Online supplementary data

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Supplemental Table 1: Search strategy for controlled trials assessing the effect of oral honey intake on cardiometabolic outcomes

Databases and Search Terms		
MEDLINE	Embase	Cochrane
1. honey.mp. 2. exp Honey/ 3. 1 or 2 4. body weight.mp. 5. exp body weight/ 6. body fat.mp. 7. body fat/ 8. body mass index/ 9. BMI.mp. 10. waist circumference.mp. 11. exp waist circumference/ 12. waist-hip ratio.mp. 13. waist-hip ratio/ 14. exp Obesity/ 15. obes*.mp. 16. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 17. 3 and 16 18. lipids.mp. 19. exp Lipids/ 20. exp Cholesterol/ 21. exp Dyslipidemia/ 22. triglyceride*.mp. 23. triacylglycerol.mp. 24. dyslipidem*.mp. 25. lipoprotein*.mp. 26. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 27. 3 and 26 28. IL-6.mp. 29. Interleukin-6/	1. honey.mp. 2. exp Honey/ 3. 1 or 2 4. body weight.mp. 5. exp body weight/ 6. body fat.mp. 7. body fat/ 8. body mass index/ 9. BMI.mp. 10. waist circumference.mp. 11. exp waist circumference/ 12. waist-hip ratio.mp. 13. waist-hip ratio/ 14. exp Obesity/ 15. obes*.mp. 16. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 17. 3 and 16 18. lipids.mp. 19. exp Lipids/ 20. exp Cholesterol/ 21. exp Dyslipidemia/ 22. triglyceride*.mp. 23. triacylglycerol.mp. 24. dyslipidem*.mp. 25. lipoprotein*.mp. 26. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 27. 3 and 26 28. IL-6.mp. 29. Interleukin-6/	1. honey.mp. 2. exp Honey/ 3. 1 or 2 4. body weight.mp. 5. exp body weight/ 6. body fat.mp. 7. body fat/ 8. body mass index/ 9. BMI.mp. 10. waist circumference.mp. 11. exp waist circumference/ 12. waist-hip ratio.mp. 13. waist-hip ratio/ 14. exp Obesity/ 15. obes*.mp. 16. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 17. 3 AND 16 18. lipids.mp. 19. exp Lipids/ 20. exp Cholesterol/ 21. exp Dyslipidemia/ 22. triglyceride*.mp. 23. triacylglycerol.mp. 24. dyslipidem*.mp. 25. lipoprotein*.mp. 26. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 27. 3 AND 26 28. IL-6.mp. 29. Interleukin-6/

30. CRP.mp. 31. C-Reactive Protein/ 32. hs-CRP.mp. 33. TNF-alpha.mp. 34. Tumor Necrosis Factor-alpha/ 35. 28 or 29 or 30 or 31 or 32 or 33 or 34 36. 3 and 35 37. exp hypertension/ 38. exp hypotension/ 39. Blood Pressure/ 40. blood pressure.mp. 41. Heart Rate/ 42. systol*.mp. 43. diastol*.mp. 44. mean arterial pressure.mp. 45. heart rate.mp. 46. beats per minute.mp. 47. 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 48. 3 and 47 49. exp Diabetes Mellitus/ 50. exp Hyperglycemia/ 51. exp Hyperinsulinism/ 52. exp Hypoglycemia/ 53. exp Insulins/ 54. exp Glucagon/ 55. exp Glucose/ 56. Glucose Tolerance Test/ 57. Hemoglobin A, Glycosylated/ 58. glyc?emia.mp. 59. insulin*.mp.	30. CRP.mp. 31. C-Reactive Protein/ 32. hs-CRP.mp. 33. TNF-alpha.mp. 34. Tumor Necrosis Factor-alpha/ 35. 28 or 29 or 30 or 31 or 32 or 33 or 34 36. 3 and 35 37. exp hypertension/ 38. exp hypotension/ 39. Blood Pressure/ 40. blood pressure.mp. 41. Heart Rate/ 42. systol*.mp. 43. diastol*.mp. 44. mean arterial pressure.mp. 45. heart rate.mp. 46. beats per minute.mp. 47. 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 48. 3 and 47 49. exp Diabetes Mellitus/ 50. exp Hyperglycemia/ 51. exp Hyperinsulinism/ 52. exp Hypoglycemia/ 53. exp Insulins/ 54. exp Glucagon/ 55. exp Glucose/ 56. Glucose Tolerance Test/ 57. Hemoglobin A, Glycosylated/ 58. glyc?emia.mp. 59. insulin*.mp. 60. gly* albumin.mp. 61. OGTT.mp. 62. hba1c.mp.	30. CRP.mp. 31. C-Reactive Protein/ 32. hs-CRP.mp. 33. TNF-alpha.mp. 34. Tumor Necrosis Factor-alpha/ 35. 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 36. 3 AND 35 37. exp hypertension/ 38. exp hypotension/ 39. Blood Pressure/ 40. blood pressure.mp. 41. Heart Rate/ 42. systol*.mp. 43. diastol*.mp. 44. mean arterial pressure.mp. 45. heart rate.mp. 46. beats per minute.mp. 47. 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 48. 3 AND 47 49. exp Diabetes Mellitus/ 50. exp Hyperglycemia/ 51. exp Hyperinsulinism/ 52. exp Hypoglycemia/ 53. exp Insulins/ 54. exp Glucagon/ 55. exp Glucose 56. Glucose Tolerance Test/ 57. Hemoglobin A, Glycosylated/ 58. glyc?emia.mp. 59. insulin*.mp. 60. gly* albumin.mp.

60. gly* albumin.mp. 61. OGTT.mp. 62. hba1c.mp. 63. HOMA*.mp. 64. diabet*.mp. 65. fructosamine*.mp. 66. 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 67. 3 and 66 68. 17 or 27 or 36 or 48 or 67 69. limit 68 to animals 70. 68 not 69 71. clinical trial.mp. 72. clinical trial.pt. 73. random:.mp. 74. tu.xs. 75. 71 or 72 or 73 or 74 76. 70 and 75	63. HOMA*.mp. 64. diabet*.mp. 65. fructosamine*.mp. 66. 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 67. 3 and 66 68. 17 or 27 or 36 or 48 or 67 69. limit 68 to animals 70. 68 not 69 71. limit 70 to animal studies 72. 70 not 71 73. random:.tw. 74. clinical trial:.mp. 75. exp health care quality/ 76. 73 or 74 or 75 77. 72 and 76	61. OGTT.mp. 62. hba1c.mp. 63. HOMA*.mp. 64. diabet*.mp. 65. fructosamine*.mp. 66. 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 67. 3 AND 66 68. 17 OR 27 OR 36 OR 48 OR 67

Database	Total
MEDLINE 1946 to January 11, 2021	223
Embase 1947 to January 11, 2021	349
Cochrane 1991 to January 11, 2021	235
Manual	1
Total	808

Supplemental Table 2: PICOTS framework of the search strategy for controlled trials assessing the effect of oral honey intake on cardiometabolic outcomes

PICO framework (1) defined in the present systematic review and meta-analysis					
Participants	**Interventions**	**Comparators**	**Outcomes**	**Time**	**Study design**
Individuals of all ages and health backgrounds	Oral honey intake	Any carbohydrate intake free from honey	Adiposity, glycemic control, lipids, blood pressure, uric acid, inflammatory markers, and markers of non-alcoholic fatty liver disease, mean difference and 95% confidence intervals	≥7 days	Controlled trials done in humans

PICOTS=participants, interventions, comparators, outcomes, time and study design

Supplemental Table 3: Controlled trial characteristics assessing the effect of oral honey intake on cardiometabolic outcomes

Study, Year	Participants	Setting	Mean Age, years (SD or range)	Mean BMI, kg/m^2 (SD)	Design	Feeding Control	Randomization	Honey dose, g/d (% E)	Intervention or Control	Diet	Energy Balance	Follow-up	Funding Sources	Outcomes
Abdulrhman et al. 2013[1]	20 DM1 (10F, 10M)	OP, Egypt	11.4 (4.2)	21.1 (5.3)	C	Supp	Yes	~26.6 (~4)		NR	Neutral	12 wk	NR	
Intervention									Honey added to diet					FBG, HbA1c, Tchol, LDL, HDL, FTRIG
Control									Usual diet					
Al-tamimi et al. 2019[2]	37 H (16F, 21M)	OP, USA	32.9 (10.3)	25.4 (4.3)	C	Supp	Yes	90 (13.5)			Positive	4 wk	I	
Intervention									Clover honey in 250-300mL beverage	51:33:16				FInsulin, Tchol, LDL, HDL, FTRIG, BW
Control									Sucrose in 250-300mL beverage	53:32:!5				
Bahrami et al. 2009[3]	48 DM2 (35F, 13M)	OP, Iran	57.2 (8.4)	NR	P	Supp	Yes	~125 (~33)			Positive	8 wk	A	
Intervention	25 DM2								Polyfloral honey added to diet	64:23:15				FBG, HbA1c, Tchol, LDL, HDL, FTRIG, BW
Control	23 DM2								Usual diet	60:22:15				
Despland et al. 2017[4]	8H (0F, 8M)	IP/OP, Switzerland	NR	NR	C	Met	Yes	~125 (25)		55:30:15	Neutral	7-8 d	A	
Intervention									25% of starch replaced by Robinia honey					FBG, FInsulin, HOMA-IR, BW, SBP, DBP, UA
Control									25% of starch replaced by glucose/fructose mixture					
Control									Usual diet					
Enginyurt et al. 2017 (DM2)[5]	32 DM2 (16F, 16M)	OP, Turkey	(18-80)	NR	P	Supp	Yes			NR	Positive	4 mo	NR	
Intervention								25 (3.75)	25g honey added to diet					HbA1c, Tchol, LDL, HDL, FTRIG
Intervention								15 (2.25)	15g honey added to diet					
Intervention								5 (0.75)	5g honey added to diet					
Control									Usual diet					
Enginyurt et al. 2017 (H)[5]	32 H (16F, 16M)	OP, Turkey	(18-80)	NR	P	Supp	Yes			NR	Positive	4 mo	NR	HbA1c, Tchol, LDL, HDL, FTRIG
Intervention								25 (3.75)	25g honey added to diet					

Intervention								15 (2.25)	15g honey added to diet					
Intervention								5 (0.75)	5g honey added to diet					
Control									Usual diet					
Farakla et al. 2018[6]	30 OB (15F, 0M)	OP, Greece	10.55 (1.86)	28.58 (7.67)	P	Supp	Yes	15 (2.8)		50:30:20	Neutral	24 wk	A	FBG, HbA1c, FInsulin, HOMA-IR, Tchol, LDL, HDL, FTRIG, ApoB, BW, BMI, hsCRP, TNFα
Intervention	15 OB (15F, 0M)								15g polyfloral honey					
Control	15 OB (15F, 0M)								15g marmalade					
Ghazali et al. 2017[7]	64 smokers	OP, Malaysia	38.38 (7.8)	NR	P	Supp	Yes	20 (3)		NR	Positive	12 wk	A	hsCRP, TNFα, IL-6
Intervention	32 smokers								20g Malaysia tualang honey added to diet					
Control	32 smokers								Usual diet					
Jayadi et al. 2019[8]	26 H	OP, Indonesia			P	Supp	No	70 (14)		NR	Positive	60 d	A	FBG, Tchol, LDL, HDL, FTRIG, BW, BMI, WC
Intervention	13 H		39.7 (9.24)	28.9 (3.3)					70g polyfloral honey in 250 mL water					
Control	13 H		44 (9.8)	29.57 (3)					Usual diet					
Majid et al. 2013[9]	63 H (0F, 63M)	IP, Pakistan	20.1 (0.8)	NR	P	Met	Yes	70 (10.5)		NR	Positive	4 wk	A	
Intervention	32 H (0F, 32M)		20.1 (0.1)						70g acacia modesta honey in 250 mL water					FBG, Tchol, LDL, HDL, FTRIG
Control	31 H (0F, 31M)		20.0 (0.2)						Usual diet					
Munstedt et al. 2009[10]	60 HCL (34F, 26M)	OP, Germany			P	Supp	Yes	75 (11.25)		NR	Positive	2 wk	I	
Intervention	30 HCL (17F, 13M)		62.6 (10.9)	25.3 (3.2)					75g polyfloral honey in 150mL warm water					Tchol, LDL, HDL, FTRIG
Control	30 HCL (17F, 13M)		58.8 (9.1)	25.8 (3.2)					75g glucose/fructose mixture in 150mL warm water					
Mushtaq et al. 2011 (NW-F)[11]	64 H (64F, 0M)	OP, Pakistan			P	Supp	Yes	40 (6)		NR	Positive	4 wk	NR	Tchol, LDL, HDL, FTRIG, BMI
Intervention	32 H (32F, 0M)		42.81 (3.37)	21.3 (0.58)					40g polyfloral honey in water					
Control	32 H (32F, 0M)		42.91 (2.15)	21.58 (0.55)					Usual diet					
Mushtaq et al. 2011 (NW-M)[11]	64 H (0F, 64M)	OP, Pakistan			P	Supp	Yes	40 (6)		NR	Positive	4 wk	NR	Tchol, LDL, HDL, FTRIG, BMI

Intervention	32 H (0F, 32M)		46.25 (3.51)	22.3 (0.55)					40g polyfloral honey in water					
Control	32 H (0F, 32M)		42.5 (1.78)	21.9 (0.93)					Usual diet					
Mushtaq et al. 2011 (OW/OB-F)[11]	64 OB (64F, 0M)	OP, Pakistan			P	Supp	Yes	40 (6)		NR	Positive	4 wk	NR	Tchol, LDL, HDL, FTRIG, BMI
Intervention	32 OB (32F, 0M)		40.06 (2.63)	38.2 (0.75)					40g polyfloral honey in water					
Control	32 OB (32F, 0M)		39.66 (2.53)	40.1 (0.9)					Usual diet					
Mushtaq et al. 2011 (OW/OB-M)[11]	64 H (0F, 64M)	OP, Pakistan			P	Supp	Yes	40 (6)		NR	Positive	4 wk	NR	Tchol, LDL, HDL, FTRIG, BMI
Intervention	32 H (0F, 32M)		41.72 (2.85)	38.7 (0.63)					40g polyfloral honey in water					
Control	32 H (0F, 32M)		39.87 (2.12)	40.93 (1.3)					Usual diet					
Raatz et al. 2015 (GT)[12]	28 GT (17F, 11M)	OP, USA	38.9 (20.1)	26 (4.2)	C	Supp	Yes	50 (7.5)		NR	Neutral	2 wk	I	FBG, FInsulin, HOMA-IR, Tchol, LDL, HDL, FTRIG, BW, SBP, DBP, hsCRP, IL-6
Intervention									50g polyfloral honey in fruit flavored beverage					
Control									50g sucrose in fruit flavored beverage					
Control									50g HFCS in fruit flavored beverage					
Raatz et al. 2015 (IGT)[12]	17 IGT (22F, 5M)	OP, USA	52.1 (14)	31.5 (5.2)	C	Supp	Yes	50 (7.5)		NR	Neutral	2 wk	I	FBG, FInsulin, HOMA-IR, Tchol, LDL, HDL, FTRIG, BW, SBP, DBP, hsCRP, IL-6
Intervention									50g polyfloral honey in fruit flavored beverage					
Control									50g sucrose in fruit flavored beverage					
Control									50g HFCS in fruit flavored beverage					
Rasad et al. 2018[13]	60 H (0F, 60M)	OP, Iran			P	Supp	Yes	80 (10.6)			Positive	6 wk	NR	FBG, Tchol, LDL, HDL, FTRIG, SBP, DBP
Intervention	30 H (0F, 30M)		21.53 (1.63)	23.37 (4.04)					80g honey in 250mL water	57.4:27.1: 16.2				
Control	30 H (0F, 30M)		24.23 (1.88)	22.55 (3.92)					80g sucrose in 250mL water	60.7:25.2: 15				
Rashid et al. 2019[14]	60 IGT (30F, 30M)	OP, Malaysia	51.6 (11.5)	29.7 (5.2)	P	Supp	NR	30 (4.5)		NR	Positive	4 wk	A	FBG, Tchol, LDL, HDL, FTRIG, BMI, SBP, DBP
Intervention	30 IGT (13F, 17M)		52.8 (10.4)	29.5 (4.8)					30g Kelulut honey					
Control	30 IGT (17F, 13M)		50.4 (12.5)	29.8 (5.6)					Usual diet					
Tang et al. 2020[15]	95 HIV (81 M, 14 F)	IP, Malaysia	(21-58)		P	Met	Yes			NR	Positive	6 mo	A	FBG, Tchol, LDL, HDL, FTRIG, BW, BMI, SBP, DBP, UA
Intervention	26 HIV			22 (3)				20 (3)	20g Tualang honey in water					
Intervention	24 HIV			22 (3)				40 (6)	40g Tualang honey in water					

Intervention	22 HIV			21 (2)				60 (9)	40g Tualang honey in water					
Control	23 HIV			23 (3)										
Salehi et al. 2020[16]	42 DM2 (24F, 18M)	OP, Iran	57.5 (9.8)	27.8 (3.6)	C	Supp	Yes	50 (9.9)		61.9:26.3: 11.8	Neutral	8 wk	A	
Intervention									50g milk vetch honey in tea, coffee, or milk					FBG, Tchol, LDL, HDL, FTRIG, hsCRP
Control									Usual diet					
Yaghoobi et al. 2008[17]	55 OW/OB (31F, 24M)	OP, Iran	41.2 (9.2)		P	Supp	Yes	70 (10.5)		NR	Positive	4 wk	A	FBG, Tchol, LDL, HDL, FTRIG, BW, hsCRP
Intervention	38 OW/OB		42.6 (8.6)	30.1 (3.1)					70g honey in 250mL water					
Control	17 OW/OB		39.6 (10.6)	32.6 (6.6)					70g sucrose in 250 mL water					
Zakaria et al. 2018[18]	72 Breast cancer (72F, 0M)	OP, Malaysia		NR	P	Supp	Yes	20 (4)		NR	Positive	3 mo	A	
Intervention	36 Breast cancer (72F, 0M)		56.5 (1)						20g Tualang honey					FBG, ALT
Control	36 Breast cancer (72F, 0M)		59.6 (1.29)						Usual diet					

*All values presented as mean ± SD, unless otherwise indicated.
%E=percentage of total energy intake, ALT=alanine aminotransferase, ApoB=apolipoprotein B, BMI=body mass index, BW=body weight, C=crossover, DBP=diastolic blood pressure, DMI=type 1 diabetes mellitus, DM2= type 2 diabetes mellitus F=female, FBG=fasting blood glucose, FInsulin=fasting insulin, FTRIG=fasting triglycerides, GT=glucose tolerant H=healthy, HbA1c=glycated hemoglobin, HCL=hypercholesterolemic, HDL=high density lipoprotein, HOMA-IR= Homeostatic Model Assessment of Insulin Resistance, hsCRP=high sensitivity C-reactive protein, IGT=impaired glucose tolerance, IL-6=interleukin 6, IP=in patient, LDL=low density lipoprotein, NR=not reported, M=male, Met=metabolically controlled, OB=obese, OP=out patient, OW=overweight, P=parallel, supp=supplemented, SBP=systolic blood pressure, Tchol=total cholesterol, TNFα=tumor necrosis factor α, UA=uric acid, WC=waist circumference
[a]Metabolic feeding control included provision of all study foods, supplement feeding control included provision of study supplements only, and dietary advice included dietary counselling without the provision of any dietary foods or supplements.
[b]Dose preceded by "~" represent approximates calculated on the basis of average energy intake reported by participants. In the absence of this data, an average of 2000 kcal/d was assumed.
[c]Total energy intake in the form of carbohydrate:fat:protein
[d]Positive energy balance included interventions designed to consume excess calories on top of a baseline diet. Negative energy balance included interventions designed to create a calorie deficit compared to the baseline diet. Neutral energy balance included interventions de-signed to continue habitual caloric intake.
[e]Agency funding included government, not-for-profit health agencies or University source.

Supplemental Table 4: Sensitivity analyses of the use of correlation coefficients of 0.25 and 0.75 for crossover trials in the primary analysis of the effect of oral honey intake on cardiometabolic outcomes

Cardiometabolic Outcome	MD (95% CI), P-value I^2, P-value		
	Correlation Coefficient used in the Primary Analysis	Correlation Coefficient used in Sensitivity Analyses	
	0·5	0·25	0·75
Adiposity			
Body Weight (kg)	-0·92 [-2·04, 0·19], p_{MD}=0·105 I^2=0·00%, p_Q=0·995	-0·97 [-2·11, 0·17], p_{MD}=0·096 I^2=0·00%, p_Q=0·996	-0·81 [-1·86, 0·25], p_{MD}=0·135 I^2=0·00%, p_Q=0·991
BMI (kg/m^2)	0·00 [-0·06, 0·05], p_{MD}=0·905 I^2=0·0%, p_Q=0·999	-0·00 [-0·06, 0·05], p_{MD}=0·905 I^2=0·00%, p_Q=0·999	-0·00 [-0·06, 0·05], p_{MD}=0·905 I^2=0·00%, p_Q=0·999
Blood Pressure			
SBP (mmHg)	1·00 [-0·50, 2·50], p_{MD}=0·190 I^2=6·6%, p_Q=0·190	0·39 [-0·84, 1·62], p_{MD}=0·530 I^2=0·00%, p_Q=0·490	1·73 [0·05, 3·42], p_{MD}=0·043 I^2=28·39%, p_Q=0·175
DBP (mmHg)	1·25 [-0·13, 2·64], p_{MD}=0·076 I^2=0·0%, p_Q=0·797	1·02 [-0·53, 2·57], p_{MD}=0·198 I^2=0·00%, p_Q=0·880	1·60 [0·49, 2·70], p_{MD}=0·005 I^2=0·00%, p_Q=0·569
Glycemic Outcomes			
Fasting Glucose (mmol/L)	-0·20 [-0·37, -0·04], p_{MD}=0·017 I^2=76·8%, p_Q<0.001	-0·19 [-0·36, -0·03], p_{MD}=0·022 I^2=72·09%, p_Q<0.001	-0·23 [-0·40, -0·05], p_{MD}=0·012 I^2=80·67%, p_Q<0.001
Fasting Insulin (uU/mL)	0·19 [-1·60, 1·99], p_{MD}=0·832 I^2=0·00%, p_Q=0·972	0·15 [-1·74, 2·03], p_{MD}=0·880 I^2=0·00%, p_Q=0·987	0·35 [-1·25, 1·95], p_{MD}=0·668 I^2=0·00, p_Q=0·916
HbA1c (%)	-0·25 [-0·52, 0·04], p_{MD}=0·086 I^2=63·0%, p_Q=0·004	-0·24 [-0·51, 0·04], p_{MD}=0·093 I^2=59·54%, p_Q=0·008	-0·25 [-0·53, 0·03], p_{MD}=0·079 I^2=67·02, p_Q=0.001
HOMA-IR	0·03 [-0·35, 0·41], p_{MD}=0·872 I^2=0·00%, p_Q=0·951	0·02 [-0·33, 0·36], p_{MD}=0·927 I^2=0·00%, p_Q=0·973	0·02 [-0·19, 0·23], p_{MD}=0·835 I^2=0·00%, p_Q=0·874
Cholesterol Outcomes			
Total Cholesterol (mmol/L)	-0·18 [-0·33, -0·04], p_{MD}=0·011 I^2=65·1%, p_Q<0.001	-0·19 [-0·33, -0·05], p_{MD}=0·001 I^2=60·90%, p_Q<0.001	-0·18 [-0·32, -0·04], p_{MD}=0·013 I^2=68·61%, p_Q<0.001
LDL (mmol/L)	-0·16 [-0·37, -0·02], p_{MD}=0.024 I^2=73·8%, p_Q<0.001	-0·16 [-0·30, 0·02], p_{MD}=0·023 I^2=71·83%, p_Q<0.001	-0·15 [-0·29, -0·02], p_{MD}=0·026 I^2=77·13%, p_Q<0.001
HDL (mmol/L)	0·07 [0·04, 0·10], p_{MD}<0.001 I^2=33·0%, p_Q=0·046	0·07 [0·04, 0·10], p_{MD}<0.001 I^2=25·02%, p_Q=0·112	0·06 [0·03, 0·09], p_{MD}<0.001 I^2=46·30%, p_Q=0·004
Fasting Triglycerides (mmol/L)	-0·13 [-0·20, -0·07], p_{MD}<0.001 I^2=63·4%, p_Q<0.001	-0·13 [-0·20, 0·07], p_{MD}<0.001 I^2=58·19%, p_Q<0.001	-0·12 [-0·19, -0·05], p_{MD}=0·001 I^2=70·97%, p_Q<0.001
Markers of Inflammation			
hsCRP (mg/L)	-0·03 [-0·08, 0·02], p_{MD}=0.236 I^2=0·00%, p_Q=0·940	-0·03 [-0·08, 0·02], p_{MD}=0.232 I^2=0·00%, p_Q=0·956	-0·03 [-0·08, 0·02], p_{MD}=0·244 I^2=0·00%, p_Q=0·897
IL-6 (pg/mL)	0·37 [0·01, 0·74], p_{MD}=0.046 I^2=0·00%, p_Q=0·847	0·37 [-0·04, 0·79], p_{MD}=0·075 I^2=0·00%, p_Q=0·917	0·38 [0·09, 0·68], p_{MD}=0·012 I^2=0·0%, p_Q=0·635
TNFα (pg/mL)	1·44 [0·24, 2·64], p_{MD}=0.019 I^2=22·9%, p_Q=0·255	1·44 [0·24, 2·64], p_{MD}=0·019 I^2=22·9%, p_Q=0·255	1·44 [0·24, 2·64], p_{MD}=0·019 I^2=22·92%, p_Q=0·255
Uric Acid (mg/dL)			
Uric Acid (mg/dL)	-0·07 [-0·21, 0·07], p_{MD}=0·340 I^2=0·00%, p_Q=0·997	-0·07 [-0·21, 0·07], p_{MD}=0·340 I^2=0·00%, p_Q=0·997	-0·07 [-0·21, 0·07], p_{MD}=0·340 I^2=0·00%, p_Q=0·997

Supplemental Table 5: GRADE certainty of evidence assessment* for the effect of oral honey intake on cardiometabolic outcomes

Trial (N)	Design	Quality assessment						Effect (MD [95%CI], P_{MD})		Quality
		Downgrades					Upgrades			
		Study limitations (Risk of Bias)	Inconsistency	Indirectness	Imprecision	Publication bias	Dose response			
Adiposity										
Body Weight (kg)										
14	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.92 [-2.04, 0.19], P=0.105	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-2.04, 0.19kg) crossed the MID (0.5kg)	Non-significant funnel plot				
BMI (kg/m^2)										
10	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.00 [-0.06, 0.05], P=0.905	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.06, 0.05kg/m^2) did not cross the MID (0.2kg/m^2)[19]	Non-significant funnel plot				
Waist circumference (cm)										
1	Non-randomized trials	Serious	Not serious	Serious	Serious	None	N/A	↔	-0.30 [-4.90, 4.30], P=0.898	⊕◯◯◯ Very low
Justification		The trial included was rated to have a high risk of bias	No evidence of heterogeneity (1 trial)	Number and type of trials limited the generalizability of the results	The confidence interval (-4.90, 4.30cm) crossed the MID (2cm)	Insufficient number of trials to assess				
Blood Pressure										
SBP (mmHg)										

11	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	Upgrade	↔	1.00 [-0.50, 2.50], P=0.190	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.50, 2.50mmHg) crossed the MID (2mmHg)[20]	Non-significant funnel plot	Significant linear dose response: -0.072 (95% CI -0.127, -0.017) P=0.010			
DBP (mmHg)										
11	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	1.25 [-0.13, 2.64], P=0.076	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.13, 2.64mmHg) crossed the MID (2mmHg)[20]	Non-significant funnel plot				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
20	Randomized and non-randomized trials	Not serious	Serious	Not serious	Not serious	Serious	N/A	↓	-0.20 [-0.37, -0.04], P=0.017	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=76.8% P_q<0.001)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.37, -0.04mmol/L) did not cross the MID (0.5mmol/L)[21]	Significant funnel plot. Trim and fill analyses resulted in a non-significant reduction (P=0.303)				
Fasting Insulin (uU/mL)										
8	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.19 [-1.60, 1.99], P=0.832	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.60, 1.99uU/mL) crossed the MID (0.72uU/mL)[21]	Insufficient number of trials to assess				
HbA1c (%)										
10	Randomized trials	Not serious	Serious	Not serious	Not serious	None	N/A	↔	-0.25 [-0.52, 0.04], P=0.086	⊕⊕⊕◯ Moderate

Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=63% P_q=0.004)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.52, 0.04%) did not cross the MID (3%)[22]	Non-significant funnel plot				
HOMA-IR										
7	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.03 [-0.35, 0.41], P=0.872	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.35, 0.41) did not cross the MID (1)	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
29	Randomized and non-randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.18 [-0.33, -0.04], P=0.011	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=75.1% P_q<0.001)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.33, -0.04mmol/L) crossed the MID (0.1mmol/L)[23]	Non-significant funnel plot				
LDL Cholesterol (mmol/L)										
29	Randomized and non-randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.16 [-0.30, -0.02], P=0.024	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=73.8% P_q<0.001)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.30, -0.02mmol/L) crossed the MID (0.1mmol/L)[23]	Non-significant funnel plot				
HDL Cholesterol (mmol/L)										
29	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↑	0.07 [0.04, 0.10], P<0.001	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit	The confidence interval (0.04, 0.10mmol/L) did not cross	Significant funnel plot. No studies imputed in the				

				generalizability of the results	the MID (0.1mmol/L)[23]	trim-and-fill analyses.				
Fasting triglycerides (mmol/L)										
29	Randomized and non-randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.13 [-0.20, -0.07], P<0.001	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=63.4% P_q<0.001)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.20, -0.07mmol/L) crossed the MID (0.1mmol/L)[23]	Significant funnel plot. Trim and fill analyses imputed 3 studies but maintained a significant reduction.				
Apolipoprotein B (mg/dL)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	-2.07 [-14.64, 10.50], P=0.747	⊕⊕◯◯ Low
Justification		The trial included was rated to have a low risk of bias	No evidence of heterogeneity (1 trial)	Number and type of trials limited the generalizability of the results	The confidence interval (-14.64, 10.50mg/dL) crossed the MID (4mg/dL)	Insufficient number of trials to assess				
Markers of Inflammation										
hsCRP (mg/L)										
8	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	-0.03 [-0.08, 0.02], P=0.236	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.08, 0.02mg/L) did not the MID (0.5mg/L)[24,25]	Insufficient number of trials to assess				
IL-6 (pg/mL)										
5	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	0.37 [0.01, 0.74], P=0.046	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.01, 0.74pg/mL) crossed the MID (0.18pg/mL)[26,27]	Insufficient number of trials to assess				
TNFα (pg/mL)										
2	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	1.44 [0.24, 2.64], P=0.019	⊕⊕⊕◯ Moderate

Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.24, 2.64pg/mL) crossed the MID (0.28pg/mL)[28,29,30,31]	Insufficient number of trials to assess				
Uric acid										
Uric acid (mg/dL)										
5	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.07 [-0.21, 0.07], P=0.340	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.21, 0.07mg/dL) crossed the MID (0.113mg/dL)[32]	Insufficient number of trials to assess				
Markers of NAFLD										
Alanine aminotransferase (U/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↓	-9.75 [-18.29, -1.21], P=0.025	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-18.29, -1.21U/L) crossed the MID (2.85U/L)[33]					

*Since all included trials were randomized or non-randomized controlled trials, the certainty of the evidence was graded as high for all outcomes by default and then downgraded or upgraded based on pre-specified criteria. Criteria for downgrades included risk of bias (downgraded if the majority of trials were considered to be at high risk of bias); inconsistency (downgraded if there was substantial unexplained heterogeneity [$I^2 \geq 50\%$, $P < 0.1$]; indirectness (downgraded if there were factors absent or present relating to the participants, interventions, or outcomes that limited the generalizability of the results); imprecision (downgraded if the 95% confidence interval crossed the minimally important difference [MID] for harm set at ±0.113mg/dL); and publication bias (downgraded if there is evidence of publication bias based on funnel plot asymmetry and/or significant Egger's or Begg's tests (P<0.1) with confirmation by adjustment by Duval and Tweedie trim-and-fill analysis). Criteria for upgrades included a significant dose-response gradient.

CI= confidence interval; MD=mean difference; MID=minimally important difference; N/A=not applicable.

Supplemental Table 6: GRADE certainty of evidence assessment* for the effect of raw vs processed honey intake on cardiometabolic outcomes

Trial (N)	Design	Quality assessment						Effect (MD [95%CI], P_{MD})		Quality
		Downgrades					Upgrades			
		Study limitations (Risk of Bias)	Inconsistency	Indirectness	Imprecision	Publication bias	Dose response			
RAW HONEY										
Adiposity										
Body Weight (kg)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↓	-1.80 [-3.54, -0.06], P=0.0.043	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited generalizability of the results	The confidence interval (-3.54, -0.06kg) crossed the MID (0.5kg)	Insufficient number of trials to assess				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
5	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-1.05 [-1.90, -0.20], P=0.015	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=90.35 % P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.90, -0.20mmol/L) crossed the MID (0.5mmol/L)[21]	Insufficient number of trials to assess				
HbA1c (%)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.21 [-0.52, 0.11], P=0.200	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=88.79% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.52, 0.11%) crossed the MID (0.3%)[22]	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										

5	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-0.61 [-1.07, -0.14], P=0.011	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=87.66 % P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.07, -0.14mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
LDL Cholesterol (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.47 [-1.01, 0.08], P=0.092	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=93.61% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.01, 0.08mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
HDL Cholesterol (mmol/L)										
5	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↑	0.11 [0.02, 0.20], P=0.021	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=69.10% P_q=0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (0.02, 0.20mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
Fasting triglycerides (mmol/L)										
5	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-0.27 [-0.43, -0.10], P<0.001	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=75.74% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.43, -0.10mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
Markers of Inflammation										
hsCRP (mg/L)										
1	Randomized trial	Not serious	Not serious	Serious	Not serious	None	N/A	↔	-0.03 [-0.08, 0.02], P=0.225	⊕⊕⊕◯ Moderate
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited generalizability of the results	The confidence interval (-0.08, 0.02mg/L) crossed the MID (0.5mg/L)[24,25]	Insufficient number of trials to assess				

PROCESSED HONEY										
Adiposity Outcomes										
Body Weight (kg)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.61 [-2.34, 3.57], P=0.683	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-2.34, 3.57kg) crossed the MID (0.5kg)	Insufficient number of trials to assess				
BMI (kg/m^2)										
3	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.21 [-1.29, 1.72], P=0.782	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.29, 1.72kg/m^2) crossed the MID (0.2kg/m^2)[19]	Insufficient number of trials to assess				
Blood Pressure										
SBP (mmHg)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	3.78 [0.76, 6.80], P=0.014	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.76, 6.80mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
DBP (mmHg)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	2.26 [0.35, 4.17], P=0.021	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.35, 4.17mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
7	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.03 [-0.11, 0.16], P=0.721	⊕⊕⊕⊕ High

Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.11, 0.16mmol/L) did not cross the MID (0.5mmol/L)[21]	Insufficient number of trials to assess				
Fasting Insulin (uU/mL)										
4	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.12 [-3.28, 3.52], P=0.945	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-3.82, 3.52uU/mL) crossed the MID (0.72uU/mL)[21]	Insufficient number of trials to assess				
HOMA-IR										
4	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.13 [-0.84, 1.09], P=0.797	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.84, 1.09) did not cross the MID (1)	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.04 [-0.23, 0.32], P=0.761	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.23, 0.32mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
LDL Cholesterol (mmol/L)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.06 [-0.14, 0.27], P=0.541	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.14, 0.27mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess.				
HDL Cholesterol (mmol/L)										
7	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.02 [-0.06, 0.10], P=0.609	⊕⊕⊕⊕ High

Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.06, 0.10mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess.				
Fasting triglycerides (mmol/L)										
7	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.05 [-0.19, 0.28], P=0.709	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.19, 0.28mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
Markers of Inflammation										
hsCRP (mg/L)										
4	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.57 [-0.78, 1.93], P=0.407	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.78, 1.93mg/L) crossed the MID (0.5mg/L)[24,25]	Insufficient number of trials to assess				
IL-6 (pg/mL)										
4	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	0.36 [-0.10, 0.81], P=0.121	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.10, 0.81pg/mL) crossed the MID (0.18pg/mL)[26,27]	Insufficient number of trials to assess				
Uric acid										
Uric acid (mg/dL)										
3	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.10 [-0.95, 0.75], P=0.818	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.95, 0.75mg/dL) crossed the MID (0.113mg/dL)[32]	Insufficient number of trials to assess				

*Since all included trials were randomized or non-randomized controlled trials, the certainty of the evidence was graded as high for all outcomes by default and then downgraded or upgraded based on pre-specified criteria. Criteria for downgrades included risk of bias (downgraded if the majority of trials were considered to be at high risk of bias); inconsistency (downgraded if there was substantial unexplained heterogeneity [$I^2 \geq 50\%$, $P < 0.1$]; indirectness (downgraded if there were factors absent or present relating to the participants, interventions, or outcomes that limited the generalizability of the results); imprecision (downgraded if the 95% confidence interval crossed the minimally important difference [MID] for harm set at ±0.113mg/dL); and publication bias (downgraded if there is evidence of publication bias based on funnel plot asymmetry and/or significant Egger's or Begg's tests ($P<0.1$) with confirmation by adjustment by Duval and Tweedie trim-and-fill analysis). Criteria for upgrades included a significant dose-response gradient.
CI= confidence interval; MD=mean difference; MID=minimally important difference; N/A=not applicable.

Supplemental Table 7: GRADE certainty of evidence assessment* for the effect of difference floral sources of honey on cardiometabolic outcomes

Trial (N)	Design	Quality assessment						Effect (MD [95%CI], P_{MD})		Quality
		Downgrades					Upgrades			
		Study limitations (Risk of Bias)	Inconsistency	Indirectness	Imprecision	Publication bias	Dose response			
CLOVER HONEY										
Adiposity										
Body Weight (kg)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↔	0.40 [-4.37, 5.18], P=0.869	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited generalizability of the results	The confidence interval (-4.37, 5.18kg) crossed the MID (0.5kg)	Insufficient number of trials to assess				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
2	Randomized trials	Not serious	Serious	Serious	Serious	None	N/A	↓	-1.82 [-2.35, -1.30], P<0.001	⊕◯◯◯ Very low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=85.74% P_q<0.001)	Number and type of trial did limit generalizability of the results	The confidence interval (-2.35, -1.30mmol/L) crossed the MID (0.5mmol/L)[21]	Insufficient number of trials to assess				
Fasting Insulin (uU/mL)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↔	2.90 [-8.57, 14.37], P=0.620	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited generalizability of the results	The confidence interval (-8.57, 14.37uU/mL) crossed the MID (0.72uU/mL)[21]	Insufficient number of trials to assess				
HbA1c (%)										
2	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-0.68 [-1.10, -0.26], P=0.001	⊕⊕◯◯ Low

Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=84.81% P_q=0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.10, 0.26%) crossed the MID (0.3%)[22]	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-0.44 [-0.63, -0.26], P=0.011	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=91.99% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.63, -0.26mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
LDL Cholesterol (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.38 [-0.56, -0.20], P<0.001	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=93.31% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.56, -0.20mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
HDL Cholesterol (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↑	0.08 [0.02, 0.15], P=0.011	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=86.50% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (0.02, 0.15mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
Fasting triglycerides (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↓	-0.31 [-0.39, -0.24], P<0.001	⊕⊕◯◯ Low
Justification		Studies were rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=88.36% P_q<0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.39, -0.24mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
ROBINIA HONEY										
Adiposity										

Body Weight (kg)										
2	Randomized trial	Serious	Not serious	Serious	Serious	None	N/A	↔	1.26 [-4.08, 6.61], P=0.643	⊕⊕◯◯ Low
Justification		Some studies were rated to have a high risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-4.08, 6.61kg) crossed the MID (0.5kg)	Insufficient number of trials to assess				
Blood Pressure										
Systolic Blood Pressure (mmHg)										
2	Randomized trials	Serious	Not serious	Serious	Serious	None	N/A	↔	-0.71 [-5.22, 3.80], P=0.758	⊕◯◯◯ Very low
Justification		Some studies were rated to have a high risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-5.22, 3.80mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
Diastolic Blood Pressure (mmHg)										
2	Randomized trials	Serious	Not serious	Not serious	Serious	None	N/A	↔	1.95 [-1.37, 5.27], P=0.249	⊕◯◯◯ Very low
Justification		Some studies were rated to have a high risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-1.37, 5.27mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
3	Randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.02 [-0.12, 0.07], P=0.621	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=78.02% P_q=0.01)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.12, 0.07mmol/L) crossed the MID (0.5mmol/L)[21]	Insufficient number of trials to assess				
Fasting Insulin (uU/mL)										
2	Randomized trials	Serious	Not serious	Serious	Serious	None	N/A	↔	0.02 [-2.21, 2.24], P=0.989	⊕◯◯◯ Very low
Justification		Some studies were rated to have a high risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-2.21, 2.24uU/mL) crossed the					

					MID (0.72uU/mL)[21]					
HOMA-IR										
2	Randomized trials	Serious	Not serious	Serious	Not serious	None	N/A	↔	0.0 [-0.42, 0.42], P=0.99	⊕⊕◯◯ Low
Justification		Some studies were rated to have a high risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-0.42, 0.42) did not cross the MID (1)	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↓	-0.69 [-1.04, -0.34], P<0.001	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited the generalizability of the results	The confidence interval (-1.04, -0.34mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
LDL Cholesterol (mmol/L)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↓	-0.52 [-0.78, -0.26], P<0.001	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial limited the generalizability of the results	The confidence interval (-0.78, -0.26mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
HDL Cholesterol (mmol/L)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↔	0.06 [-0.01, 0.13], P=0.096	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.01, 0.13mmol/L) crossed the MID (0.1mmol/L)[23]	Insufficient number of trials to assess				
Fasting triglycerides (mmol/L)										
1	Randomized trial	Not serious	Not serious	Serious	Serious	None	N/A	↓	-0.20 [-0.37, -0.03], P=0.023	⊕⊕◯◯ Low
Justification		Risk of bias domains for this trial were rated as low or unclear	No evidence of heterogeneity (1 trial)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.37, -0.03mmol/L) crossed the	Insufficient number of trials to assess				

					MID (0.1mmol/L)[23]					
Uric acid										
Uric acid (mg/dL)										
2	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.07 [-0.21, 0.07], P=0.340	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.21, 0.07mg/dL) crossed the MID (0.113mg/dL)[32]	Insufficient number of trials to assess				
POLYFLORAL HONEY										
Adiposity Outcomes										
Body Weight (kg)										
10	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-1.04 [-2.32, 0.24], P=0.112	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-2.32, 0.24kg) crossed the MID (0.5kg)	Non-significant funnel plot				
BMI (kg/m^2)										
10	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.00 [-0.06, 0.05], P=0.905	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.06, 0.05kg/m^2) did not cross the MID (0.2kg/m^2)[19]	Non-significant funnel plot				
Waist circumference (cm)										
1	Non-randomized trials	Serious	Not serious	Serious	Serious	None	N/A	↔	-0.30 [-4.90, 4.30], P=0.898	⊕◯◯◯ Very low
Justification		The trial included was rated to have a high risk of bias	No evidence of heterogeneity (1 trial)	Number and type of trials limited the generalizability of the results	The confidence interval (-4.90, 4.30cm) crossed the MID (2cm)	Insufficient number of trials to assess				

Blood Pressure										
SBP (mmHg)										
8	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	3.91 [1.45, 6.38], P=0.002	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (1.45, 6.38mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
DBP (mmHg)										
8	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	2.20 [0.32, 4.09], P=0.022	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.32, 4.09mmHg) crossed the MID (2mmHg)[20]	Insufficient number of trials to assess				
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
12	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Not serious	Not serious	N/A	↔	-0.02 [-0.13, 0.09], P=0.731	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.13, 0.09mmol/L) did not cross the MID (0.5mmol/L)[21]	Non-significant funnel plot				
Fasting Insulin (uU/mL)										
5	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.35 [-2.80, 3.49], P=0.828	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-2.80, 3.49uU/mL) crossed the MID (0.72uU/mL)[21]	Insufficient number of trials to assess				
HbA1c (%)										

8	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	-0.09 [-0.30, 0.12], P=0.385	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.30, 0.12%) did not cross the MID (0.3%)[22]	Insufficient number of trials to assess				
HOMA-IR										
5	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	N/A	↔	0.15 [-0.69, 1.00], P=0.720	⊕⊕⊕⊕ High
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.69, 1.00) did not cross the MID (1)	Insufficient number of trials to assess				
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
22	Randomized and non-randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.07 [-0.22, -0.07], P=0.325	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=37.03% P_q=0.04)	Number and type of trial did not limit generalizability of the results	c	Non-significant funnel plot				
LDL Cholesterol (mmol/L)										
22	Randomized and non-randomized trials	Not serious	Serious	Not serious	Serious	None	N/A	↔	-0.09 [-0.21, 0.02], P=0.117	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	Evidence of serious heterogeneity (I^2=41.92% P_q=0.02)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.21, 0.02mmol/L) crossed the MID (0.1mmol/L)[23]	Significant funnel plot. No studies imputed in the trim-and-fill analyses.				
HDL Cholesterol (mmol/L)										
22	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	0.09 [0.06, 0.11], P<0.001	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity (I^2=0.00% P_q=0.58)	Number and type of trial did not limit	The confidence interval (0.06, 0.11mmol/L) crossed the	Significant funnel plot. Trim and fill analyses imputed 17 studies but				

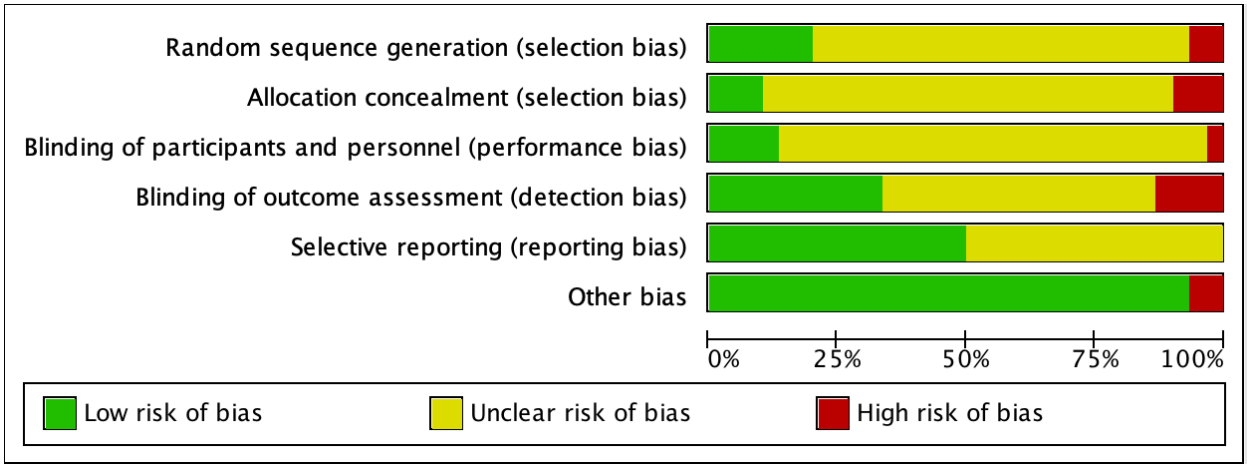
				generalizability of the results	MID (0.1mmol/L)[23]	maintained a significant increase.				
Fasting triglycerides (mmol/L)										
22	Randomized and non-randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.15 [-0.17, -0.12], P<0.001	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity (I^2=0.00% P_q=0.53)	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.17, -0.12mmol/L) crossed the MID (0.1mmol/L)[23]	Significant funnel plot. Trim and fill analyses imputed 2 studies but maintained a significant reduction.				
Apolipoprotein B (mg/dL)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	-2.07 [-14.64, 10.50], P=0.747	⊕⊕◯◯ Low
Justification		The trial included was rated to have a low risk of bias	No evidence of heterogeneity (1 trial)	Number and type of trials limited the generalizability of the results	The confidence interval (-14.64, 10.50mg/dL) crossed the MID (4mg/dL)	Insufficient number of trials to assess				
Markers of Inflammation										
hsCRP (mg/L)										
6	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	0.43 [-0.35, 1.21], P=0.277	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.35, 1.21mg/L) crossed the MID (0.5mg/L)[24,25]	Insufficient number of trials to assess				
IL-6 (pg/mL)										
5	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↑	0.37 [0.01, 0.74], P=0.046	⊕⊕⊕◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.01, 0.74pg/mL) crossed the MID (0.18pg/mL)[26,27]	Insufficient number of trials to assess				
TNFα (pg/mL)										

2	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	1.44 [0.24, 2.64], P=0.019	⨁⨁⨁◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (0.24, 2.64pg/mL) crossed the MID (0.28pg/mL)[28,29,30,31]	Insufficient number of trials to assess				
Uric acid										
Uric acid (mg/dL)										
3	Randomized trials	Not serious	Not serious	Not serious	Serious	None	N/A	↔	-0.10 [-0.95, 0.75], P=0.818	⨁⨁⨁◯ Moderate
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did not limit generalizability of the results	The confidence interval (-0.95, 0.75mg/dL) crossed the MID (0.113mg/dL)[32]	Insufficient number of trials to assess				
Milk Vetch Honey										
Glycemic Outcomes										
Fasting Glucose (mmol/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	-0.10 [-0.76, 0.56], P=0.767	⨁⨁◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-0.13, 0.09mmol/L) did not cross the MID (0.5mmol/L)[21]					
Cholesterol Outcomes										
Total cholesterol (mmol/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	0.10 [-0.21, 0.41], P=0.511	⨁⨁◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-0.21, 0.41mmol/L) crossed the MID (0.1mmol/L)[23]					
LDL cholesterol (mmol/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↑	0.38 [0.15, 0.60], P<0.001	⨁⨁◯◯ Low
Justification		Majority of studies rated	No evidence of heterogeneity	Number and type of trial did	The confidence interval (0.15,					

		with low/unclear risk of bias		limit generalizability of the results	0.60mmol/L) crossed the MID (0.1mmol/L)[23]					
HDL cholesterol (mmol/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	0.00 [-0.10, 0.09], P=0.957	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-0.10, 0.09mmol/L) crossed the MID (0.1mmol/L)[23]					
Fasting triglycerides (mmol/L)										
1	Randomized trials	Not serious	Not serious	Serious	Serious	None	N/A	↔	-0.13 [-0.38, 0.13], P=0.258	⊕⊕◯◯ Low
Justification		Majority of studies rated with low/unclear risk of bias	No evidence of heterogeneity	Number and type of trial did limit generalizability of the results	The confidence interval (-0.38 0.13mmol/L) crossed the MID (0.1mmol/L)[23]					

Supplemental Figures

Supplemental Figure 1: Risk of bias proportion graph for the effect of oral honey intake on cardiometabolic outcomes



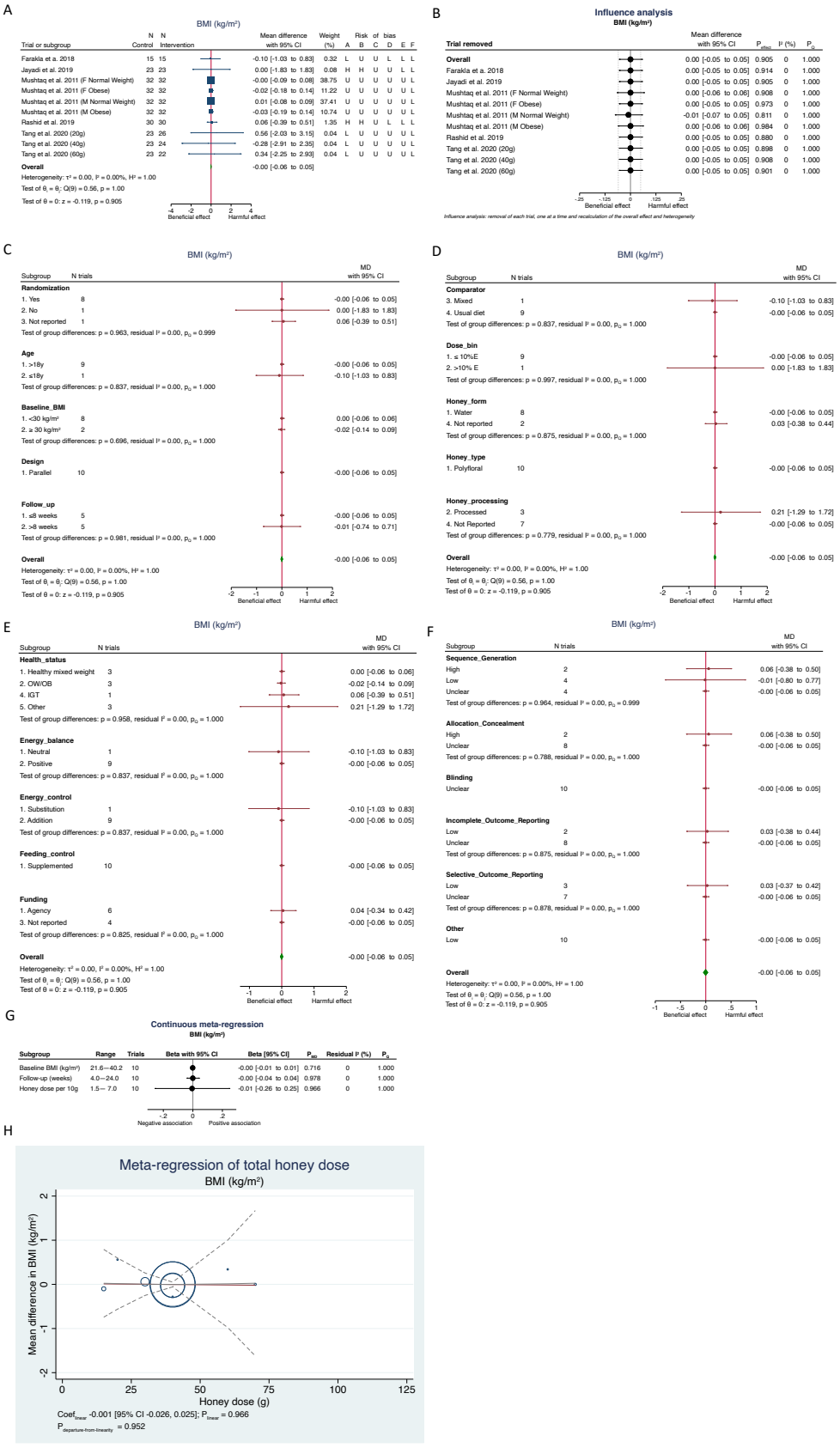
Colored bars represent the proportion of trials assessed as low (green), unclear (yellow) or high (red) risk of bias for the six domains of bias above according to criteria set by the Cochrane Risk of Bias tool in the 49 included controlled trial comparisons.
High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

Supplemental Figure 2. Body weight analyses



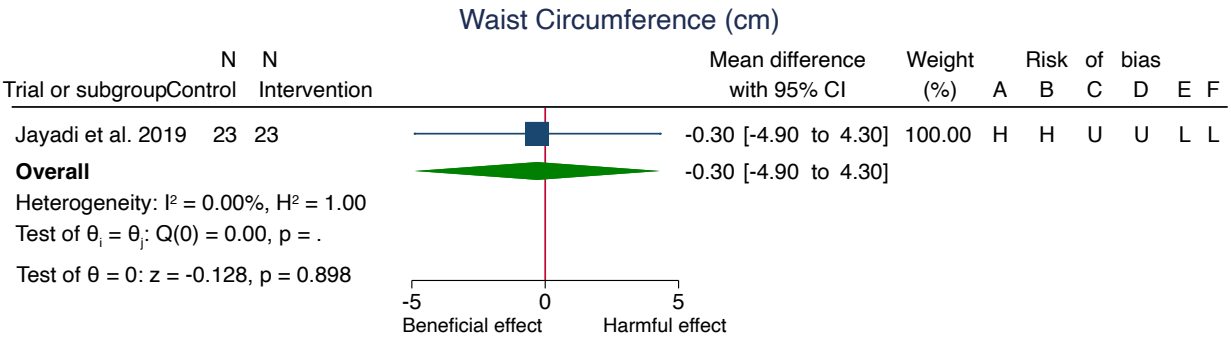
A: Forest plot for the effect of oral honey intake on body weight (kg) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on body weight (kg)
C. (1/3) Subgroup analyses for the effect of oral honey intake on body weight (kg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on body weight (kg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on body weight (kg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on body weight (kg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on body weight (kg). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on body weight (kg) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake on body weight (kg) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

Supplemental Figure 3. BMI analyses



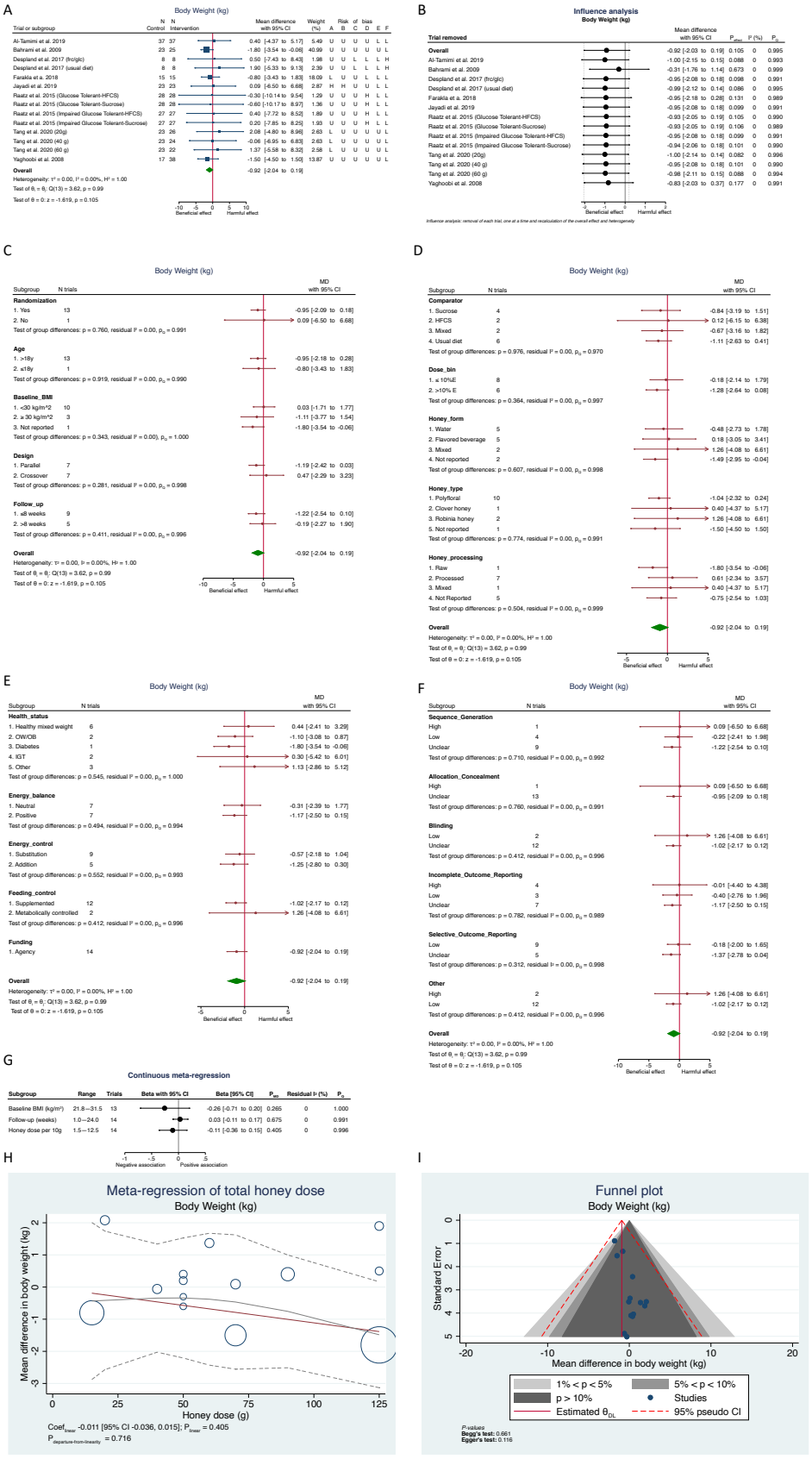
A: Forest plot for the effect of oral honey intake on BMI (kg/m^2) Refer to supplemental figure 1 for figure explanation.
B. Sensitivity analyses for the effect of oral honey intake on BMI (kg/m^2)
C. (1/3) Subgroup analyses for the effect of oral honey intake on BMI (kg/m^2)Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on BMI (kg/m^2) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on BMI (kg/m^2) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on BMI (kg/m^2) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on BMI (kg/m^2) Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on BMI (kg/m^2) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

Supplemental Figure 4. Waist circumference analyses



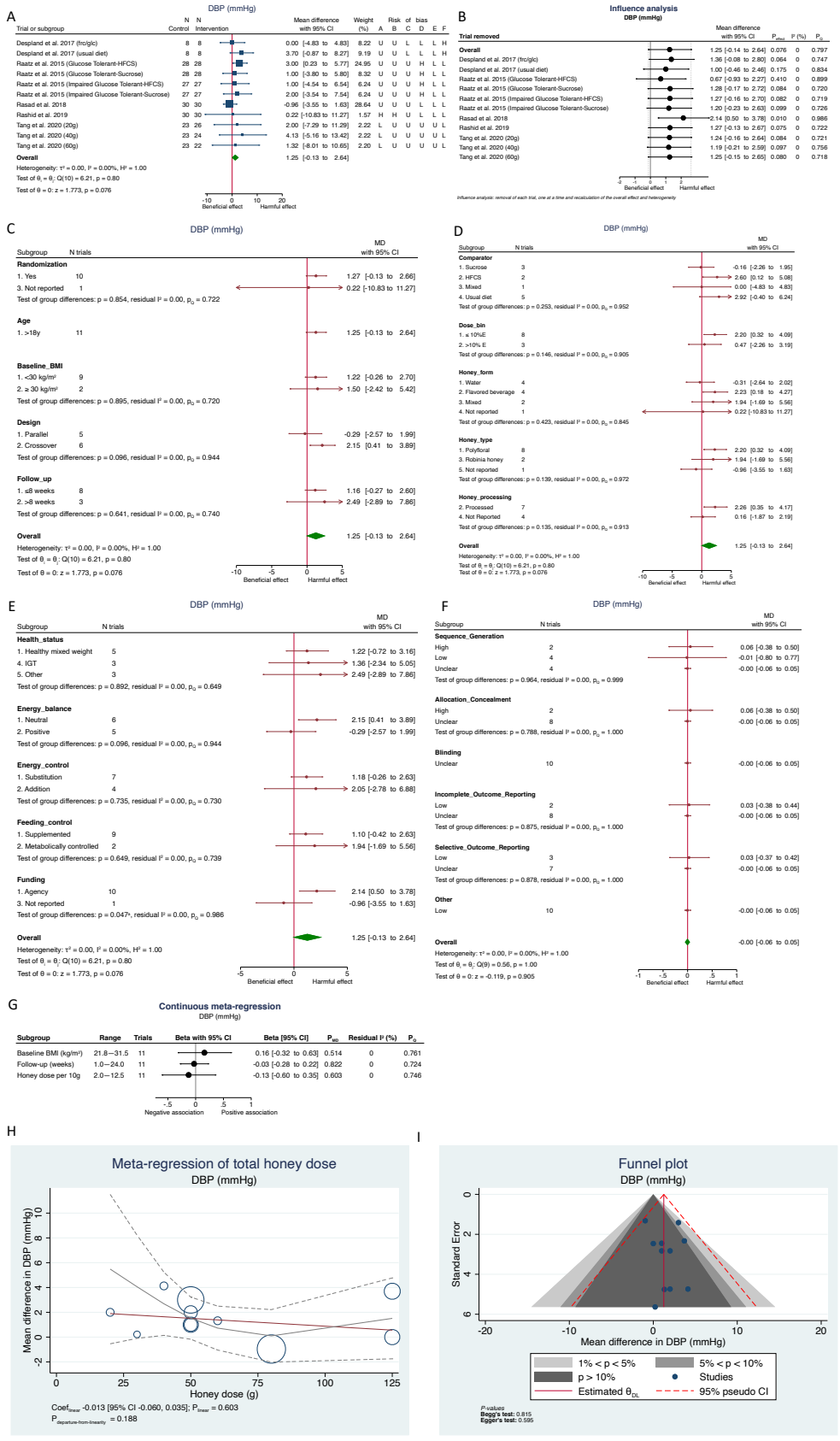
Forest plot for the effect of oral honey intake on BMI (kg/m^2) Refer to supplemental figure 1 for figure explanation.

Supplemental Figure 5. SBP analyses



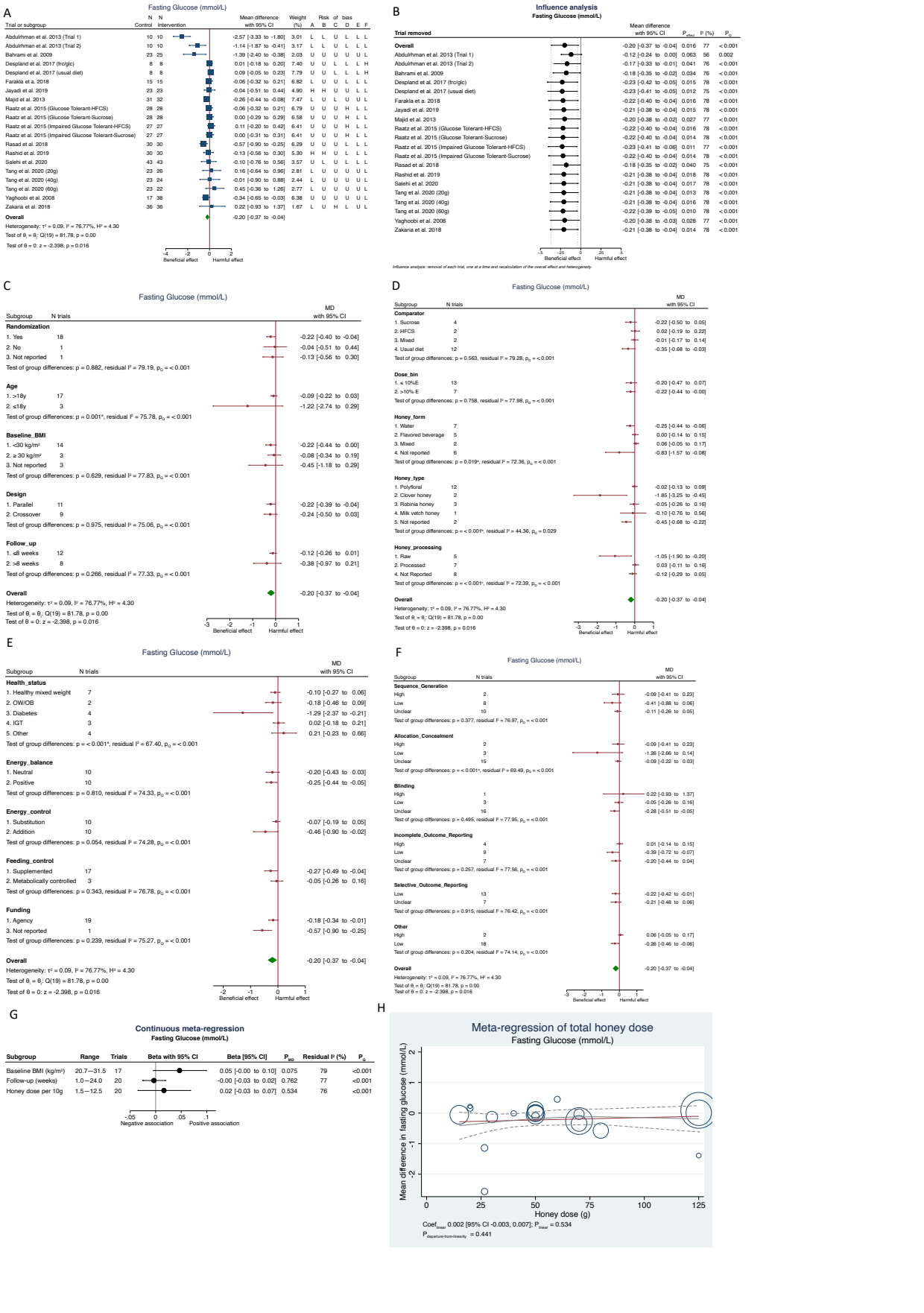
A: Forest plot for the effect of oral honey intake on SBP (mmHg) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on SBP (mmHg)
C. (1/3) Subgroup analyses for the effect of oral honey intake on SBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on SBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on SBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on SBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on SBP (mmHg). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on SBP (mmHg) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake on SBP (mmHg) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.
J. Trim and fill funnel plots for the effect of oral honey intake on SBP (mmHg) Figure explanation: The horizontal line represents the pooled effect estimate expressed as mean difference. The diagonal lines represent the pseudo-95% confidence limits, the circles represent the effect estimate for each included study, and squares represent the effect estimate for each imputed “missed” study. Imputed random mean difference is provided, p<0.05 is considered evidence of small-study effects.

Supplemental Figure 6. DBP analyses

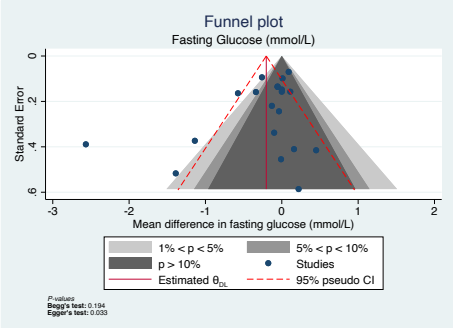


A: Forest plot for the effect of oral honey intake on DBP (mmHg) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on DBP (mmHg)
C. (1/3) Subgroup analyses for the effect of oral honey intake on DBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on DBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on DBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on SBP (mmHg) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on DBP (mmHg). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on DBP (mmHg) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake on DBP (mmHg) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

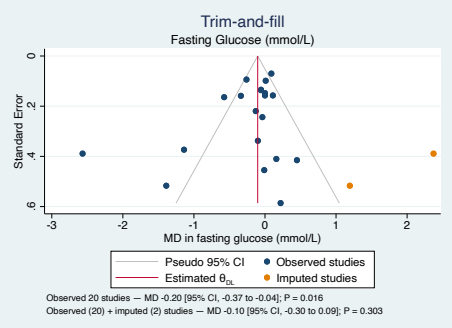
Supplemental Figure 7. Fasting glucose analyses



I

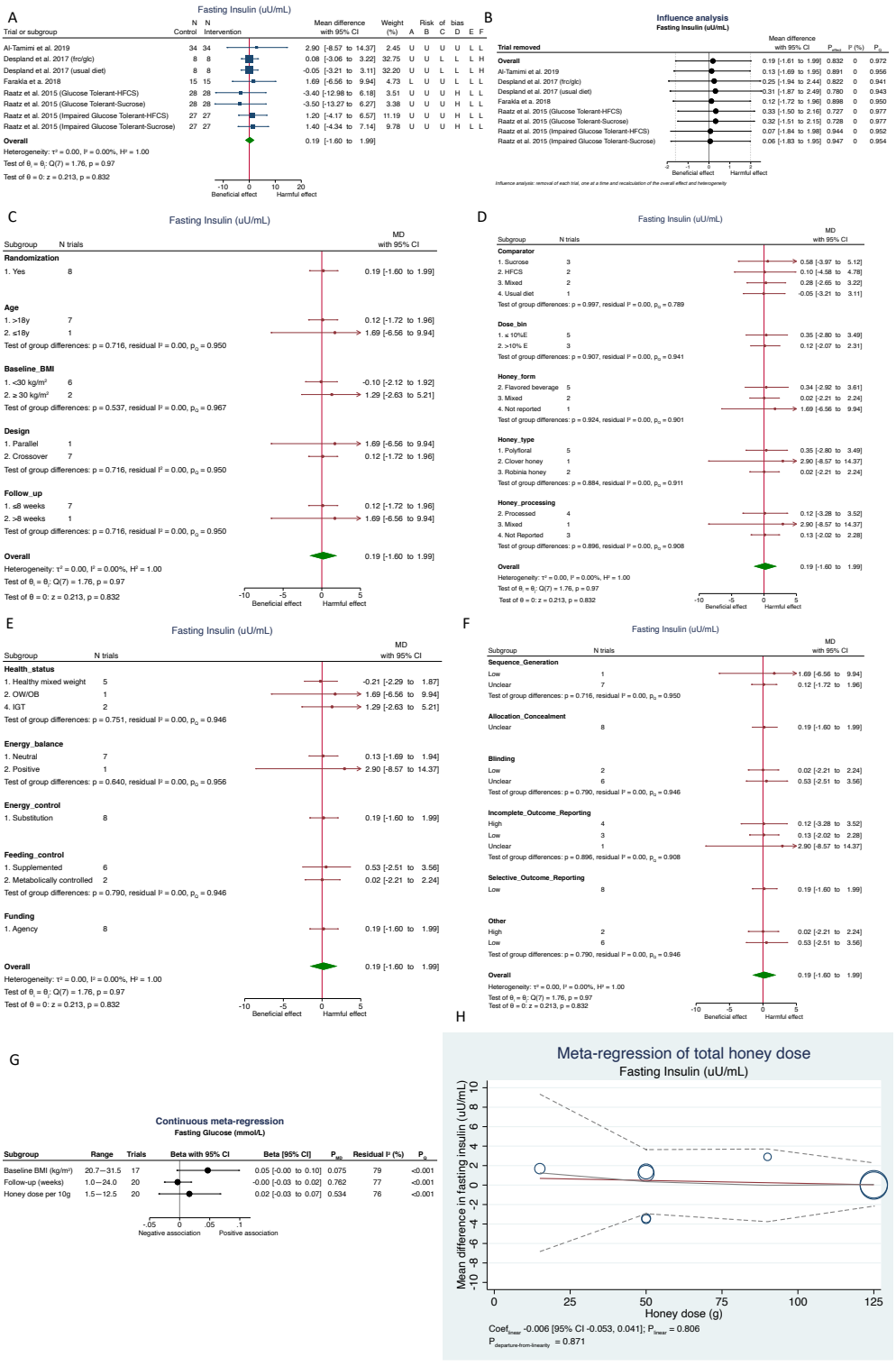


J



A: Forest plot for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
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Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on fasting glucose (mmol/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on fasting glucose (mmol/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on fasting glucose (mmol/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake fasting glucose (mmol/L) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.
J. Trim and fill funnel plots for the effect of oral honey intake on fasting glucose (mmol/L) Figure explanation: The horizontal line represents the pooled effect estimate expressed as mean difference. The diagonal lines represent the pseudo-95% confidence limits, the circles represent the effect estimate for each included study, and squares represent the effect estimate for each imputed “missed” study. Imputed random mean difference is provided, p<0.05 is considered evidence of small-study effects.

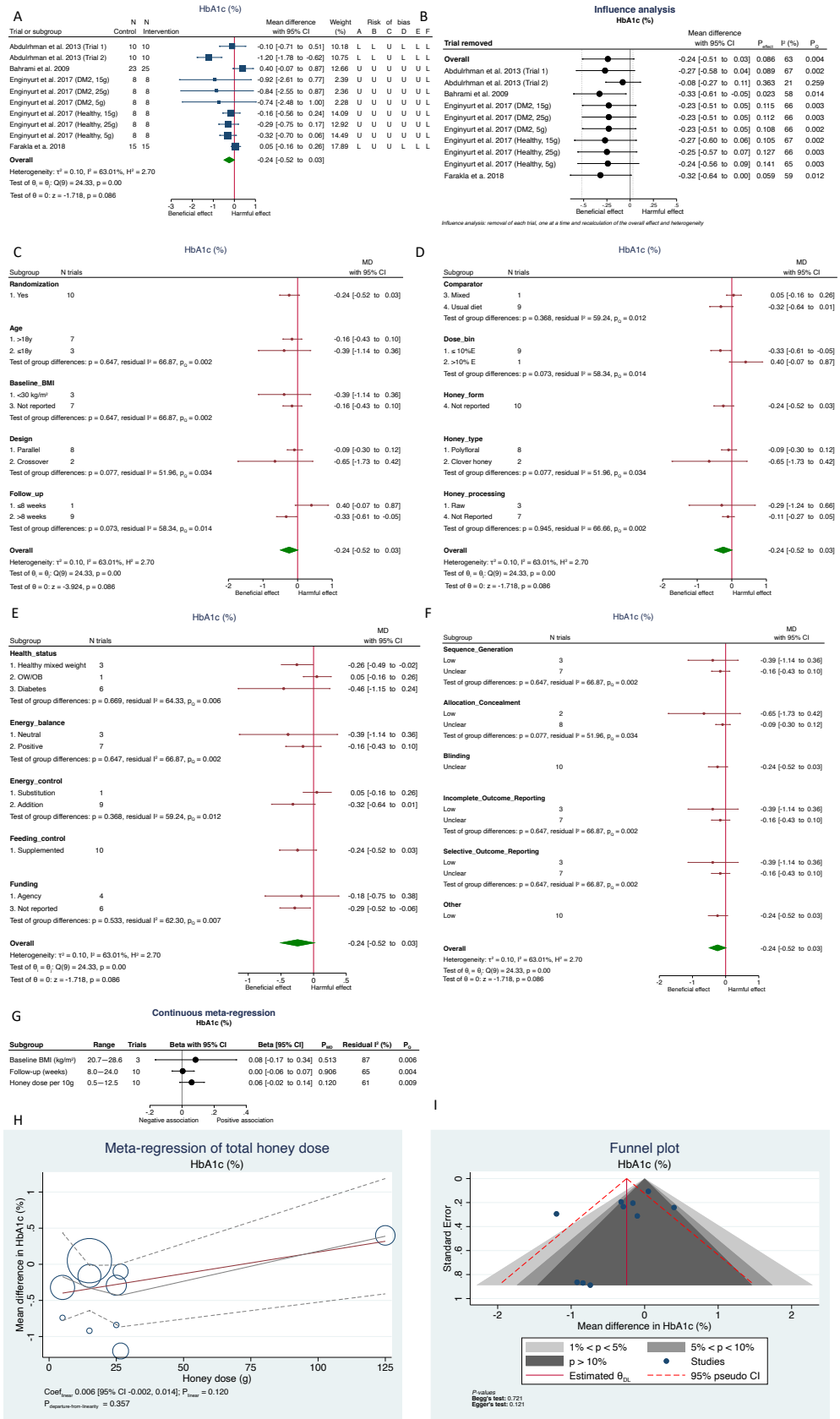
Supplemental Figure 8. Fasting insulin analyses



A: Forest plot for the effect of oral honey intake on fasting insulin (uU/mL) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

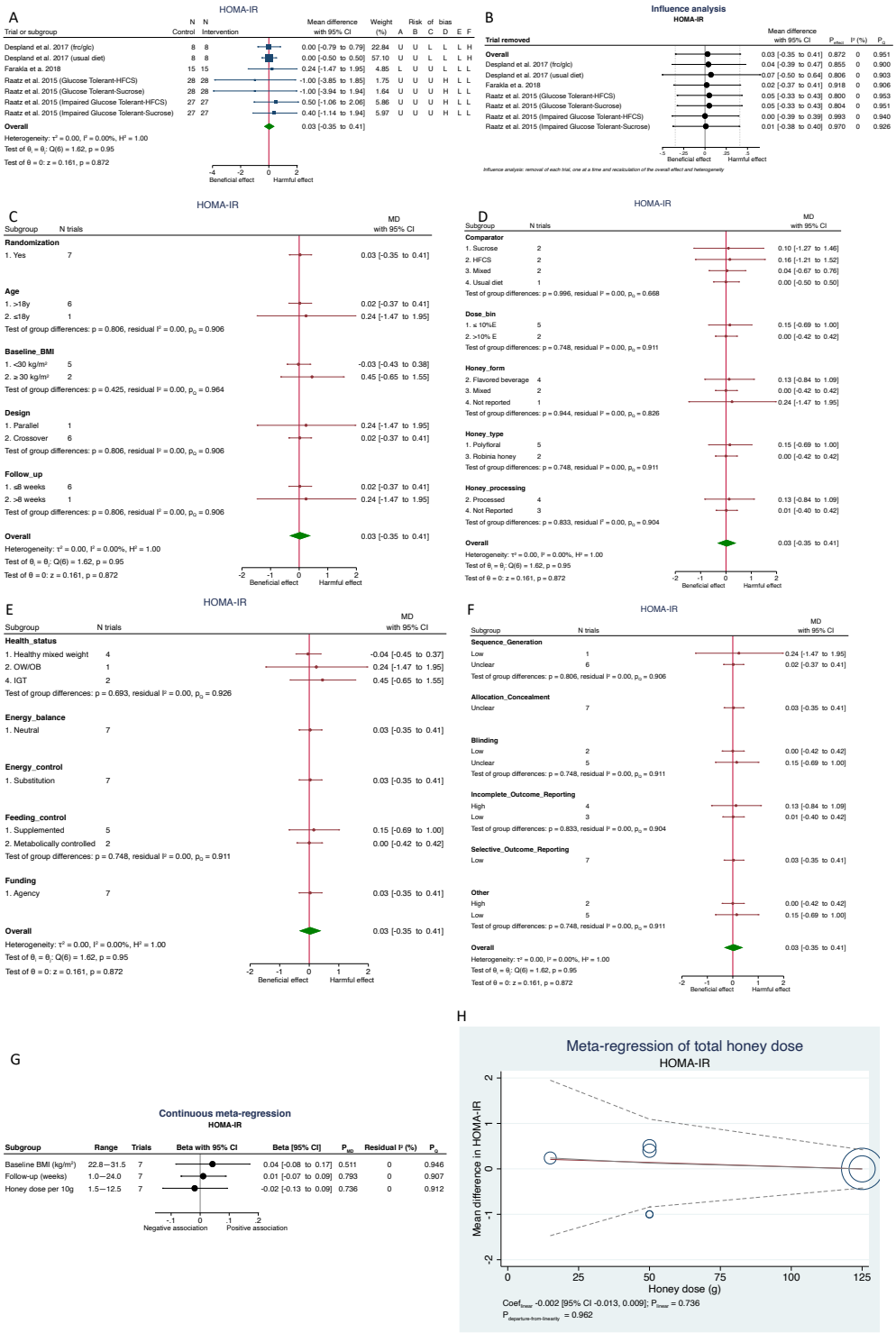
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on fasting insulin (uU/mL)
C. (1/3) Subgroup analyses for the effect of oral honey intake on fasting insulin (uU/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on fasting insulin (uU/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on fasting insulin (uU/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on fasting insulin (uU/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on fasting insulin (uU/mL). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on fasting insulin (uU/mL) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake fasting insulin (uU/mL) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

Supplemental Figure 9. HbA1c analyses



A: Forest plot for the effect of oral honey intake on HbA1c (%) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on HbA1c (%)
C. (1/3) Subgroup analyses for the effect of oral honey intake on HbA1c (%) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on HbA1c (%) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on HbA1c (%) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on HbA1c (%) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on HbA1c (%). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on HbA1c (%) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake HbA1c (%) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

Supplemental Figure 10. HOMA-IR analyses



A: Forest plot for the effect of oral honey intake on HOMA-IR Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.

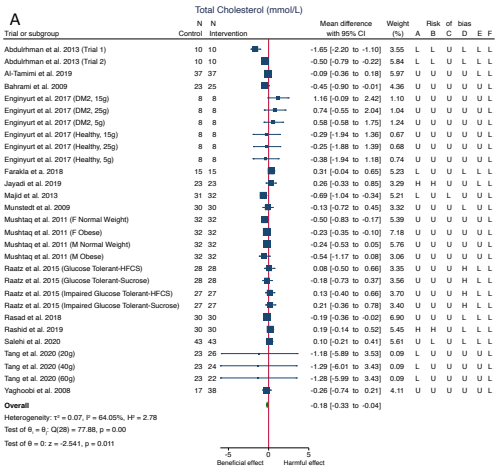
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

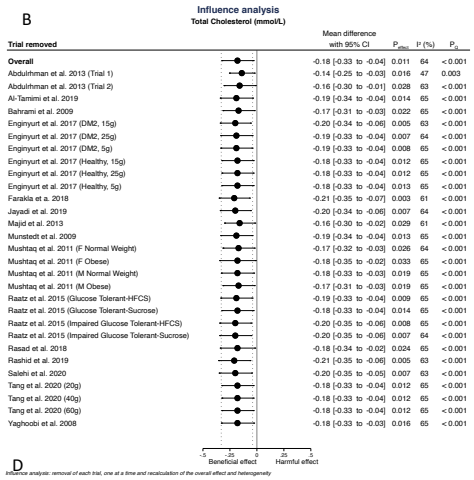
Pooled effect summary calculated with the ⍰2 test. Test for group differences calculated with meta-regression, which uses the Wald test.

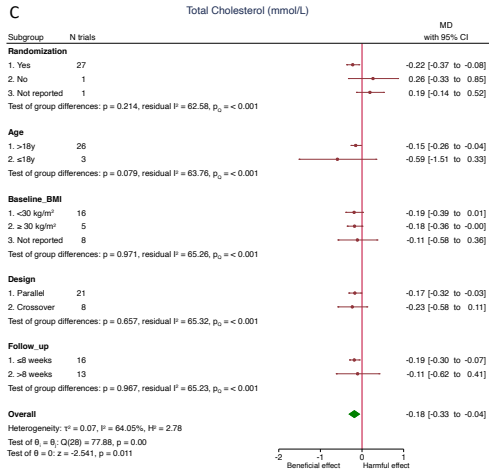
B. Sensitivity analyses for the effect of oral honey intake on HOMA-IR

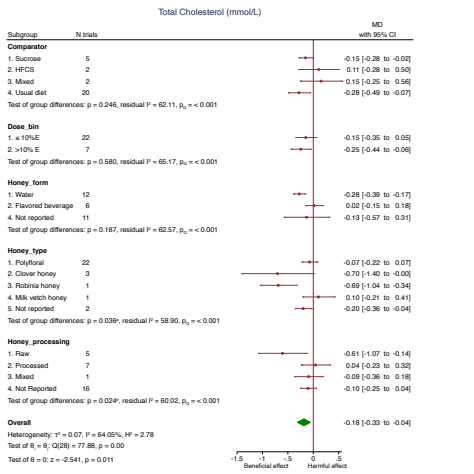
C. (1/3) Subgroup analyses for the effect of oral honey intake on HOMA-IR Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on HOMA-IR Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on HOMA-IR Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on HOMA-IR Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on HOMA-IR. Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on HOMA-IR Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake HOMA-IR Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

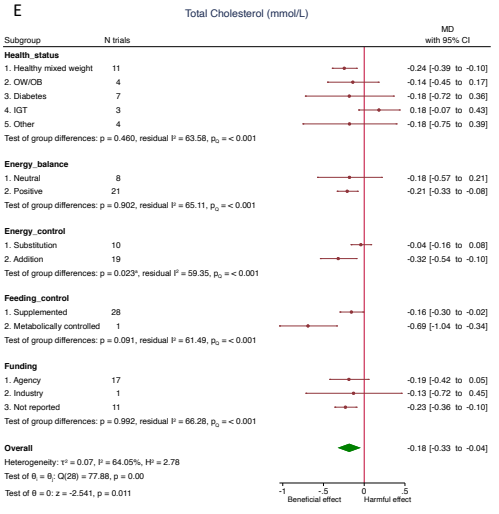
Supplemental Figure 11. Total cholesterol analyses

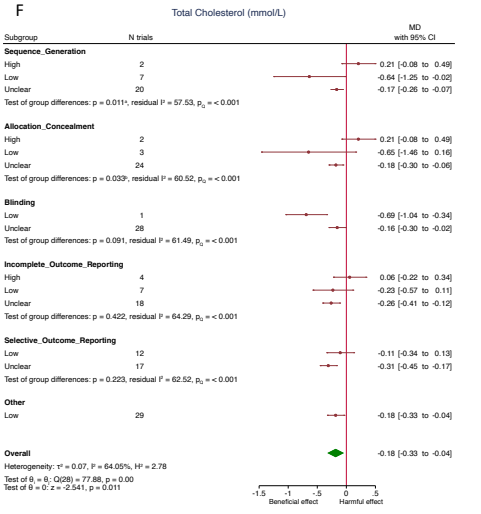


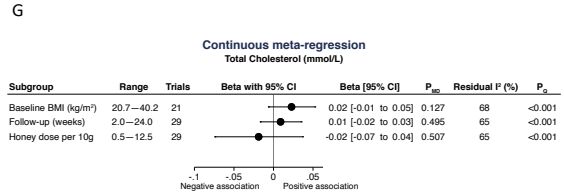


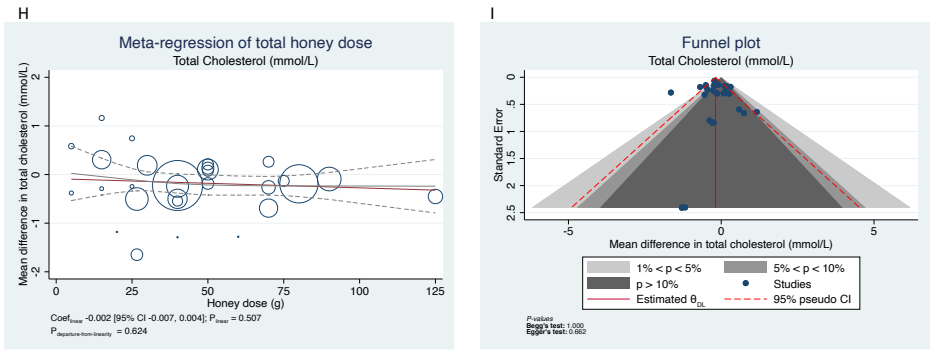






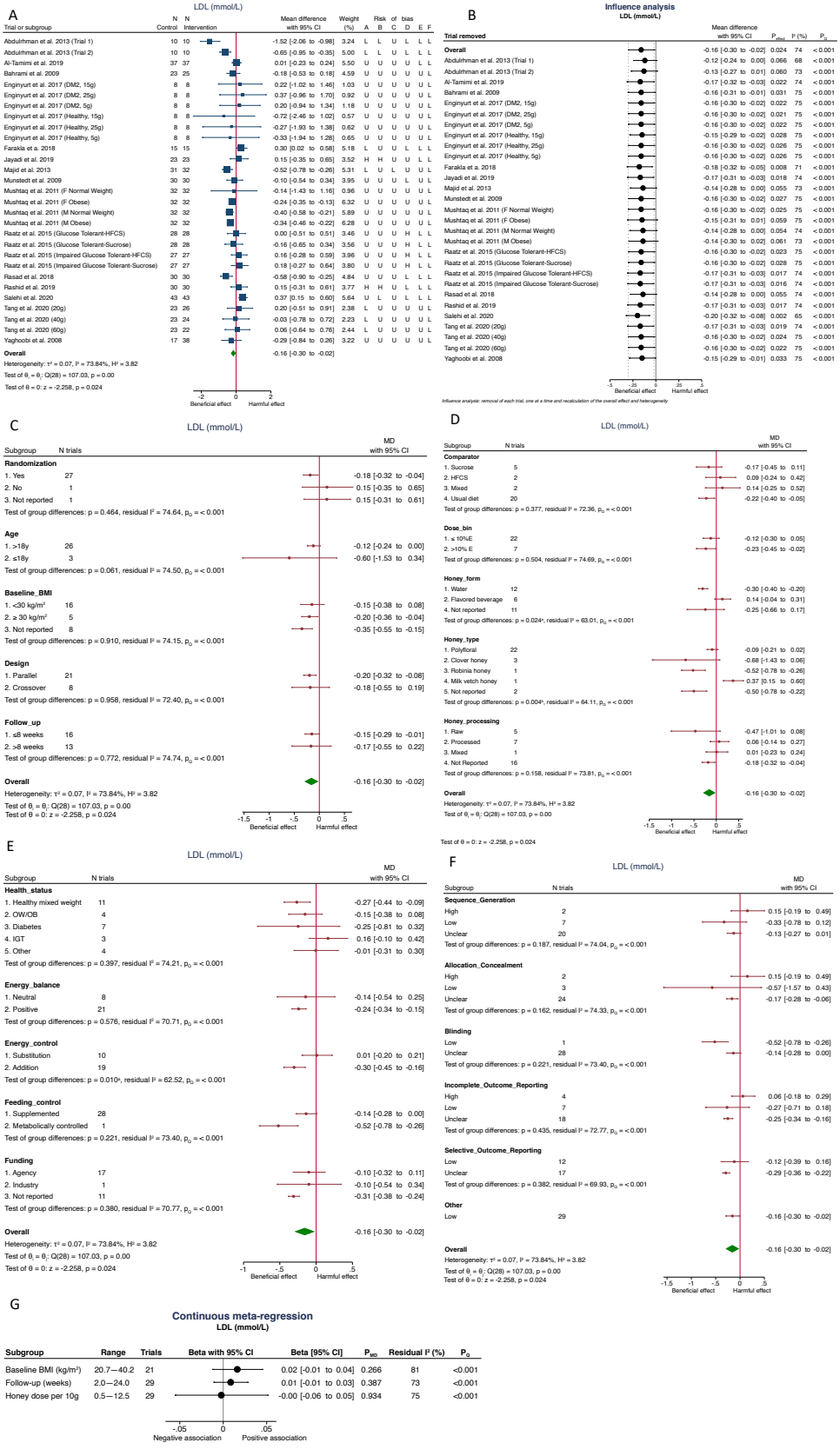


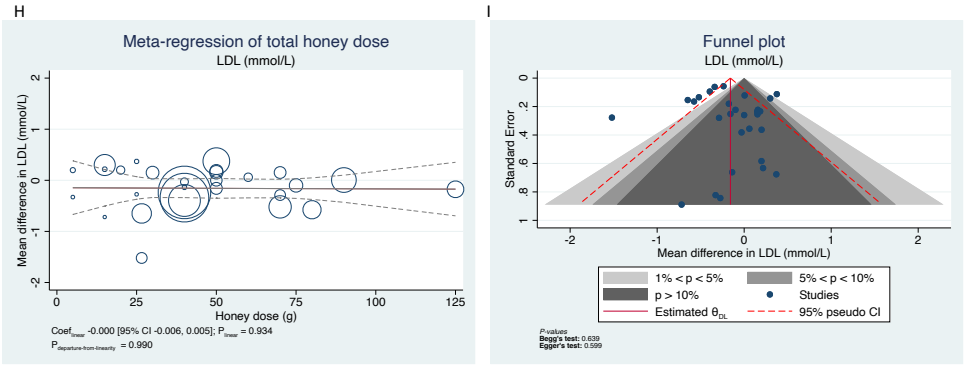




A: Forest plot for the effect of oral honey intake on total cholesterol (mmol/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on total cholesterol (mmol/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on total cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on total cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on total cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on total cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on total cholesterol (mmol/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on total cholesterol (mmol/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake total cholesterol (mmol/L) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

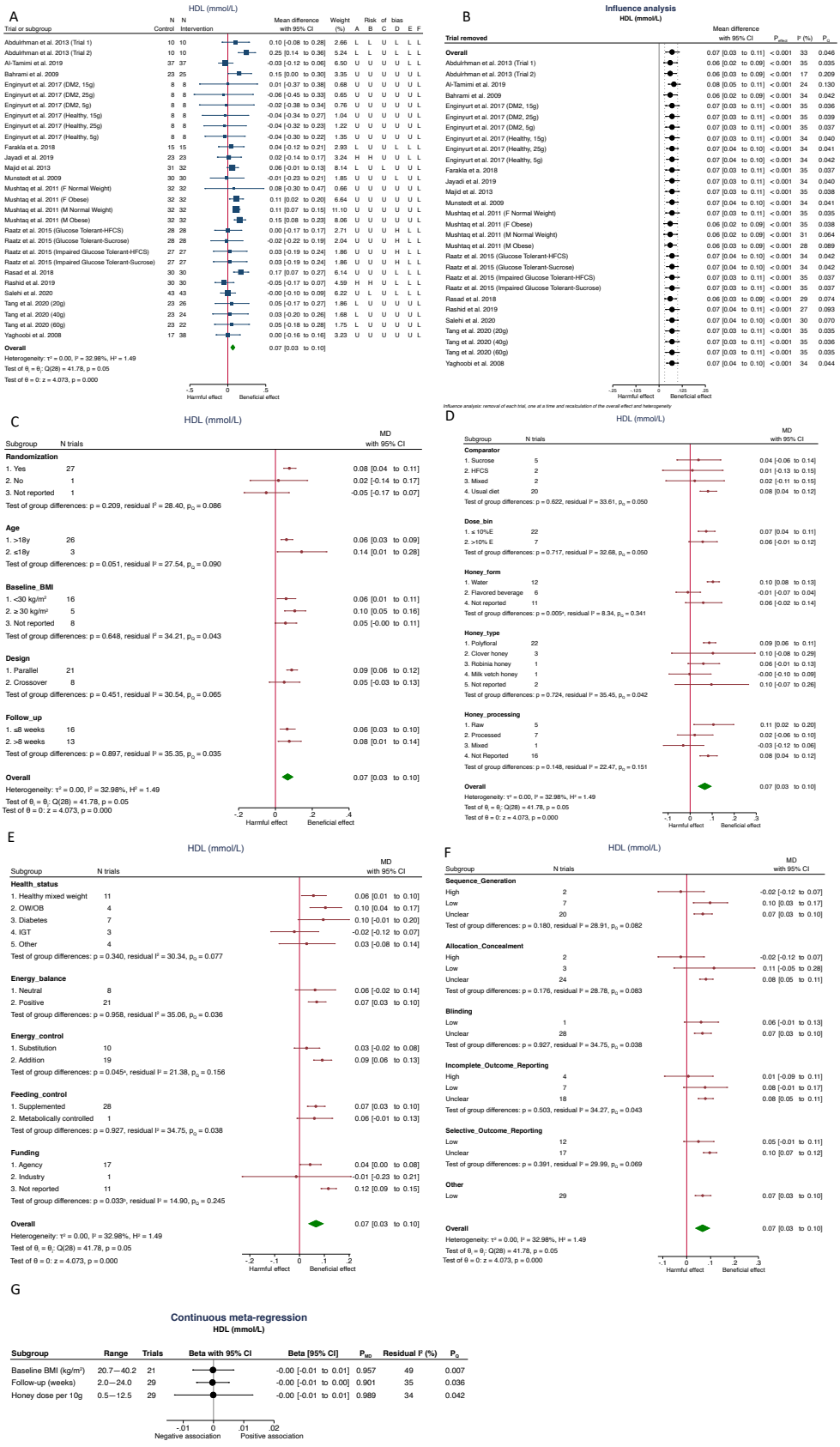
Supplemental Figure 12. LDL cholesterol analyses



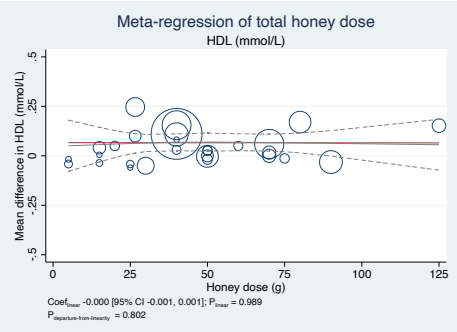


A: Forest plot for the effect of oral honey intake on LDL cholesterol (mmol/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ⍰2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on LDL cholesterol (mmol/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on LDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on LDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on LDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on LDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on LDL cholesterol (mmol/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on LDL cholesterol (mmol/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.
I. Publication bias funnel plots for the effect of oral honey intake LDL cholesterol (mmol/L) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

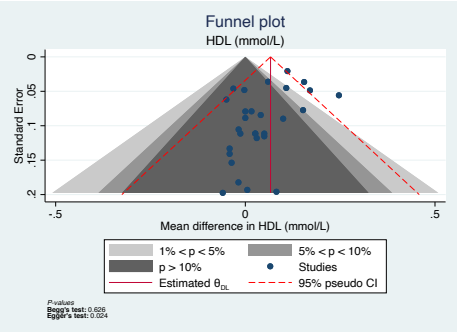
Supplemental Figure 13. HDL cholesterol analyses



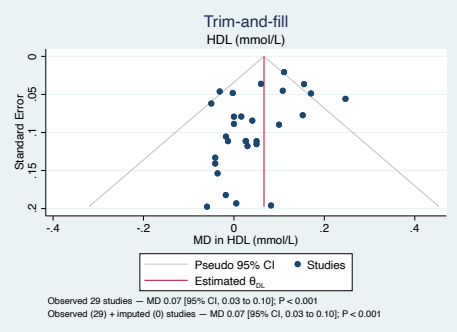
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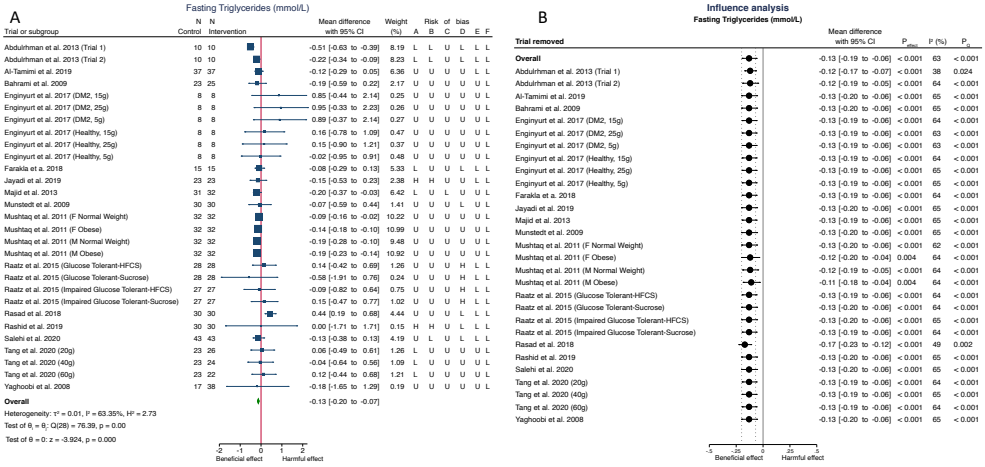
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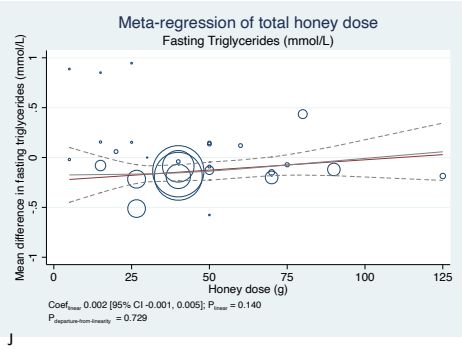
A: Forest plot for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on HDL cholesterol (mmol/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on HDL cholesterol (mmol/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on HDL cholesterol (mmol/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

I. Publication bias funnel plots for the effect of oral honey intake HDL cholesterol (mmol/L) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.
J. Trim and fill funnel plots for the effect of oral honey intake on HDL cholesterol (mmol/L) Figure explanation: The horizontal line represents the pooled effect estimate expressed as mean difference. The diagonal lines represent the pseudo-95% confidence limits, the circles represent the effect estimate for each included study, and squares represent the effect estimate for each imputed “missed” study. Imputed random mean difference is provided, p<0.05 is considered evidence of small-study effects.

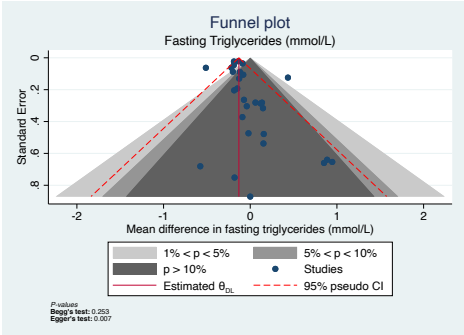
Supplemental Figure 14. Fasting triglyceride analyses



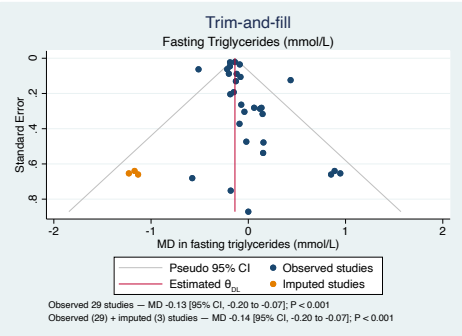
H



I



J

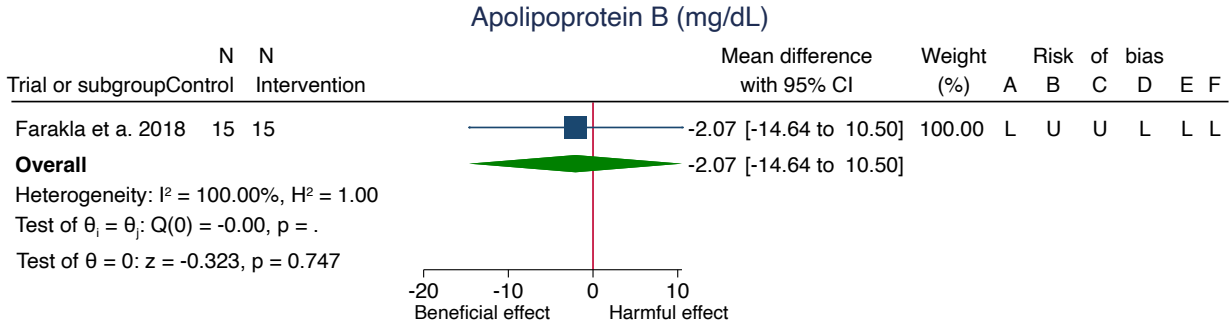


A: Forest plot for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on fasting triglycerides (mmol/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on fasting triglycerides (mmol/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on fasting triglycerides (mmol/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

I. Publication bias funnel plots for the effect of oral honey intake fasting triglycerides (mmol/L) Figure explanation: Contour-enhanced funnel plot is a scatterplot of each trial weighted mean difference on the x-axis with the standard error representing precision on the y-axis. The vertical solid red line represents the pooled effect estimate and the dashed red lines represent the pseudo-95% confidence limits. The blue dots represent individual trials. The contour regions define the regions for the test of significance of individual trial effect size for a given P-value range >0.100 (dark grey), 0.500 to <0.100 (medium grey), 0.010 to <0.500 (light grey), <0.0100 (white)]. The contour-enhanced funnel plots may suggest funnel-plot asymmetry is due to publication bias when less precise (smaller) trials are missing in the non-significant regions. Quantitative assessment of publication bias was also per-formed using Egger's and Begg's tests set at a significance level of P<0.100.

J. Trim and fill funnel plots for the effect of oral honey intake on fasting triglycerides (mmol/L) Figure explanation: The horizontal line represents the pooled effect estimate expressed as mean difference. The diagonal lines represent the pseudo-95% confidence limits, the circles represent the effect estimate for each included study, and squares represent the effect estimate for each imputed "missed" study. Imputed random mean difference is provided, p<0.05 is considered evidence of small-study effects.

Supplemental Figure 15. Apolipoprotein B analyses

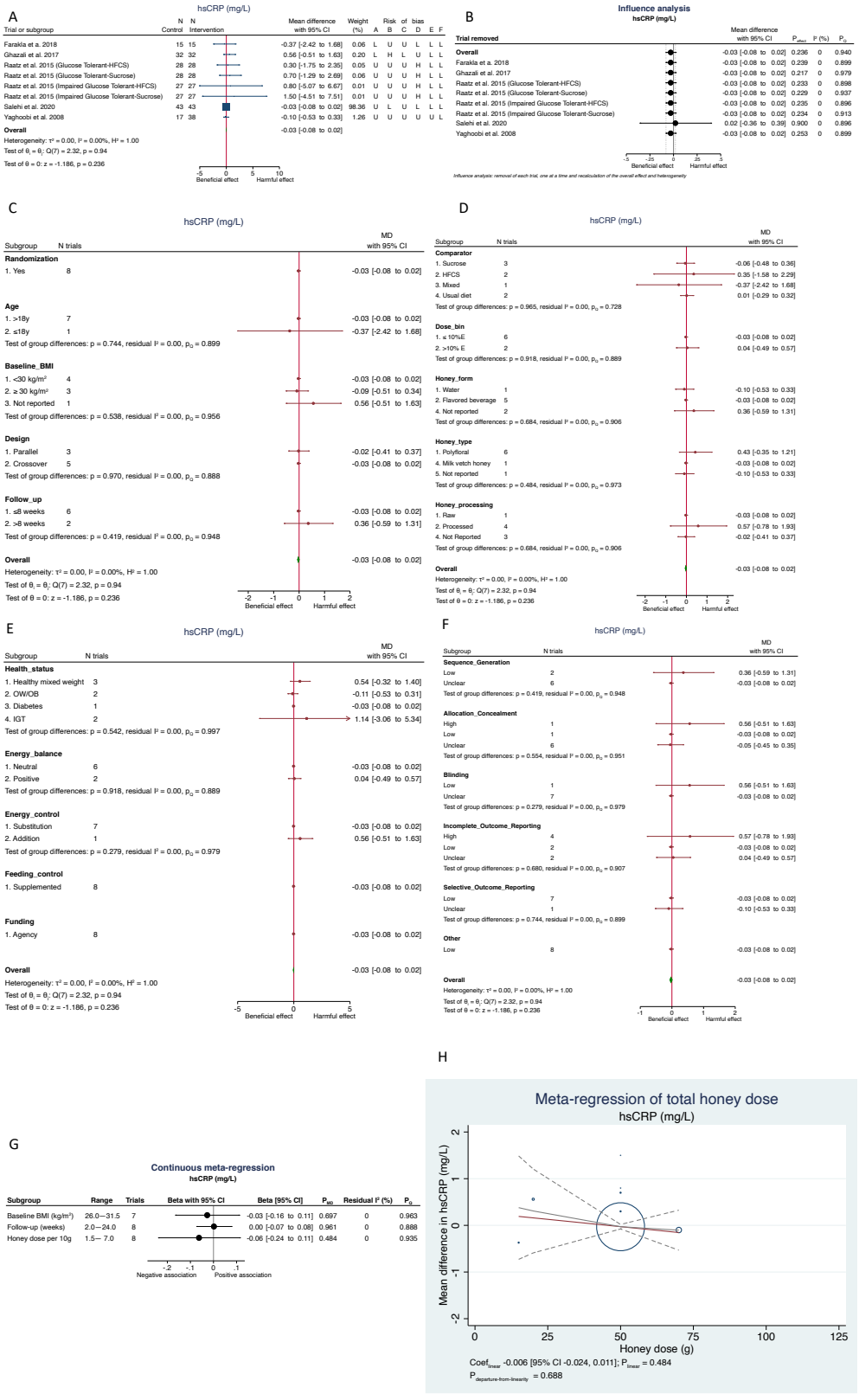


Forest plot for the effect of oral honey intake on apolipoproteing B (mg/dL) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.

Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

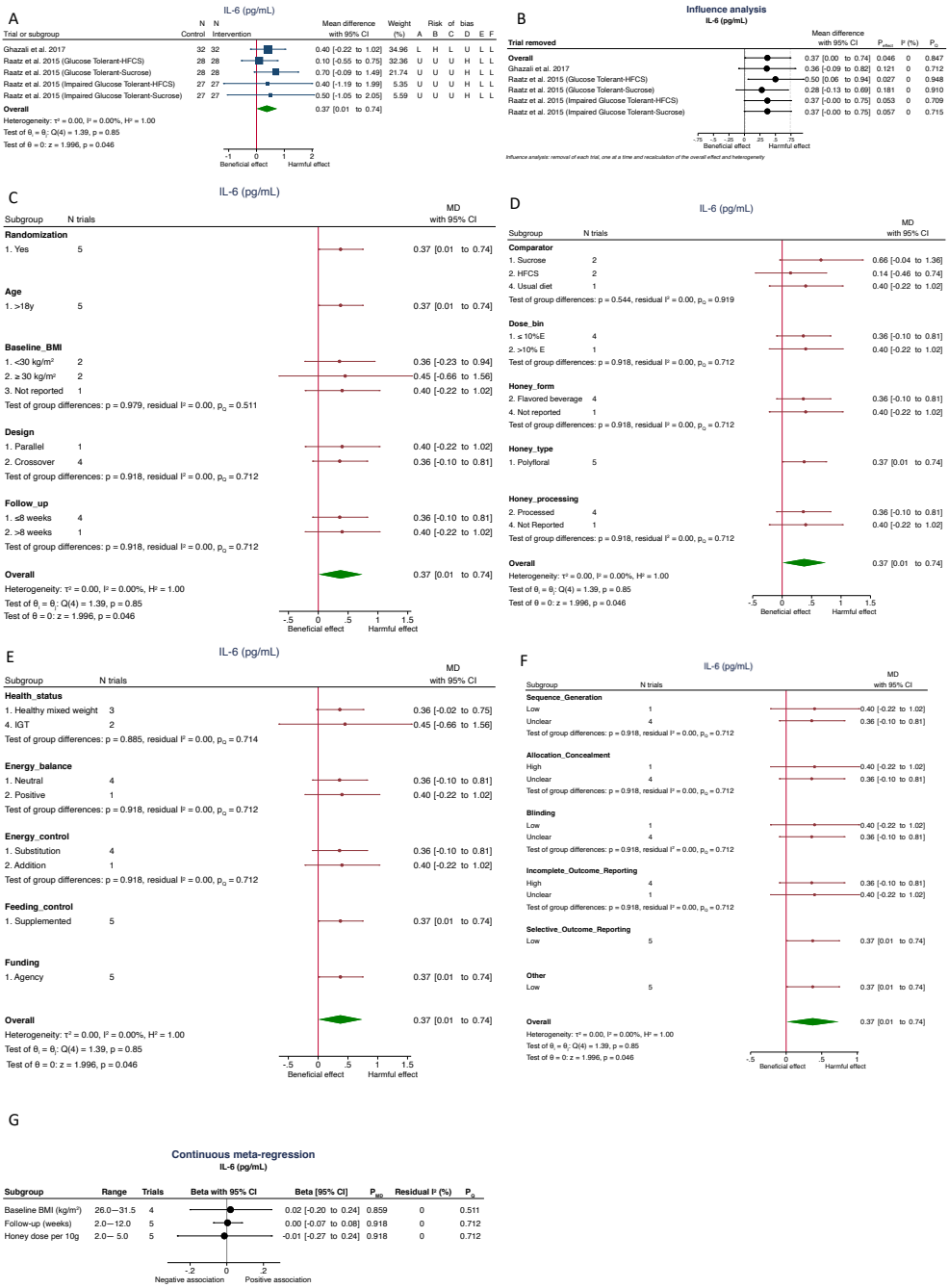
Pooled effect summary calculated with the ⍰2 test. Test for group differences calculated with meta-regression, which uses the Wald test.

Supplemental Figure 16. hsCRP analyses



A: Forest plot for the effect of oral honey intake on hsCRP (mg/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the 2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on hsCRP (mg/L)
C. (1/3) Subgroup analyses for the effect of oral honey intake on hsCRP (mg/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
D. (2/3) Subgroup analyses for the effect of oral honey intake on hsCRP (mg/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on hsCRP (mg/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on hsCRP (mg/L) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on hsCRP (mg/L). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on hsCRP (mg/L) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

Supplemental Figure 17. IL-6 analyses



A: Forest plot for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.

Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

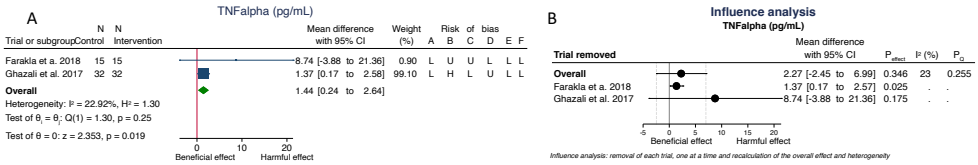
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.

B. Sensitivity analyses for the effect of oral honey intake on IL-6 (pg/mL)

C. (1/3) Subgroup analyses for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.

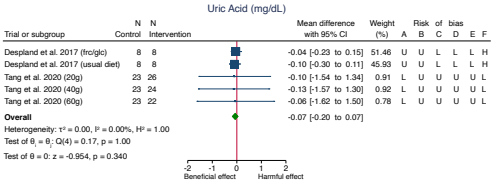
D. (2/3) Subgroup analyses for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on IL-6 (pg/mL). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on IL-6 (pg/mL) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

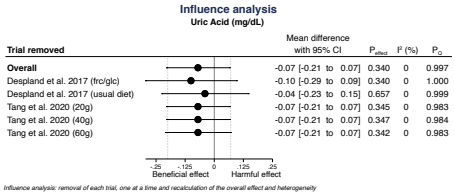
Supplemental Figure 18. IL-6 analyses

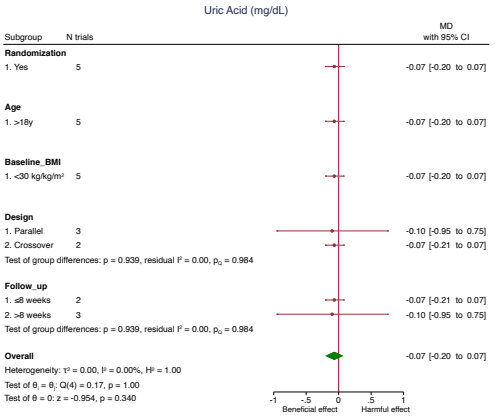


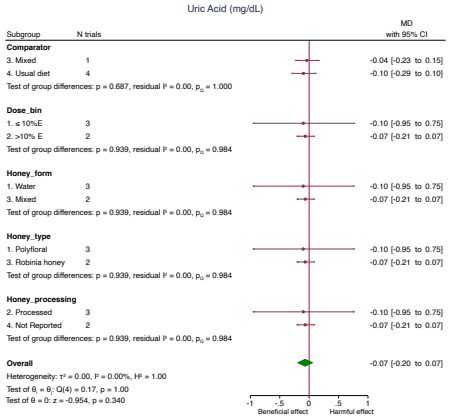
A: Forest plot for the effect of oral honey intake on IL-6 (pg/mL) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.
B. Sensitivity analyses for the effect of oral honey intake on IL-6 (pg/mL)

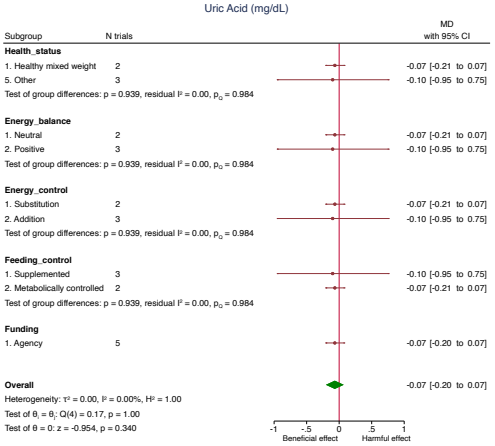
Supplemental Figure 19. Uric acid analyses

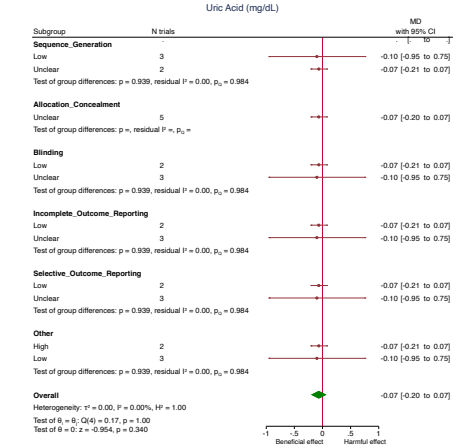


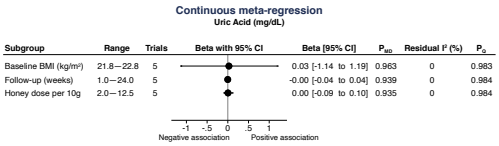












A: Forest plot for the effect of oral honey intake on uric acid (mg/dL) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.

Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.

Pooled effect summary calculated with the ⍰2 test. Test for group differences calculated with meta-regression, which uses the Wald test.

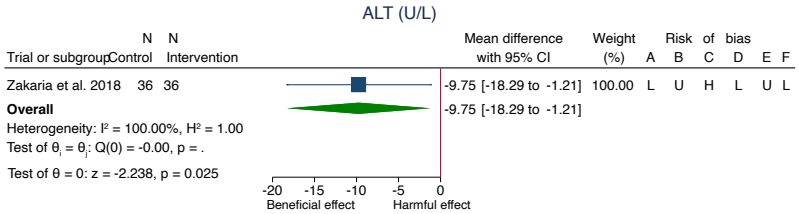
B. Sensitivity analyses for the effect of oral honey intake on uric acid (mg/dL)

C. (1/3) Subgroup analyses for the effect of oral honey intake on uric acid (mg/dL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.

D. (2/3) Subgroup analyses for the effect of oral honey intake on uric acid (mg/dL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance

method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
E. (3/3) Subgroup analyses for the effect of oral honey intake on uric acid (mg/dL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
F. Risk of bias (using The Cochrane Collaboration Tool) subgroup analysis for the effect of oral honey intake on uric acid (mg/dL) Figure explanation: The green diamond represents the pooled estimate for the overall analysis of oral honey intake on body weight. Within subgroup mean differences are the pooled effect estimates represented by a red circle. 95% confidence intervals are represented by the line through the circle. Data are expressed as mean differences with 95% confidence intervals using the generic inverse-variance method and random effects DerSimonian-Laird model. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity. P<0.050 indicates that the effect size differed between levels of the subgroup.
G. Continuous meta-regression analysis for the effect of oral honey intake on uric acid (mg/dL). Figure explanation: Data is presented as between group mean difference (95% confidence intervals) for a 1-unit change in the predictor variable, except for honey dose which is for a 10-unit change in the predictor variable. ß–coefficients were estimated using continuous meta-regression analysis. A positive ß-coefficient implies an increase in body weight with the oral honey intake intervention as the subgroup variable increases, and a negative ß-coefficient implies a decrease in body weight. Residual I2 reports inter-study heterogeneity not explained by the subgroup and was estimated using the Cochrane Q statistic.
H. Linear and non-linear meta-regression analyses for the effect of oral honey intake dose (g) on uric acid (mg/dL) Figure explanation: Individual trials are represented by the circles, with their weight in the overall analysis represented by the size of the circles. The straight line represents the estimate dose response for amount of honey consumed (g) and the dashed lines represent the upper and lower 95% Confidence Intervals.

Supplemental Figure 20. ALT analyses



A: Forest plot for the effect of oral honey intake on ALT (U/L) Figure explanation: Pooled effect estimates for each subgroup and overall effect are represented by the diamonds. Data are expressed as weighted mean differences with 95% confidence intervals using the generic in-verse-variance method and random effects DerSimonian-Laird model. Paired analyses were applied to all crossover trials. Inter-study heterogeneity was assessed using the Cochrane Q statistic and quantified using the I2 statistic, with significance set at P<0.100 and I2≥50% considered to be evidence of substantial heterogeneity.
Risk of Bias Legend: (H) High Risk; (L) Low Risk; (U) Unclear. The letters represent the following risk of bias domains: A, random sequence generation (selection bias); B, allocation concealment (selection bias); C, blinding of participants and personnel and outcome assessors (performance bias); D, incomplete outcome data (attrition bias); E, selective reporting (reporting bias); and F, other bias (carry-over effects). High other risk of bias was given to crossover trials which had no washout between interventions (carry-over effects). Trials which did not have this characteristic were rated as Low.
Pooled effect summary calculated with the ?2 test. Test for group differences calculated with meta-regression, which uses the Wald test.

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