

Pathological eating behaviours and risk of retinopathy in diabetes: a systematic review and meta-analysis

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Abstract (249/250)

Background: Diabetes mellitus can cause several long-term macrovascular and microvascular complications including nephropathy, neuropathy, and retinopathy (DR). Several studies have reported positive associations between eating pathologies and DR; however, these studies have not been aggregated and sub-grouped into type of pathological eating behaviour, and the differences in risk according to type of eating behaviour is unknown. The aim of this review, therefore, was to aggregate risks of DR in populations with and without pathological eating behaviours, stratified according to eating behaviour.

Methods: A systematic review and meta-analysis was conducted. Major databases and grey literature were search from inception until 1/6/2021. Studies reporting the prevalence of pathological eating behaviours (against a control group with no pathological eating behaviours) in diabetic people with and without DR were included. Odds ratios were calculated from primary data.

Results: Seven studies with eight independent outcomes with a total of 1162 participants were included. The odds ratio of DR in the total pooled analysis was 2.94 (95%CI 1.86-4.64; $p < 0.001$; $I^2 = 29.59$). Two types of eating behaviour yielded enough data for sub-group analysis. Eating disorder not otherwise specified yielded an odds ratio of 2.73 (95%CI 1.81-4.10; $p < 0.001$; $I^2 = 0.00$), and binge eating disorder yielded an non-significant odds ratio of 0.92 (95%CI 0.31-2.77; $p = 0.887$; $I^2 = 0.00$).

Discussion: The likelihood of DR increases almost three times in the presence of pathological eating behaviours. More studies are required to confirm this in clinical populations stratified by eating disorder. Practitioners working with people with diabetes should closely monitor eating behaviours to preclude this risk.

Keywords: diabetes; diabetic retinopathy; eating disorder; disordered eating

Declarations

Funding: No funding was received for this study

Conflict of interest: All authors declare no conflict of interest.

Availability of data and material: All data from this study are available from pre-published papers.

Ethics approval: As this was a review on already published papers, no ethical approval was required.

Introduction

Diabetes mellitus is a condition characterised by elevated blood glucose concentrations, which can lead to tissue damage in several parts of the body, including the eyes, heart, and feet [1]. The most common eye disease amongst people with diabetes is diabetic retinopathy (DR) [2], a condition in which microvascular changes in the retina can cause visual impairment, and if left untreated, blindness [3]. Although it has been reported that almost all people with diabetes are likely to suffer with some form of DR over a 20-year period, with 10 year incidence rates being reported as 48% and 28% for type I and II respectively [4], not all cases may lead to registrable visual impairment [3]. Indeed, the presence or absence of several factors can regress or accelerate the progression of DR. For example, levels of physical activity have been shown to be independently negatively associated with DR progression, and sedentary behaviour has been shown to be independently positively correlated [5]. Furthermore, several co-morbidities have been associated with the risk of any type of DR in diabetic people, for example, several large cohort studies have shown that systolic blood pressure is positively associated with a higher risk of DR [6–9].

Another important positive association reported in the literature is between pathological eating behaviours and DR risk. A recent study found that food addiction (characterised as a behavioural pattern, similar to other substance addictions, where an individual cannot control food consumption rationally, and generally consumes highly palatable foods) was much higher in diabetic populations with DR than with no DR [10]. Several studies have found associations between eating disorders and DR risk, especially bulimia nervosa [11, 12]. Bulimia nervosa is characterised by periods of binge eating (often with a feeling of loss of control), followed by purging behaviours to get rid of these calories and prevent weight gain, by means of self-induced vomiting, the use of laxatives, or diuretics [13].

There are few systematic reviews that aggregate and quantify the risk of DR in the presence (versus absence) of pathological eating behaviours. The most recent, conducted in 2002, reported a four-fold increase in DR risk in type 1 people with diabetes who have an eating disorder [14], however the data were not sub-grouped according to type of eating disorder, and did not include any studies that examined type 2 diabetes. Furthermore, binge eating disorder (BED; a condition where a person

frequently consumes a large amount of food over discrete periods and feels a lack of control over eating during the episode [13]), was not a recognised eating disorder at the time of the review, and therefore was not included in its analyses. The aggregated risk of DR in people with BED is therefore currently unknown. Primary studies examining associations between BED and DR have, to date, yielded non-significant results. It is the aim of this review, therefore, to examine and aggregate the current literature regarding pathological eating behaviours and DR risk in people with diabetes, stratified by pathological eating behaviour is appropriate. This review has the potential to inform practitioners working with (a) people with diabetes, and/or (b) people with pathological eating behaviours about the respective risks of DR.

Methods

Protocol and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[15], and was registered on 28th May 2021 with the international prospective register of systematic reviews (PROSPERO: protocol ID CRD42021257761). Note that all deviations from the published protocol are described and justified in Supplementary Table 1.

Search strategy

Databases were searched from inception to 1/6/2021 including Pubmed, Embase, Cinahl, PSYCinfo, Cochrane library of systematic reviews, and Opengrey, using the following search terms: ((eating disorder OR anorexia OR bulimia OR EDNOS OR anorexia nervosa OR bulimia nervosa OR binge eating disorder OR eating disorder not otherwise specified) AND (diabetic retinopathy OR diabetic macular edema OR diabetic macular oedema OR proliferative diabetic retinopathy OR proliferative retinopathy OR sight threatening retinopathy OR retinopathy)). No other limiters were applied. Note that the full search strategy for each database can be found in Supplementary Table 2. Results of the searches were imported in a bibliographic database and duplicates removed automatically. Titles and abstracts of the studies obtained were independently screened for inclusion by two authors. Following title and abstract screening, the full texts of all potentially eligible papers were reviewed independently by two reviewers (MT,EI), with senior reviewer (SP) mediating any disputes.

Inclusion criteria

To be eligible for inclusion, studies had to include the following:

1. Populations with diabetes reporting prevalence/incidence rates of DR versus no DR, and pathological eating behaviours versus no pathological eating behaviours.

2. All types of study design were considered if they reported the above information
3. Written in English, French, Spanish, or Italian

Data extraction

Data were extracted by two reviewers (MT; RD) and included: first author; study title; publication date; country; study type; type of diabetes; type of pathological eating behaviour; type of DR; method of DR diagnosis/screening; total participants; total participants with and without DR with and without eating disorders; demographic variables.

Quality assessment

Risk of bias was respectively assessed by two independent researchers (MT; RD) using the Joanna Briggs Institute (JBI) critical appraisal checklists for (a) cohort studies [16] (b) case-control studies [17], and (c) analytical cross-sectional studies [18]. Any discrepancies over the final risk of bias verdict were solved by consensus, with involvement of a third review author (SP) where necessary.

Statistical analysis

A random-effects meta-analysis was conducted using the DerSimonian and Laird method, with studies weighted according to the inverse variance, using Comprehensive Meta-Analysis [19]. The meta-analysis was conducted using the following steps:

(1) Odds ratios (ORs) were calculated from the number of participants with (a) no indicated pathological eating behaviours and no DR; (b) no indicated pathological eating behaviours and DR; (c) indicated pathological eating behaviours and no DR, and (d) indicated pathological eating behaviours and DR.

(2) Heterogeneity between studies was assessed using the I^2 statistic, with <50% considered low heterogeneity, 50-75% considered moderate heterogeneity, and >75% considered high heterogeneity [20].

(3) Publication bias was assessed with a visual inspection of funnel plots and with the Egger bias test [21]. As per the recommendations by Sterne et al [22], the Egger test was only conducted if the number of studies in each analysis exceeded ten. If an analysis had fewer than 10 studies, visual inspection of the funnel plot was conducted. Furthermore, sensitivity analyses were conducted to assess the robustness of analyses through the one study removed method.

(4) All analyses were stratified according to type of eating disorder, if applicable. If a study does not indicate a specific type of eating disorder (for example, using a questionnaire such as the EAT-26), these were categorized as eating disorder not otherwise specified (EDNOS).

(5) The robustness of results was determined via the use of the one-study removed method.

(6) To further determine the credibility of evidence, prediction intervals (PIs) for all ORs with more than three studies were also calculated.

Certainty of evidence

To ascertain the certainty of the evidence, the Grading of Recommendations, Assessment, Development and Evaluations [23] (GRADE) framework was used.

Results

Out of 126 hits initially identified, after automatic duplicate removal, 87 studies were assessed at title/abstract level. After full text review – seven studies [10, 24–29], with eight independent outcomes were included in the meta-analysis, with a total of 1162 participants. The flow diagram of search, selection and inclusion process is fully reported in Figure 1. Table 1 shows descriptive statistics of included studies and Supplementary Table 3 shows a list of full text studies that were excluded, with justifications. Four outcomes were classified as assessing DR risk and EDNOS [10, 24, 25, 27], two outcomes examined DR risk and BED [26, 29], one study pooled both anorexia and bulimia nervosa [28], and one outcome examined bulimia nervosa exclusively [29]. All included studies were of sufficiently low risk of bias according to the JBI tools and were included.

Meta-analysis

Overall, the pooled random effects model yielded an OR of 2.94 with low levels of heterogeneity (95% CI 1.86-4.64; $p < 0.001$; $PI = 1.05-8.21$ $I^2 = 29.59$), see Figure 2 and Table 2. As there were fewer than 10 studies included in the analysis, visual inspection of the funnel plot showed no evidence of publication bias (see Supplementary Figure 1). The removal of any one study did not change the direction or magnitude of results (see Supplementary Figure 2), and the PI did not exclude the null hypothesis. This evidence has been classified as ‘high’ level of certainty according to the GRADE criteria.

Sub-group analysis

Two types of eating disorders had more than one outcome and were therefore included in the sub-group analyses of EDNOS and BED. The EDNOS sub-group yielded a significant OR of 2.73 (95% CI 1.81-4.10; $p < 0.001$; $PI = 1.81-4.10$; $I^2 = 0.00$), and the BED yielded a non-significant OR of 0.92 (95% CI 0.31-2.77; $p = 0.887$; $I^2 = 0.00$), see Figure 3 and Table 2. The magnitude and significance of results for both EDNOS and BED did not change with one-study removed (see Supplementary Figures 3 and 4), and the PI in the EDNOS group did not exclude the null hypothesis. The EDNOS subgroup was classified as ‘high’ certainty of evidence according to the GRADE criteria. Due to the inconsistency of included studies and the general lack of studies

(and hence unknown likelihood of publication bias), the BED subgroup has been classified as 'low' certainty of evidence.

Discussion

The current systematic review and meta-analysis, including seven primary studies with eight independent outcomes, examines associations between the presence (versus absence) of pathological eating behaviours and the risk of DR. This review also attempts to stratify analyses according to the type of eating pathology.

The pooled results showed that the likelihood of DR is almost three-fold higher (OR=2.94) in the presence of pathological eating behaviours. A review conducted in 2002 yielded an OR of 4.84 [14], which is much higher than this study's estimate. One possible reason for this is we were unable to verify the underlying data from some studies included in the 2002 review (i.e., one included study was a 'personal communication'), and therefore were not included in this analysis. In addition, this review includes three studies in addition to those that were meta-analysed in 2002. The most likely mechanism behind the increased DR risk with pathological eating behaviours is poor glycaemic control that has been linked to higher prevalence of diabetic complications. Indeed, binge and purging behaviour has widely been associated with changes in glycaemic control [14]. Further, it has been widely reported that poor insulin control amongst people with Type I and Type II diabetes is associated with increased risk of several microvascular complications, including earlier presentation of diabetic retinopathy [30, 31].

Two types of pathological eating yielded enough studies to be included in sub-group analyses: EDNOS and BED. The association between indicated EDNOS and DR risk yielded an OR of 2.73. This was slightly lower than the pooled OR because of the omission of two studies examined both AN and BN, and another than measured BN exclusively, that had much higher ORs. This result is in broad agreement with the literature. Indeed, it has been reported that people with BN have much higher prevalence of DR than other eating disorders [11]. Our results show, however, that unspecified, pathological eating behaviours (such as food addiction and weight-related insulin omission) also yield significant increases in DR risk and should be monitored in people with both Type I and Type II diabetes. With regards to BED, this study found no significant association between BED and DR risk, although the

certainty of evidence was graded as low, mainly due to a paucity of studies. One possible reason for this non-significant result could be because BED exerts a lesser effect on glycaemic control than other pathological eating behaviours that include purging behaviors, like BN or weight-related insulin omission [26, 32]. Indeed, one of the included studies examining BED found no significant differences in several biochemical glycaemic parameters (including HbA1c and fasting plasma) glucose in the BED group versus control [26]. The low certainty of this evidence warrants further primary studies to confirm or refute this study's findings.

Strengths and limitations: This study found significant associations between pathological eating behaviours and risk of DR, with a high degree of certainty. The findings of this review should be considered within its limitations. Firstly, several of the tools used for measuring pathological eating behaviours were self-report questionnaires, which increases the chances of false-negative results, possibly because of the secretive nature of sufferers of eating disorders [33] – future studies should aim to use clinician diagnosed eating disorders wherever possible. Secondly, all but one study was either cross-sectional or case-control in study design, making the direction of correlation (and therefore causation) difficult to determine. Thirdly, all but one study failed to stratify results according to type of DR (e.g., sight-threatening versus non sight threatening, or non-proliferative versus proliferative), therefore the extent in which pathological eating has in the progression of DR is unknown. Furthermore, due to the paucity of studies, the results were not stratified according to the type of diabetes, therefore the effects according to diabetes type is unknown. Lastly, both the number of studies and number of participants was low – primary studies examining pathological eating behaviours and complications of diabetes especially DR are warranted.

Conclusion

The presence of pathological eating behaviours increases the risk of diabetic retinopathy in people with diabetes by around 3 times. Practitioners working with people with diabetes should closely monitor eating behaviours so that any pathological eating behaviour can be addressed swiftly to reduce the risk of DR and consequent blindness if not treated. Furthermore, more primary studies examining DR risk and pathological eating behaviours are required, particularly in populations with clinical eating disorders such as AN, BN, and BED.

References

1. diabetes.co.uk (2020) Dry mouth and diabetes. <https://www.diabetes.co.uk/diabetes-complications/dry-mouth.html>. Accessed 28 Jul 2020
2. Hirai FE, Tielsch JM, Klein BE, Klein R (2011) Ten-year change in vision-related quality of life in type 1 diabetes: Wisconsin epidemiologic study of diabetic retinopathy. *Ophthalmology* 118:353–358
3. Forbes JM, Cooper ME (2013) Mechanisms of Diabetic Complications. *Physiological Reviews* 93:137–188. <https://doi.org/10.1152/physrev.00045.2011>
4. Mathur R, Bhaskaran K, Edwards E, et al (2017) Population trends in the 10-year incidence and prevalence of diabetic retinopathy in the UK: a cohort study in the Clinical Practice Research Datalink 2004–2014. *BMJ Open* 7:e014444. <https://doi.org/10.1136/bmjopen-2016-014444>
5. Ren C, Liu W, Li J, et al (2019) Physical activity and risk of diabetic retinopathy: a systematic review and meta-analysis. *Acta diabetologica* 56:823–837
6. Kim TK, Won JY, Shin JA, et al (2016) The association of metabolic syndrome with diabetic retinopathy: the Korean national health and nutrition examination survey 2008–2012. *PloS one* 11:e0157006
7. Tapp RJ, Shaw JE, Harper CA, et al (2003) The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes care* 26:1731–1737
8. Zhang X, Saaddine JB, Chou C-F, et al (2010) Prevalence of diabetic retinopathy in the United States, 2005–2008. *Jama* 304:649–656
9. Kostev K, Rathmann W (2013) Diabetic retinopathy at diagnosis of type 2 diabetes in the UK: a database analysis. *Diabetologia* 56:109–111
10. Nicolau J, Romerosa JM, Rodríguez I, et al (2020) Associations of food addiction with metabolic control, medical complications and depression among patients with type 2 diabetes. *Acta diabetologica* 57:1093–1100
11. Takii M, Uchigata Y, Nozaki T, et al (2002) Classification of type 1 diabetic females with bulimia nervosa into subgroups according to purging behavior. *Diabetes Care* 25:1571–1575
12. Rodin G, Olmsted MP, Rydall AC, et al (2002) Eating disorders in young women with type 1 diabetes mellitus. *Journal of psychosomatic research* 53:943–949
13. American Psychiatric Association (2013) DSM-V
14. Nielsen S (2002) Eating disorders in females with type 1 diabetes: an update of a meta-analysis. *European Eating Disorders Review: The Professional Journal of the Eating Disorders Association* 10:241–254

15. Page MJ, McKenzie JE, Bossuyt PM, et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71.
<https://doi.org/10.1136/bmj.n71>
16. Joanna Briggs Institute Checklist for Cohort Studies.
https://jbi.global/sites/default/files/2021-03/Checklist_for_Cohort_Studies.docx.
Accessed 24 Jun 2021
17. Joanna Briggs Institute Checklist for Case Control Studies.
https://jbi.global/sites/default/files/2021-03/Checklist_for_Case_Control_Studies.docx. Accessed 24 Jun 2021
18. Joanna Briggs Institute Checklist for Analytical Cross Sectional Studies.
https://jbi.global/sites/default/files/2021-03/Checklist_for_Analytical_Cross_Sectional_Studies.docx. Accessed 24 Jun 2021
19. Borenstein M, Hedges L, Higgins J, Rothstein H (2013) *Comprehensive Meta Analysis*. Biostat, Englewood, NJ
20. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. *Statistics in medicine* 21:1539–1558
21. Egger M, Smith GD, Schneider M, Minder C (1997) Bias in meta - analysis detected by a simple, graphical test. *BMJ : British Medical Journal*.
<https://doi.org/10.1136/bmj.315.7109.629>
22. Sterne JA, Egger M, Moher D (2008) Addressing reporting biases. *Cochrane handbook for systematic reviews of interventions: Cochrane book series* 297–333
23. Guyatt GH, Oxman AD, Vist GE, et al (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *Bmj* 336:924–926
24. Rydall AC, Rodin GM, Olmsted MP, et al (1997) Disordered eating behavior and microvascular complications in young women with insulin-dependent diabetes mellitus. *New England Journal of Medicine* 336:1849–1854
25. Cantwell R, Steel JM (1996) Screening for eating disorders in diabetes mellitus. *Journal of psychosomatic Research* 40:15–20
26. Nicolau J, Simó R, Sanchís P, et al (2015) Eating disorders are frequent among type 2 diabetic patients and are associated with worse metabolic and psychological outcomes: results from a cross-sectional study in primary and secondary care settings. *Acta diabetologica* 52:1037–1044
27. Polonsky WH, Anderson BJ, Lohrer PA, et al (1994) Insulin omission in women with IDDM. *Diabetes care* 17:1178–1185
28. Colas C (1991) Eating disorders and retinal lesions in type 1 (insulin-dependent) diabetic women. *Diabetologia* 34:288–288

29. Takii M, Komaki G, Uchigata Y, et al (1999) Differences between bulimia nervosa and binge-eating disorder in females with type 1 diabetes: the important role of insulin omission. *Journal of Psychosomatic Research* 47:221–231
30. Goldstein DE, Blinder KJ, Ide CH, et al (1993) Glycemic Control and Development of Retinopathy in Youth-onset Insulin-dependent Diabetes Mellitus: Results of a 12-year Longitudinal Study. *Ophthalmology* 100:1125–1132. [https://doi.org/10.1016/S0161-6420\(93\)31516-2](https://doi.org/10.1016/S0161-6420(93)31516-2)
31. Henricsson M, Nilsson A, Janzon L, Groop L (1997) The effect of glycaemic control and the introduction of insulin therapy on retinopathy in non-insulin-dependent diabetes mellitus. *Diabetic medicine* 14:123–131
32. Çelik S, Kayar Y, Önem Akçakaya R, et al (2015) Correlation of binge eating disorder with level of depression and glycemic control in type 2 diabetes mellitus patients. *General Hospital Psychiatry* 37:116–119. <https://doi.org/10.1016/j.genhosppsych.2014.11.012>
33. Fairburn CG, Beglin SJ (1994) Assessment of eating disorders: Interview or self-report questionnaire? *International journal of eating disorders* 16:363–370

Tables and Figures

Table 1: Descriptive characteristics of included studies

Authors	Study Design	Country	Type of diabetes	Type of eating pathology	Eating pathology measurement	Diabetic retinopathy measurement	Total participants	Mean age (SD)	Follow-up (SD)	Duration of diabetes	Conflict of interest
Rydall et al. [24]	Cohort	Canada	T1DM	'Highly and moderately disordered eating'	Diagnostic Survey for Eating Disorders.	Indirect ophthalmoscopy and slit-lamp biomicroscopy (after pupillary dilation) and grading of seven-field stereoscopic color fundus photographs	71	NR	4.4 (0.3) years	NR	NR
Cantwell et al. [25]	Cross-sectional	UK	T1DM	Indicated eating disorder	>18 or above on the EAT-40	Interview	48	High EAT= 24.4 (4.4); Low EAT= 22.5 (3.9)	NA	high EAT=13.1 (6.2); low EAT=9.8(5.0)	NR
Nicolau et al. [26]	Cross-sectional	Spain	T2DM	BED	EAT-26 and QEWP-R	Clinical report and self-report	306	No BED =63.3 (10.3) BED= 57.5 (11.1)	NA	No ED=12.1 (9.6); BED=8.5(6.1)	Reported - none declared
Nicolau et al. [10]	Cross-sectional	Spain	T2DM	Food addiction	YFAS 2.0	Clinical interview	300	63.8 (11.8)	NA	12 (9.4)	Reported - none declared
Polonsky et al. [27]	Cross-sectional	USA	T1DM	Weight-related insulin omission	BULIT-R	Clinical chart	282	NR	NA	NR	NR
Colas et al. [28]	Case-control	France	T1DM	AN and BN	NR (clinical patients)	Retinal angiography	58	AN and BN= 26.2 (0.9) No AN or BN= 27.8 (0.9)	NA	AN and BN= 9.2 (0.7) No AN or BN= 10.9 (1.3)	NR
Takii et al. [29]	Case-control	Japan	T1DM	BN	Clinician interview DSM-IV criteria	Medical records	54	BN=23.2 (4.4); Control: 23.9 (3.8)	NA	BN=8.7 (5.7); Control=7.9 (5.5)	NR
		Japan	T1DM	BED			43	BED= 24.8 (7.5) Control= 23.9 (3.8)	NA	BED= 4.7 (1.8); Control= 7.9 (5.5)	

SD= standard deviation; T1DM=Type 1 diabetes mellitus; T2DM=Type 2 diabetes mellitus; BED=binge eating disorder; AN=anorexia nervosa; BN=bulimia nervosa; EAT 40= Eating attitudes test 40; EAT 26=eating attitudes test 26; QEWP-R=Questionnaire of Eating and Weight Patterns-Revised; YFAS 2.0= Yale Food Addiction Scale 2.0; BULIT-R= Bulimia Test-Revised; NR=not reported; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders IV.

Table 2: Meta-analysis results

Study details			Meta-analysis			Heterogeneity
Type of eating pathology	<i>n</i> studies (<i>k</i> outcomes)	<i>n</i> participants	Odds ratio (95% CI)	<i>p</i> -value	Prediction interval	<i>I</i> ²
EDNOS	4(4)	701	2.73 (1.81-4.10)	<0.001	1.81-4.10	0.00
BED	2 (2)	349	0.92 (0.31-2.77)	0.887	NA	0.00
BN	1(1)	54	10.29 (1.96-54.14)	0.010	NA	0.00
AN and BN	1 (1)	58	6.27 (1.95-20.22)	<0.001	NA	0.00
Total pooled	7 (8)	1162	2.94 (1.86-4.64)	<0.001	1.05-8.21	29.59

EDNOS=eating disorder not-otherwise-specified; BED=binge eating disorder; BN=bulimia nervosa; AN=anorexia nervosa

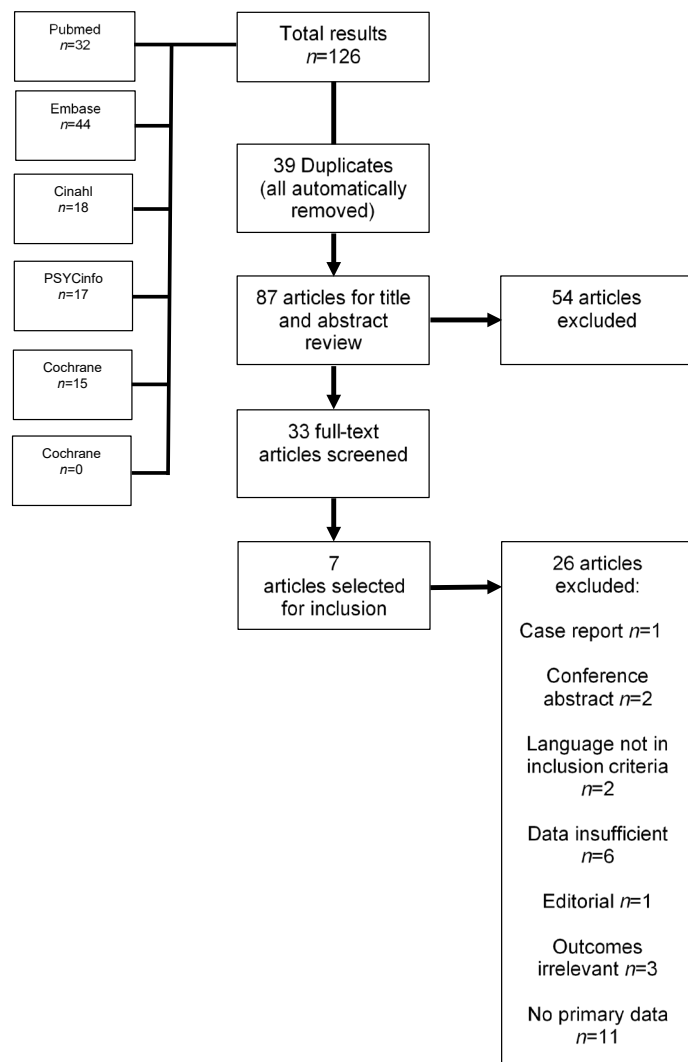


Figure 1: PRISMA flowchart showing included studies

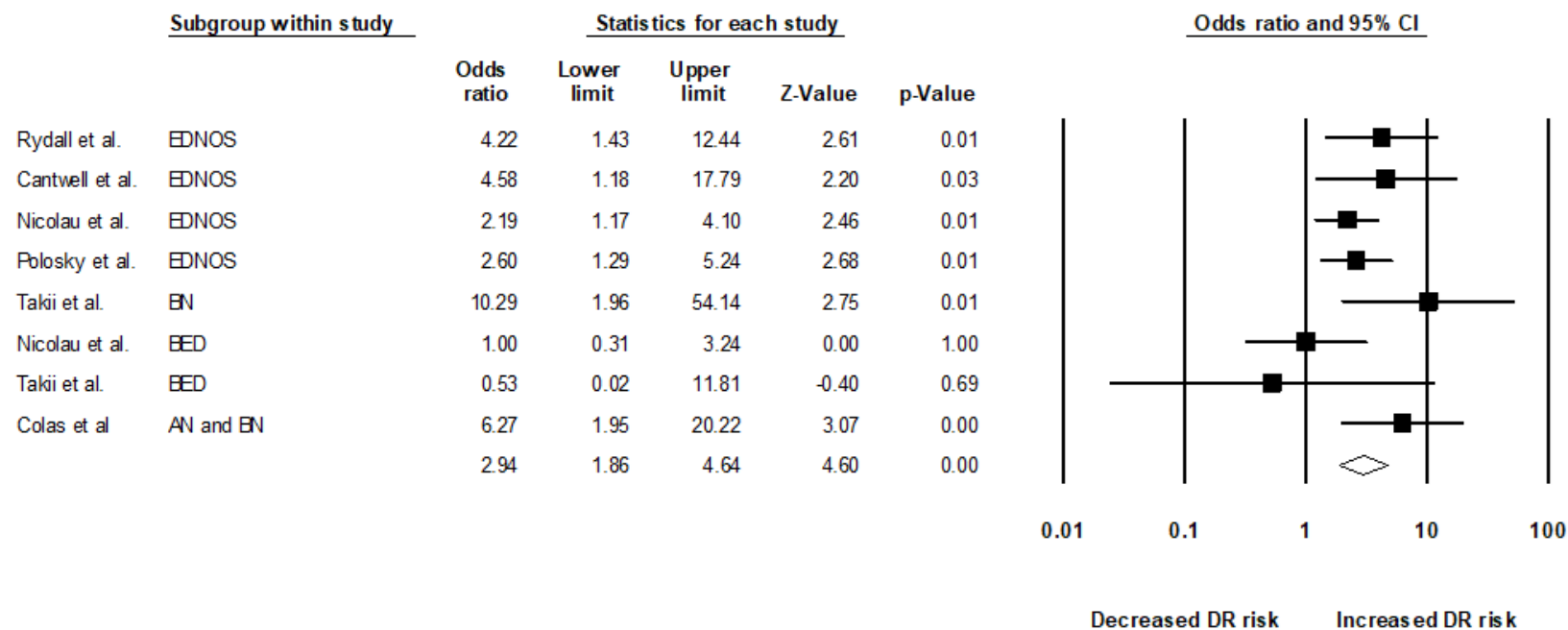


Figure 2: Odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without pathological eating behaviors. Note EDNOS=eating disorder not otherwise specified; BN=bulimia nervosa; AN=anorexia nervosa; BED=binge eating disorder; DR=diabetic retinopathy

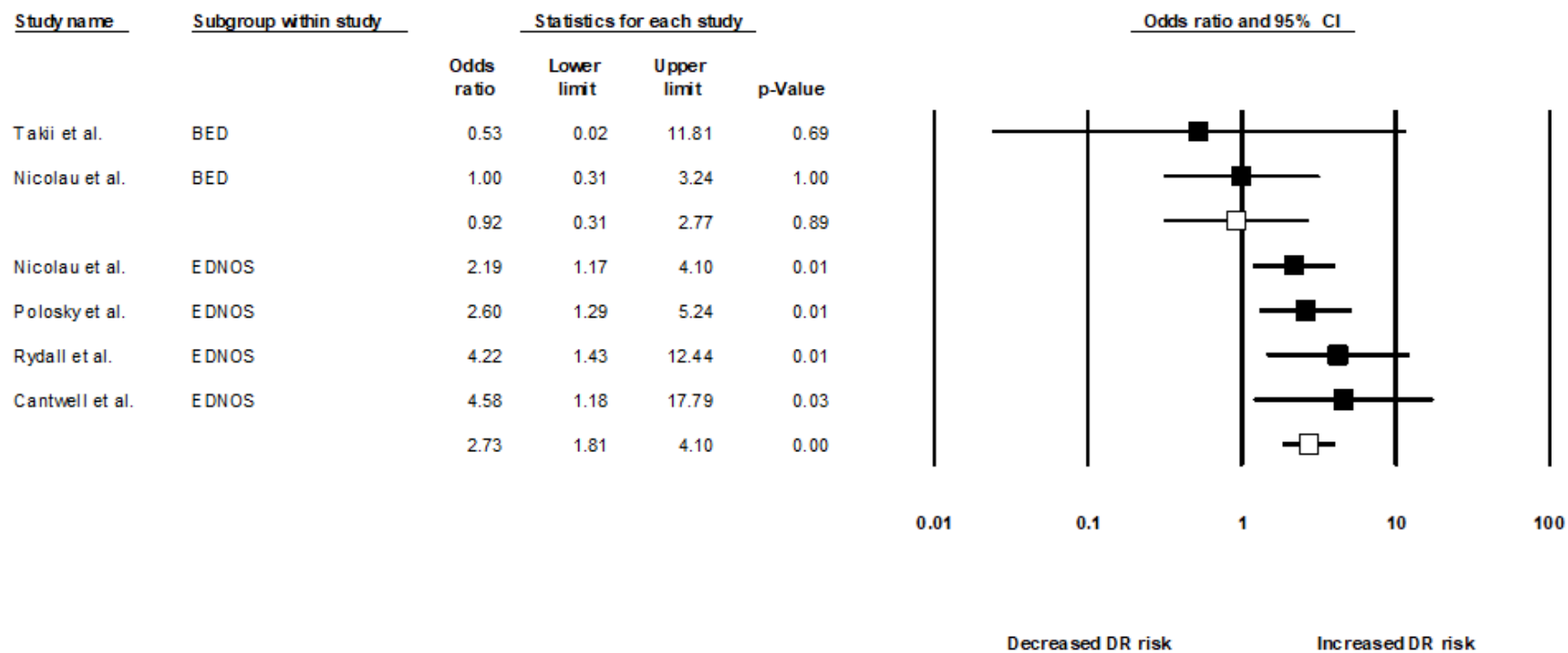


Figure 3: Odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without pathological eating behaviors, stratified by eating disorder not-otherwise-specified and binge eating disorder. Note EDNOS=eating disorder not otherwise specified; BED=binge eating disorder; DR=diabetic retinopathy.

Supplementary Tables and Figures

Supplementary Table 1: Justifications of deviations from the pre-published protocol

Type of change	Justification
Inclusion of studies changed from eating disorders to pathological eating behaviours	After initial searches, it was clear that there was a paucity of studies that examined eating disorders, so the inclusion criteria was broadened to include all types of pathological eating behaviour.

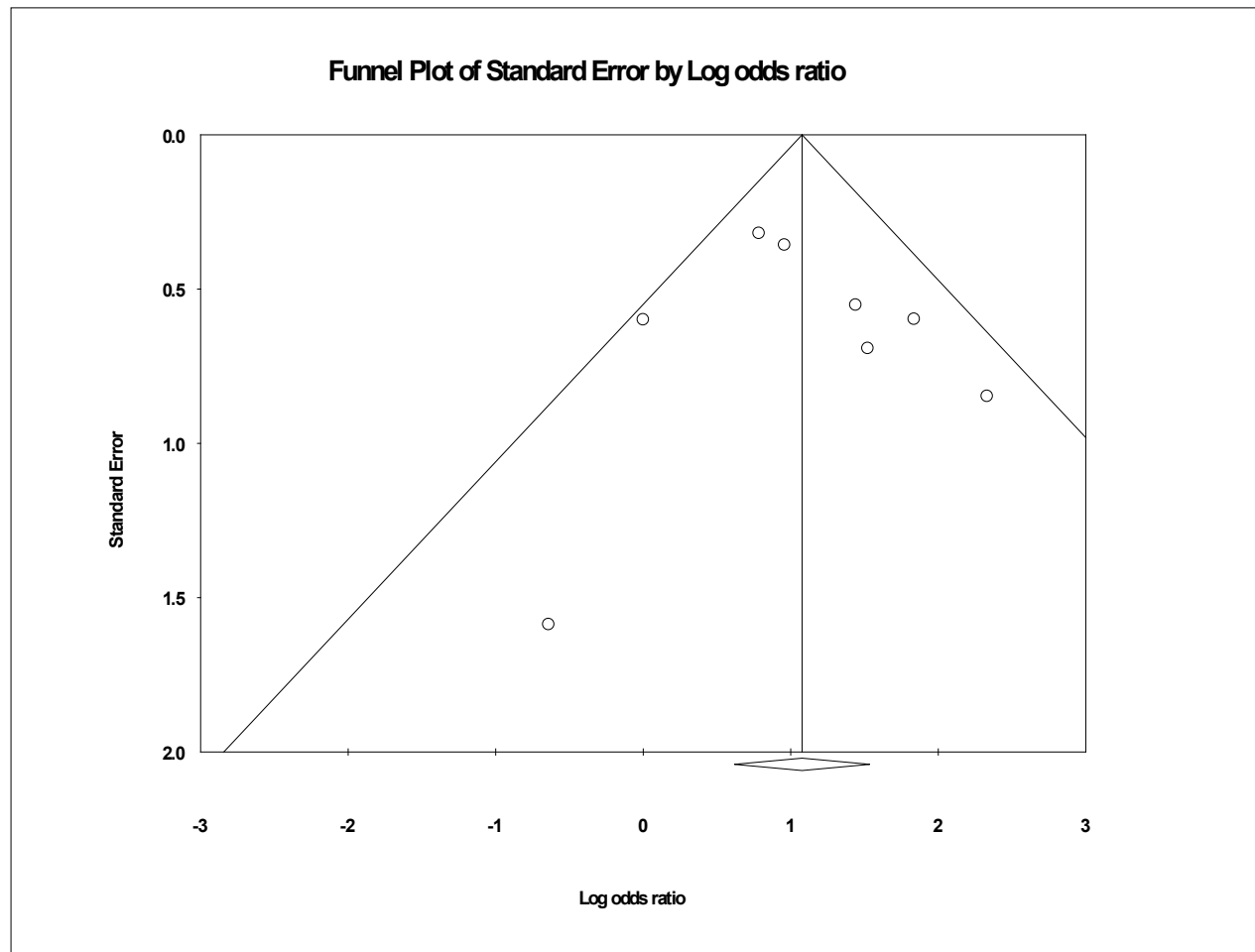
Supplementary Table 2: Search strategy

Database	Search terms
PubMed	(eating disorder[Title/Abstract] OR anorexia[Title/Abstract] OR bulimia[Title/Abstract] OR EDNOS[Title/Abstract] OR anorexia nervosa[Title/Abstract] OR bulimia nervosa[Title/Abstract] OR binge eating disorder[Title/Abstract] OR 'eating disorder not otherwise specified'[Title/Abstract]) AND (diabetic retinopathy[Title/Abstract] OR diabetic macular edema[Title/Abstract] OR diabetic macular oedema[Title/Abstract] OR proliferative diabetic retinopathy[Title/Abstract] OR proliferative retinopathy[Title/Abstract] OR sight threatening retinopathy[Title/Abstract] OR retinopathy[Title/Abstract])
Embase	(((eating disorder or anorexia or bulimia or EDNOS or anorexia nervosa or bulimia nervosa or binge eating disorder or eating disorder) not otherwise specified) and (diabetic retinopathy or diabetic macular edema or diabetic macular oedema or proliferative diabetic retinopathy or proliferative retinopathy or sight threatening retinopathy or retinopathy)).ab,ti.
Cinahl, PsycInfo, Cochrane, and Opengrey	(eating disorder OR anorexia OR bulimia OR EDNOS OR anorexia nervosa OR bulimia nervosa OR binge eating disorder OR eating disorder not otherwise specified) AND (diabetic retinopathy OR diabetic macular edema OR diabetic macular oedema OR proliferative diabetic retinopathy OR proliferative retinopathy OR sight threatening retinopathy OR retinopathy)

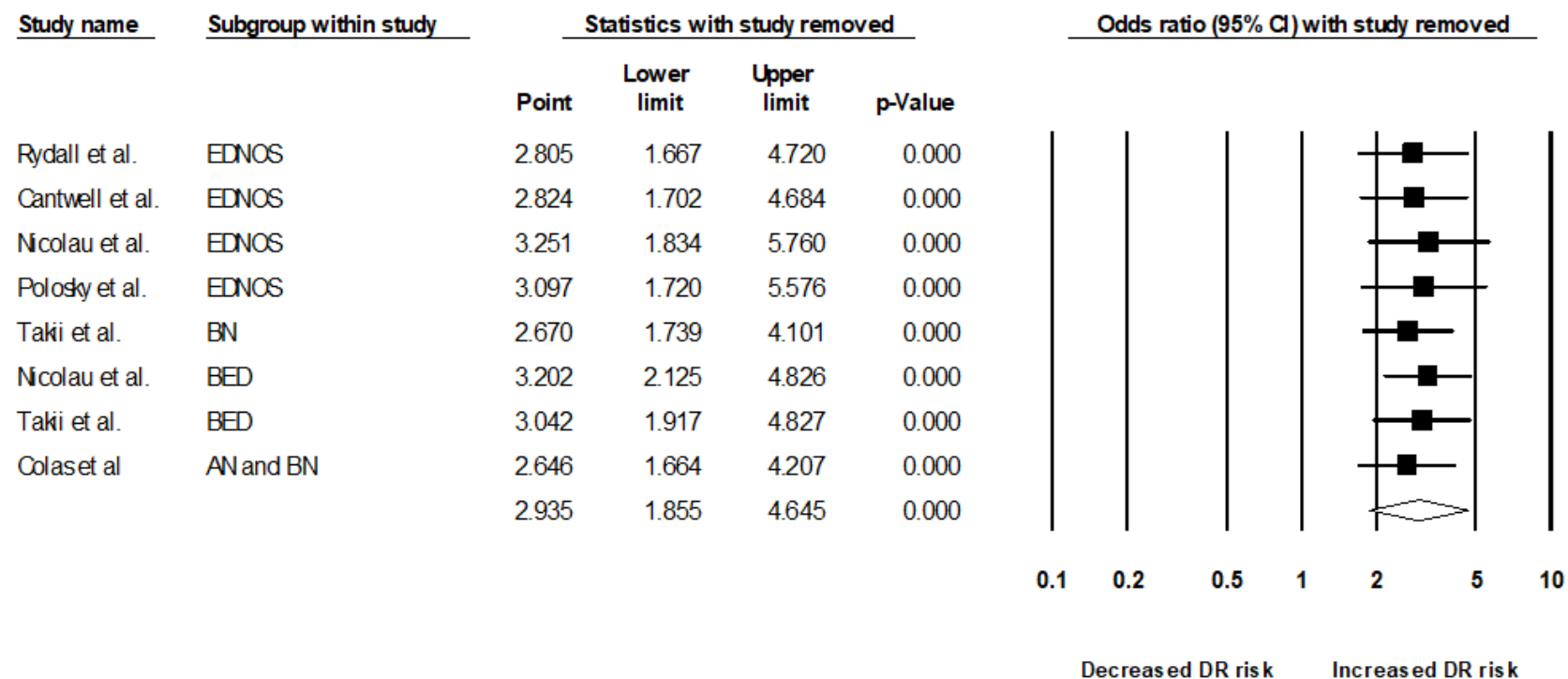
Supplementary Table 3: List of excluded studies with justifications

Author(s)	Title	Reason for exclusion
Herpertz et al.	Eating disorders and diabetes mellitus.	Article in German
Bernardczyk-Meller et al.	Disadvantageous course of ophthalmological changes in young women with long-lasting diabetes mellitus followed by the symptoms of anorexia nervosa	Article in Polish
Brown and Mehler	Anorexia nervosa complicated by diabetes mellitus: the case for permissive hyperglycemia.	Case report
Bergman and D'Emden	Eating disorders	Conference abstract
Pieper and Freitas	The impact of education in the prevention of eating disorders in patients with diabetes and their families	Conference abstract
Scheuing et al.	Clinical characteristics and outcome of 467 patients with a clinically recognized eating disorder identified among 52,215 patients with type 1 diabetes: a multicenter german/austrian study.	Data insufficient
Steel et al.	Abnormal eating attitudes in young insulin-dependent diabetics.	Data insufficient
Takii et al.	The duration of severe insulin omission is the factor most closely associated with the microvascular complications of Type 1 diabetic females with clinical eating disorders.	Data insufficient
Philpot	Eating disorders in young people with diabetes: Development, diagnosis and management.	Editorial - no primary data
Tamburrino and McGinnis	Anorexia nervosa. A review.	No DR
Gonzalez-Cantu	Eating behaviors and emotional distress are predicted by treatment and adverse outcome in patients with type 2 diabetes.	No ED screen
Krochik	Diabetes mellitus tipo 1 en niños y adolescentes: Factor de riesgo para trastornos de la conducta alimentaria? = Diabetes Mellitus Type 1 in children and adolescents: Risk factor for eating disorders?	Data insufficient
Steel et al.	Clinically apparent eating disorders in young diabetic women: associations with painful neuropathy and other complications.	No non-ED control group
Takii et al.	Classification of type 1 diabetic females with bulimia nervosa into subgroups according to purging behavior.	No non-ED control group
Delhayé et al.	Diabète insulino-dépendant et troubles des conduites alimentaires: Quels progrès? = Insulin-dependent diabetes mellitus and eating disorders: A review	No primary data

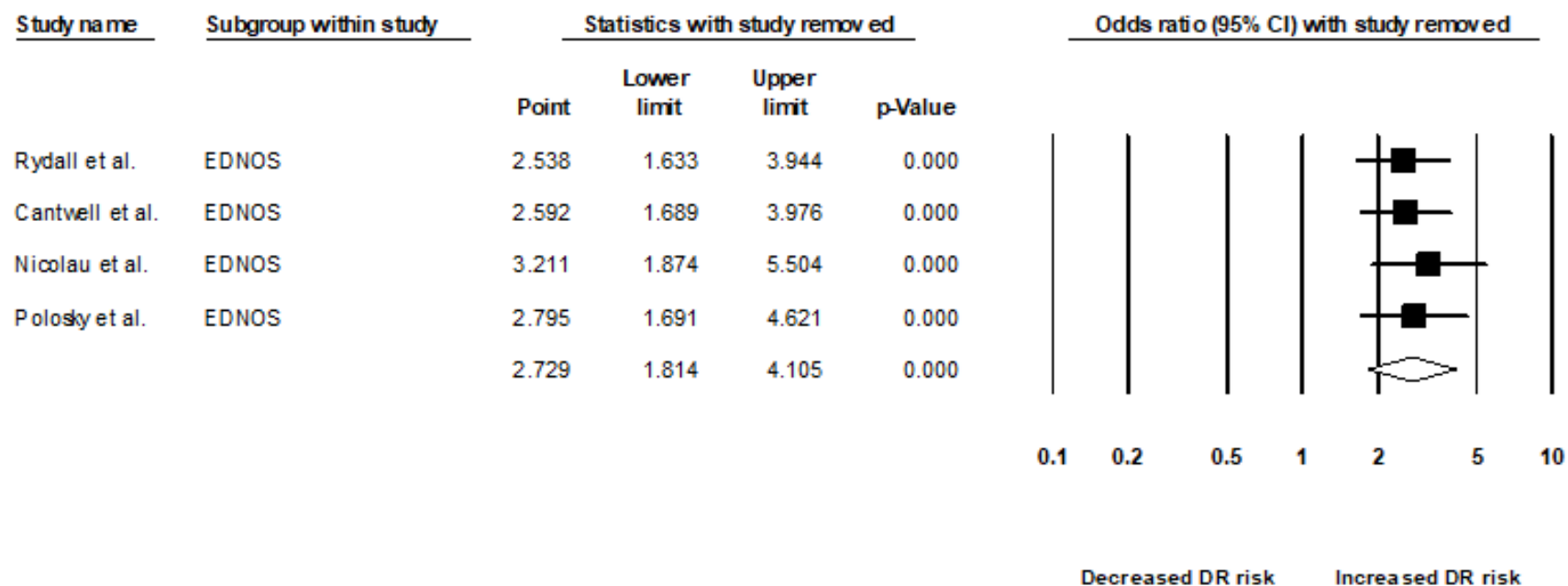
Geisbusch and Buhren	Eating disorders with diabetes mellitus	No primary data
Goebel-Fabbri et al.	Identification and treatment of eating disorders in women with type 1 diabetes mellitus.	No primary data
Kelly et al.	Disordered eating behaviors in youth with type 1 diabetes.	No primary data
Lamisse	Frequency and severity of eating disorders in young diabetics of type 1 diabetes mellitus: Review of literature	No primary data
Maronian et al.	Troubles DSMâ€“IV, l'equilibre m'etabolique et complications somatiques dans le diab'ete insulino-d'ependant de l'enfant et de l'adolescent = DSMâ€“IV disorders, metabolic control and somatic complications in insulin-dependent diabetes mellitus of child and adolescent	No primary data
Grethe and Soren	Eating disorder and type 1 diabetes: Overview and summing-up	No primary data
Nissim et al.	[Eating disturbances in adolescent girls with type 1 diabetes mellitus].	No primary data
Racicka and Brynska	Eating Disorders in children and adolescents with Type 1 and Type 2 Diabetes: prevalence, risk factors, warning signs.	No primary data
Rodin, Gary et al.	Eating disorders in young women with type 1 diabetes mellitus.	No primary data
Nielsen, Soren	Eating disorders in females with type 1 diabetes: An update of a meta-analysis	No primary data - MT to check references
Trial number: NCT04837989	Effectiveness of the Diabetes Body Project Among Females With Type 1 Diabetes	Ongoing clinical trial, no results published yet estimated end 2026



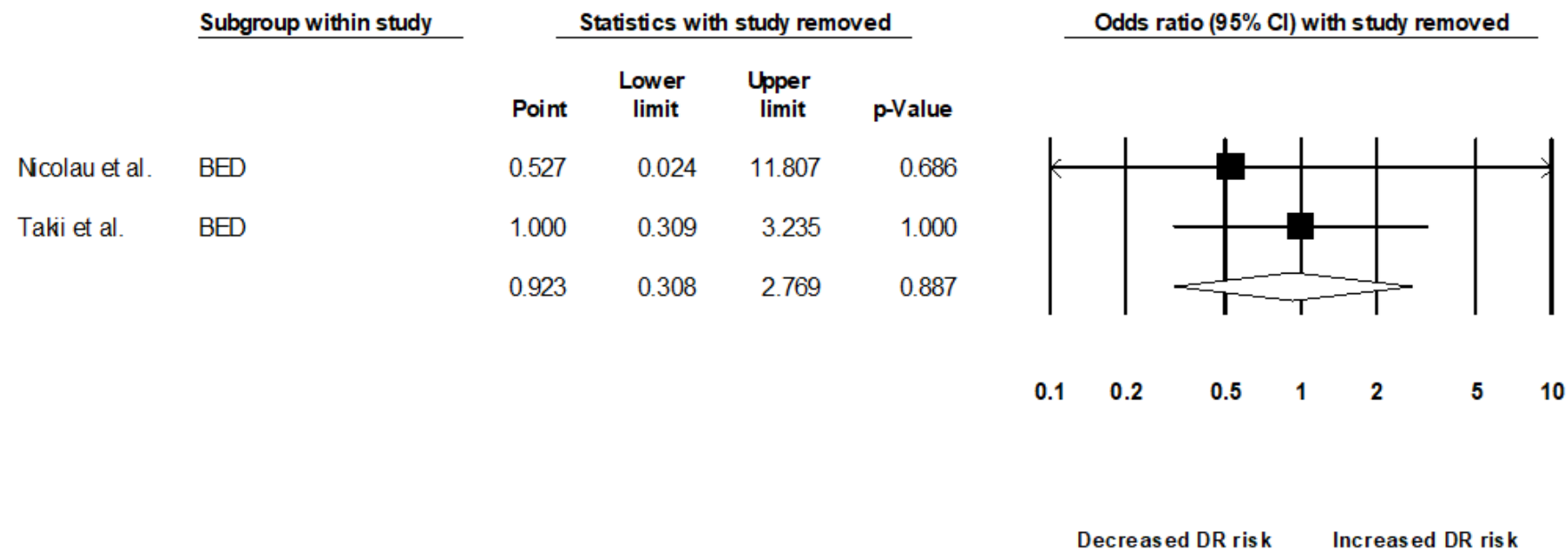
Supplementary Figure 1: Funnel plot showing standard errors and log odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without pathological eating behaviors



Supplementary Figure 2: Odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without pathological eating behaviors with one-study removed. Note EDNOS=eating disorder not otherwise specified; BN=bulimia nervosa; AN=anorexia nervosa; BED=binge eating disorder; DR=diabetic retinopathy



Supplementary Figure 3: Odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without eating disorder not-otherwise-specified with one-study removed.
 Note EDNOS=eating disorder not otherwise specified; DR=diabetic retinopathy



Supplementary Figure 4: Odds ratios of diabetic retinopathy risk amongst people with diabetes with versus without binge eating disorder with one-study removed. Note BED=binge eating disorder; DR=diabetic retinopathy