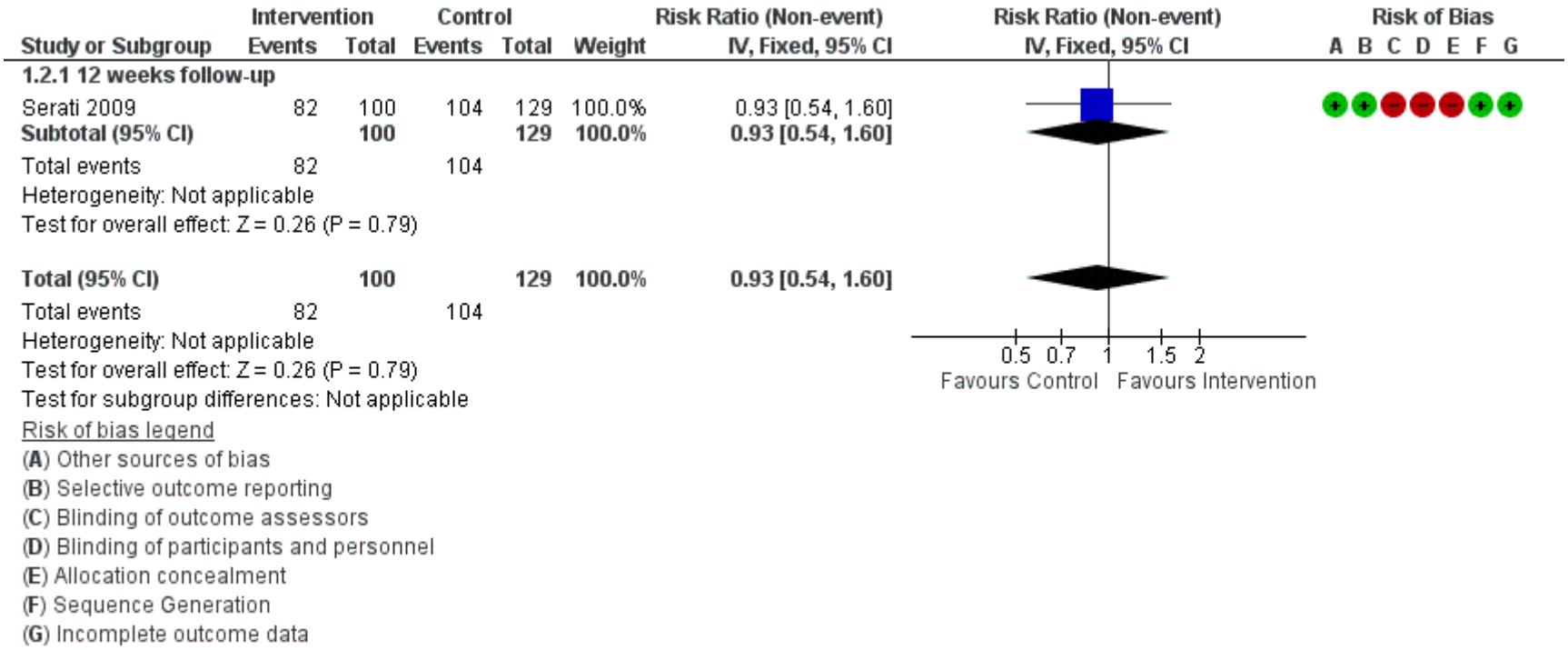
Figures

Figure 1 (Analysis 1.1)



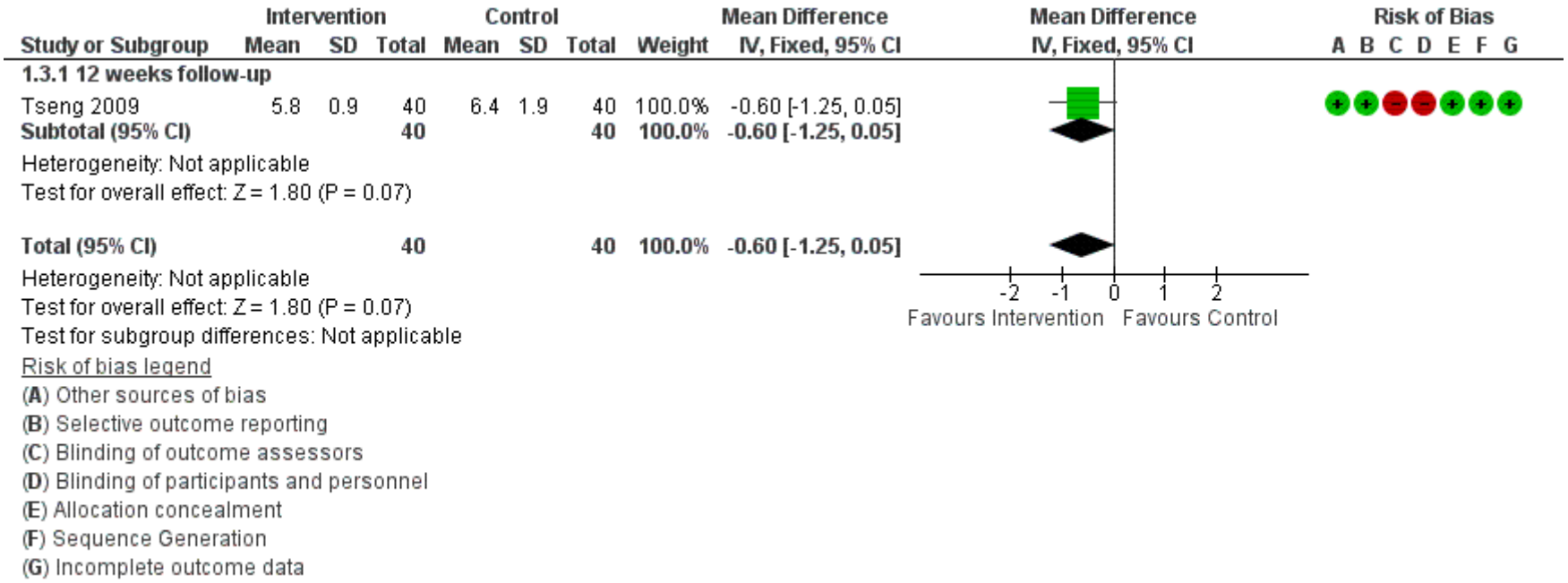
Forest plot of comparison: 1 Intervention vs Control, outcome: 1.1 Patientoplevet effekt.

Figure 2 (Analysis 1.2)



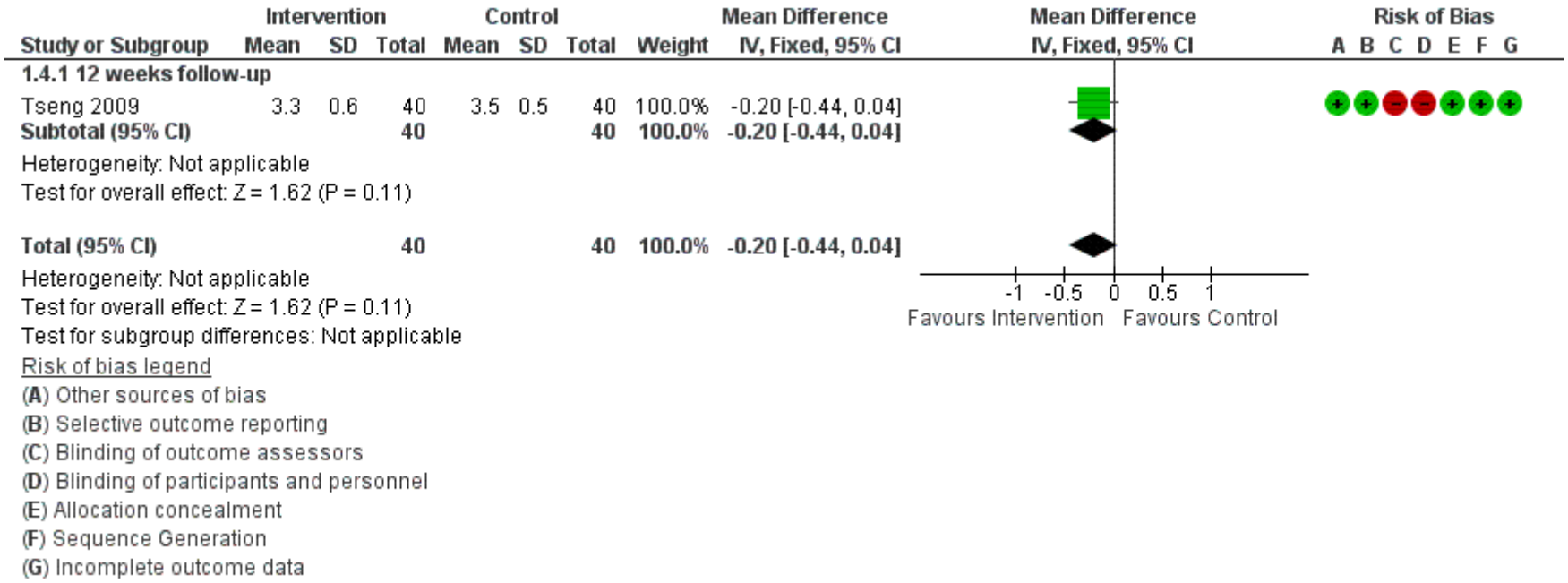
Forest plot of comparison: 1 Intervention vs Control, outcome: 1.2 Patientoplevet effekt (patientreported effect) - End of treatment.

Figure 3 (Analysis 1.3)



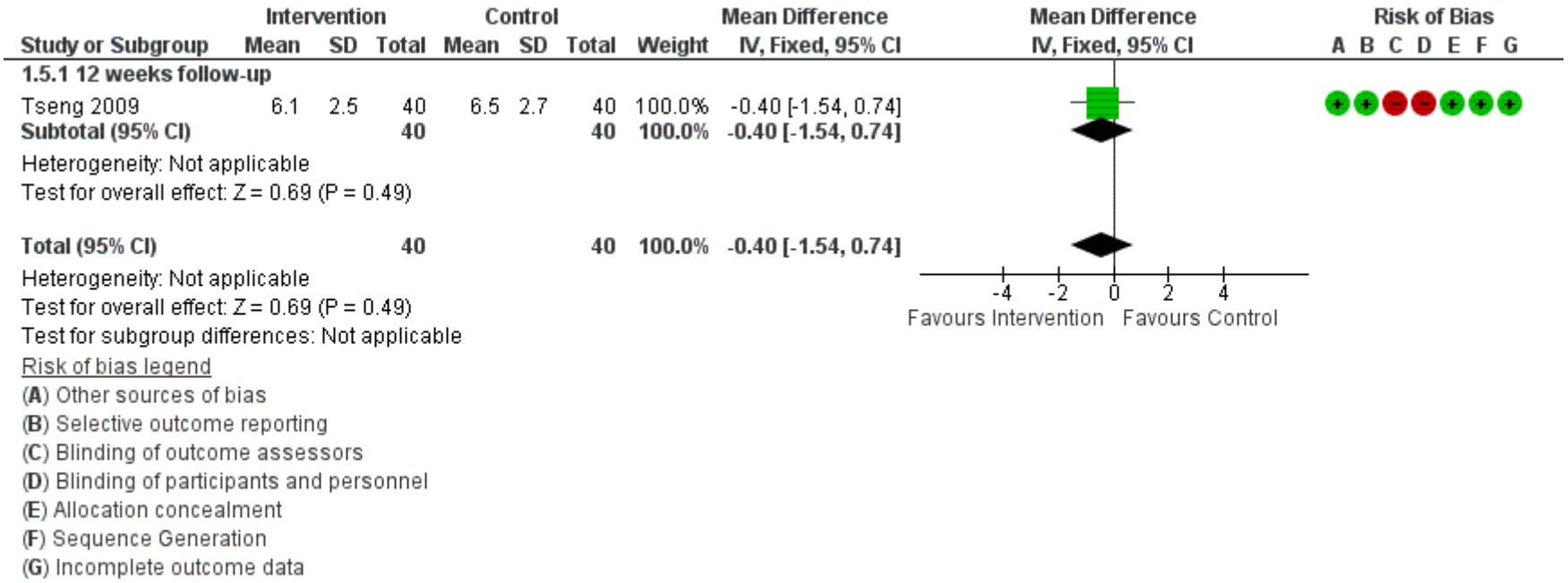
Forest plot of comparison: 1 Intervention vs Control, outcome: 1.3 Antal vandladninger per døgn.

Figure 4 (Analysis 1.4)



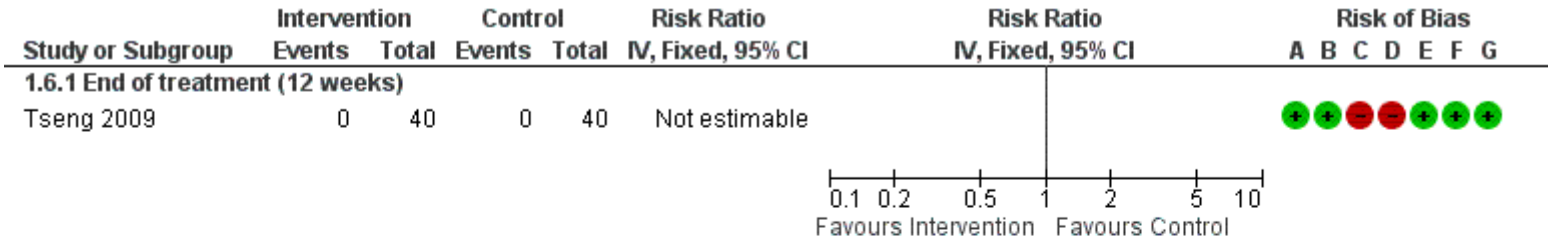
Forest plot of comparison: 1 Intervention vs Control, outcome: 1.4 Antal tilfælde af urgency inkontinens per døgn.

Figure 5 (Analysis 1.5)



Forest plot of comparison: 1 Intervention vs Control, outcome: 1.5 Inkontinensrelateret livskvalitet.

Figure 6 (Analysis 1.6)



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

Forest plot of comparison: 1 Intervention vs Control, outcome: 1.6 Frafald.