Title: Lifestyle interventions for weight loss in adults with severe obesity: a systematic review

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Keywords:

Overweight, Obesity, Severe Obesity, Morbid Obesity, Lifestyle, Weight Loss, Weight Reduction

Running title; Lifestyle interventions in adults with severe obesity.

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LIST OF ABBREVIATIONS

BMI	body mass index
CENTRAL	Cochrane Central Register of Controlled Trials
HbA1c	Glycated haemoglobin
kg	kilograms
Kg/m2	weight in kilograms divided by height squared in metres
NHS	National Health Services
NICE	National Institute for Health and Clinical Excellence
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
SD	Standard deviation
WHO	World Health Organisation
UK	United Kingdom
USA	United States of America

Background

Severe obesity is an increasingly prevalent condition and is often associated with long-term comorbidities, reduced survival and higher health care costs. Non-surgical methods avoid the side effects, complications and costs of surgery but it is unclear which non-surgical method is most effective.

Objective

To systematically review the effectiveness of lifestyle interventions compared to standard or minimal care for weight loss in adults with severe obesity.

Methods

MEDLINE, EMBASE, CENTRAL, databases of on-going studies, reference lists of any relevant systematic reviews and The Cochrane Library database were searched from inception to February 2016 for relevant randomised controlled trials. Inclusion criteria were participants with severe obesity (body mass index (BMI>40 kg/m² or BMI>35 kg/m² with comorbidity)) and interventions with a minimal duration of twelve weeks that were multi-component combinations of diet, exercise or behavioural therapy. Risk of bias was evaluated using the Cochrane risk of bias criteria. Meta-analysis was not possible because of methodological heterogeneity.

<u>Results</u>

Seventeen randomised controlled trials met the inclusion criteria. Weight change in kilograms of participants from baseline to follow up was reported for 14 studies. Participants receiving the lifestyle intervention had a greater decrease in weight than participants in the control group for all studies (1.0 to 11.5kg). Lifestyle interventions varied greatly between the studies. Overall lifestyle interventions with combined diet and exercise components achieved the greatest weight loss.

Conclusion

Lifestyle interventions for weight loss in adults with severe obesity were found to result in increased weight loss when compared to minimal or standard care, especially those with combined diet and exercise components.

Introduction

The prevalence of obesity, defined as a body mass index (BMI) greater than or equal to 30 kg/m2, is rapidly increasing in the developed world; more than doubling since 1980.[1,2] Worldwide approximately 13% of the adult population are estimated to have obesity.[2] The prevalence of severe obesity is also rising globally.[3] The prevalence of severe obesity in adults in England rose from 0.8% in 1993 to 2.7% in 2014.[4] Projections suggest that the severe obesity trend will continue to rise over the next decade.[3] Severe or morbid obesity is defined by the National Institute of Clinical Excellence (NICE) as either a BMI greater than or equal to 40 kg/m² or a BMI greater than 35 kg/m² and less than 40 kg/m² in an individual with weight-related co-morbidities.[1] These definitions are important because local healthcare organisations use them to design clinical pathways which influence individual patients' care.[5]

Adult with obesity are at risk of co-morbidities [6] such as type II diabetes, cardiovascular disease, musculoskeletal disorders and certain types of cancer.[7,8] BMI is positively correlated with mortality with studies indicating that median survival could be reduced by ten years in individuals with severe obesity.[9] The NHS costs in England attributable to obesity are projected to reach £10 billion, with wider costs to society estimated to reach £49.9 billion per year by 2050.[2] Severe obesity is likely to be associated with higher costs per individual as it is associated with more comorbidity, secondary care management and reduced capacity for employment.[10] The NICE guidance states weight loss of 5-10% of baseline weight is associated with health benefits.[1]

Non-surgical or surgical options are available to individuals with severe obesity. Reviews comparing bariatric surgery to non-surgical interventions show bariatric surgery to have increased efficacy, sustainability and acceptable cost-effectiveness.[10] Although bariatric surgery has benefits [11], access is limited, with 1% or less of eligible patients receiving it due to demand exceeding supply, and due to high healthcare costs.[12] However lifestyle interventions are an accessible option for all patients adults with severe obesity [13] and a recent systematic review found them to be safe and effective for management of adults with obesity.[14] Furthermore, bariatric surgery is associated with significant surgical complications [11] and needs long-term follow up. [15] The NICE guidance on bariatric surgery suggests that many candidates can show maintenance of lifestyle changes.[1,15] Therefore, there is need for lifestyle interventions targeted specifically at individuals with severe obesity to reduce the demand for bariatric surgery and the burden on healthcare providers. Furthermore, successful pre-operative lifestyle interventions may improve postoperative outcomes. Lifestyle interventions that combine diet, exercise and behavioural therapy [16] are the most effective treatment of people with obesity, other than surgical or pharmacological treatments.[4] Lifestyle interventions may include components aimed at improving diet, exercise, group support and psychosocial support.[17] Therefore, research needs to be done to determine what components, or active ingredients, of a lifestyle intervention are most effective for participants with severe obesity.

Currently, there is no systematic review evaluating the effectiveness of lifestyle interventions targeted specifically at individuals with severe obesity. This review aims to systematically review multi-component lifestyle interventions in participants with severe obesity compared to usual care in randomised controlled trials. The primary outcome of interest is weight loss. Secondary outcomes include change in co-morbidities, functioning and quality of life.

Methods

A systematic review was undertaken. MEDLINE, EMBASE and CENTRAL were searched (inception to February 2016). Clinicaltrials.gov and the WHO Trials Registry were searched to identify any relevant on-going studies. The reference lists of any systematic reviews relevant to the management of adults with obesity from the search strategy results and the database The Cochrane Library were searched to identify any further relevant studies.

Randomised controlled trials (RCT) with a minimum duration of twelve weeks for the intervention were included. This was chosen as it is the minimal amount of time to achieve satisfactory weight loss that is recognised according to NICE guidance.[4] Conference proceedings and abstracts were included if they contained sufficient details for data extraction. There were no language restrictions on the search. Studies without baseline BMI reporting were excluded because the participants could not be confirmed to have severe obesity. Only studies examining severe obesity in adults were included. Severe or morbid obesity was defined as either a BMI greater than or equal to 40 kg/m^2 or a BMI greater than 35 kg/m^2 and less than 40 kg/m^2 in an individual with weight-related comorbidities. [1]

Only multicomponent lifestyle interventions (defined as a combination of at least two of diet, exercise or behavioural therapy within any setting) were included. Eligible comparators for inclusion included standard care, no treatment or minimal intervention. Studies including pharmacological therapies were excluded.

The primary outcome was weight measured as change in kg, change in BMI or percentage weight loss from baseline weight. Secondary outcomes included: comorbidity measured as change in measures of comorbidity associated with excess weight and health related quality of life measured using validated tools.

Two reviewers carried out screening and identified studies independently (YH and VH). Differences were resolved through consensus or by a third author (JF).

One reviewer extracted relevant data on population, interventions and outcomes from each study using a specifically designed data extraction form. A second reviewer checked the completed data extraction forms independently; discussion or a third independent reviewer

resolved any disagreements. If there was any missing data, an attempt to contact the authors of the study by e-mail was made to request more information. Included studies were assessed for homogeneity. Meta-analysis was not suitable because of considerable heterogeneity.

Risk of bias was assessed using the Cochrane Risk of Bias tool.[18] One reviewer independently evaluated each study for risk of bias. A second reviewer then checked completed risk of bias evaluations independently; discussion or a third independent reviewer resolved any disagreements.

Results

The electronic search of databases found 3992 titles and abstracts, and of these 205 were categorised as meeting the inclusion criteria or being unclear for which full studies were obtained, of which 17 were included in the review (Figure 1). Included studies were published between 2004 and 2014. The details of the included studies are shown in Table S1. In 12 studies change in weight was a primary outcome and in five studies change in a comorbidity associated with excess weight was a primary outcome. Of the included studies, 11 involved a behavioural, diet and exercise lifestyle intervention, 10 of which were compared to minimal intervention and one compared to a diet and exercise lifestyle intervention. Two studies involved a behavioural and diet intervention, one of which was compared to standard care and the other to minimal intervention. Four of the studies involved a diet and exercise intervention which in two studies was compared to standard care and in two with diet alone.

Participants

The baseline characteristics of included participants are presented Table 1. The total number of participants randomised in the studies was 7,981 (range 27-5145) with a mean age of 54.2 years, mean BMI of 37.1 kg/m² and 70% female. In two of the studies all participants were female and in 1 study all participants were of African American ethnicity. One of the studies had a participant group with a mean BMI greater than 40 kg/m², the rest of the study participants had a comorbidity associated with excess weight. In eight studies the comorbidity was diabetes mellitus, in two it was musculoskeletal impairment and in a further two it was metabolic syndrome. In remaining studies it was hypertension, urinary incontinence, cardiovascular risk (diabetes, hypertension or hypercholestorolaemia) and obstructive sleep apnoea.

Interventions

The follow up duration of the studies ranged from three months to 48 months. Interventions in the studies included educational classes on lifestyle change and behavioural techniques, group sessions, individual support, support and monitoring through technology, self-monitoring, prescribed diet programmes, prescribed physical activity programmes, meal replacements, access to facilities for physical activity and individual counselling (Table 1). The intensity and frequency of interventions varied between studies.

Setting

Eleven studies had single-centre designs and six had multi-centre designs. The setting for 13 studies was the USA, two studies were set in Australia, one in the Netherlands and one in Germany. Sixteen studies were based in the community, one study, involving a very low calorie diet, was set in a hospital outpatients department.

The study by Look and colleagues (Look 2010) was the largest with 5,145 participants, making up 64.5% of all participants included in this systematic review, and had the longest follow up period of 48 months. This study consisted of diet, exercise and behavioural intervention for participants with diabetes mellitus.

Risk of bias in included studies

The details of the risk of bias in included studies are presented in Table 2. No study fulfilled all of the criteria used to assess risk of bias and therefore all had methodological limitations. In 8 studies there was a high risk of bias regarding sequence generation in randomisation. In 14 studies allocation concealment was unclear and had a high risk of bias. The latter two limitations might have resulted in intervention and control groups being systematically different. Participants were not blinded for any of the studies creating a high risk of bias. Risk of bias from incomplete data was low in all but one study. Selective reporting was present in 3 studies associated with a high risk of bias. 15 studies utilised intention to treat analysis creating a low risk of bias. One of the studies had a funding conflict of the company producing the product being used in the intervention and one study did not state the source of funding. Four of the studies had a high risk of bias from participants not being comparable at baseline; two studies stated the groups were not comparable and for two studies it was unclear.

Effects of Interventions

Weight change outcomes

The weight change of participants within intervention or control groups during trials was statistically significantly greater for participants receiving the lifestyle intervention, compared to participants in the control groups, for 12 studies. Overall lifestyle interventions with diet and exercise components achieved the greatest mean weight loss.

The weight change in kilograms of participants from baseline to follow up was reported for 14 studies (Table S2). The range of difference in changes between intervention and control groups was -1.0 to -11.5kg and the range of follow up was 3 to 24 months.

Change in BMI was reported for 11 studies (Table S3). The range of difference in changes between intervention and control groups was -0.3 to -4.0 kg/m². The range of follow up was 3 to 24 months. Luley 2011 had the greatest weight change outcomes for BMI and Kg.[26]

Percentage change from baseline total body weight was reported for five studies (Table S4),. The range of difference in changes between intervention and control groups was -1.0 to -6.5%. The range of follow up was 6 to 48 months.

Co-morbidity change outcomes

Change in HbA1c was reported in eight studies, in seven of which participants receiving the lifestyle intervention had a greater decrease than participants in the control group. The range of difference in changes between intervention and control groups was 0.0 to -0.9 % and the range of follow up was 3 to 48 months.

Change in total cholesterol was reported for seven studies, in three of which participants receiving the lifestyle intervention had a greater decrease than participants in the control group. Studies used two different units for measuring cholesterol so the results cannot be compared effectively.

Change in triglycerides was reported for nine studies, in eight of which participants receiving the lifestyle intervention had a greater decrease than participants in the control group. Studies used two different units for measuring triglycerides so the results cannot be compared directly.

Change in systolic blood pressure was reported for nine studies, in seven of which participants receiving the lifestyle intervention had either a greater decrease or smaller increase than

participants in the control group. The range of difference in changes between intervention and control groups was -1 to -8.6 mmHg and the range of follow up was 3 to 48 months.

Change in quality of life was reported in two studies, in one of which participants receiving the lifestyle intervention had a greater increase than participants in the control group. The range of difference in changes between intervention and control groups was 1.0 to 9.8 and the range of follow up was 3 to 6 months.

Measures for other co-morbidities including urinary incontinence, physical function and obstructive sleep apnoea were included in one study each so cannot be compared between studies.

Behavioural, diet and exercise intervention outcomes

Of the ten studies comparing a behavioural, diet and exercise lifestyle intervention with minimal intervention, eight reported absolute weight changes and the difference in changes between intervention and control groups ranged from -1.0 to -10.2 kg; the range of follow up was 3 to 24 months. The other studies on a combined behavioural, diet and exercise lifestyle intervention were not comparable as one compared this to a diet and exercise lifestyle intervention and one reported change in weight only as percentage change from baseline. The two studies on a behaviour and diet intervention were not compared it to standard care and the other to minimal intervention.

Two of the four studies on diet and exercise interventions compared them to standard care. They reported weight change outcomes as change in kg and BMI, of which the range of difference in changes between intervention and control groups was -5.2 to -11.5 kg and -1.6 to -4.0 kg/m^2 respectively and the range of follow up was 4 to 6 months. The other two studies compared to diet alone and reported weight change outcomes as change in kg and BMI, of which the range of difference in changes between intervention and control groups was -2.7 to -3.5 kg and -0.8 kg/m² respectively and the range of follow up was 4 to 6 months. Overall lifestyle interventions with diet and exercise components achieved the greatest mean weight loss.

Discussion

This is the first systematic review to review the multi-component lifestyle interventions for adults with severe obesity. All studies reported a greater reduction in weight in the lifestyle intervention arm compared to control. Overall lifestyle interventions with combined diet and exercise components achieved the greatest mean weight loss. Quality of life outcomes were poorly reported throughout the studies.

Strengths and limitations

The search strategy was designed to be broad by including the term 'obesity' so studies could be identified if they did not specifically include the term 'morbid' or 'severe' in the title or abstract. There were no language or date restrictions and grey literature was specifically sought.

The methods for selection of studies were robust and included two independent reviewers, this reduced the possibility of relevant studies being discarded. The methods for data extraction, analysis and assessment of risk of bias were carried out by one reviewer and then checked by another reviewer independently. Authors of studies for which there was missing data were contacted but only one responded.

The duration of follow up in studies varied from 3 to 48 months and so the short-term and medium-term effects of interventions could be assessed. Another strength of this review was that there were a suitable number of studies reporting weight change outcomes, HbA1c, cholesterol, triglycerides and systolic blood pressure as outcome measures to compare and collate. A limitation of this review was that measures for other co-morbidities of urinary incontinence, physical function and obstructive sleep apnoea were included in one study each and so could not be compared between studies. Furthermore, quality of life was only reported in two studies. None of the studies fulfilled the full Cochrane risk of bias tool criteria indicating that the evidence may be of low quality. The majority of included studies had a high risk of bias for sequence generation, allocation concealment and blinding of researchers, with no explanation or justification of these limitations from the authors. Participants were not blinded for any of the studies, because due to the nature of the intervention it would not be possible to blind participants.

A limitation of this review was that combining of results using meta-analyses was not suitable as there was considerable methodological heterogeneity.

What the results mean

Overall, lifestyle interventions were found to reduce weight in adults with severe obesity. Of the five studies reporting percentage change from baseline weight, three achieved the recommended 5-10% loss of baseline weight for the intervention group. Participants in the control groups for all the studies, excluding two, had a decrease in weight from baseline that reduced the between-group differences. This may be due to the Hawthorne effect by which an individual's behaviour is modified if they are under observation. A degree of Hawthorne or placebo effect is likely in the intervention arm, especially because those who choose to participate in trials are willing to change. Furthermore a perceived positive allocation to the intervention arm may further motivate individuals. Some weight reduction in both arms might also just be due to regression to the mean, that is, when participants are recruited into a trial when their weight is unusually high and then their weight decreases due to factors unrelated to the trial. Policy makers and clinicians face the challenge of achieving these results in "real life". For the majority of comorbidity loutcomes, except for cholesterol, participants in the intervention group had a greater improvement compared to the control group suggesting lifestyle interventions are effective for improving overall health. However the randomised trial design allowed the effect of interventions over and above Hawthorne or placebo effects or regression to the mean to be estimated.

A key finding of this review was that there only one study of a lifestyle intervention for weight loss exclusively confined to adults with a BMI of greater than 40 kg/m^2 . Lifestyle interventions compared to surgical interventions are favoured by patients [36] and are key in improving the outcomes of bariatric surgery in this population group, it is important that effective services are developed. This review found that lifestyle interventions with diet and exercise components were most effective.

Another key finding of this review is that quality of life was only reported as an outcome measure in two studies. Quality of life is arguably the most important outcome to individuals with severe obesity.[37] It is an expression of weight loss, impact on co-morbidities, functioning and crucially mental health. Change in BMI and % weight loss are most commonly used, but more patient focused research on how a lifestyle intervention can improve overall participant quality of life and wellbeing is needed, using quality of life measures sensitive to people with obestity

How does this review compare to other research

This is the first systematic review investigating the effectiveness of lifestyle interventions for weight loss in adults with severe obesity.

A Health Technology Assessment systematic review considered the clinical effectiveness of long-term weight management schemes for adults [17] that included studies with a multicomponent intervention for participants who were overweight or with obesity. These

results support our findings; that weight management interventions were generally shown to promote weight loss in adults who were overweight or with obesity.[17]

Leblanc and colleagues completed a systematic review on the effectiveness of primary care relevant weight-loss interventions for adults with overweight and obesity.[14] The authors concluded that primary care relevant weight loss interventions are effective [14], which is consistent with the findings of this review.

Implications for practice

Lifestyle interventions for weight loss in adults with severe obesity have been found to result in increased weight loss when compared to minimal or standard care. Overall lifestyle interventions with combined diet and exercise components achieved the greatest mean weight loss. Improved lifestyle interventions for adults with severe obesity can lead to decreased demand for or better outcomes of bariatric surgery and therefore contribute to successful management of adults with severe obesity.[4] Policy makers and clinicians should consider multi-faceted lifestyle interventions when designing services.

Implications for research

Studies comparing lifestyle interventions, as part of the overall patient pathway, in patients with a BMI greater than or equal to 40 kg/m² are needed. Future studies on lifestyle interventions need to take measures to reduce risk of bias in order to increase the quality of available literature. As more and longer term research is done into lifestyle interventions, comparisons can start to be made with surgical interventions and achievement and sustainability of results. There were only two studies that had an outcome measure of quality of life, which would be valuable to research further in order to supplement data on objective outcome measures. There was too much heterogeneity between studies to determine which components of lifestyle interventions correlate with a greater weight loss. Development of a robust coding system for components of each lifestyle intervention which would allow metaregression would be useful. Further sufficiently powered RCTs, which focus specifically on answering this question, are needed before a systematic review can assess it. In trials or individual patient meta-analyses that include both participants with both obesity and severe obesity it would be valuable to compare the effects between these two subgroups. The costeffectiveness of lifestyle interventions for the management of adults with severe obesity needs to be investigated to provide more evidence on the subject. Cost and resource use of lifestyle interventions is priority for further research as this will allow a more definite comparison with bariatric surgery and would be useful to modify any future guidelines and policies.

The material is original research, has not been previously published and has not been submitted for publication elsewhere while under consideration. The authors declare that there are no conflicts of interest.

Yasmeen Hassan, John Ford, Shamsher Diu and Max Bachman conceived the review. All authors were involved in the design and interpretation of the review. Yasmeen Hassan, Vicky Head and John Ford were involved in reviewing titles and abstracts. Yasmeen Hassan, Diyva Jacob and John Ford were involved in data extraction. Yasmeen Hassan drafted the initial manuscript. All authors contributed to and approved the final paper.

The training, teaching and library staff at the University of East Anglia and Norfolk Public Health offered guidance towards this systematic review.

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Study	Interventions	Number	Mean age, years (SD)	Mean BMI (kg/m ²) (SD)	Female
Anderson- Loftin 2005.[19]	Culturally competent behavioral intervention	49	58.9 (10.1)	35.39 (8.1)	78%
	Traditional diabetes class	48	55.7 (12.1)	35.75 (8.5)	74%
Anton 2011.[20]	Weight loss plus exercise	17	63.7 (4.5)	37.8 (5.5)	100%
	Educational control	17	63.7 (6.7)	35.8 (6.8)	100%
Appel	Remote support	139	55.8 (9.7)	36.0 (4.7)	63.3%
2011.[21]	In-person support	138	53.3 (10.5)	36.8 (5.2)	63.8%
	Educational control	138	52.9 (10.1)	36.8 (5.1)	63.8%
Bennett 2012.[22]	Behavioural weight loss Intervention	180	54.6 (10.8)	37.0(5.0)	71.1%
	Educational control	185	54.7 (11.0)	37.0 (5.2)	65.9%
Delany 2010. [23]	Initial activity and dietary intervention	67	46.1 (6.5)	43.5 (4.8)	88.5%
	Dietary intervention	63	47.5 (6.2)	43.7 (5.9)	
Foster 2009.[24]	Intensive lifestyle intervention	135	61.2 (6.6)	36.8 (5.8)	61.6%
	Diabetes support and education	139	61.3 (6.4)	36.5 (5.7)	56.8%
Foster2 2009.[25]	Portion controlled diet	35	52.1 (7.7)	39.1 (5.5)	74.3%
	Diabetes support and education	34	52.8 (11.2)	38.9 (6.9)	67.7%
Look 2010.[26]	Intensive lifestyle intervention	2570	58.6 (6.8)	35.9 (6.0)	59.3%
	Diabetes support and education	2575	58.9 (6.9)	36.0 (5.8)	59.6%
Luley 2011 [27]	The ABC program	35	57.0 (9.0) 35.3 (5.7)		57%
2011.[27]	Standard care	35	58.0 (7.0)	34.8 (5.9)	46%

Table 1: Interventions and participants' baseline characteristics in each study

Pettman 2009.[28]	Prescriptive group lifestyle education program	103	45.0	36.7 (0.6)	72%
	Educational control	50		36.3 (0.9)	72%
Rock	Low fat	74	37	36.2 (4.3)	51.1%
2014.[29]	diet and exercise counselling				
	Low carbohydrate	77	38.5	36.2 (4.7)	
	diet and exercise counselling				
	Usual care	76	38	36.3 (4.4)	
Snel 2012.[30]	Very low calorie diet and exercise	13	53.0 (2.5)	36.4 (1.1)	38%
	Very low calorie diet	14	56.1 (2.4)	37.9 (1.4)	57%
Villareal 2011.[31]	Weight management programme and exercise training	28	70.0 (4.0)	37.2(5.4)	57%
	Educational control	27	69.4 (4.0)	37.3 (4.7)	67%
Wadden 2011.[32]	Brief lifestyle counselling	131	52.0 (12.2)	38.5 (4.6)	84%
	Enhanced lifestyle counselling	129	51.0 (10.1)	37.8 (4.7)	79.8%
	Standard care	130	51.7 (12.1)	39 (4.8)	75.4%
Wing 2012.[33]	Behavioural weight loss programme	226	53 (11.0)	36 (6.0)	100%
	Structured education program	112	53 (10.0)	36 (5.0)	100%
Wolf 2004 [24]	Case management	73	53.5 (8.6)	37.6 (7.7)	62%
2004.[34]	Standard care	71	53.4 (8.0)	37.5 (6.4)	58%
Wycherley 2010.[35]	High protein diet and resistance-training program	14	56.1 (7.5)	36.6 (5.0)	-
	Standard carbohydrate diet	16		34.8 (4.9)	

Table 2: Risk of bias

Study	Sequence generation	Allocation concealment	Blinding: Participants;	Incomplete data	Selective reporting	Power calculation	Intention to treat analysis	Funding: Conflicting	Comparable at baseline
			Researchers					interests	
Anderson-Loftin 2005.[19]	Low	High	High; Low	Low	Low	Low	Low	Low	High
Anton 2011.[20]	Low	High	High; Low	Low	Low	High	Low	Low	High
Appel 2011.[21]	Low	Low	High; Low	Low	High	Low	Low	Low	High
Bennett 2012.[22]	Low	High	High; High	Low	Low	Low	Low	Low	Low
Delaney 2010.[23]	High	High	High High	Low	Low		Low	Low	Low
Foster 2009.[24]	Low	High	High; Low	Low	Low	Low	High	Low	Low
Foster2 2009.[25]	Low	High	High; High	Low	Low	High	Low	High	Low
Look 2010.[26]	High	High	High; Low	Low	Low	Low	Low	Low	Low
Luley 2011.[27]	High	High	High; High;	Low	Low	Low	Low	High	Low
Pettman 2009.[28]	Low	High	High; High	Low	Low	Low	Low	Low	High
Rock 2014.[29]	Low	Low	High High	Low	Low	Low	Low	Low	Low
Snel 2012.[30]	High	High	High; High	High	High	Low	High	Low	Low
Villareal 2011.[31]	High	High	High; Low	Low	Low	Low	Low	Low	Low
Wadden 2011.[32]	Low	High	High; High	Low	Low	Low	Low	Low	Low
Wing 2012.[33]	High	Low	High; Low	Low	Low	Low	Low	Low	Low

Wolf 2004.[34]	High	High	High; High	Low	High	Low	Low	Low	Low
Wycherley 2010.[35]	High	High	High; High	Low	Low	High	Low	Low	Low