Study or Subgroup	Honey Events	Total	Control Events	Total	Weight	Odds Ratio M–H, Fixed, 95% CI
5.1.1 Grade2 1w						
Amanat 2017	3	41	6	41	5.3%	0.46 [0.11, 1.98]
Biswal 2003	0	20	1	20	1.4%	0.32 [0.01, 8.26]
Jayachandran 2012	14	20	4	20	1.1%	9.33 [2.18, 39.96]
Rashad 2009	0	20	1	20	1.4%	0.32 [0.01, 8.26]
Subtotal (95% CI)		101		101	9.3%	1.52 [0.68, 3.36]
Total events	17		12			
Heterogeneity: Chi² = 10.33, df = 3 (P = 0.02); I² = 71%						
Test for overall effect: Z = 1.03 (P = 0.31)						
5.1.2 Grade2 2w						
Amanat 2017	8	41	16	41	12.3%	0.38 [0.14, 1.02]
Biswal 2003	3	20	8	20	6.5%	0.26 [0.06, 1.21]
Jayachandran 2012	15	20	5	20	1.2%	9.00 [2.15, 37.66]
Rashad 2009	3	20	9	20	7.3%	0.22 [0.05, 0.98]
Subtotal (95% CI)		101		101	27.4%	0.69 [0.39, 1.22]
Total events	29		38			
Heterogeneity: Chi² = 17.55, df = 3 (P = 0.0005); I² = 83%						
Test for overall effect: Z = 1.29 (P = 0.20)						
5.1.3 Grade2 3w						
Amanat 2017	17	41	20	41	11.2%	0.74 [0.31, 1.78]
Biswal 2003	5	20	8	20	5.7%	0.50 [0.13, 1.93]
Rashad 2009	7	20	9	20	5.6%	0.66 [0.18, 2.35]
Subtotal (95% CI)		81		81	22.6%	0.66 [0.35, 1.24]
Total events	29		37			
Heterogeneity: Chi² = 0.23, df = 2 (P = 0.89); I² = 0%						
Test for overall effect: Z = 1.28 (P = 0.20)						
5.1.4 Grade2 4w						
Amanat 2017	14	41	15	41	9.5%	0.90 [0.36, 2.22]
Biswal 2003	6	20	2	20	1.3%	3.86 [0.67, 22.11]
Rashad 2009	8	20	4	20	2.3%	2.67 [0.65, 10.97]
Subtotal (95% CI)		81		81	13.1%	1.51 [0.77, 2.98]
Total events	28		21			
Heterogeneity: Chi² = 2.99, df = 2 (P = 0.22); I² = 33%						
Test for overall effect: Z = 1.19 (P = 0.23)						
5.1.5 Grade2 5w						
Amanat 2017	13	41	15	41	9.8%	0.80 [0.32, 2.01]
Biswal 2003	3	20	5	20	4.1%	0.53 [0.11, 2.60]
Rashad 2009	5	20	7	20	5.0%	0.62 [0.16, 2.43]
Subtotal (95% CI)		81		81	18.9%	0.70 [0.35, 1.38]
Total events	21		27			
Heterogeneity: Chi² = 0.24, df = 2 (P = 0.89); I² = 0%						
Test for overall effect: Z = 1.04 (P = 0.30)						
5.1.6 Grade2 6w						
Amanat 2017	8	41	4	41	3.1%	2.24 [0.62, 8.14]
Biswal 2003	3	20	3	20	2.4%	1.00 [0.18, 5.67]
Rashad 2009	3	20	4	20	3.3%	0.71 [0.14, 3.66]
Subtotal (95% CI)		81		81	8.8%	1.33 [0.56, 3.12]
Total events	14		11			
Heterogeneity: Chi² = 1.30, df = 2 (P = 0.52); I² = 0%						
Test for overall effect: Z = 0.65 (P = 0.52)						
Total (95% CI)		526		526	100.0%	0.92 [0.70, 1.22]
Total events	138		146			
Heterogeneity: Chi² = 39.23, df = 19 (P = 0.004); I² = 52%						
Test for overall effect: Z = 0.56 (P = 0.57)						
Test for subgroup differences: Chi² = 6.98, df = 5 (P = 0.22), I² = 28.4%						

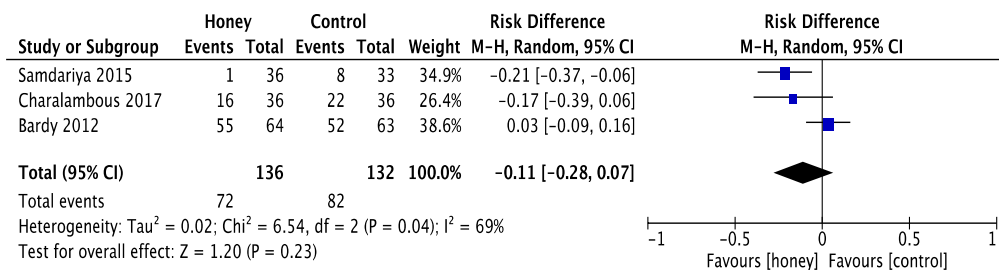Odds Ratio M–H, Fixed, 95% CI

0.01 0.1 1 10 100
Favours [honey] Favours [control]

Supplemental figure1. Forest plot of the incidence of radiotherapy-induced mucositis (Grade 2) (honey vs. control intervention)

Study or Subgroup	Honey Events	Total	Control Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Samdariya 2015	1	36	8	33	34.9%	-0.21 [-0.37, -0.06]
Charalambous 2017	16	36	22	36	26.4%	-0.17 [-0.39, 0.06]
Bardy 2012	55	64	52	63	38.6%	0.03 [-0.09, 0.16]
Total (95% CI)		136		132	100.0%	-0.11 [-0.28, 0.07]
Total events	72		82			

Heterogeneity: Tau^2 = 0.02; Chi^2 = 6.54, df = 2 (P = 0.04); I^2 = 69%
Test for overall effect: Z = 1.20 (P = 0.23)

Supplemental figure 2. Forest plot of the incidence of severe pain after radiotherapy (honey vs. control intervention)
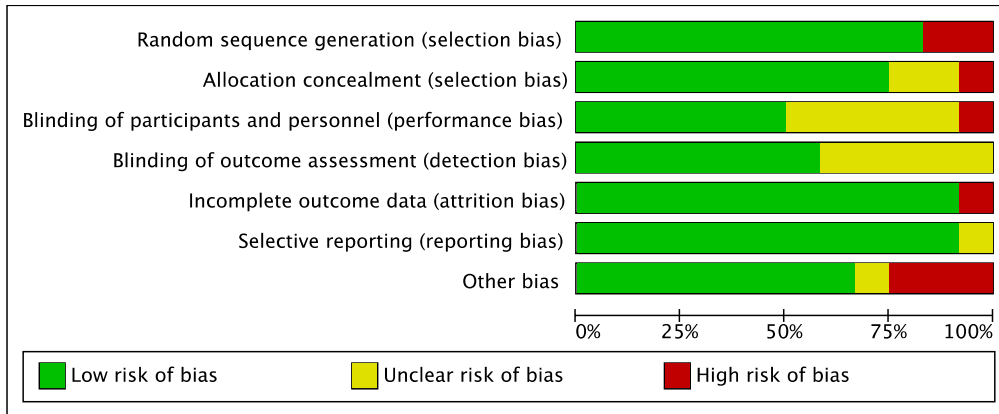
Supplemental figure 3. Percentage risk of bias in the included studies

Supplemental figure 4. Types of potential bias in the included studies

Grade 1
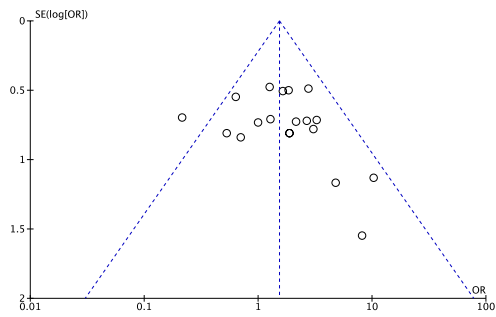
Grade 2
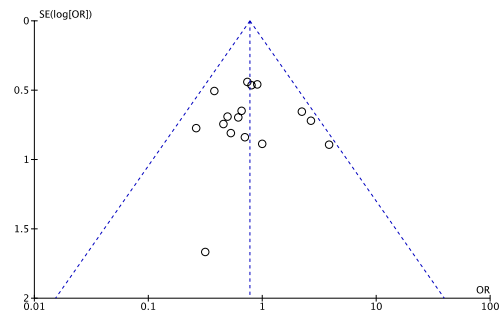
Grade 3
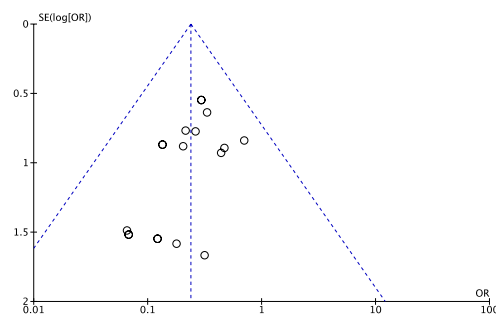
Grade 4
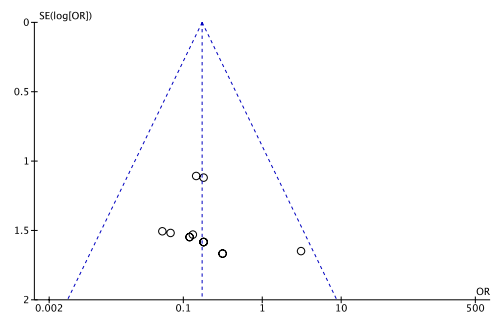
Supplemental figure 5. Analysis of publish bias by funnel plot in different grade of mucositis.

Supplement table 1.

Characteristics of patients and trails associated with honey treatment arm vs control arm

	OR,95%(CI)	Heterogeneity
Age	-0.71 (-2.87, 1.45)	Chi² = 1.57, P = 0.95, I² = 0%
Sex		
Overall results	1.01 (0.78, 1.30)	Chi² = 25.60, P = 0.08; I² = 34%
male	1.34 (0.94, 1.91)	Chi² = 10.42, P = 0.24; I² = 23%
female	0.78(0.54,1.11)	Chi² = 10.73, P = 0.22; I² = 25%
Tumor location		
Overall results	0.92(0.70,1.20)	Chi² = 10.88, P = 0.90, I² = 0%
Oral cavity	0.85 [0.55, 1.30]	Chi² = 1.87, P = 0.87, I² = 0%
Oropharynx+ hypopharynx	0.96 [0.64, 1.44]	Chi² = 3.98, P = 0.55, I² = 0%
Nasopharynx cavity	1.57(0.66,3.72)	Chi² = 1.20, P = 0.55, I² = 0%
Others	0.49(0.17,1.44)	Chi² = 1.17, P = 0.76, I² = 0%

Supplement table 2.

Subgroup analysis for the of the mild mucositis between honey vs. control intervention

Outcome and subgroups	participants	OR,95%(CI)	Heterogenetiy (I^2 and P)	
County				
Overall results	79/97	0.71(0.49,1.05)	I^2=78%	P<0.01
Aisa	47/66	0.60(0.38,0.95)	I^2=82%	P<0.01
Non-Asia	32/31	1.12(0.54,2.33)	I^2=2%	P=0.31
mucositis cause				
Overall results	79/97	0.71(0.49,1.05)	I^2=78%	P<0.01
Radiotherapy	38/38	1.00(0.57,1.74)	I^2=87%	P<0.01
Radiotherapy + chemotherapy	41/59	0.52(0.31,0.90)	I^2=74%	P=0.01
Radiation dose				
Overall results	79/97	0.71(0.49,1.05)	I^2=78%	P<0.001
<60Gy	78/81	0.94(0.62,1.42)	I^2=76%	P<0.001
≥60Gy	1/16	0.04(0.00,0.29)	--	--
Assessment scale				
Overall results	79/97	0.71(0.49,1.05)	I^2=78%	P<0.01
WHO	11/23	0.29(0.11,0.73)	I^2=68%	P=0.08
RTOG	68/74	0.87(0.57,1.34)	I^2=87%	P<0.01
Control arm				
Overall results	79/97	0.71(0.49,1.05)	I^2=78%	P<0.001
placebo	26/23	1.45(0.59,3.56)	––	--
saline	25/58	0.28(0.15,0.49)	I^2=67%	P=0.003
other	28/16	2.43(1.13,5.23)	I^2=84%	P=0.002

Supplement table 3.

Subgroup analysis for the of the severe mucositis between honey vs. control intervention

Outcome and subgroups	participants	OR,95%(CI)	Heterogenetiy (I^2 and P)	
County				
Overall results	79/145	0.30(0.20,0.44)	I^2=78%	P<0.01
Asia	14/80	0.10(0.05,0.19)	I^2=56%	P=0.04
Non-Asia	65/65	0.98(0.54,1.80)	I^2=12%	P=0.29
mucositis cause				
Overall results	79/145	0.30(0.20,0.44)	I^2=73%	P<0.01
Radiotherapy	56/89	0.32(0.18,0.54)	I^2=84%	P<0.01
Radiotherapy + chemotherapy	23/56	0.28(0.15,0.50)	I^2=73%	P=0.01
Radiation dose				
Overall results	79/145	0.30(0.20,0.44)	I^2=78%	P<0.01
<60Gy	52/66	0.47(0.25,0.90)	I^2=93%	P<0.01
≥60Gy	27.79	0.22(0.13,0.37)	I^2=67%	P<0.01
Assessment scale				
Overall results	79/145	0.30(0.20,0.44)	I^2=78%	P<0.01
WHO	2/22	0.04(0.01,0.19)	I^2=0%	P=0.92
RTOG	77/123	0.37(0.24,0.56)	I^2=77%	P<0.01
Control arm				
Overall results	79/145	0.30(0.20,0.44)	I^2=78%	P<0.01
placebo	65/65	0.98(0.54,1.80)	I^2=12%	P=0.29
saline	13/53	0.14(0.07,0.28)	I^2=68%	P=0.02
other	1/27	0.03(0.01,0.17)	I^2=0%	P=0.75