

Table S1: The risk of bias within individual studies for observational studies by the NOS.

Sategna-Guidetti et al.1998

Study type	Cross-sectional study
Participants	Patients: adult N: 132 cases, 53 controls Gender: 43 males/ 89 females case, 12 males/ 41females control Location: Italy
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of prevalence of autoimmune thyroid disease and thyroid dysfunction Available outcomes: the risk of prevalence of autoimmune thyroid disease and thyroid dysfunction
<i>Risk of bias</i>	
Bias	Authors' judgment Support for judgment
Is the case definition adequate (Selection)	1 yes, with independent validation
Representativeness of the cases(Selection)	1 consecutive or obviously representative series of cases
Selection of Controls(Selection)	0 hospital controls
Definition of Controls(Selection)	1 no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2 study controls age and gender between case and control
Ascertainment of exposure(Exposure)	0 not described
Same method of ascertainment for cases and controls(Exposure)	1 yes
Non-Response rate(Exposure)	0 not described

Toscano et.al.2000

Study type	Cross-sectional study
Participants	<p>Patients: adolescent</p> <p>N: 25 cases, 19 controls</p> <p>Gender: 16 males, 28 females</p> <p>Location: Italy</p>
Comparison	<p>Comparison: GFD in Patients with CD vs. control</p> <p>Case: GFD in Patients with CD</p> <p>Control: Non- GFD in Patients with CD</p>
Outcomes	<p>Main study outcome: the risk of ATPO and ATG positivity and thyroid dysfunction</p> <p>Available outcomes: the risk of ATPO and ATG positivity and thyroid dysfunction</p>

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	not described
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls age between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Ansaldi et al.2003

Study type	Cross-sectional study
Participants	<p>Patients: children</p> <p>N: 256 cases, 87 controls</p> <p>Gender: 77 males/ 179 females case, 36 males/ 51 females control</p> <p>Location: Italy</p>
Comparison	<p>Comparison: GFD in Patients with CD vs. control</p> <p>Case: GFD in Patients with CD</p> <p>Control: Non- GFD in Patients with CD</p>
Outcomes	<p>Main study outcome: the risk of prevalence of autoimmune thyroid disease and thyroid dysfunction</p> <p>Available outcomes: the risk of prevalence of autoimmune thyroid disease and thyroid dysfunction</p>

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	hospital controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2	study controls age and gender between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Naiyer et al.2008

Study type	Cross-sectional study
Participants	Patients: children N: 46 cases, 40 controls Location: Italy
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of ATPO and ATG positivity Available outcomes: the risk of ATPO and ATG positivity

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	not described
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls age between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Toumi et al.2008

Study type	Cross-sectional study
Participants	Patients: adult N: 21 cases, 56 controls Location: Tunisia
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of thyroid dysfunction Available outcomes: the risk of thyroid dysfunction

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	hospital controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls age between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Meloni et al.2008

Study type	Cross-sectional study
Participants	Patients: children N: 324 cases, 313 controls Location: Italy
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of ATPO and ATG positivity and prevalence of autoimmune thyroid disease Available outcomes: the risk of ATPO and ATG positivity and prevalence of autoimmune thyroid disease

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	hospital controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls age between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Norström et al. 2012

Study type	Cross-sectional study
Participants	Patients: adult N: 973 cases, 1031 controls Location: Sweden
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of prevalence of autoimmune thyroid disease Available outcomes: the risk of prevalence of autoimmune thyroid disease

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	not described
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2	study controls age and gender between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Pals et.al.2014

Study type	Cross-sectional study
Participants	Patients: children N: 93 cases, 242 controls Location: Sweden
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of ATPO positivity Available outcomes: the risk of ATPO positivity

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	community controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls sex between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Imperatore et.al.2016

Study type	Cross-sectional study
Participants	Patients: adult N: 1148 cases, 1255 controls Location: Italy
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of prevalence of autoimmune thyroid disease Available outcomes: the risk of prevalence of autoimmune thyroid disease

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	0	hospital controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	0	not described
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Norström et.al.2018

Study type	Cross-sectional study
Participants	Patients: children N: 89 cases, 220 controls Location: Sweden
Comparison	Comparison: GFD in Patients with CD vs. control Case: GFD in Patients with CD Control: Non- GFD in Patients with CD
Outcomes	Main study outcome: the risk of ATPO positivity and thyroid dysfunction Available outcomes: the risk of ATPO positivity and thyroid dysfunction

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	community controls
Definition of Controls(Selection)	1	no history of disease (endpoint)
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study only controls sex between case and control
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	not described

Table S2. The Summary of Findings (SoF) with GRADE system.

GFD on Patients diagnosed with CD and normal diet on Patients diagnosed with CD in risk of thyroid autoimmunity

Population: GFD in Patients with CD vs. Normal Diet in Control

Settings: Five of the studies were conducted in southern Europe, three studies in northern Europe, one study in North America and one study in North Africa

Cases: Gluten-free diet in Patients diagnosed with CD

Controls: Normal diet or regular diet in Patients diagnosed with CD

Outcomes	OR (95% CI)	No. of participants(studies)	Quality of the evidence Comments (GRADE)
The risk of thyroid autoimmunity	0.87(0.47, 1.63) ¹	6423(10 observational studies)	⊕ ⊕ ⊕ ⊖ Moderate ²

Abbreviations: OR: odd ratio; CI: Confidence interval;

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹Results for the risk of thyroid autoimmune of primary outcomes

²Upgraded by one level due to all the results of the included studies were almost identical

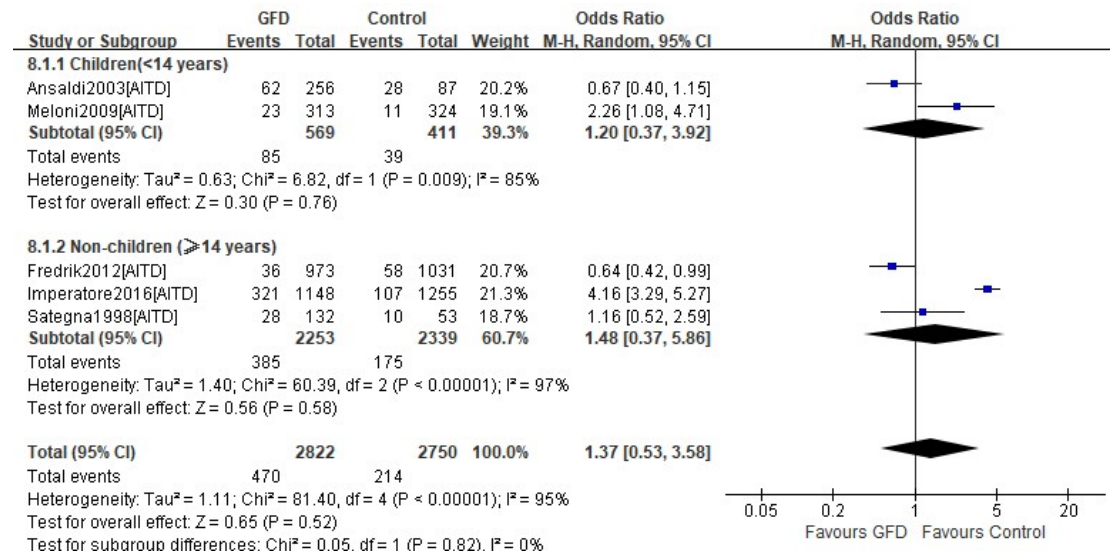


Figure S1 Subgroup analysis of children (<14 years) vs. non-children (≥ 14 years) for the risk of developing AITD in CD patients who adhered GFD vs. Controls.

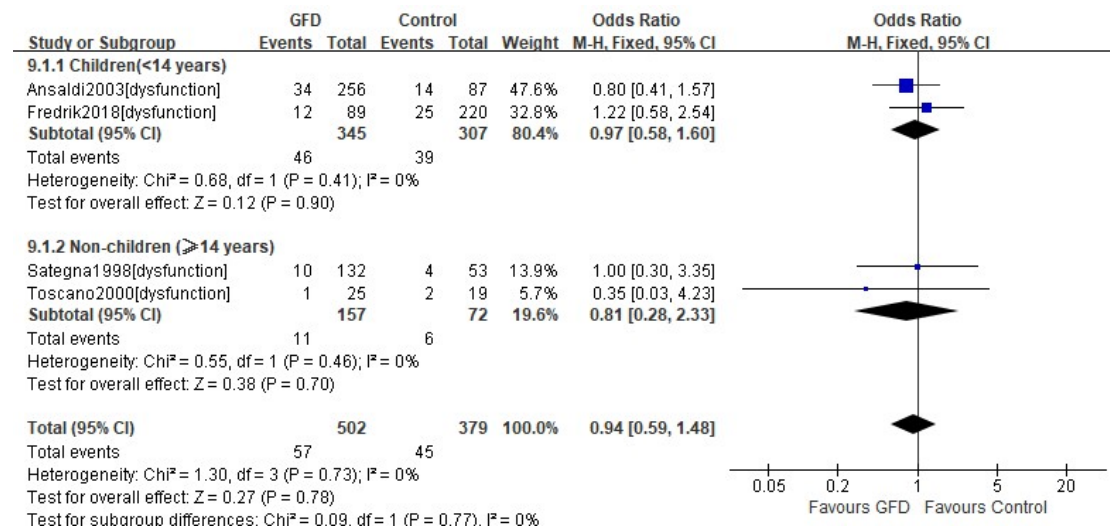


Figure S2 Subgroup analysis of children (<14 years) vs. non-children (≥14 years) for the risk of developing immune-related thyroid dysfunction in CD patients who adhered GFD vs. Controls.

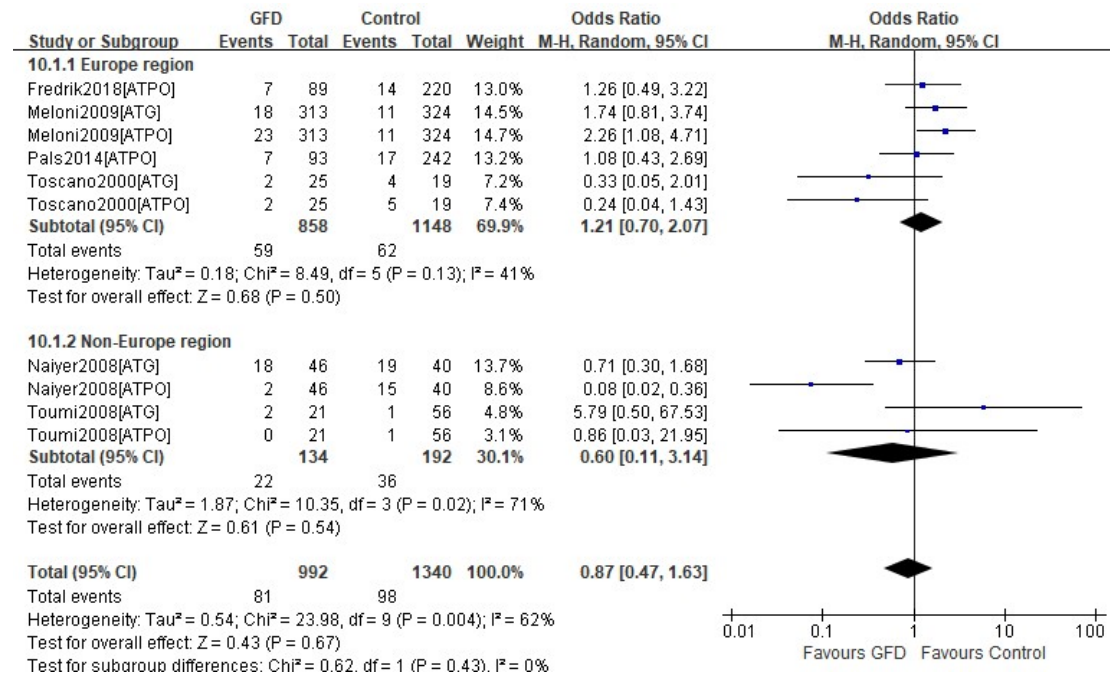
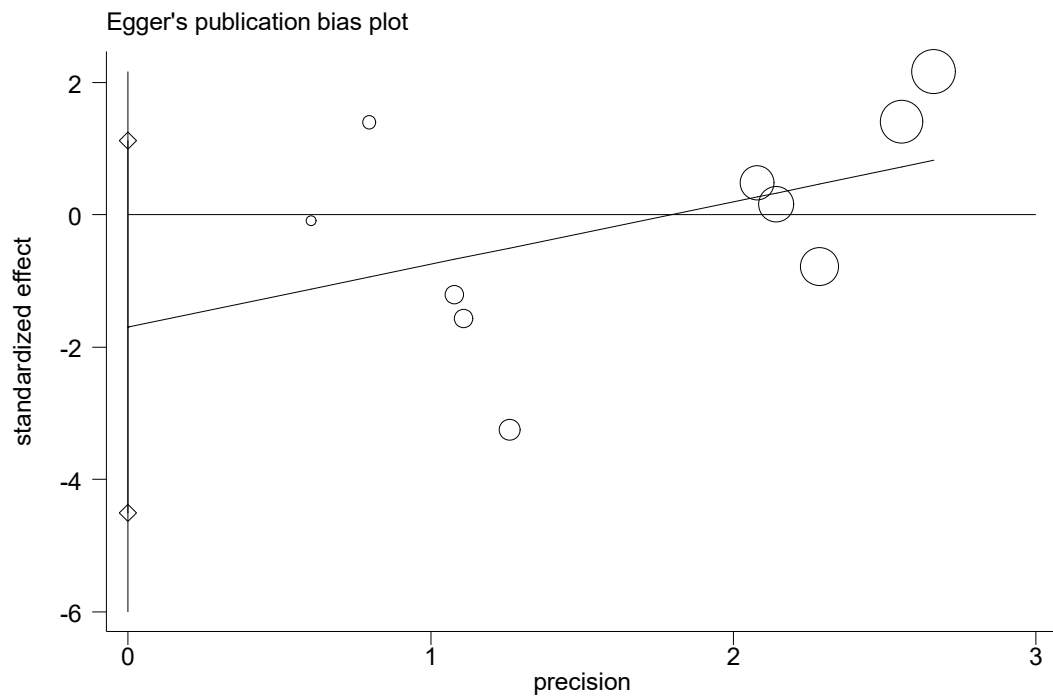
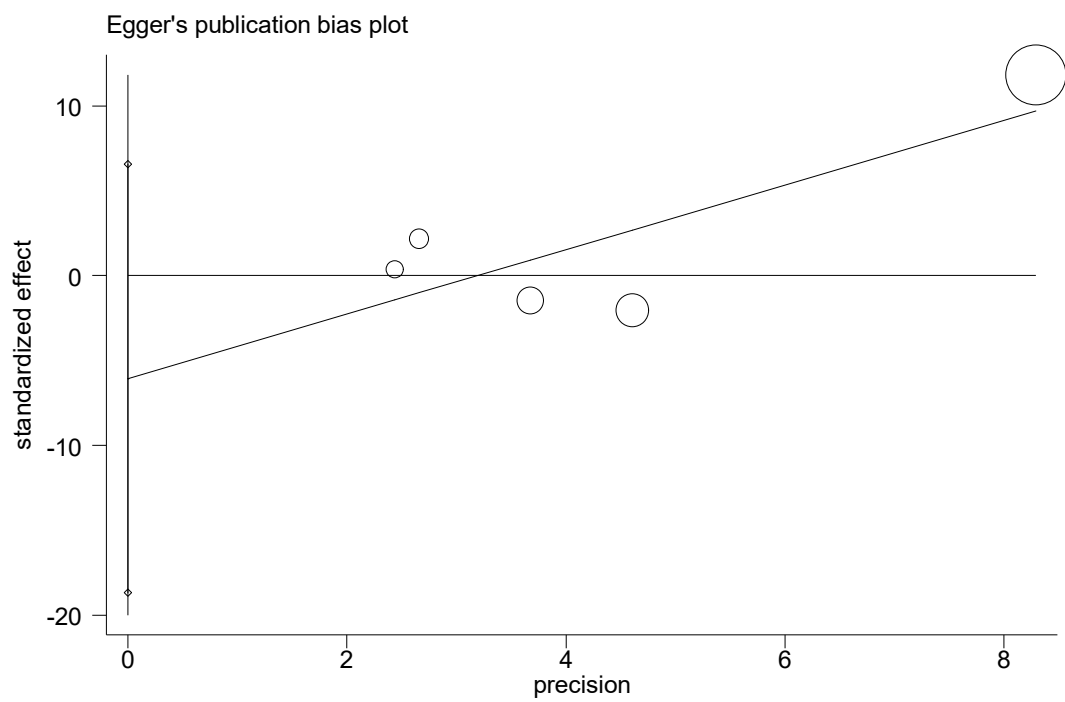


Figure S3 Subgroup analysis of Europe region vs. non-Europe region for the risk of ATPO and ATG antibody positivity in CD patients who underwent GFD vs. Controls.

(a)



(b)



(c)

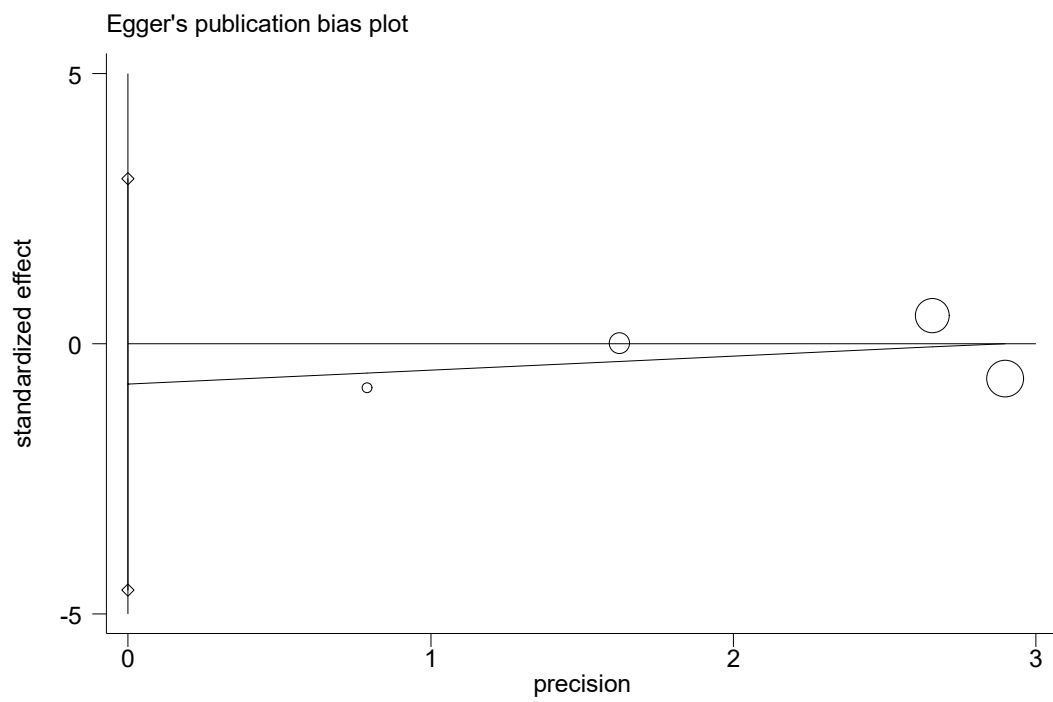


Figure S4 Funnel plot of publication bias for involved studies. (a) Publication bias in the risk of ATPO and ATG antibody positivity; (b) Publication bias in the risk of developing AITD; (c) Publication bias in the risk of developing thyroid dysfunction.