

## **PICO 5: Hvad er effekten af et superviseret aerobt træningsprogram af lav til moderat intensitet sammenlignet med råd om øget fysisk aktivitet ved type 2 diabetes?**

### **Methods**

#### **Criteria for considering studies for this review**

##### ***Types of outcome measures***

##### **Primary outcomes**

HbA1c  $\geq$  1 år - kritisk

Fysisk kapacitet ( $VO_2$  max)  $<$  1 år - kritisk

Bivirkninger, ved endt forløb - kritisk

##### **Secondary outcomes**

##### **Følgende outcomes er vurderet vigtige:**

BMI  $<$  1 år

Vægt  $<$  1 år

HbA1c  $<$  1 år

SF-36 fysisk begrænsning  $<$  1 år

SF-36 mental sundhed  $<$  1 år

Komplikationer  $\geq$  1 år

Hjertekarsygdom  $\geq$  1 år

Frafaldsrate - efter endt forløb

QoL - længste follow-up

## Characteristics of studies

### Characteristics of included studies

#### Backx 2011

<b>Methods</b>	<p><b>Study design:</b> Randomized controlled trial</p> <p><b>Study grouping:</b> Parallel group</p> <p><b>Open Label:</b> YES</p> <p><b>Cluster RCT:</b></p>
<b>Participants</b>	<p><b>Baseline Characteristics</b></p> <p>control</p> <ul style="list-style-type: none"> <li>● Age <math>43.86 \pm 10.3</math> years:</li> <li>● Mænd (males)%:</li> <li>● Alder (age) yrs:</li> <li>● DM varighed (duration) yrs:</li> <li>● HbA1c %:</li> <li>● vægt (weight) kg:</li> <li>● BMI:</li> </ul> <p>intervention</p> <ul style="list-style-type: none"> <li>● Age <math>43.86 \pm 10.3</math> years:</li> <li>● Mænd (males)%:</li> <li>● Alder (age) yrs:</li> <li>● DM varighed (duration) yrs:</li> <li>● HbA1c %:</li> <li>● vægt (weight) kg:</li> <li>● BMI:</li> </ul> <p><b>Included criteria:</b> Treatment-naive patients with Type 2 diabetes diagnosed in the preceding 3 months were recruited from a diabetes clinic.</p> <p><b>Excluded criteria:</b> current treatment with oral anti-diabetic drugs or insulin, and severe complications of diabetes, such as evidence of hepatic disease, changes of ischaemia or cardiac disease at rest or during an exercise. Cardiac anomalies observed during the exercise, tolerance test identified by electrocardiogram, problems with mobility, current</p>

	<p>use of anti-inflammatory drugs, severe asthma, taking corticosteroids, thyroxine or growth hormones. None of the participants had previously participated in an exercise intervention.</p>
<p><b>Interventions</b></p>	<p><b>Intervention Characteristics</b> control</p> <ul style="list-style-type: none"> <li>● 12 weeks supervised exercise training three times 35-40 min weekly with 40-50% of max heart rate in 15-20 min per exercise session:</li> </ul> <p>intervention</p> <ul style="list-style-type: none"> <li>● 12 weeks supervised exercise training three times 35-40 min weekly with 40-50% of max heart rate in 15-20 min per exercise session:</li> </ul>
<p><b>Outcomes</b></p>	<p><i>Continuous:</i></p> <ul style="list-style-type: none"> <li>● SF-36 fysisk funktion</li> <li>● SF-36 Generelt helbred</li> <li>● SF-36 fysisk begrænsning</li> <li>● fysisk kapacitet</li> <li>● BMI</li> <li>● SF-36 bodily pain</li> <li>● SF-36 social funktion</li> <li>● SF-36 vitalitet</li> <li>● SF 36 psykisk begrænsning</li> <li>● SF-36 mental helbred</li> <li>● vægt</li> <li>● HbA1c %</li> </ul> <p><i>Dichotomous:</i></p> <ul style="list-style-type: none"> <li>● komplikationer</li> <li>● hjertekarsygdom</li> <li>● andre utilsigtede hændelser</li> <li>● frafaldsrate %</li> </ul> <p><i>Adverse Events:</i></p> <ul style="list-style-type: none"> <li>● utilsigtet hændelse</li> </ul>

<b>Notes</b>	<p><b>Identification:</b></p> <p><b>Participants:</b></p> <p><b>Study design:</b></p> <p><b>Baseline characteristics:</b>  <i>Jens Steen Nielsen</i> data are given as median and range thus do not fit in this table</p> <p><b>Intervention characteristics:</b></p> <p><b>Pretreatment:</b></p> <p><b>Continuous outcomes:</b>  <i>Simon Tarp</i> Body mass (kg) SCP Pre 102.5 [82.1–123.2]; Post 101.1 [78.0–123.3]. SEP pre 91.7 [74.3–113.7]; post 87.9 [69.9–112.7] p=0.007. Diff NS.Body mass index (kg m<sup>2</sup>) SCP 32.3 [26.4–40.5] 32.0 [25.0–41.2] POST SEP 30.0 [25.3–40.1] 28.7 [23.1–39.4] 0.006 Diff NS.HbA1c (%)* SCP 6.6 [5.6–7.9] 6.7 [5.7–9.7] N.S. N.S. POST: SEP 6.4 [5.7–8.5] 6.0 [5.5–7.1] 0.007. Diff NS</p> <p><i>Jens Steen Nielsen</i> data is given as median and range thus can not fit in to this table</p> <p><b>Dichotomous outcomes:</b></p> <p><b>Adverse outcomes:</b></p>
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**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	Low risk	

**Cuff 2003**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Comment: only stated: Subjects were then randomly assigned to one of three groups: Insufficient details.
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	Comment: Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	Unclear risk	NR

**Giannopoulou 2005**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	High risk	
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	Unclear risk	NR

***Hordern 2008***

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Quote: "After baseline testing, patients were randomly allocated to either usual care (n = 112) or exercise training groups (n = 111) by an independent statistician using random number generation."
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	Comment: personnel was not blinded. this is not possible during exercise intervention.
Blinding of outcome assessment (detection bias)	Unclear risk	Comment: not described
Incomplete outcome data (attrition bias)	High risk	Quote: "After randomization to exercise training or usual care, five declined the intervention and, over the 4-week period, five patients withdrew from the study and 13 did not attend for follow-up." Comment: only 132 out of 222
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	Unclear risk	NR

**Johannsen 2013**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

*Jorge 2011*

<b>Methods</b>
<b>Participants</b>
<b>Interventions</b>
<b>Outcomes</b>
<b>Notes</b>

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	Unclear risk	NR



Selective reporting (reporting bias)	Low risk
Other bias	Low risk

**Kadoglou 2007**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	Unclear risk	NR

**Karstoft 2013**

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<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

Risk of bias table

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Quote: "Subjects with type 2 diabetes (22) were recruited by advertisements in news- papers and by contacting local diabetes patient organizations. All volunteers un- derwent medical screening, including a health status interview, physical exam, blood chemistry analysis, and oral glu- cose tolerance test (OGTT). Exclusion cri- teria included the use of exogenous insulin, weight instability (.2 kg/6 months), physical activity (.150 min/ week), and evidence of liver, renal, and cardiopulmonary disease and diseases contraindicating physical activity (23)."
Allocation concealment (selection bias)	Low risk	Comment: Subjectes draw blinded envelopes where in group allocation was stated.
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	Low risk	Comment: all lab values - no soft data.
Incomplete outcome data (attrition bias)	Low risk	Quote: "intervention, of whom n = 5 underwent both CON and either CWT or IWT. Therefore, n = 32 pre- and posttrials were included for statistical analysis (CON, n = 8; CWT, n = 12; IWT, n = 12)."
Selective reporting (reporting bias)	Low risk	Quote: "If a single subject with rapidly progressing (3 years since diagnosis), severe disease (fasting glucose = 16.3 mmol/L; HbA 1c = 8.2%), who experienced serious deterioration in classical glycemc control variables after the training intervention (fasting glucose = 18.3 mmol/L; HbA 1c = 9.8%), was removed from the statistical analysis, significant improvements in HbA 1c were encountered in the IWT group (DHbA 1c = 20.25 6 0.08%, P,"

Other bias	Low risk
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**Negri 2010**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

**Risk of bias table**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "by a randomization table,"
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	Comment: not possible to blind the participants
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	Low risk	Comment: seems to be OK
Selective reporting (reporting bias)	High risk	Comment: Presentation of specific data for all participants are missing
Other bias	Low risk	

**Ribeiro 2008**

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	

<b>Notes</b>
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**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	Unclear risk	NR
Incomplete outcome data (attrition bias)	High risk	
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	High risk	

**Sigal 2007**

<b>Methods</b>
<b>Participants</b>
<b>Interventions</b>
<b>Outcomes</b>
<b>Notes</b>

**Risk of bias table**

<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Comment: central block randomization based on gender and 2 age groups
Allocation concealment (selection bias)	Low risk	Comment: allocation concealment before randomization

Blinding of participants and personnel (performance bias)	High risk	Comment: unable to blind patients and personnel
Blinding of outcome assessment (detection bias)	Low risk	Comment: main study outcomes were measured by blinded technologist using objective methods
Incomplete outcome data (attrition bias)	Low risk	Comment: Attrition and missing values were reported. Analysis was intention-to-treat
Selective reporting (reporting bias)	Unclear risk	NR
Other bias	High risk	Comment: larger drop-out (12) in intervention compared to control (3)

### Tomar 2013

<b>Methods</b>	
<b>Participants</b>	
<b>Interventions</b>	
<b>Outcomes</b>	
<b>Notes</b>	

### Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: were randomly allocated
Allocation concealment (selection bias)	High risk	Comment: not indicated
Blinding of participants and personnel (performance bias)	High risk	Comment: unblinded for patient and personnel
Blinding of outcome assessment (detection bias)	High risk	Comment: not indicated
Incomplete outcome data (attrition bias)	High risk	Comment: 2 out 12 dropped out in the intervention group, with the small number it might of significance

Selective reporting (reporting bias)	Unclear risk	Comment: not discussed
Other bias	Unclear risk	Comment: Not clear, and this study should be considered further

*Footnotes*

**Characteristics of excluded studies**

*Footnotes*

**Characteristics of studies awaiting classification**

*Footnotes*

**Characteristics of ongoing studies**

*Footnotes*

**Summary of findings tables**

**Additional tables**

**References to studies**

**Included studies**

**Backx 2011**

Backx K, McCann A, Wasley D, Dunseath G, Luzio S, Owens D. The effect of a supported exercise programme in patients with newly diagnosed Type 2 diabetes: a pilot study. *J Sports Sci* 2011;29(6):579-86.

### ***Cuff 2003***

Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care* 2003;26(11):2977-82.

### ***Giannopoulou 2005***

Giannopoulou I, Fernhall B, Carhart R, Weinstock RS, Baynard T, Figueroa A, et al.. Effects of diet and/or exercise on the adipocytokine and inflammatory cytokine levels of postmenopausal women with type 2 diabetes. *Metabolism* 2005;54(7):866-75.

### ***Hordern 2008***

Hordern MD, Cooney LM, Beller EM, Prins JB, Marwick TH, Coombes JS. Determinants of changes in blood glucose response to short-term exercise training in patients with Type 2 diabetes. *Clin Sci (Colch)* 2008;115(9):273-81.

### ***Johannsen 2013***

Johannsen NM, Sparks LM, Zhang Z, Earnest CP, Smith SR, Church TS, et al.. Determinants of the Changes in Glycemic Control with Exercise Training in Type 2 Diabetes: A Randomized Trial. *PLoS ONE* 2013;Article Number: e6;8 (6):-.

### ***Jorge 2011***

Jorge ML, de Oliveira VN, Resende NM, Paraiso LF, Calixto A, Diniz AL, et al.. The effects of aerobic, resistance, and combined exercise on metabolic control, inflammatory markers, adipocytokines, and muscle insulin signaling in patients with type 2 diabetes mellitus. *Metabolism* 2011;60(9):1244-52.

### ***Kadoglou 2007***

Kadoglou NP, Iliadis F, Angelopoulou N, Perrea D, Ampatzidis G, Liapis CD, et al.. The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus.. *Eur J Cardiovasc Prev Rehabil* 2007;14(6):837-43.

### ***Karstoft 2013***

Karstoft K, Winding K, Knudsen SH, Nielsen JS, Thomsen C, Pedersen BK, et al.. The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in type 2 diabetic patients: a randomized, controlled trial. *Diabetes Care* 2013;36(2):228-36.

### ***Negri 2010***

Negri C, Bacchi E, Morgante S, Soave D, Marques A, Menghini E, et al.. Supervised walking groups to increase physical activity in type 2 diabetic patients. *Diabetes Care* 2010;33(11):2333-5.

**Ribeiro 2008**

Ribeiro IC, Iborra RT, Neves MQ, Lottenberg SA, Charf AM, Nunes VS, et al.. HDL atheroprotection by aerobic exercise training in type 2 diabetes mellitus. *Med Sci Sports Exerc* 2008;40(5):779-86.

**Sigal 2007**

Sigal RJ, Kenny GP, Boule NG, Wells GA, Prud'homme D, Fortier M, et al.. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med* 2007;147(6):357-69.

**Tomar 2013**

Tomar RH, Hashim MH, Al-Qahtani MH. Effects of a 12-week aerobic training on glycemic control in type 2 diabetes mellitus male patients. *Saudi Med J* 2013;34:757-9.

**Excluded studies****Studies awaiting classification****Ongoing studies****Other references****Additional references****Other published versions of this review****Data and analyses****1 control vs intervention**

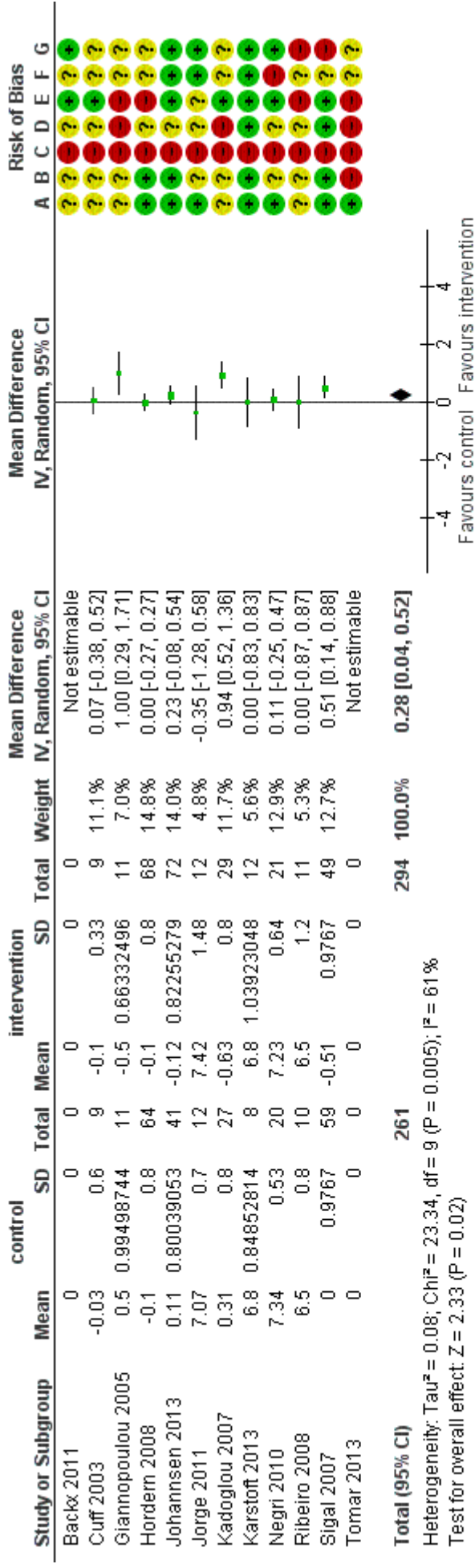
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 HbA1c% <1år	12	555	Mean Difference (IV, Random, 95% CI)	0.28 [0.04, 0.52]
1.2 BMI <1år	9	439	Mean Difference (IV, Random, 95% CI)	0.57 [0.26, 0.87]
1.3 vægt <1år	9	414	Mean Difference (IV, Random, 95% CI)	1.82 [0.93, 2.71]



1.4 SF-36 fysisk begrænsning <1år	2	175	Mean Difference (IV, Random, 95% CI)	-2.96 [-6.58, 0.67]
1.5 SF-36 mentalt helbred <1år	2	175	Mean Difference (IV, Random, 95% CI)	1.22 [-2.21, 4.65]
1.6 V02-max <1år	8	507	Mean Difference (IV, Random, 95% CI)	-1.79 [-2.77, -0.80]
1.9 andre utilsigtede hændelser	4	317	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.19, 1.84]
1.10 frafald (antal)	5	296	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.19, 2.69]

## Figures

Figure 1 (Analysis 1.1)

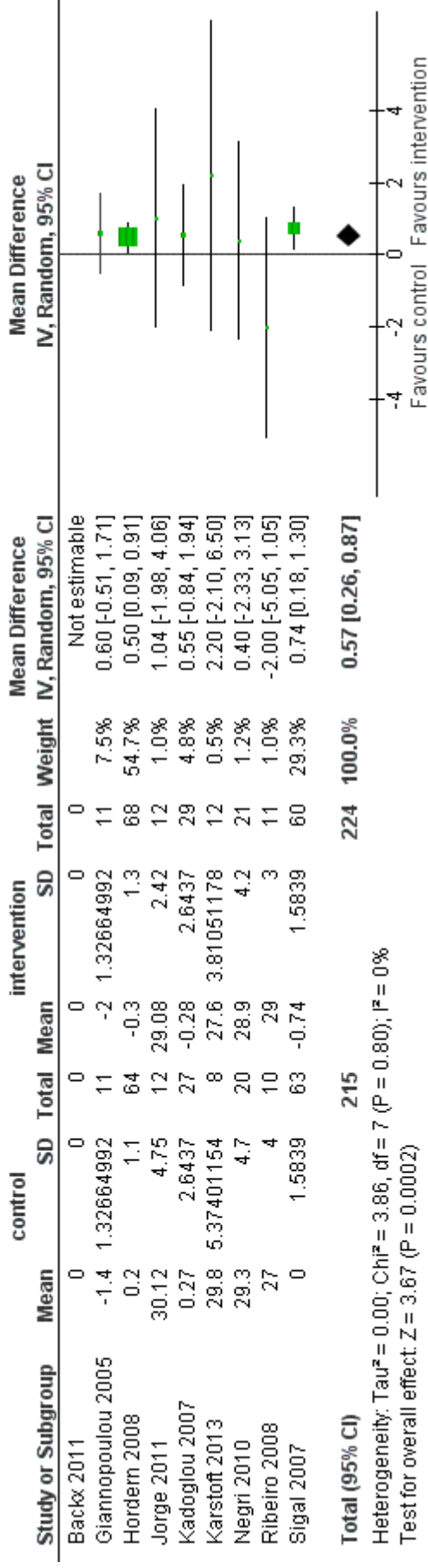


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

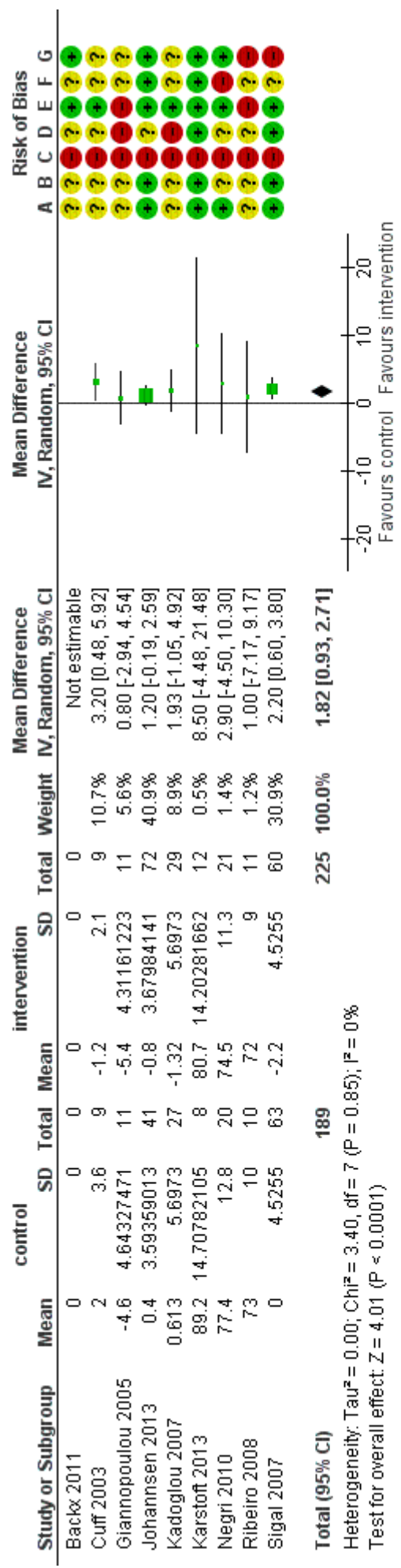
Forest plot of comparison: 1 control vs intervention, outcome: 1.1 HbA1c% < 1år.

Figure 2 (Analysis 1.2)



Forest plot of comparison: 1 control vs intervention, outcome: 1.2 BMI <1år.

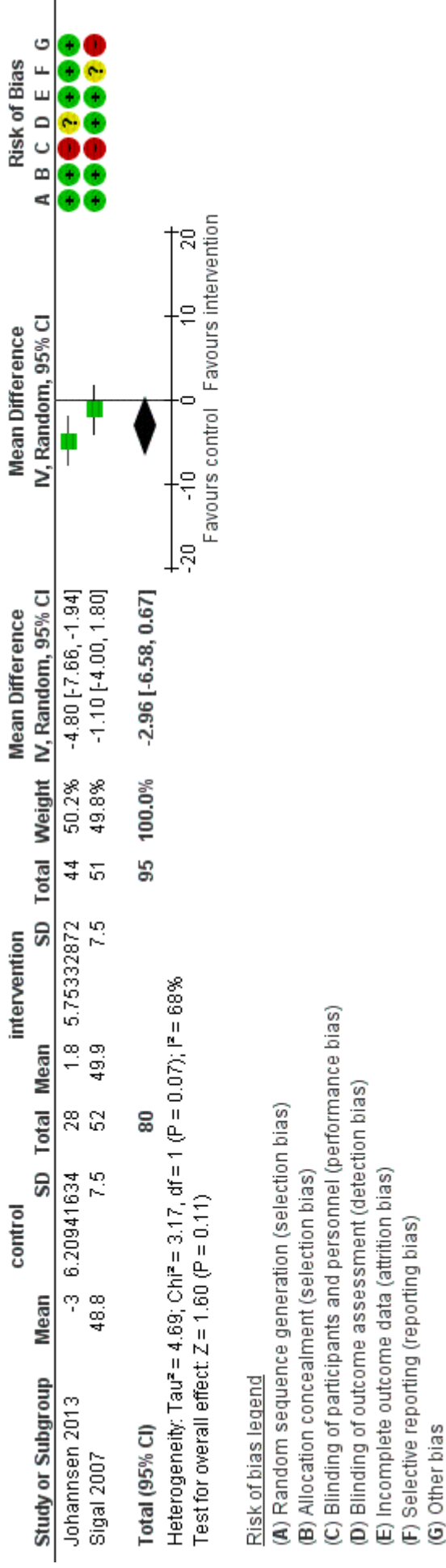
Figure 3 (Analysis 1.3)



- Risk of bias legend
- (A) Random sequence generation (selection bias)
  - (B) Allocation concealment (selection bias)
  - (C) Blinding of participants and personnel (performance bias)
  - (D) Blinding of outcome assessment (detection bias)
  - (E) Incomplete outcome data (attrition bias)
  - (F) Selective reporting (reporting bias)
  - (G) Other bias

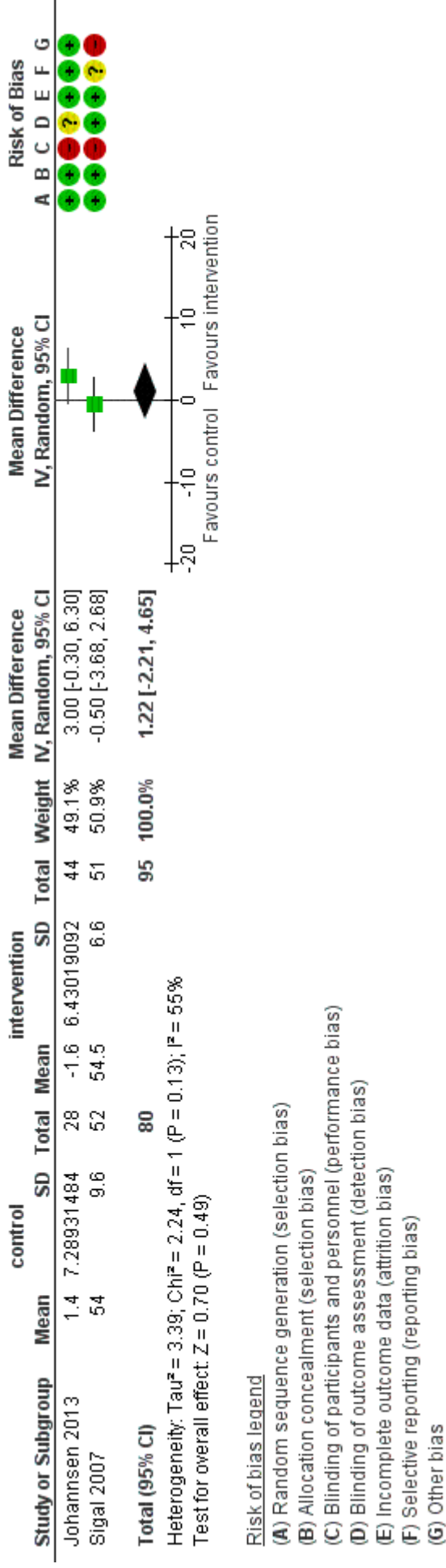
Forest plot of comparison: 1 control vs intervention, outcome: 1.3 vægt <1år.

Figure 4 (Analysis 1.4)



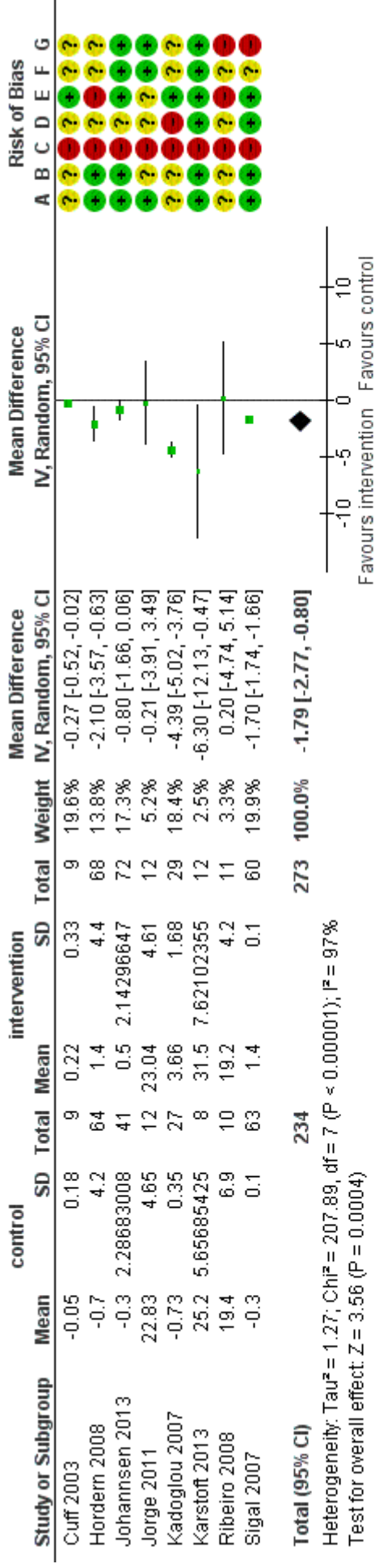
Forest plot of comparison: 1 control vs intervention, outcome: 1.4 SF-36 fysisk begrænsning <1år.

Figure 5 (Analysis 1.5)



Forest plot of comparison: 1 control vs intervention, outcome: 1.5 SF-36 mentalt helbred <1år.

**Figure 6 (Analysis 1.6)**

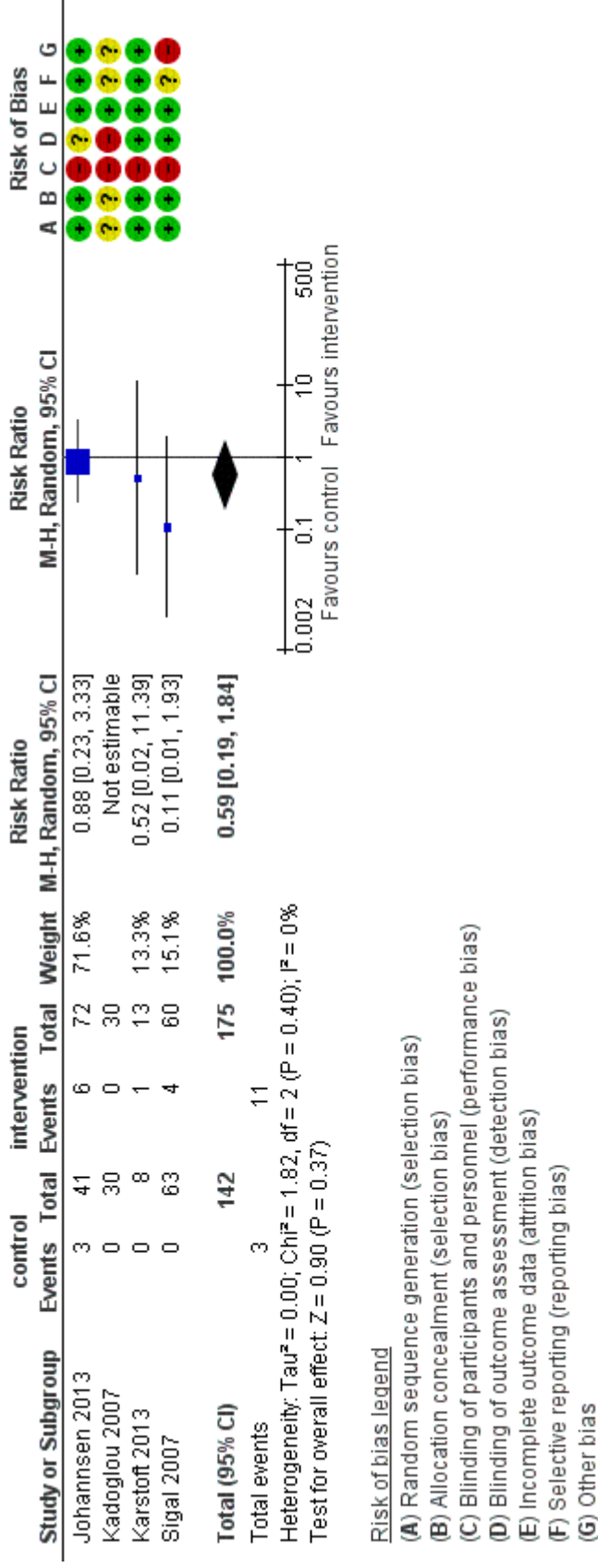


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Forest plot of comparison: 1 control vs intervention, outcome: 1.6 V02-max <1år.

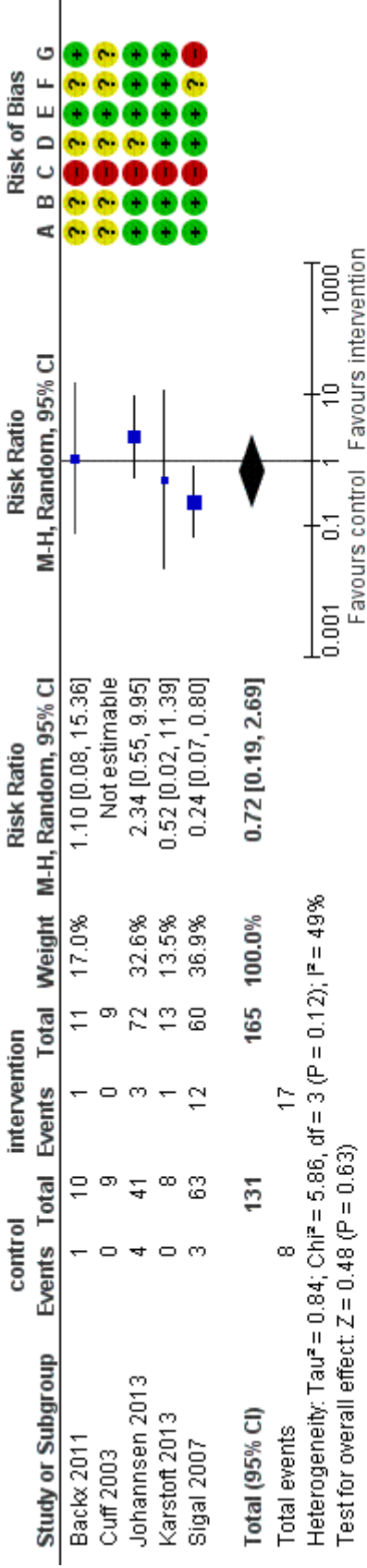
Figure 7 (Analysis 1.9)



Forest plot of comparison: 1 control vs intervention, outcome: 1.9 andre utilsigtede hændelser.

Figure 8 (Analysis 1.10)





- Risk of bias legend
- (A) Random sequence generation (selection bias)
  - (B) Allocation concealment (selection bias)
  - (C) Blinding of participants and personnel (performance bias)
  - (D) Blinding of outcome assessment (detection bias)
  - (E) Incomplete outcome data (attrition bias)
  - (F) Selective reporting (reporting bias)
  - (G) Other bias

Forest plot of comparison: 1 control vs intervention, outcome: 1.10 frafald (antal).