Supplementary Online Content

Nagy R, Gede N, Ocskay K, et al. Association of body mass index with clinical outcomes in patients with cystic fibrosis: a systematic review and meta-analysis. *JAMA Netw Open*. 2022;5(3):e220740. doi:10.1001/jamanetworkopen.2022.0740

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

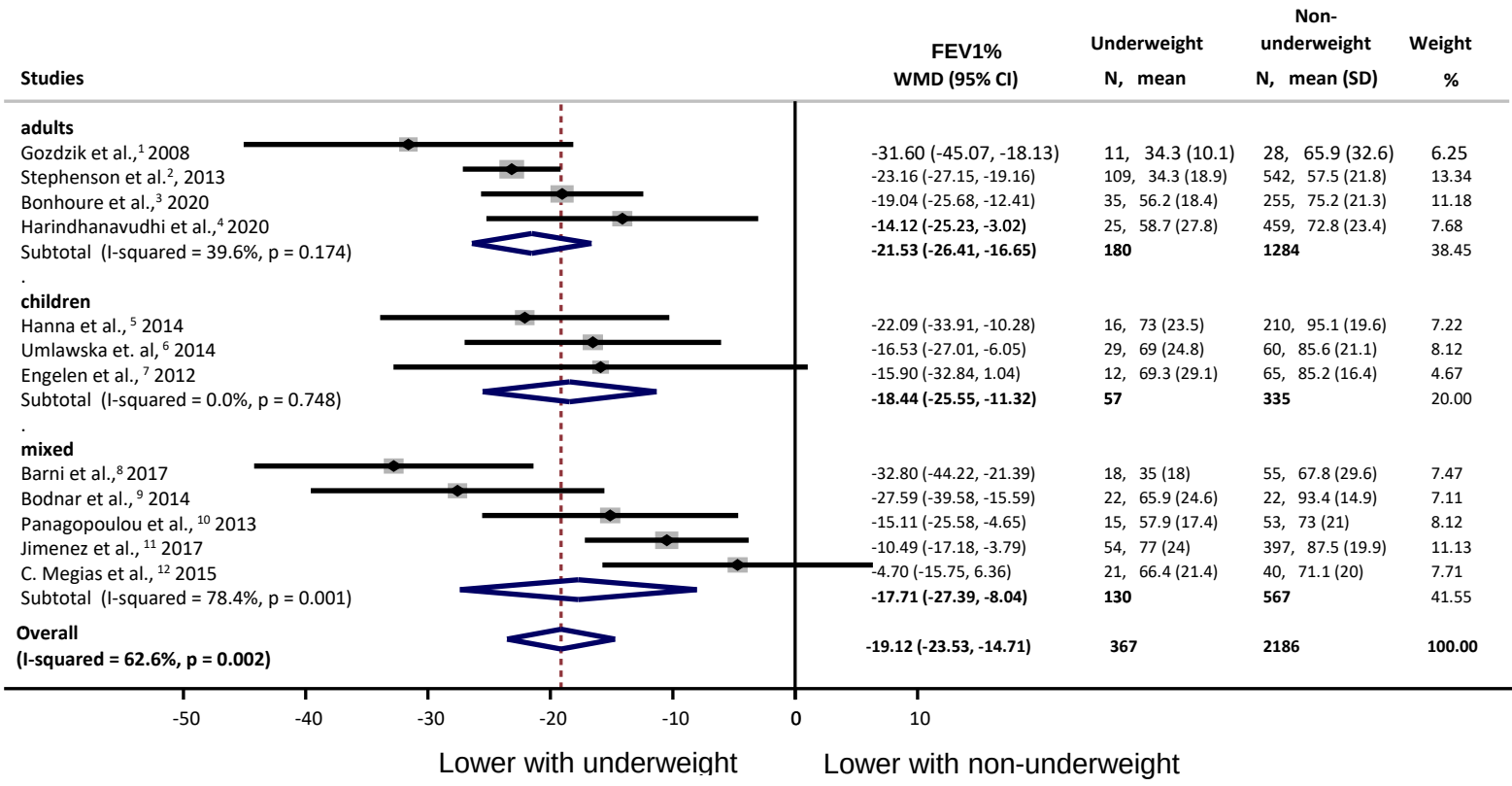
Search strategy and selection

The literature search was conducted on November 2, 2020, in three databases: MEDLINE (via PubMed), Embase, and Cochrane Central Register of Controlled Trials (CENTRAL). The following search key was used: ("cystic fibrosis" OR mucoviscidosis) AND ("body fat" OR bmi OR "body mass" OR "body composition" OR "fat free mass" OR "muscle mass" OR "lean body mass" OR adiposity OR obes* OR "body weight" OR overweight OR sarcopen*), without any restrictions.

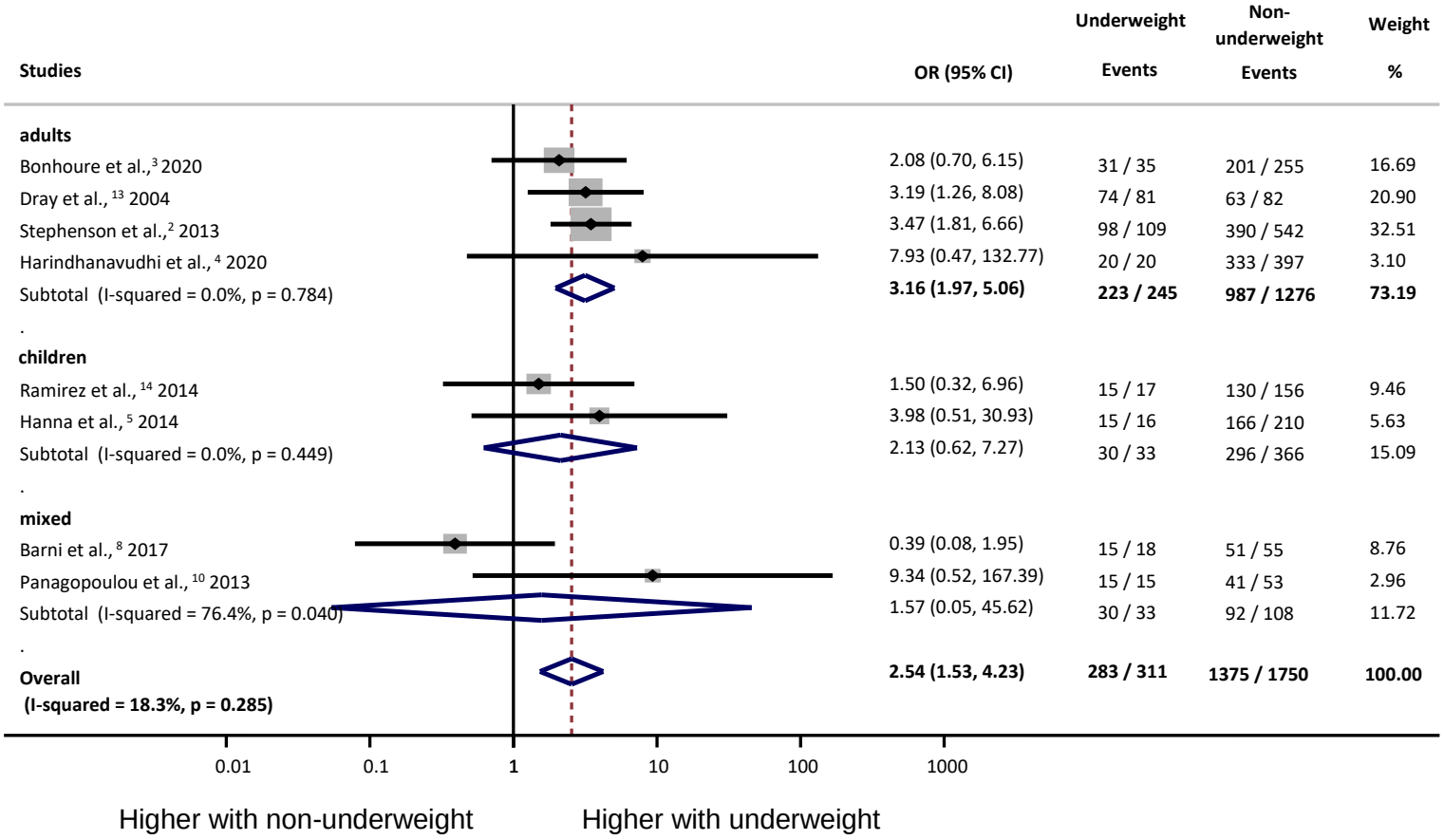
The following data were extracted from each eligible article: study name, first author, publication year, Digital Object Identifier (DOI), recruitment period, gender distribution, age distribution, genotype, patient number and mean or median values of outcomes of interest. Correlation coefficients were also extracted regarding the association of BMI or body composition and clinical outcomes.

eFigure 1. Forest plot showing pulmonary function in adults, children and mixed patient population in the comparison of underweight and non-underweight patients.

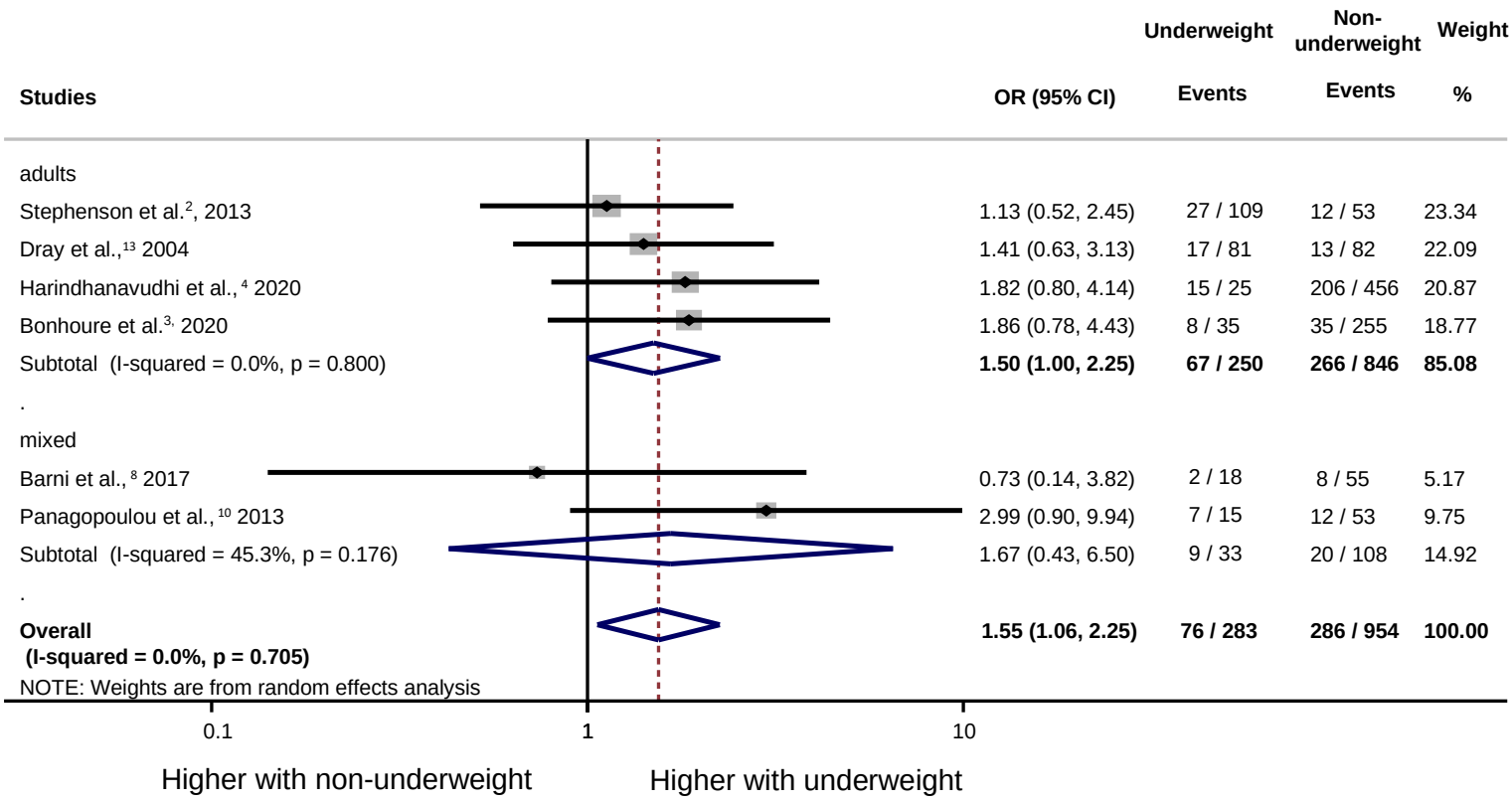
Note: substantial heterogeneity can be detected.



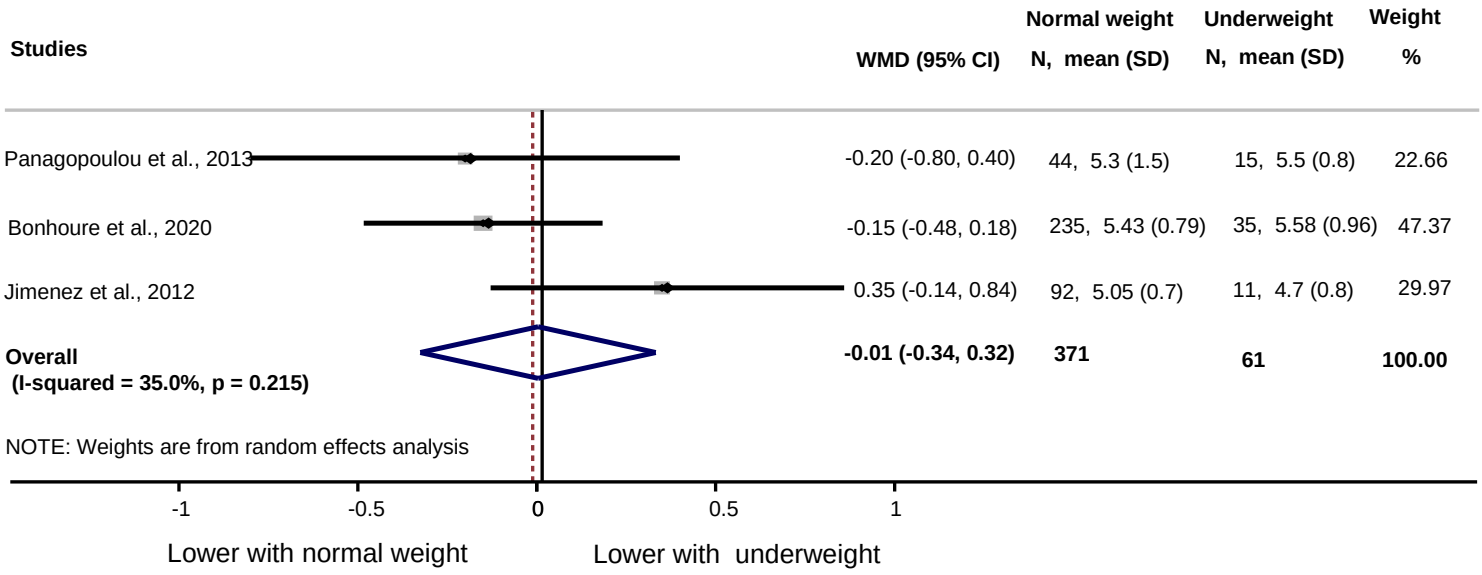
eFigure 2. Forest plot displaying the risk for exocrine insufficiency in subgroup analysis in the comparison of underweight and non-underweight patients.

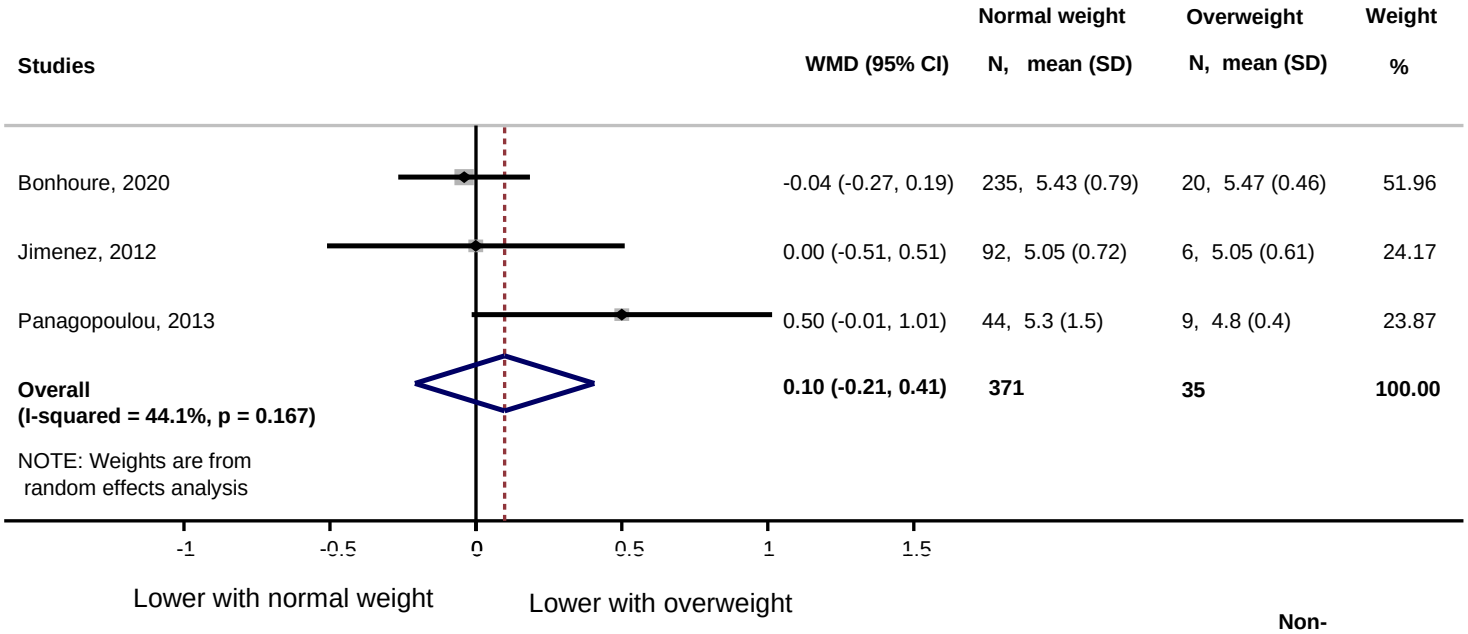


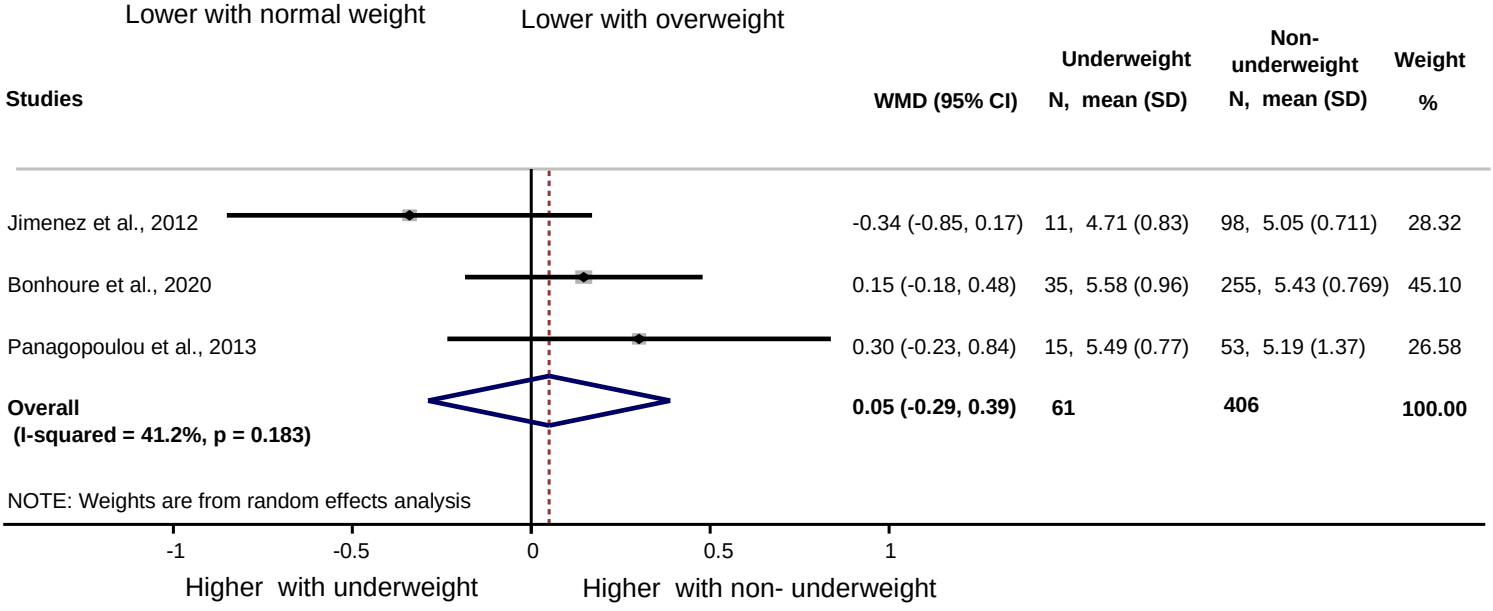
eFigure 3. - Forest plot displaying the risk for CF-related diabetes in the comparison of underweight and non-underweight.



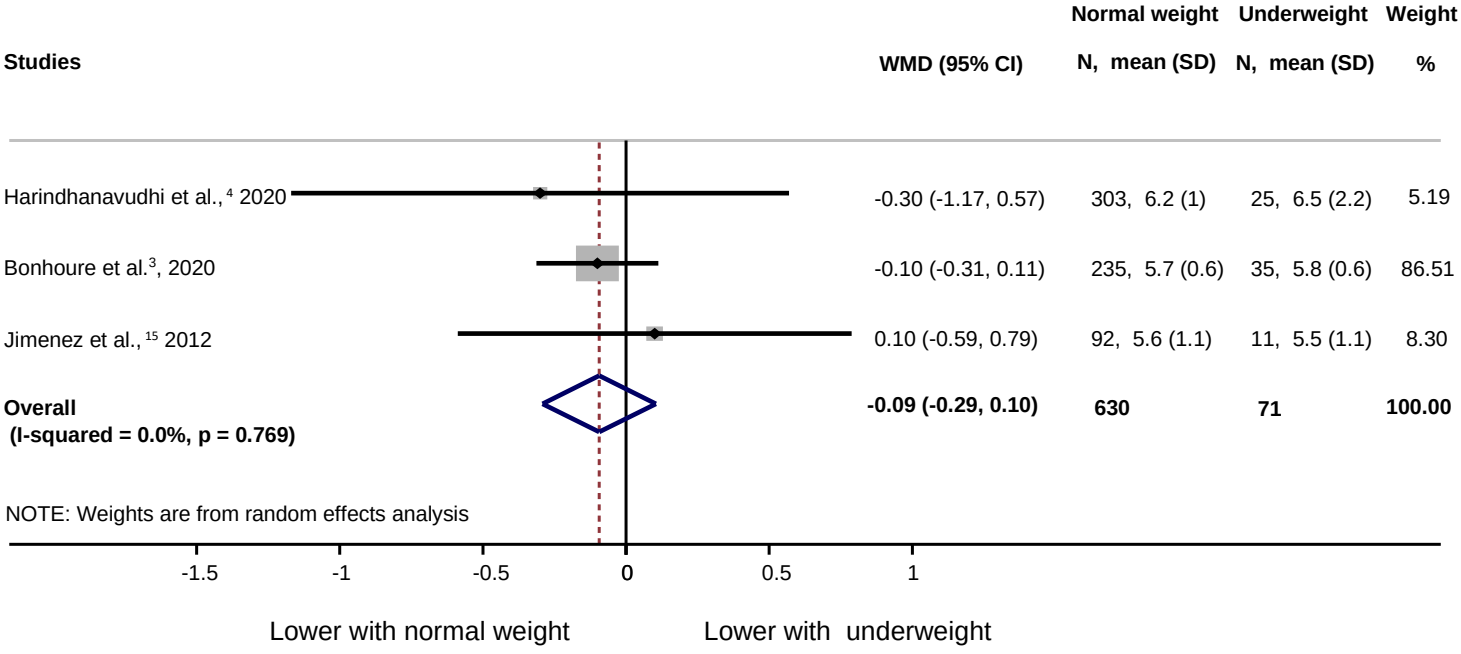
eFigure 4. - Forest plots showing fasting glucose level in the comparison of different BMI categories.

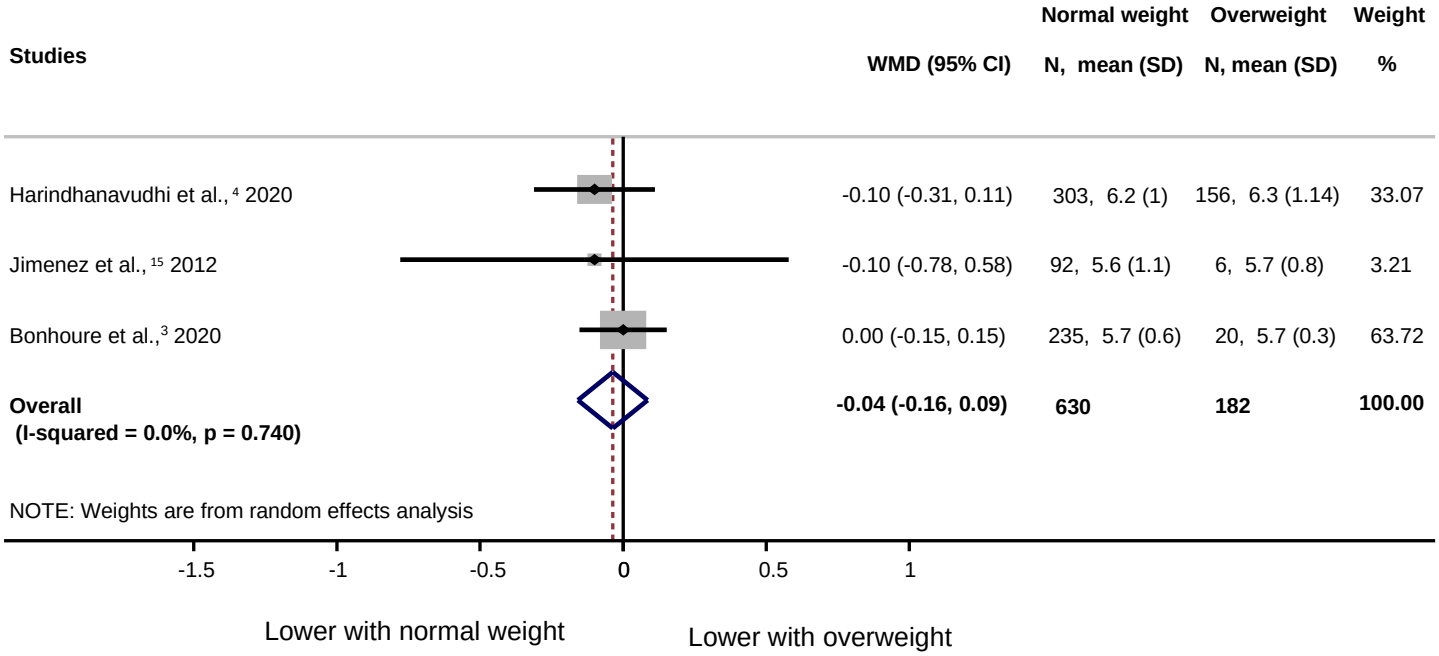




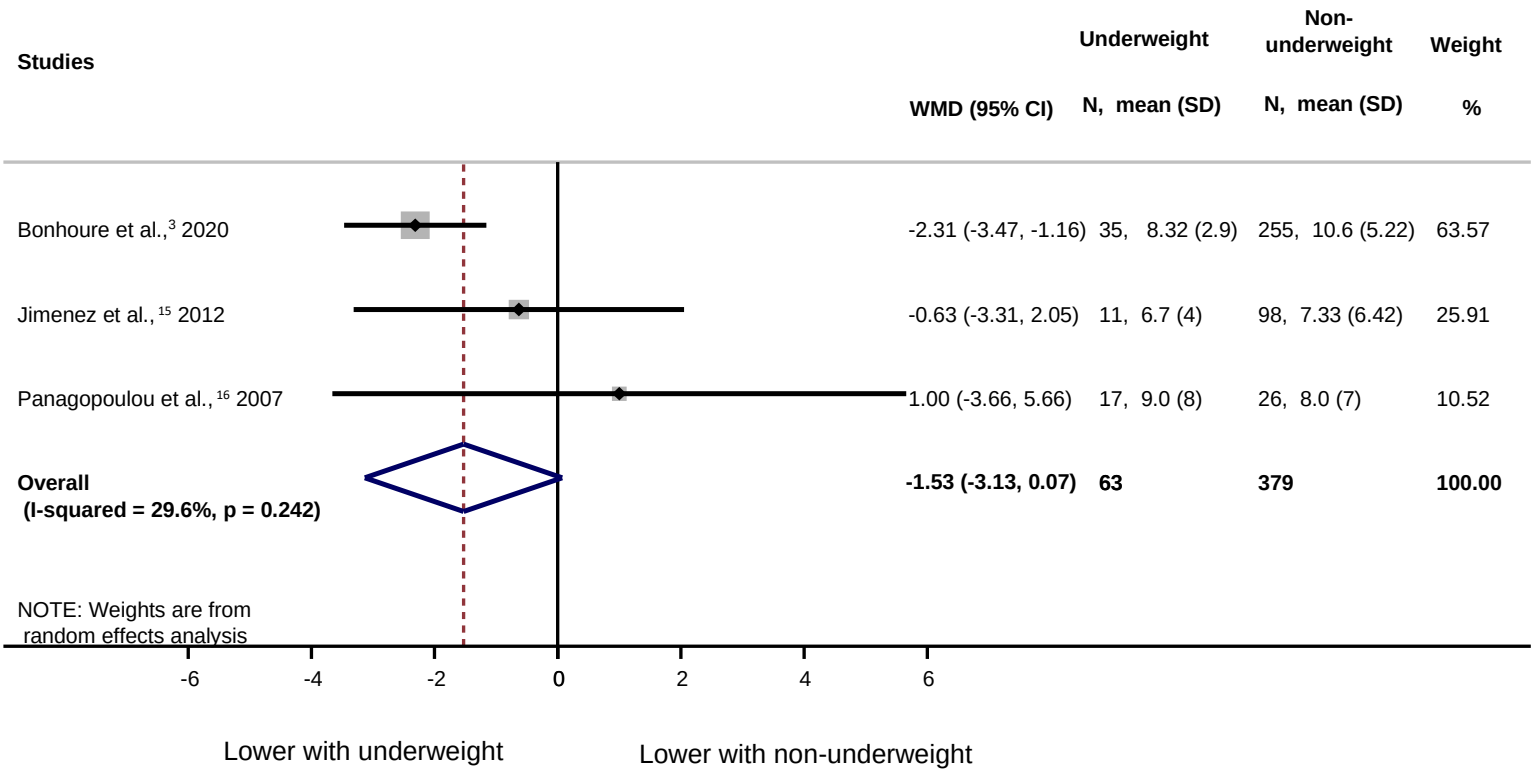


eFigure 5. Forest plots showing HbA1c% level in the comparison of different BMI categories

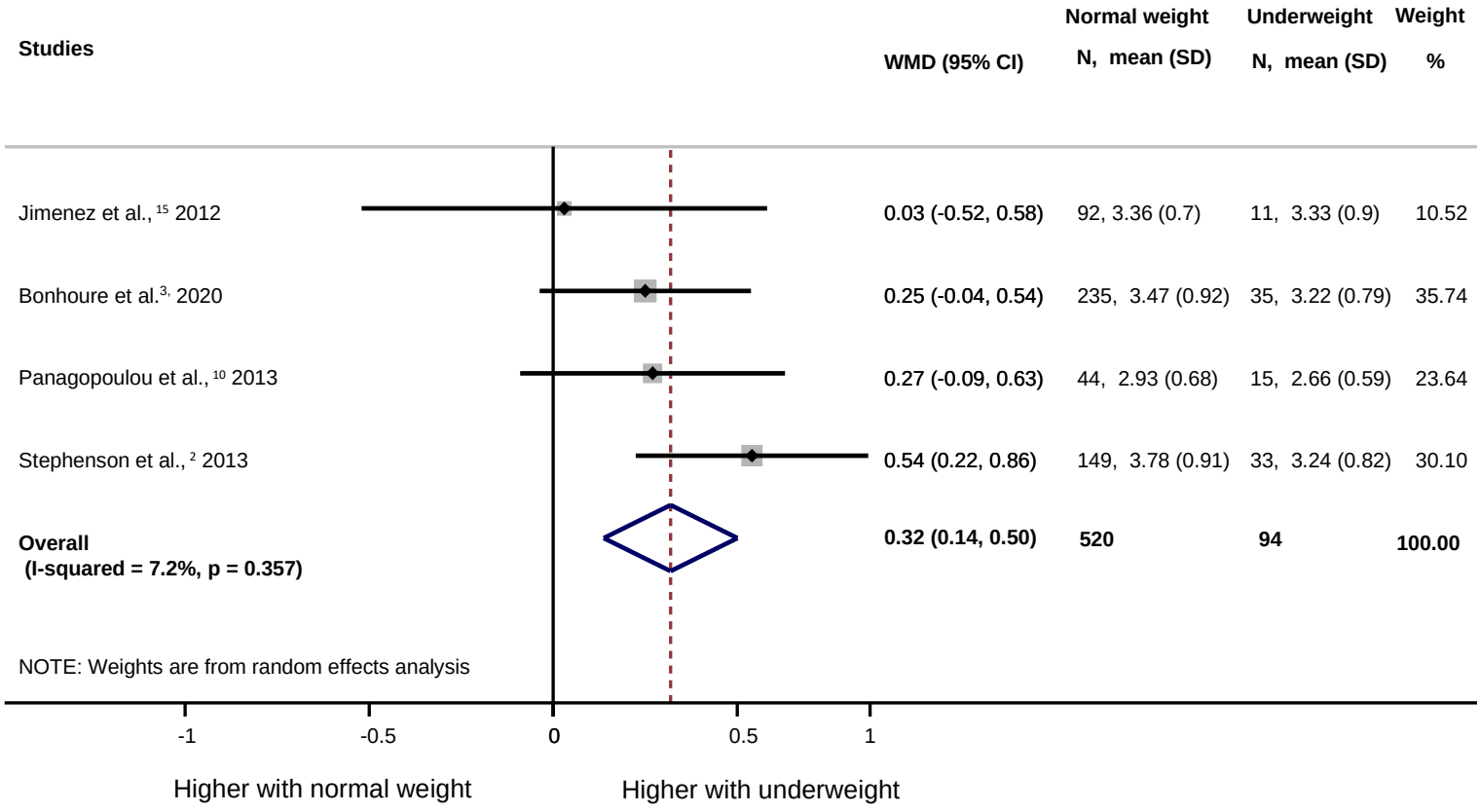


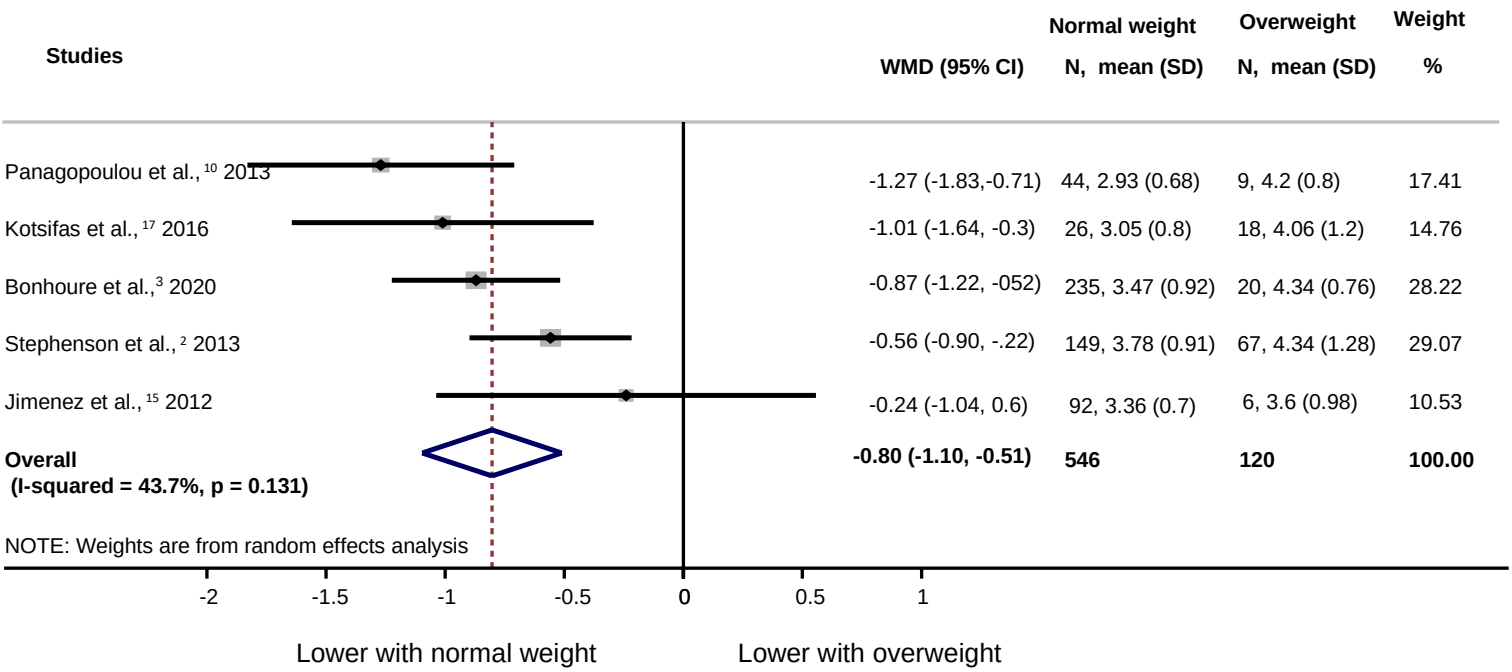


eFigure 6. Forest plot displaying fasting insulin level in the comparison of underweight and non-underweight patients.

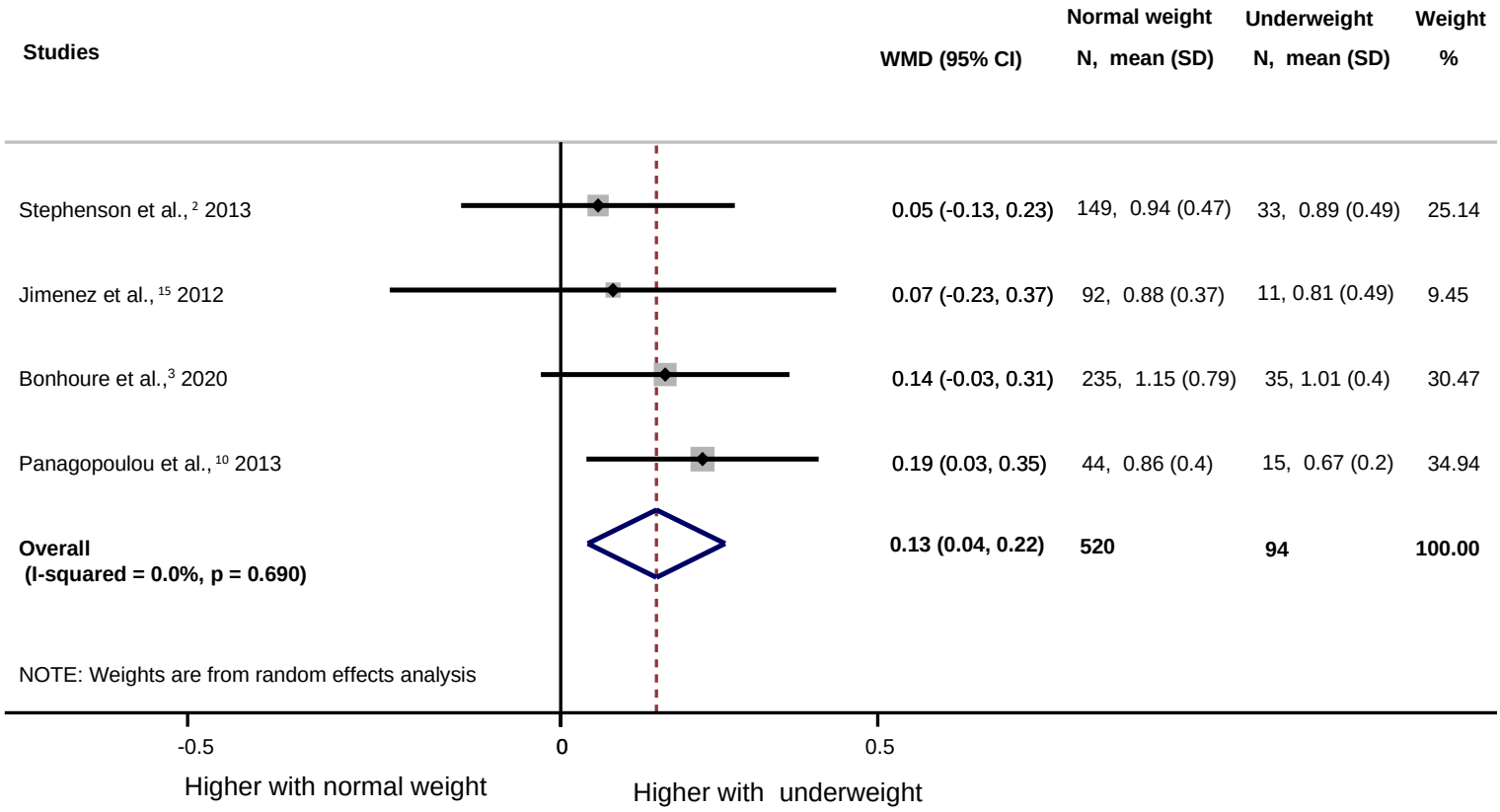


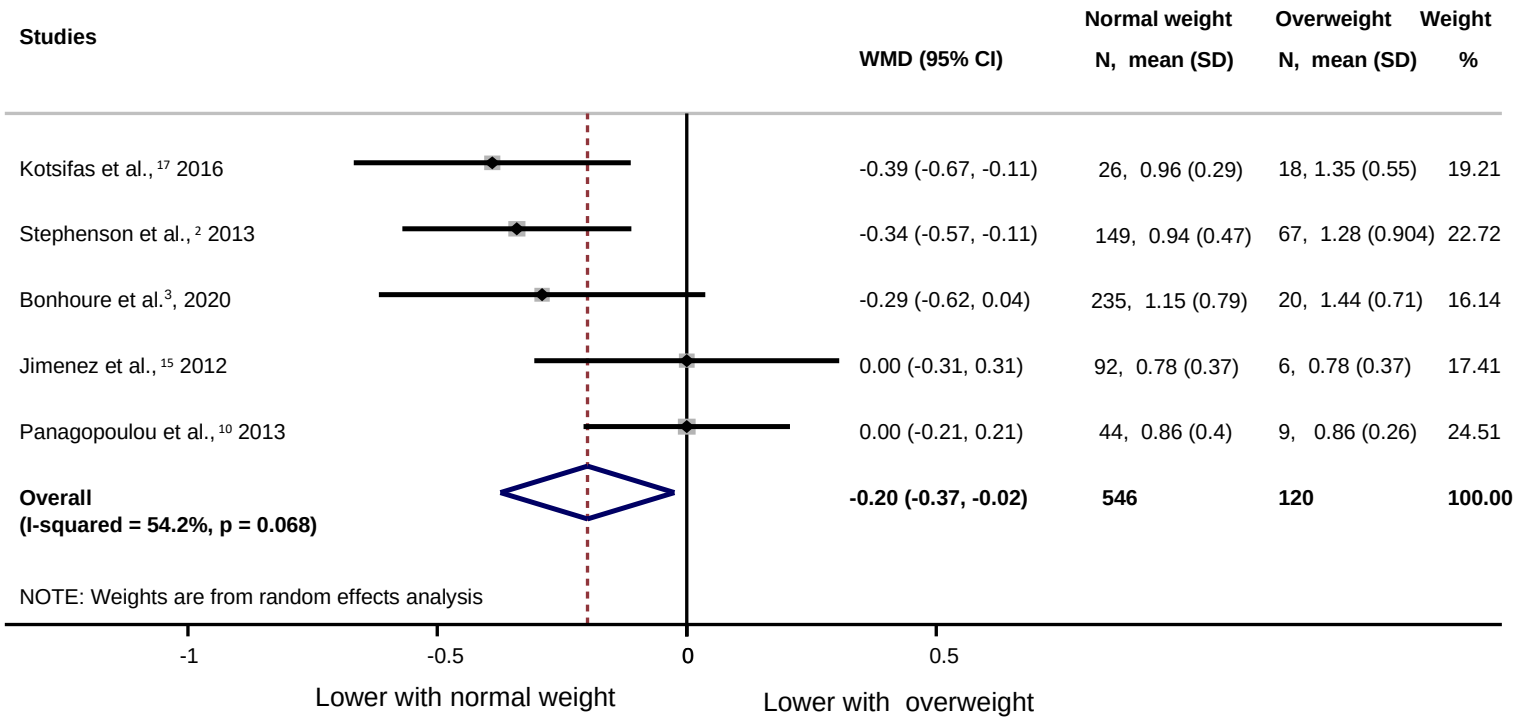
eFigure 7. Forest plots showing total cholesterol level in the comparison of different BMI categories.



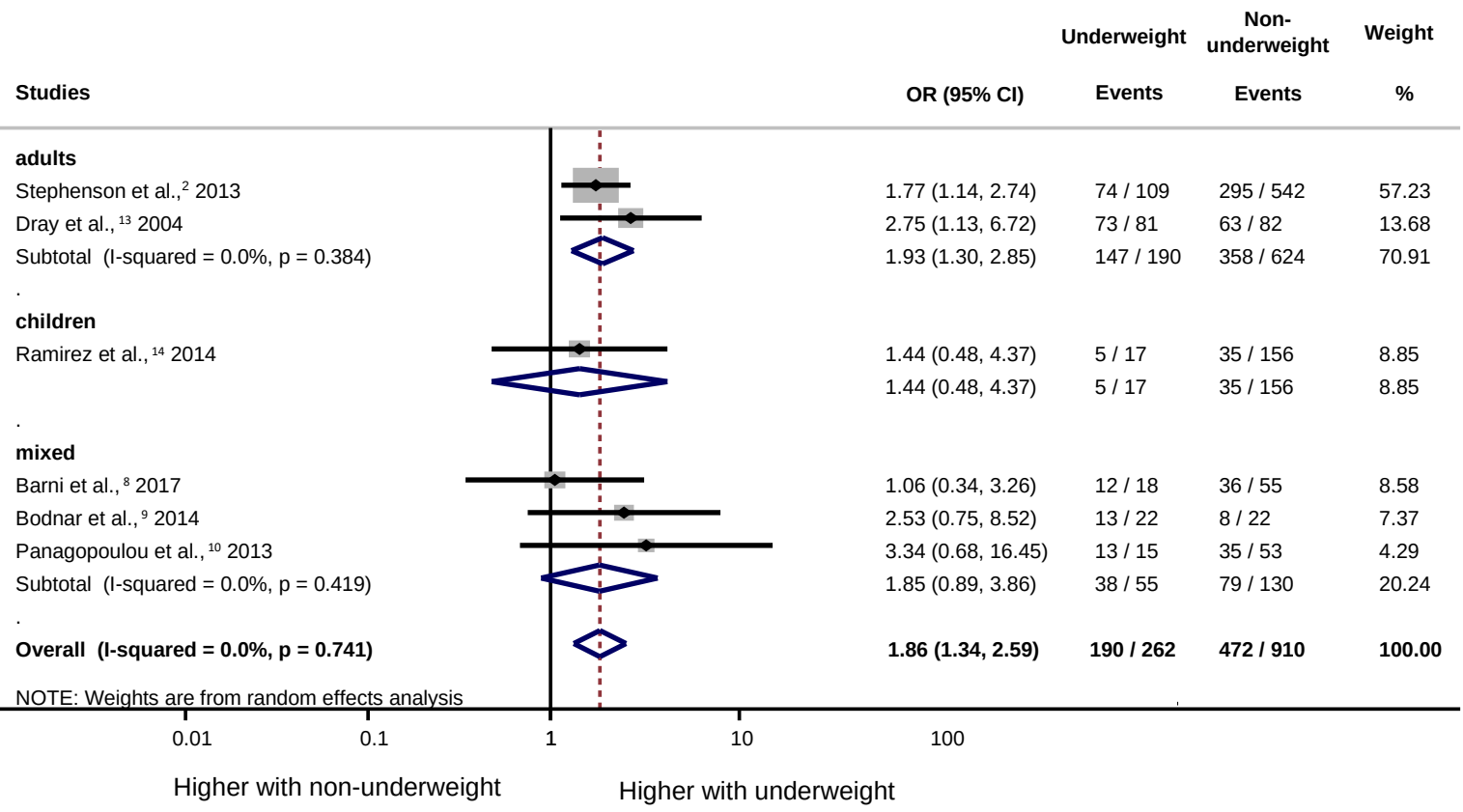


eFigure 8. Forest plots showing triglyceride level in the comparison of different BMI categories.





eFigure 9. Forest plot showing *Pseudomonas aeruginosa* colonization in the comparison of underweight and non-underweight.



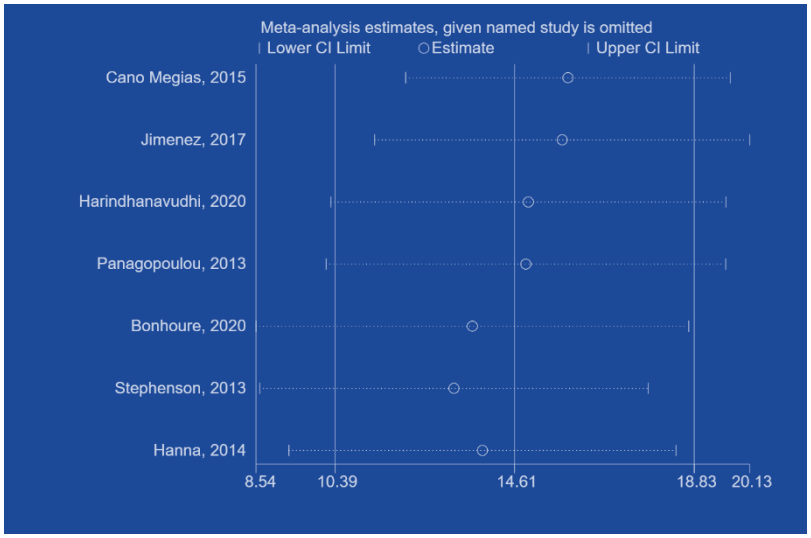
eTable. Table of correlation coefficients.

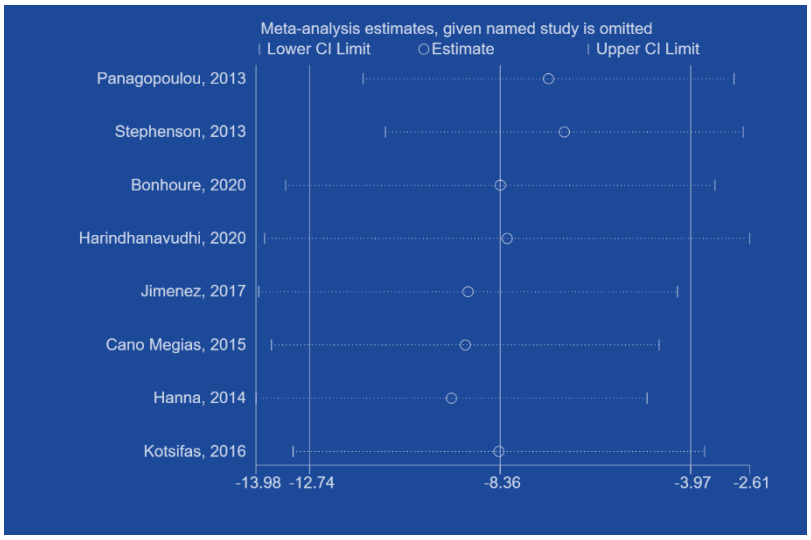
Author	Parameters	r-value	p-value	Patient number	Age group
Barja et al.[18]	FEV1% - BMI z score	0.459	0.02	25	children
Pedreira et al. [19]	FEV1% - BMI z-score	0.59	0.0001	50	children
Asseiceire et al.[20]*	FEV1% - BMI z-score	0.414	0.026	34	children
Junge et al.[21]*	FEV1% - BMI z-score	0.326	<0.001	156	children
Mexia et al.[22]*	FEV1% - BMI z-score	0.530	0.002	39	children
Cherniak et al. [23]	FEV1% - BMI z-score	0.47	< 0.001	291	mixed
Vukic et al.[24]*	FEV1% - BMI	0.31	0.09	30	adults
Bell et al. [25]	FEV1% - BMI	0.51	<0.0001	81	adult
Gozdzik et al.[1]	FEV1% - BMI	0.34	≤0.03	39	adult
Callela et al. [26]	FEV1% - BMI	0.52	<0.001	96	children
Coderre et al. [27]	FEV1% - BMI	0.32	<0.01	187	adult
Dray et al.	et al.FEV1% - BMI	0.46	<0.001	163	adult
Er et al. [28]	FEV1% - BMI	0.46	< 0.001	76	adults
Ionescu et al. [29]	FEV1% - BMI	0.30	<0.02	56	adult
Jarad et al. [30]	FEV1% - BMI	0.42	< 0.0001	34	adult
Belson et al.[31]*	FEV1% - BMI	0.23	<0.005	190	adults
Cardenas et al. [32]*	FEV1% - BMI	0.35	0.001	96	adults
Bianchi et al. [33]	FEV1% - BMI	0.30	non-sign.	136	mixed
Moco et al. [34]	FEV1% - BMI	0.1	non-sign.	21	adults
Spirevska et al. [35]*	FEV1% - BMI	0.37	NA	49	mixed
Papalexopoulou et al. [36]	FEV 1% z-score - BMI z-score	0.097	0.616	29	mixed
Panagopoulou et al.[10]	FEV1% - BMI-SDS	0.498	0.000	68	mixed
Souza et al. [38]	FEV1% - BMIp	0.312	0.004	85	children
Engelen et al.[7]	FEV1% - FFMI %	0.39	< 0.001	77	mixed
Bolton et al. [37]	FEV1% - FFMI	0.418	0.003	511	adults
Ionescu et al. [29]	FEV1% - FFM	0.44	< 0.01	56	adults
Bianchi et al. [33]	FEV1% - FFM	0.61	< 0.01	136	mixed
Moco et al. [34]	FEV1% - FFM	0.2	non-sign.	21	adults
Asseiceire et al. [20]*	FEV1% - FFMI	0.413	0.045	34	children
Bisogno et al.[1]*	FEV1% - FFMI	0.55	<0.0001	85	adults
Vukic et al. [24]*	FEV1% - FFMI	0.52	0.0002	30	adults
King et al.[39]	FEV1% - FFMI z-score	0.41	<0.0001	86	adults
Sermet et al. [40]	FEV1% - FFM z -score	0.41	0.001	114	children
Pedreira et al. [19]	FEV1% - FFM z -score	0.30	0.03	50	children

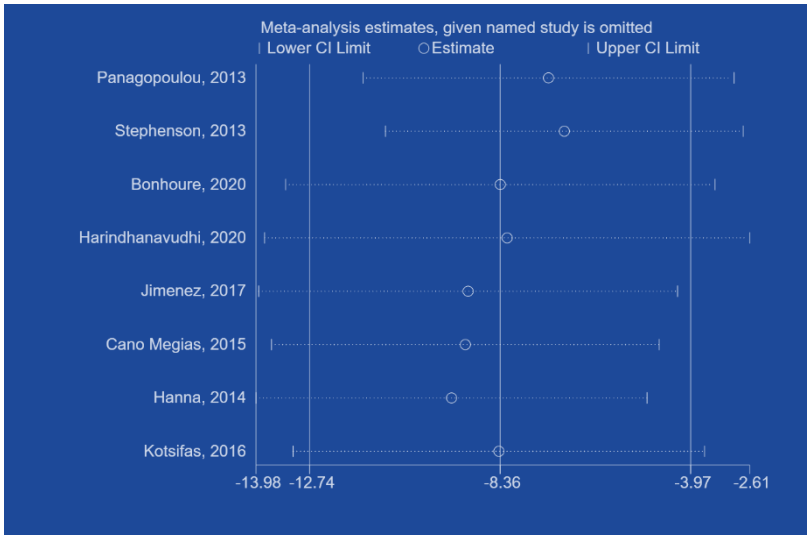
Callela et al. [26]	FEV1% - LBM	0.68	<0.001	96	children
Rochat et al.[41]	FEV 1%- T-LBM	0.847	0.0005	12	adults
Sripalan et al.[42]*	FEV 1%- T-LBM	0.39	0.04	34	adults
Papalexopoulou et al. [36]	FEV1% z-score - FFMI	0.299	0.115	29	mixed
Boat et al.[43]*	FEV1% - LMI	0.676	0.011	13	mixed
Panagopoulou et al.[10]	FEV1% - BF%	0.349	0.023	68	mixed
Belson et al. [31]*	FEV1% - BF %	0.19	<0.05	190	adults
Sills et al.[44]*	absolute FEV1 - BF%	- 0.2	0.03	103	adults
Engelen et al.[7]	FEV1% - FMI %	0.30	< 0.01	77	mixed
Belson et al. [31]*	FEV1% - FM	0.18	<0.05	190	adults
Bellissimo et al.[45]*	FG - VFM	0.45	0.04	22	adults

r value indicates the strength of the kinear relationship between two variables. p value represents the probability that the correlation between the two variables occured by chance. * conference abstract

eFigure 10. Leave-1-out sensitivity analysis regarding pulmonary function in the comparison of different BMI categories.

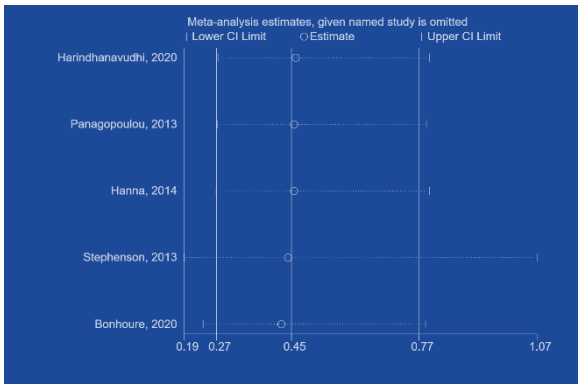






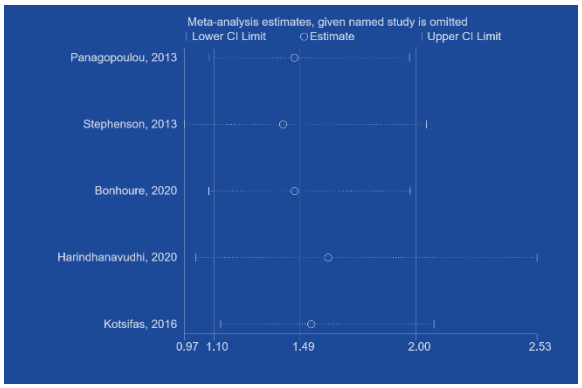
Omitting a study does not influence the result in any case.

eFigure 11. Leave-1-out sensitivity analysis regarding exocrine insufficiency in the comparison of normal weight and underweight patients.



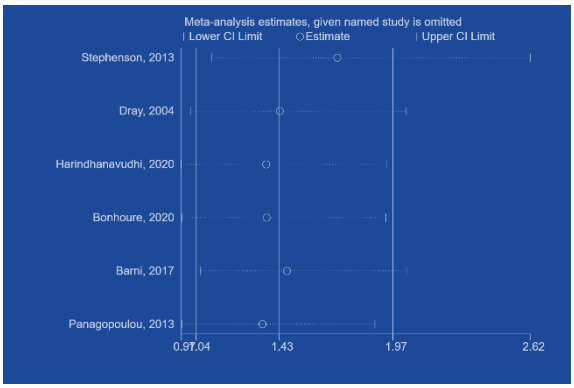
Leaving out the study of Stephenson will alter the result.

eFigure 12. Leave-1-out sensitivity analysis regarding CF-related diabetes in the comparison of normal weight and overweight plus obese groups.



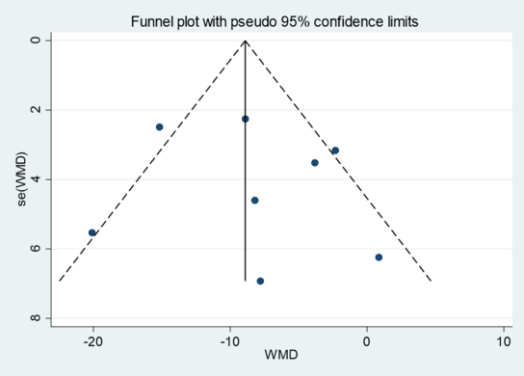
Leaving out the study of Stephenson et al.[2] will alter the significancy of the result.

eFigure 13. Leave-1-out sensitivity analysis regarding CF-related diabetes in subgroup analysis in the comparison of underweight and non-underweight patients.



Leaving out the study of Bonhoure[3] and Harindhanavudhi[4] will alter the significancy of the result.

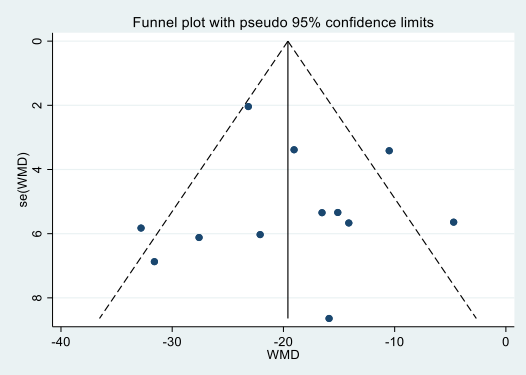
eFigure 14. Funnel plot of the included 8 studies regarding pulmonary function in the comparison of normal weight and overweight patients.



Egger's test: P = 0.650
(no small study effect)

The visual assessment and Egger's test (p>0.05) does not indicate asymmetry, thus publication bias is unlikely.

eFigure 15. Funnel plot of the included 12 studies regarding pulmonary function in subgroup analysis in the comparison of underweight and non-underweight patients.

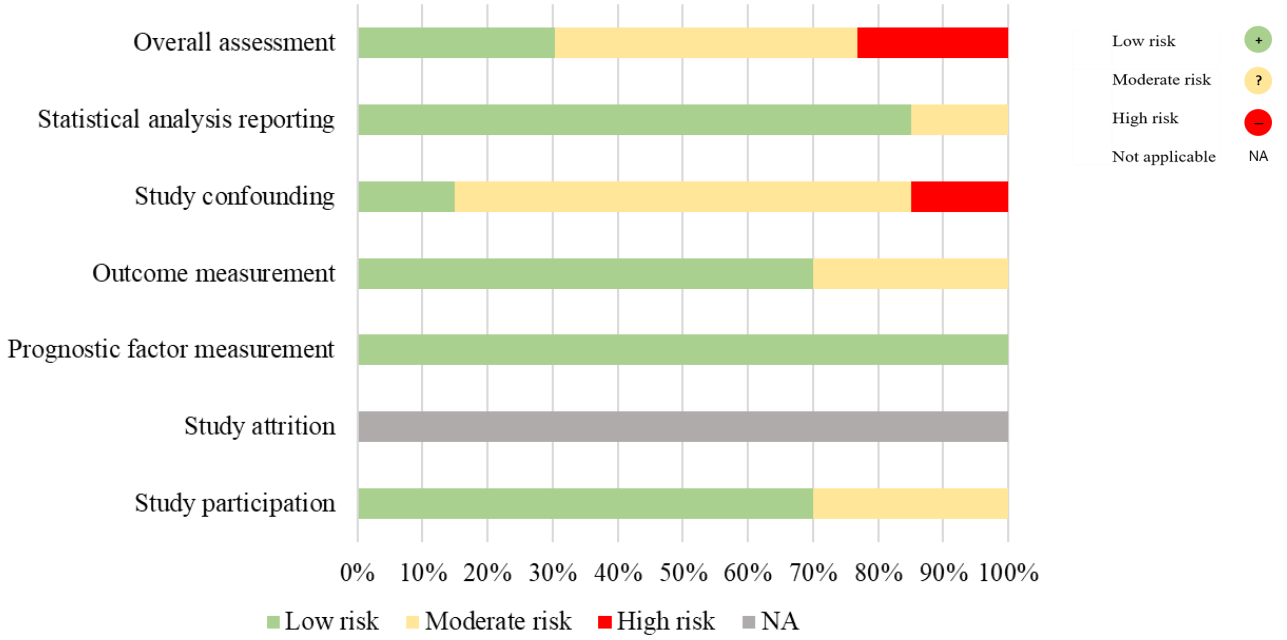


Egger's test: P = 0.751
(no small study effect)

The visual assessment and Egger's test (p>0.05) does not indicate asymmetry, thus publication bias is unlikely.

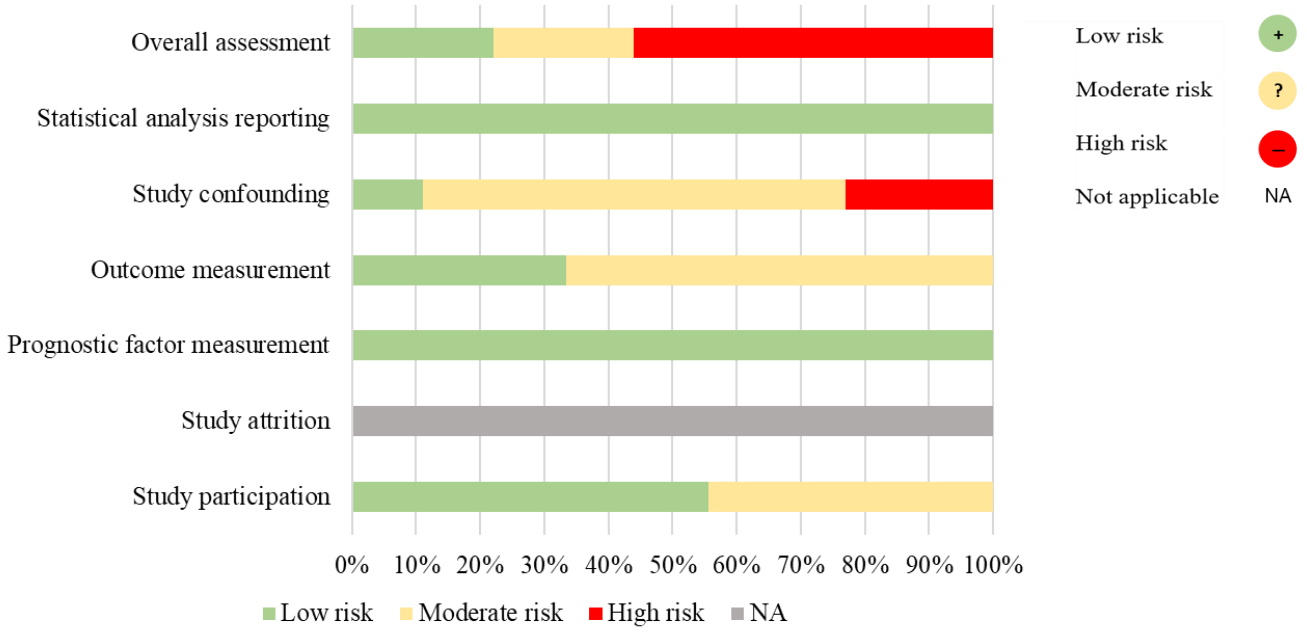
eFigure 16. Risk of bias assessment at study and domain level regarding pulmonary function (FEV1%).

Study	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Panagopoulou et al., 2013[10]	3	NA	3	2	2	3	2	yes
Stephenson et al, 2013[2]	3	NA	3	3	1	3	1	yes
Bonhoure et al, 2020[3]	3	NA	3	3	2	2	3	yes
Harindhanavudhi et al.,2020[4]	2	NA	3	3	1	3	1	yes
Jimenez et al., 2017[11]	3	NA	3	2	2	3	2	yes
C. Megias et al.,2015[12]	3	NA	3	3	2	2	2	yes
Hanna et al., 2014[5]	3	NA	3	2	2	3	2	yes
Gozdzik et al.,2008[1]	2	NA	3	3	2	3	2	yes
Engelen et al.,2012[7]	3	NA	3	3	2	3	3	yes
Umlawska et al.,2014[6]	2	NA	3	3	2	3	2	yes
Barni et al.,2017[8]	3	NA	3	3	3	3	3	yes
Bodnar et al, 2014[9]	3	NA	3	3	3	3	3	yes
Kotsifas et al.,2016[17]	2	NA	3	2	2	3	1	yes
Total	low	9		13	9	2	11	4	
Total	moderate	4			4	9	2	6	
Total	high					2		3	
Total	NA		13						



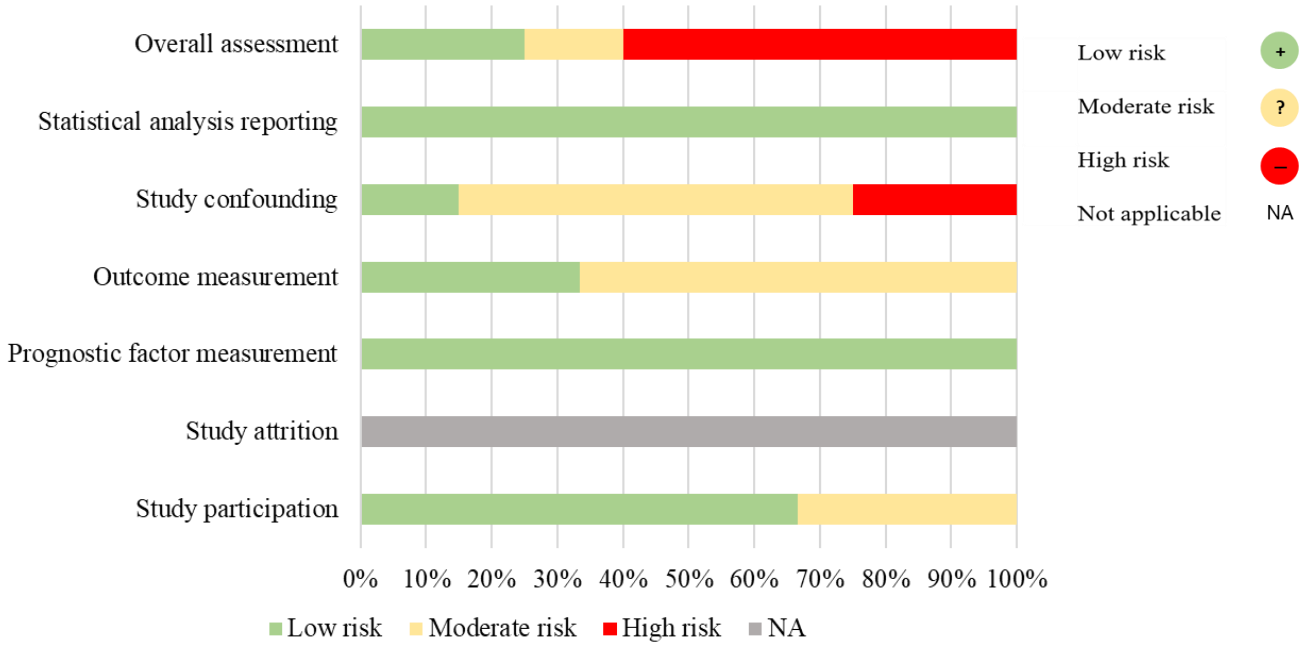
eFigure 17. Risk of bias assessment at study and domain level regarding exocrine insufficiency.

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Panagopoulou et al., 2013[10]		3	NA	3	3	2	3	3	yes
Stephenson et al, 2013[2]		3	NA	3	2	1	3	1	yes
Bonhoure et al, 2020[3]		3	NA	3	2	2	3	2	yes
Harindhanavudhi et al.,2020[4]		2	NA	3	2	1	3	1	yes
Hanna et al., 2014[5]		3	NA	3	2	2	3	2	yes
Ramirez et al.,2014[14]		2	NA	3	2	2	3	1	yes
Barni et al.,2017[8]		3	NA	3	3	3	3	3	yes
Dray et al.,2004[13]		2	NA	3	2	2	3	1	yes
Kotsifas et al.,2016[17]		2	NA	3	2	2	3	1	yes
Total	low	5		9	3	1	9	2	
Total	moderate	4			6	6		2	
Total	high					2		5	
Total	NA		9						



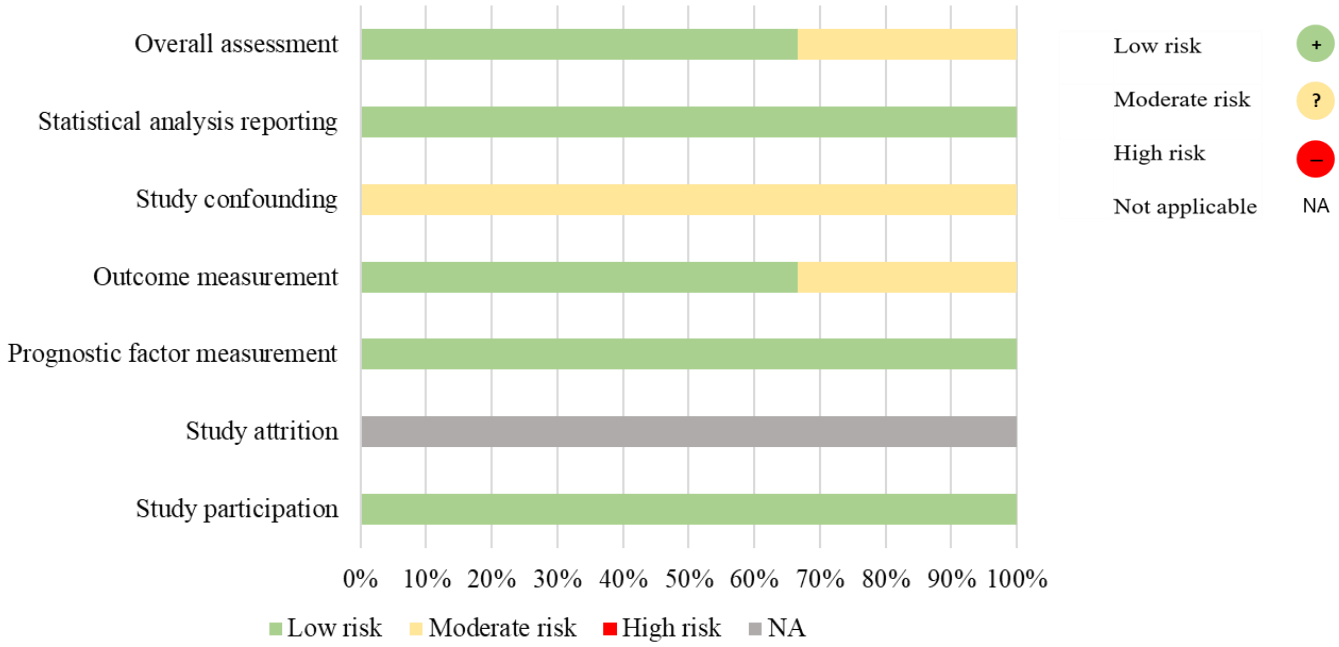
eFigure 18. **Risk of bias assessment at study and domain levevel ragarding CFRD.**

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Panagopoulou et al., 2013[10]		3	NA	3	3	2	3	3	yes
Stephenson et al, 2013[2]		3	NA	3	2	1	3	1	yes
Bonhoure et al, 2020[3]		3	NA	3	3	2	3	3	yes
Harindhanavudhi et al.,2020[4]		2	NA	3	3	1	3	1	yes
Dray et al.,2004[13]		2	NA	3	2	2	3	1	yes
Barni et al.,2017[8]		3	NA	3	2	3	3	2	yes
Kotsifas et al.,2016[17]		2	NA	3	2	2	3	1	yes
Total	low	4		7	3	1	7	2	
Total	moderate	3			4	4		1	
Total	high					2		4	
Total	NA		7						



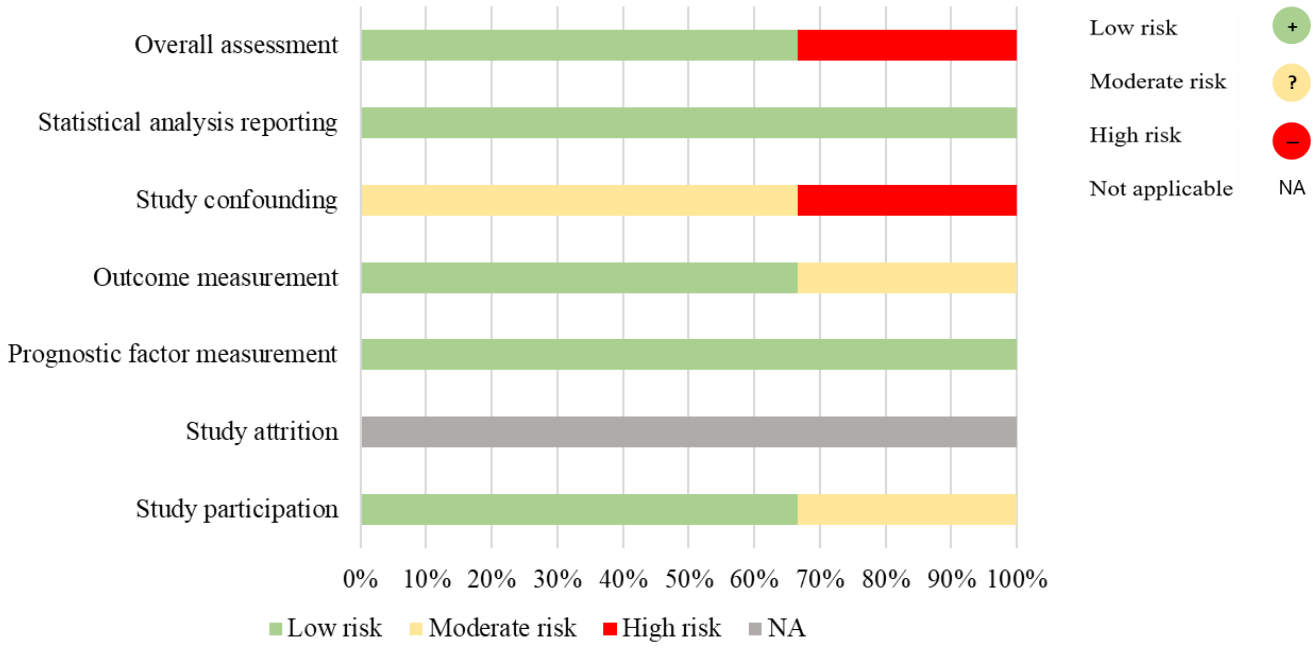
eFigure 19. Risk of bias assessment at study and domain level regarding fasting glucose.

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Panagopoulou et al.,2013[10]		3	NA	3	2	2	3	2	yes
Bonhoure et al., 2020[3]		3	NA	3	3	2	3	3	yes
Jimenez et al., 2012[15]		3	NA	3	3	2	3	3	yes
Total	low	3		3	2		3	2	
Total	moderate				1	3		1	
Total	high								
Total	NA		3						



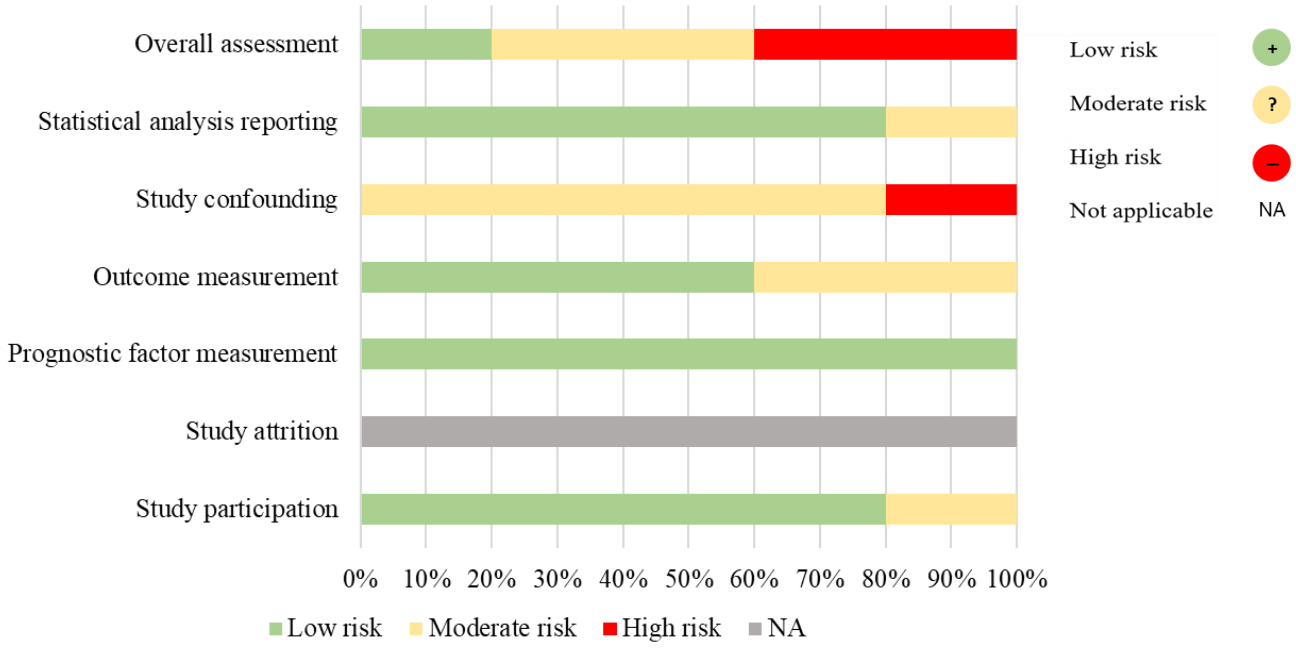
eFigure 20. Risk of bias assessment at study and domain level regarding HbA1c%.

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Harindhanavudhi et al., 2020[4]		2	NA	3	2	1	3	1	yes
Bonhoure et al.,[3] 2020		3	NA	3	3	2	3	3	yes
Jimenez et al., 2012[15]		3	NA	3	3	2	3	3	yes
Total	low	2		3	2		3	2	
Total	moderate	1			1	2			
Total	high					1		1	
Total	NA		3						



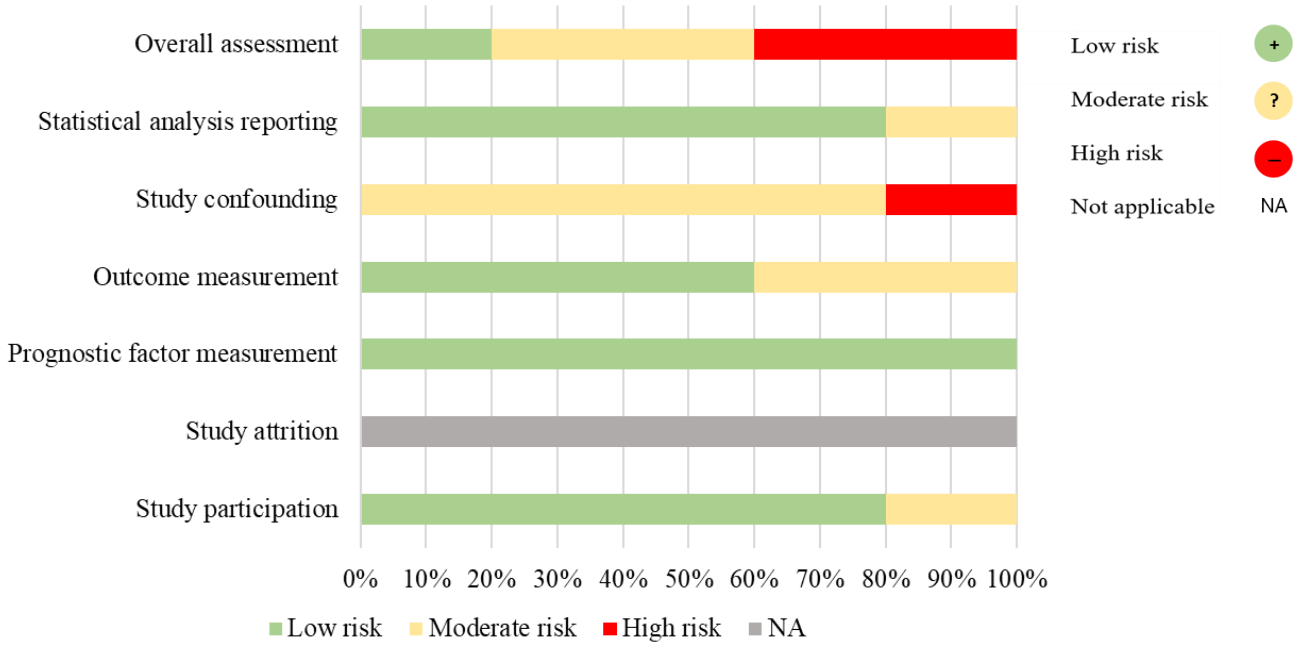
eFigure 21. Risk of bias assessment at study and domain level regarding total cholesterol.

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Harindhanavudhi et al.,2020[4]		2	NA	3	3	2	2	1	no
Stephenson et al.,[2] 2013		3	NA	3	3	1	3	1	yes
Bonhoure et al., 2020[3]		3	NA	3	3	2	3	3	yes
Panagopoulou et al.,2013[10]		3	NA	3	2	2	3	2	yes
Jimenez et al., 2012[15]		3	NA	3	2	2	3	2	yes
Total	low	4					4	1	
Total	moderate	1			4	4	1	2	
Total	high			5	1	1		2	
Total	NA		5						



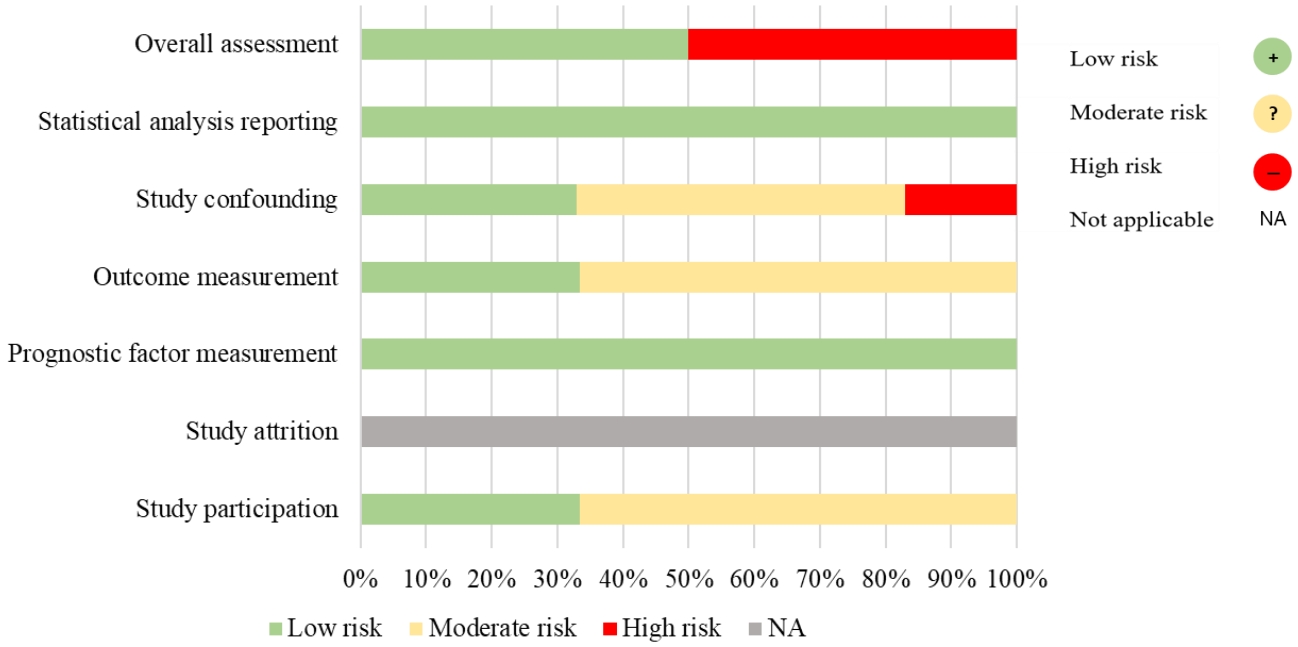
eFigure 22. Risk of bias assessment at study and domain level regarding triglycerides

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Harindhanavudhi et al.,2020[4]		2	NA	3	3	2	2	1	no
Stephenson et al., 2013[2]		3	NA	3	3	1	3	1	yes
Bonhoure et al.,[3] 2020		3	NA	3	3	2	3	3	yes
Panagopoulou et al.,2013[10]		3	NA	3	2	2	3	2	yes
Jimenez et al., 2012[15]		3	NA	3	2	2	3	2	yes
Total	low	4					4	1	
Total	moderate	1			4	4	1	2	
Total	high			5	1	1		2	
Total	NA		5						



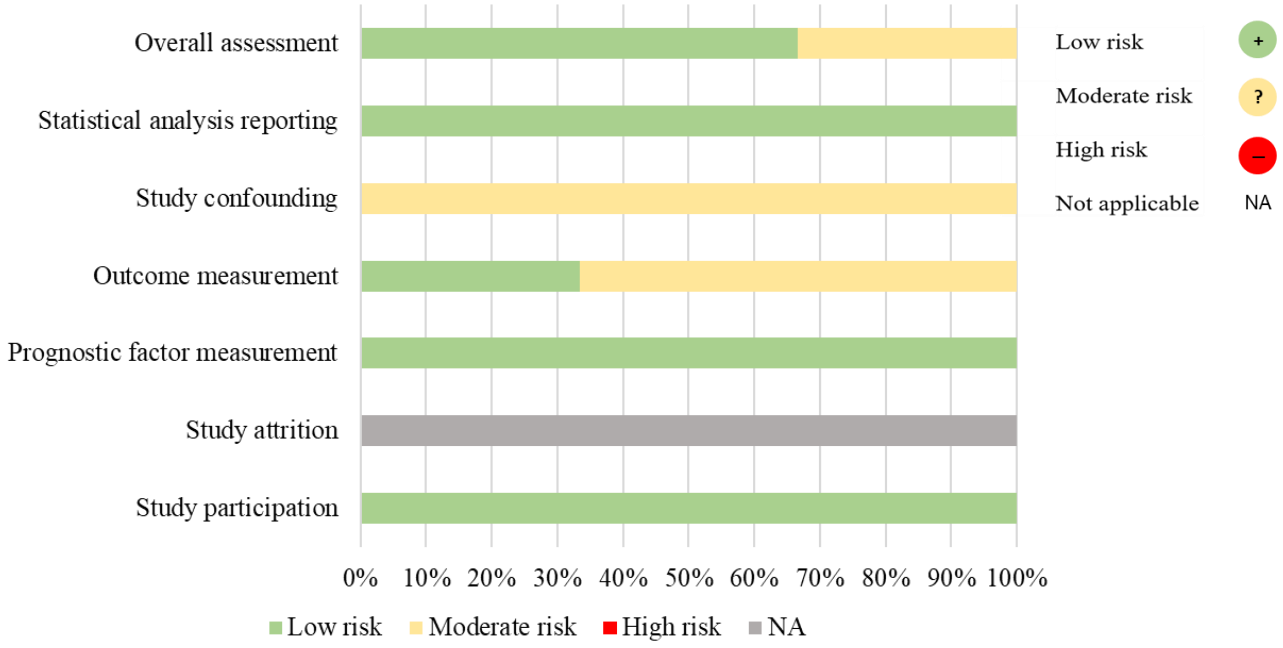
eFigure 23. Risk of bias assessment at study and domain level regarding *Pseudomonas aeruginosa* colonization

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Stephenson et al., 2013[2]		3	NA	3	3	1	3	1	yes
Dray et al., 2004[13]		2	NA	3	2	2	3	1	yes
Ramirez et al., 2014[14]		2	NA	3	2	2	3	1	yes
Panagopoulou et al.,2013[10]		3	NA	3	3	2	3	3	yes
Barni et al.,2017[8]		3	NA	3	3	3	3	3	yes
Bodnar et al.,2014[9]		3	NA	3	3	3	3	3	yes
Total	low	4		6	4	2	6	3	
Total	moderate	2			2	3			
Total	high					1		3	
Total	NA		6						



eFigure 24. Risk of bias assessment at study and domain level regarding fasting insulin.

Study		Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis reporting	**Overall risk of bias**	**Included in the MA**
Bonhoure et al., 2020[3]		3	NA	3	3	2	3	3	yes
Panagopoulou et al., 2013[10]		3	NA	3	2	2	3	2	yes
Jimenez et al., 2012[15]		3	NA	3	3	2	3	3	yes
Total	low	3		3	2		3	2	
Total	moderate				1	3		1	
Total	high								
Total	NA		3						



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