Appendix

Appendix table 1-Adverse events

Study ID	Intervention groups	Description	Control groups	Description
Lin RX2016	3(49)	1:Nausea and vomiting 2:Rash	1(49)	1:Vomiting
Wu J2001	2(80)	2:Nausea	32(80)	25:Nausea 5:Loss of appetite 2:Rash
Qin HL2010	0(60)	0	8(46)	2:Vomiting 6:Rash
Geng Y2012	1(49)	1:Vomiting	0(49)	0

Appendix Table2 Summary of secondary outcomes of randomized controlled trials on berberine for diarrhea

	Certainty assessment					№ of patients		Effect		Outstate		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Berberine	erberine vs no berberine-Stool bacterial culture											
2	randomised trials	serious ^a	serious ^b	not serious	serious ^c	not suspected	50/67 (74.6%)	43/65 (66.2%)	RR 1.15 (0.70 to 1.88)	99 more per 1,000 (from 198 fewer to 582 more)	⊕⊖⊖⊖ VERY LOW	NOT IMPORTANT
Berberine	vs no-Duration	n of hospitalizati	on							l l		
2	randomised trials	serious ^a	serious ^b	not serious	serious °	not suspected	109	109	-	MD 2.35 lower (4.82 lower to 0.12 higher)	⊕⊖⊖⊖ VERY LOW	NOT IMPORTANT
Berberine	vs no berberin	ne -Isoenzyme-C	K							<u>l</u>		
2	randomised trials	serious ^a	not serious	not serious	serious ^c	not suspected	74	74	-	MD 51.59 lower (57.84 lower to 45.34 lower)	⊕⊕⊖⊖ Low	NOT IMPORTANT
Berberine	vs no berberin	ne-Isoenzyme-Ch	(-MB							<u> </u>		
3	randomised trials	serious ^a	very serious ^b	not serious	serious ^c	not suspected	109	109	-	MD 7.04 lower (9.1 lower to 4.97 lower)	⊕⊖⊖⊖ VERY LOW	NOT IMPORTANT
Berberine	vs no berberin	ne-Inflammatory	factors-TNF-α				ı	ı		<u>. </u>		
4	randomised trials	serious ^a	serious ^b	not serious	serious ^c	not suspected	147	147	-	MD 0.81 lower (0.88 lower to 0.74 lower)	⊕⊖⊖ VERY LOW	NOT IMPORTANT

	Certainty assessment						№ of patients		Effect		•	
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
3	randomised trials	serious ^a	serious ^b	not serious	serious ^c	not suspected	112	112		MD 32.69 lower (36.42 lower to 28.96 lower)	⊕○○○ VERY LOW	NOT IMPORTANT
Berberine	vs no berberin	e-Inflammatory	factors-IL-10									
3	randomised trials	serious ^a	serious ^b	not serious	serious ^c	not suspected	112	112	-	MD 3.47 lower (4.39 lower to 2.54 lower)	⊕○○○ VERY LOW	NOT IMPORTANT
Berberine	vs no berberin	e-Myocardial en	zyme-ALT									
3	randomised trials	serious ^a	not serious	not serious	serious ^c	not suspected	109	109	-	MD 13.43 lower (15.49 lower to 11.37 lower)	ФФОО	NOT IMPORTANT
Berberine	Berberine vs no berberine-Myocardial enzyme-AST											
2	randomised trials	serious ^a	not serious	not serious	serious ^c	not suspected	80	80	-	MD 14.71 lower (16 lower to 13.42 lower)	ФФСО Low	NOT IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference

Explanations

- a. All the trials had a high risk of performance bias not blinding the participants. Methodological quality of these trials was graded as "high risk of bias" due to the design of comparison is difficult to blind personnel and participants.
- b. There is significant statistical heterogeneity indicating by a large I2 value.
- c. For dichotomous outcomes, the total number of events is less than 300; for continuous outcomes, the total population size is less than 400; or pooled results included no effects.

Study ID	Inclusion criteria
Berberine VS No	berberine
Lin RX2016 ^[29]	(1)Stool frequency> 3 times / d, and accompanied by changes in fecal characteristics; (2)The patient's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(3)The patient is accompanied by frequent vomiting, fever or thirst, etc;(4)Red blood cells and phagocytes can be seen in stool routine;(5)According to the duration of diarrhea, diarrhea is divided into acute and persistent types;(6)Age ≥18 years old;(7)The patient signed an informed consent form.
Ye J2013 ^[34]	(1)The course of chronic diarrhea> 2 months;(2)Stool frequency> 3 times / d, and accompanied by changes in fecal characteristics;(3)Patients can cooperate with treatment and follow-up.
Hu YX2009 ^[40]	(1)The course of chronic diarrhea> 2 months;(2)Stool frequency 4-10 times / d, and accompanied by changes in fecal characteristics;(3)Patients can cooperate with treatment and follow-up.
Zhang HF2015 ^[43]	(1) The patient is between 18-65 years old;(2)Stool frequency> 3 times / d, and accompanied by changes in fecal characteristics; (3)The patient's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(4)The patient is accompanied by frequent vomiting, fever or thirst, etc;(5)Red blood cells and phagocytes can be seen in stool routine;(6)According to the duration of diarrhea, diarrhea is divided into acute and persistent types; (7)Onset did not exceed 48 hours; (8)The patient signed an informed consent form;(9)The patient also has at least two of the main symptoms of abdominal pain, fever, diarrhea, and changes in stool characteristics
Dang GL2011 ^[44]	(1)The patient is between 2-12 years old;(2)The course of disease was within 72 hours; (3)The frequency of diarrhea ≥5 times / 24 h; (4)Loose stools, mucous pus and bloody stools, and / or abdominal pain, tenesmus;(4)The fecal leukocytes in stool routine≥15 / p / HP; (5)Red blood cells and phagocytes can be seen in stool routine;(6)The patients did not receive antibiotics before enrollment.
Wu J2001 ^[45]	(1)Stool frequency> 3 times / d, and accompanied by changes in fecal characteristics; (2)The patient's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(3)The patient is accompanied by frequent vomiting, fever or thirst, etc;(4)Red blood cells and phagocytes can be seen in stool routine;(5)According to the duration of diarrhea, diarrhea is divided into acute and persistent types;(6)Age 16~58 years old;(7)Gender is not limited; (8)The acute course is less than 5d, the chronic course is 2mo~1a;(9)Chronic patients did not receive drug treatment 2mo before the trial;(10)The patient signed an informed consent form.
Khin-Maung-U M K1985 ^[10]	(1)Patients had a history of watery diarrhea within 48 hours before enrollment; (2)The patient has no history of antibiotic intake, coexisting diseases such as pneumonia, systemic diseases such as diabetes or hypertension, or diarrhea within the past two weeks were taken into the study.
Berberine + Montm	orillonite VS No Berberine + Montmorillonite
Huang HH2011 ^[49]	(1)The children's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(2)The course of disease ≥14d;(3)The frequency of stool increased;(4)Age from 3 month to four years;(5)Children's parents with informed consent.
Gan YL2009 ^[52]	(1)The children's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(2)The course of disease ≥14d;(3)The frequency of stool increased.
Guo XH2009 ^[53]	(1)The children's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool;(2)The course of disease ≥14d;(3)The frequency of stool increased.

Wang HQ2009 ^[54]	(1)The stool frequency is $5 \sim 16$ times / d;(2)The stool is yellow water-like, no mucus and pus blood, no smell, and some milk;(3)In the microscopic examination of stool routine, there were no or 1 to 2 white blood cells / HP, and no or + \sim + + fat globules;(4)Most patients are accompanied by fever, bloating, vomiting, mild or moderate dehydration;(5) The course of disease ≤ 2 weeks.							
Berberine + Bifidol	pacterium subtilisVS No Berberine + bifidobacterium subtilis							
Geng Y2012 ^[59]	(1)The patient's stool traits changed, showing loose stools, watery stools, sticky pus stools or pus bloody stool; (2)The frequency of stool increase; (3)The course of disease ≤14 days.							
Berberine + Montmorillonite + Vitamin B VS No Berberine + Montmorillonite + Vitamin B								
Lu M2008 ^[60]	(1) The course of disease \leq 7 days; (2) The frequency of stools \geq 4 times / day.							
Yi Q2008 ^[61]	(1)The frequency of stool increased;(2)The patient cannot eat normally;(3)The patient is accompanied by frequent vomiting, fever, obvious thirst, and bloody stools.							

NR: Not reported

Appendix the modification of the Cochrane Risk of Bias tool

	1=low risk of bias (mention of "randomized" e.g. random number table, computer random number generator, coins, dice, drawing lots, minimizing)
Was generation randomization of sequence adequate	2=probably low risk of bias (mention of "randomized" but not detailed protocol) 3=probably high risk of bias (mention of "randomized", generate random sequence by an open random allocation schedule) 4=high risk of bias (mention of "randomized", randomization protocol is determined by the clinician, etc.)

"1=low risk of bias (e.g. central allocation (including telephone, web-based, and pharmacy-controlled randomization)

Was allocation concealed?

2=probably low risk of bias (e.g. sequentially numbered drug entainers of identical appearance; opaque, sealed envelopes;)

3=probably high risk of bias (mention of "randomized" but not detailed protocol; not mention of "randomized")

4=high risk of bias, Quasi-RCT, Using an open random allocation schedule: (e.g. Date of birth; Case record number; Any other explicitly unconcealed procedure))

For the next 5 questions regarding blinding, when high risk of bias explicit statement about blinding status is provided, consider the following assumptions:

Placebo controlled drug trial → probably low risk of bias

Active control drug trial (A vs. B) and mention of "double dummy" or that medications were identical or matched → probably low risk of bias

Active control drug trial (A vs. B) but high risk of bias mention of "double dummy" or that medications were identical or matched → probably high risk of bias

high risk of biasn drug trial→ probably high risk of bias

When high risk of biasne of the above applies, but still high risk of bias explicit statement of patient blinding is provided, consider the following assumptions:

"single blinded" → "probably low risk of bias" for patients; "probably high risk of bias" for healthcare providers, data collectors, outcome assessors, and data analysts.

" double blinded" → "probably low risk of bias" for patients, health care providers and "probably

high risk of bias	' for the rest.
	" →"probably low risk of bias" for patients, health care providers and outcome obably high risk of bias" for the rest.
Blinding of patients	1=low risk of bias (explicit statement that a group of interest was blinded) 2=probably low risk of bias trial (described as "single blinded" "double blinded" or "triple blinded") 3=probably high risk of bias(not mentioned) 4=Definitely high risk of biast (explicit statement that a group of interest was NOT blinded, explicit description of the trial as "open label" or "unblinded")
Blinding of health care providers	1=low risk of bias (explicit statement that a group of interest was blinded) 2=probably low risk of bias trial (described as "double blinded" or "triple blinded") 3=probably high risk of bias(not mentioned) 4=Definitely high risk of biast (explicit statement that a group of interest was NOT blinded, explicit description of the trial as "open label" or "unblinded")
Blinding of lata collectors	1=low risk of bias (explicit statement that a group of interest was blinded) 2=probably low risk of bias 3=probably high risk of bias (trial described as "single blinded" "double blinded" "triple blinded" or not mentioned) 4=Definitely high risk of biast (explicit statement that a group of interest was NOT blinded, explicit description of the trial as "open label" or "unblinded")

Blinding of adjudicators	1=low risk of bias (explicit statement that a group of interest was blinded) 2=probably low risk of bias ("triple blinded") 3=probably high risk of bias (trial described as "single blinded" "double blinded" or not mentioned) 4=Definitely high risk of biast (explicit statement that a group of interest was NOT blinded, explicit description of the trial as "open label" or "unblinded")
Blinding of data analysts	1=low risk of bias(explicit statement that a group of interest was blinded) 2=probably low risk of bias 3=probably high risk of bias (trial described as "single blinded" "double blinded" "triple blinded" or not mentioned) 4=Definitely high risk of biast (explicit statement that a group of interest was NOT blinded, explicit description of the trial as "open label" or "unblinded")
Lost to follow-up/missi ng data	0=0% 1= <5% 2= 5-9.9% 3= 10-19.9% 4= 20+% 5=not mentioned Difference between n randomized and n available for analysis.
Selective report	

^{*}Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, high risk of biasrris S, Falck-Ytter Y, Glasziou P, DeBeer H, Jaeschke R, Rind D, Meerpohl J, Dahm P, Schünemann HJ. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011; 64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026

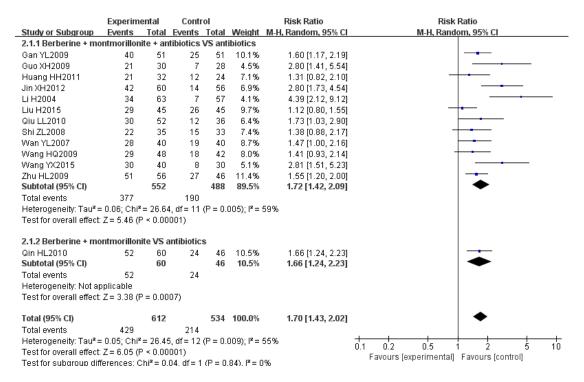


	Experime Events		Contro ents		Weight	Risk Ratio M-H, Fixed, 95% Cl		Risk Ratio M-H, Fixed, 95% Cl
1.1 Berberine + antil	oiotics vs	antibiotics	- child	dren di	iarrhea o	n day 3		
W2017 ei H2016	17 9	35 15	16 8	35 15	4.2% 2.1%	1.06 [0.65, 1.75] 1.13 [0.60, 2.11]		
ototal (95% CI)	9	50	0	50	6.2%	1.08 [0.73, 1.60]		
al events	26		24			,		
terogeneity: Chi² = 0			$ I^2 = 0 ^2$	%				
st for overall effect: 2	1= 0.40 (P	= 0.69)						
.2 Berberine + antil	oiotics vs	antibiotics	- child	dren d	iarrhea o	n day 7		
eng H2015	20	29	10	29	2.6%	2.00 [1.14, 3.49]		
ang YC2012 ang ZH2016	34 25	50 45	20 20	50 45	5.2% 5.2%	1.70 [1.15, 2.51] 1.25 [0.82, 1.90]		
ng CZ2017	22	38	16	38	4.2%	1.38 [0.87, 2.18]		+
btotal (95% CI)		162		162	17.1%	1.53 [1.23, 1.91]		•
tal events	101		66					
terogeneity: Chi² = 2 st for overall effect: 2			, I* = 09	%				
						rrhea in children on day 3		
YF2006 btotal (95% CI)	80	84 84	66	84 84	17.1% 17.1%	1.21 [1.07, 1.37] 1.21 [1.07, 1.37]		_
tal events	80	04	66	04	17.170	1.21[1.07, 1.37]		
terogeneity: Not app								
st for overall effect: 2	Z = 3.10 (P	= 0.002)						
.4 Berberine + antil	piotics VS	antibiotics	s - chil	dren v	with persi	stent infectious diarrhea on day 3		
ang H2010	23	40	15	40	3.9%	1.53 [0.95, 2.48]		+
btotal (95% CI)		40		40	3.9%	1.53 [0.95, 2.48]		
ital events eterogeneity: Not app	23 dicable		15					
eterogeneity. Not app est for overall effect: 2		= 0.08)						
1.5 Berberine + antil n RX2016	biotics VS 4∩	antibiotics 49	s - adul 20	ılts wit 49	th acute a 5.2%	nd persistent infectious diarrhea on 2.00 [1.39, 2.87]	day 3	
ibtotal (95% CI)	40	49	20	49	5.2%	2.00 [1.39, 2.87]		
tal events	40		20			,		
terogeneity: Not app								
st for overall effect: 2	Z= 3.75 (P	= 0.0002)						
1.6 Berberine + antil	biotics vs	antibiotics	- adul	ts wit	h acute a	nd persistent, infectious and non-infe	ectious diarrhea on day 5	
JQ2011	36	53	25	53	6.5%	1.44 [1.03, 2.02]		
ibtotal (95% CI) Ital events	36	53	25	53	6.5%	1.44 [1.03, 2.02]		
лагечетіs eterogeneity: Not app			25					
est for overall effect: 2		= 0.04)						
4.7.0	418-1-41	-1-11-1		41				
1.7 Berberine VS an ang GL2011	35	57	18	45	0.0%	1.54 [1.02, 2.32]		
ibtotal (95% CI)	33	Ö	10	0	0.070	Not estimable		
ital events	0		0					
eterogeneity: Not app		blo						
est for overall effect: N	Ant abblica	bie						
1.8 Berberine VS an								
ang HF2015	24	30	17	30	4.4%	1.41 [0.98, 2.02]		
ibtotal (95% CI) Ital events	24	30	17	30	4.4%	1.41 [0.98, 2.02]		
eterogeneity: Not app								
st for overall effect: 2	Z= 1.88 (P	= 0.06)						
I.9 Berberine VS am	tibiotics.a	dults with	acute	and n	ersistent	infectious and non-infectious diarrh	ea on day 5	
u J2001	56	80	51	80	0.0%	1.10 [0.88, 1.37]	may o	
ıbtotal (95% CI)		0		0		Not estimable		
tal events	0		0					
terogeneity: Not app		ble						
st for overall effect: N								
	hiotics VS			-				
1.10 Berberine + pro		20 35	14 16	20 33	3.6% 4.3%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22]		-
1.10 Berberine + pro 1 YX2009	19		16	30	4.2%	1.38 [0.92, 2.05]		+ :-
1.10 Berberine + pro 1 YX2009 0 YM2014 J2013		30		83	12.1%	1.40 [1.13, 1.75]		•
I.10 Berberine + pro I YX2009 O YM2014 J2013 btotal (95% CI)	19 25 22							
I.10 Berberine + pro i YX2009 o YM2014 J2013 ibtotal (95% CI) tal events	19 25 22 66	30 85	46 12 - 00	DC.				I I
i.10 Berberine + pro 1 YX2009 0 YM2014 J2013 btotal (95% CI) tal events terogeneity: Chi ² = 0	19 25 22 66 0.11, df = 2	30 85 (P = 0.95);		%				
I.10 Berberine + pro 1 YX(2009 o YM2014 J2013 bitotal (95% CI) tal events sterogeneity: Chi ² = 0 st for overall effect: 2	19 25 22 66 0.11, df = 2 Z = 3.02 (P	30 85 (P = 0.95); = 0.003)	; I*= 09					
I.10 Berberine + pro 1 YX2009 0 YM2014 J2013 btotal (95% CI) tal events eterogeneity: Chi² = 0 st for overall effect: 2 I.11 Berberine + inte	19 25 22 66 0.11, df = 2 Z = 3.02 (P	30 85 (P = 0.95); = 0.003) cosal prote	; I² = 09 ection	ı + anti		S intestinal mucosal protection + ant	ibiotics-Children with diarrhea	
1.10 Berberine + pro 1 YX2009 10 YM2014 J2013 blotal (95% CI) tal events sterogeneity: Chi ² = (st for overall effect: 2 1.11 Berberine + interpretation	19 25 22 66 0.11, df = 2 Z = 3.02 (P estinal mu 53	30 85 (P = 0.95); = 0.003) cosal prote	= 09 ection 37	n + anti 60	9.6%	1.43 [1.15, 1.78]	ibiotics-Children with diarrhea	-
1.10 Berberine + pro 1.17(2009 10 YM2014 1.J2013 10tal events 10tal events 10tergeneity: ChiF= 0 1.11 Berberine + inter 1/L2010 10u Y2013	19 25 22 66 0.11, df = 2 Z = 3.02 (P	30 85 (P = 0.95); = 0.003) cosal prote	; I² = 09 ection	ı + anti			ibiotics-Children with diarrhea	
1.10 Berberine + pro 1/X2009 10 YM2014 1/2013 1/201	19 25 22 66 0.11, df = 2 Z = 3.02 (P estinal mu 53 89	30 85 (P = 0.95); = 0.003) cosal prote 60 100 160	ection 37 68	1 + anti 60 98 158	9.6% 17.8%	1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	ibiotics-Children with diarrhea	
1.10 Berberine + pro 1/YC2009 10 YM2014 1/J2013 Ibtotal (95% CI) tal events teterogeneity. Chif = (1.11 Berberine + into YL2010 100 Y2013 Ibtotal (95% CI) tal events teterogeneity. Chif = (1.11 Berberine + into YL2010 100 Y2013 Ibtotal (95% CI) tal events teterogeneity. Chif = (19 25 22 66 0.11, df = 2 2 = 3.02 (P estinal mu 53 89 142 0.67, df = 1	30 85 (P = 0.95); = 0.003) cosal prote 60 100 160 (P = 0.41);	ection 37 68 105 	1 + anti 60 98 158	9.6% 17.8%	1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	ibiotics-Children with diarrhea	
1.10 Berberine + pro 1 YX2009 10 YM2014 1 J2013 1btotal (95% CI) tal events sterogeneity. Chif= (1st for overall effect: 2 1.11 Berberine + inter YL2010 100 V2013 1btotal (95% CI) stal events sterogeneity. Chif= (19 25 22 66 0.11, df = 2 2 = 3.02 (P estinal mu 53 89 142 0.67, df = 1	30 85 (P = 0.95); = 0.003) cosal prote 60 100 160 (P = 0.41);	ection 37 68 105 	1 + anti 60 98 158	9.6% 17.8%	1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	zibiotics-Children with diarrhea	-
1.10 Berberine + pro 1 YX2009 10 YM2014 1 J2013 bitotal (95% CI) tal events 1.11 Berberine + inter 1 L2013 bitotal (95% CI) tal over 10 to	19 25 22 66 0.11, df = 2 2 = 3.02 (P estinal mu 53 89 142 0.67, df = 1	30 85 (P = 0.95); = 0.003) cosal prote 60 100 160 (P = 0.41);	ection 37 68 105 	1 + anti 60 98 158 %	9.6% 17.8%	1.43 [1.15, 1.78] 1.28 [1.11, 1.49] 1.34 [1.18, 1.51]	ibiotics-Children with diarrhea	•
YL2010 nou Y2013 ubtotal (95% CI) utal events eterogeneity: Chi ² = 0 est for overall effect: 2 utal (95% CI) utal events	19 25 22 66 0.11, df = 2 2 = 3.02 (P estinal mu 53 89 142 0.67, df = 1 2 = 4.58 (P	30 85 (P = 0.95); = 0.003) cosal prot 60 100 160 (P = 0.41); < 0.00001)	ection 37 68 105 ; = 09	1 + anti 60 98 158 %	9.6% 17.8% 27.4 %	1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	ibiotics-Children with diarrhea	•
1.10 Berberine + pro 17/2009 o *M2014 J2013 bitotal (95% CI) tal events eterogeneity. Chi² = (st for overall effect: 2 1.11 Berberine + inte **W12010 u	19 25 22 66 0.11, df = 2 2 = 3.02 (P estinal mu 53 89 142 0.67, df = 1 2 = 4.58 (P	30 85 (P = 0.95); = 0.003) cosal prot 60 100 160 (P = 0.41); < 0.00001) 713	ection 37 68 105 ; = 09) 384 6); = =	1 + anti 60 98 158 %	9.6% 17.8% 27.4 %	1.43 [1.15, 1.78] 1.28 [1.11, 1.49] 1.34 [1.18, 1.51]	ibiotics-Children with diarrhea	05 07 1 15 2

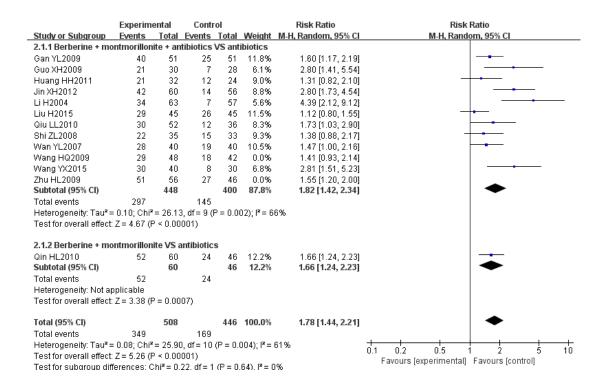
Appendix 1 Berberine vs no Berberine-clinical cure rate-sensitivity analysis(ran	ndomization, allocation concealment)

udy or Subgroup 1.1 Berberine + anti W2017	Experime Events		Contro ents		Weight	Risk Ratio M-H, Fixed, 95% Cl	Risk Ratio M-H, Fixed, 95% CI
WOLT T	ibiotics vs	antibiotics	- chil	dren d	iarrhea o	day 3	
ei H2016	17 9	35 15	16 8	35 15	6.7% 0.0%	1.06 [0.65, 1.75] 1.13 [0.60, 2.11]	
btotal (95% CI)	9	35	۰	35	6.7%	1.06 [0.65, 1.75]	
tal events	17		16			,,	
terogeneity: Not ap							
st for overall effect:	Z = 0.24 (P	= 0.81)					
.2 Berberine + ant	ibiotics vs	antibiotics	- chil	dren d	iarrhea o	day 7	
eng H2015	20	29	10	29	4.2%	2.00 [1.14, 3.49]	
iang YC2012 ang ZH2016	34 25	50 45	20 20	50 45	8.4% 8.4%	1.70 [1.15, 2.51] 1.25 [0.82, 1.90]	
ng CZ2017	22	38	16	38	6.7%	1.38 [0.87, 2.18]	
btotal (95% CI)		162		162	27.8%	1.53 [1.23, 1.91]	•
tal events	101		66				
terogeneity: Chi ² = st for overall effect:			I= 0	%			
Stroi overali ellect.	2-5.10(- 0.0002)					
						rrhea in children on day 3	
YF2006 btotal (95% CI)	80	84 0	66	84 0	0.0%	1.21 [1.07, 1.37] Not estimable	
tal events	0	·	0	U		not estillable	
terogeneity: Not ap	plicable						
st for overall effect:	Not applica	ble					
4 Perherine + anti	ihiotice VS	antihiotics	chil	ldron s	with norei	stent infectious diarrhea on day 3	
iang H2010	23	40	15	40	6.3%	1.53 [0.95, 2.48]	
btotal (95% CI)		40		40	6.3%	1.53 [0.95, 2.48]	
tal events	23		15				
eterogeneity: Not ap est for overall effect:		= 0.087					
						nd persistent infectious diarrhea on day 3	
n RX2016 ibtotal (95% CI)	40	49 0	20	49 0	0.0%	2.00 [1.39, 2.87] Not estimable	
ibiotal (95% CI) ital events	0	U	0	U		Not estimable	
eterogeneity: Not ap							
st for overall effect:		ble					
1 6 Berherine + anti	ihintice ve	antihiotice	adu	lte wit	h acuto a	nd persistent, infectious and non-infectious diarrhea	on day 5
JQ2011	36	53	25	53	10.5%	1.44 [1.03, 2.02]	- I on day 5
ıbtotal (95% CI)		53		53	10.5%	1.44 [1.03, 2.02]	
ital events	36		25				
eterogeneity: Not ap est for overall effect:		- 0.04)					
stiol overall ellect.	2-2.10 (1	- 0.04)					
1.7 Berberine VS ar							
ang GL2011	35	57	18	45	0.0%	1.54 [1.02, 2.32]	
ibtotal (95% CI) Ital events	0	0	0	0		Not estimable	
eterogeneity: Not ap							
est for overall effect:	Not applica	ble					
1.8 Berberine VS ar	ntihiotice	adulte with	infor	tione	diarrhoa (n day 7	
ang HF2015	24	30	17	30	7.2%	1.41 [0.98, 2.02]	
ibtotal (95% CI)		30		30	7.2%	1.41 [0.98, 2.02]	
ital events	24		17				
eterogeneity: Not ap est for overall effect:		_ 0.06\					
orior overall ellect.	∠- 1.00 (P	- 0.00)					
						infectious and non-infectious diarrhea on day 5	
	56	80	51	80	0.0%	1.10 [0.88, 1.37]	
u J2001	30	0	0	0		Not estimable	
u J2001 ibtotal (95% Cl)							
u J2001 I btotal (95% CI) tal events	0		۰				
u J2001 I btotal (95% CI) tal events eterogeneity: Not ap	0 plicable	ble					
u J2001 Ibtotal (95% CI) tal events eterogeneity: Not ap st for overall effect:	0 plicable Not applica			lte ne	eistant di	arrhea	
u J2001 Ibtotal (95% CI) tal events sterogeneity: Not ap st for overall effect: I.10 Berberine + pr	0 plicable Not applica obiotics V S	probiotic	s-adu	-			
J J2001 Ibtotal (95% CI) tal events sterogeneity: Not ap st for overall effect: I.10 Berberine + pr i YX2009	0 plicable Not applica			Its per 20 33	sistent di 5.9% 0.0%	arrhea 1.36 (1.00, 1.84) 1.47 (0.98, 2.22)	-
JJ2001 btotal (95% CI) tal events sterogeneity: Not ap st for overall effect: I.10 Berberine + pr IYX2009 0 YM2014 J2013	0 plicable Not applica obiotics V 9	5 probiotic : 20 35 30	s-adu 14	20 33 30	5.9% 0.0% 6.7%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05]	
JJ2001 btotal (95% CI) tal events sterogeneity: Not ap st for overall effect: I.10 Berberine + pr 1 YX2009 o YM2014 JJ2013 btotal (95% CI)	0 plicable Not applica obiotics VS 19 25 22	probiotics 20 35	s-adu 14 16 16	20 33	5.9% 0.0%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22]	
J J2001 bitotal (95% CI) tal events teterogeneity: Not ap st for overall effect: I.10 Berberine + pr 1/X2009 o YM2014 J2013 bitotal (95% CI) tal events	0 plicable Not applica obiotics VS 19 25 22	20 35 30 50	s-adu 14 16 16	20 33 30 50	5.9% 0.0% 6.7%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05]	
J2001 btotal (95% CI) al events terogeneity: Not ap at for overall effect: .10 Berberine + pr YX2009 b YM2014 J2013 btotal (95% CI) al events terogeneity: Chi² =	0 plicable Not applica obiotics VS 19 25 22 41 0.00, df = 1	35 30 50 (P = 0.96)	s-adu 14 16 16	20 33 30 50	5.9% 0.0% 6.7%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05]	
JJ2001 httotal (95% CI) tatal events rerogeneity: Not apst for overall effect: 1.10 Berberine + pr 179/2009 o YM2014 JJ2013 httotal (95% CI) tat events sterogeneity: Chi² = st for overall effect:	0 plicable Not applica obiotics V5 19 25 22 41 0.00, df = 1 Z = 2.39 (P	5 probiotic: 20 35 30 50 (P = 0.96); = 0.02)	s-adu 14 16 16 30 ; ² = 0	20 33 30 50 %	5.9% 0.0% 6.7% 12.6 %	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76]	
JJ2001 that (95% CI) tal events terogeneity. Not aps teroyeneity effect: L10 Berberine + pr 1/Y/2009 o YM2014 JJ2013 biotal (95% CI) tal events etrogeneity. Chi² = st for overall effect: L11 Berberine + int	0 plicable Not applica obiotics V5 19 25 22 41 0.00, df = 1 Z = 2.39 (P	5 probiotics 20 35 30 50 (P = 0.96); = 0.02)	s-adu 14 16 16 30 ; ² = 0	20 33 30 50 %	5.9% 0.0% 6.7% 12.6 % ibiotics V	1.36 [1.00, 1.84] 1.47 [0.38, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76]	n with diarrhea
J.J. J.	0 plicable Not applica obiotics V5 19 25 22 41 0.00, df = 1 Z = 2.39 (P	5 probiotics 20 35 30 50 (P = 0.96); = 0.02) cosal prot	s-adu 14 16 16 30 ; = 0 ectior 37	20 33 30 50 %	5.9% 0.0% 6.7% 12.6 % ibiotics V 0.0%	1.36 [1.00,1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78]	n with diarrhea
J J J J J J J J J J J J J J J J J J J	0 plicable Not applica obiotics V5 19 25 22 41 0.00, df = 1 Z = 2.39 (P	5 probiotics 20 35 30 50 (P = 0.96); = 0.02)	s-adu 14 16 16 30 ; ² = 0	20 33 30 50 %	5.9% 0.0% 6.7% 12.6 % ibiotics V	1.36 [1.00, 1.84] 1.47 [0.38, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76]	n with diarrhea
J J J J J J J J J J J J J J J J J J J	0 plicable Not applica volume 53 89 89	(P = 0.96); = 0.02) cosal prot	s-adu 14 16 16 30 ; = 0 ectior 37	20 33 30 50 % 1 + ant 60 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78]	n with diarrhea
J J J J J J J J J J J J J J J J J J J	0 plicable Not applica obiotics VS 19 25 22 41 0.00, df = 1 Z = 2.39 (P testinal mu 53 89 plicable	s probiotics 20 35 30 50 (P = 0.96); = 0.02) cosal prot 60 100	s-adu 14 16 16 30 ; = 0 ectior 37 68	20 33 30 50 % 1 + ant 60 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78]	n with diarrhea
J J J J J J J J J J J J J J J J J J J	0 plicable Not applica obiotics VS 19 25 22 41 0.00, df = 1 Z = 2.39 (P testinal mu 53 89 plicable	s probiotics 20 35 30 50 (P = 0.96); = 0.02) cosal prot 60 100	s-adu 14 16 16 30 ; = 0 ectior 37 68	20 33 30 50 % 1 + ant 60 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78]	n with diarrhea
J J J J J J J J J J J J J J J J J J J	0 plicable Not applica obiotics VS 19 25 22 41 0.00, df = 1 Z = 2.39 (P testinal mu 53 89 plicable	(P = 0.96); (P = 0.96); = 0.02) (cosal prot 60 100 100 = 0.001)	s-adu 14 16 16 30 ; = 0 ectior 37 68	20 33 30 50 % 1 + ant 60 98 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	n with diarrhea
u J2001 Initiotal (95% CI) Initi	0 plicable Not applica obiotics VS 19 25 22 41 0.00, df = 1 Z = 2.39 (P testinal mu 53 89 plicable	(P = 0.96); 00 35 30 50 (P = 0.96); 00 00 100 100 100 100 100 100 100 100 1	s-adu 14 16 16 30 ; = 0 ectior 37 68	20 33 30 50 % 1 + ant 60 98 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78]	n with diarrhea
JJ2001 thotal (95% CI) tal events terogeneity. Not aps tfor overall effect: J10 Berberine + pr 1/Y2009 o YM2014 J2013 biotal (95% CI) tal events terogeneity. Chif = st for overall effect: J11 Berberine + int YL2010 ou Y2013 biotal (95% CI) tal events terogeneity. Not aps tfor overall effect: tal (95% CI)	0 plicable Not applica vobiotics VS 22 41 0.00, df = 1 Z = 2.39 (P testinal mu 53 89 plicable Z = 3.29 (P 331 5.38, df = 1	s probiotic: 20 35 30 50 (P = 0.96); = 0.02) cosal prot 60 100 100 = 0.001) 470 0 (P = 0.86	s-adu 14 16 16 30 F= 0 ection 37 68 68	20 33 30 50 % 1 + ant 60 98 98	5.9% 0.0% 6.7% 12.6% ibiotics V 0.0% 28.9% 28.9%	1.36 [1.00, 1.84] 1.47 [0.98, 2.22] 1.38 [0.92, 2.05] 1.37 [1.06, 1.76] S intestinal mucosal protection + antibiotics-Childre 1.43 [1.15, 1.78] 1.28 [1.11, 1.49]	n with diarrhea

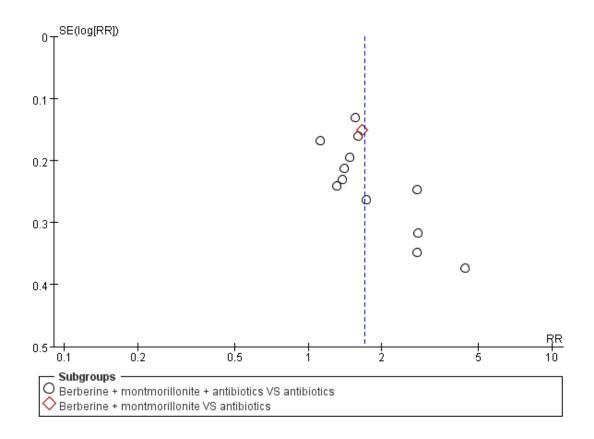
Appendix 2 Berberine vs no Berberine-clinical cure rate-sensitivity analysis(selective reporting bias)



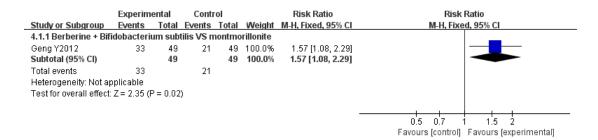
Appendix 3 Berberine+Montmorillonite versus No Berberine+Montmorillonite -clinical cure rate



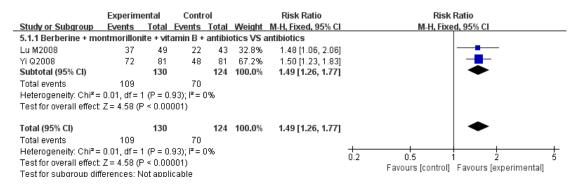
Appendix 3.A Berberine+Montmorillonite versus No Berberine+Montmorillonite -clinical cure rate-sensitivity analysis(selective reporting bias)



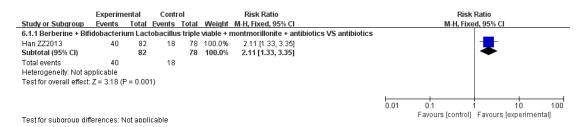
Appendix 4 Berberine+Montmorillonite versus No Berberine+Montmorillonite -clinical cure rate-funnel plot



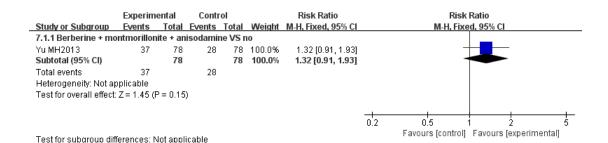
Appendix 5 Berberine + Bifidobacterium subtilis versus No Berberine + Bifidobacterium subtilis-clinical cure rate



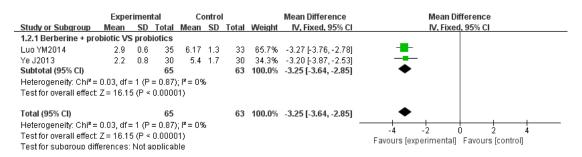
Appendix 6-Berberine + montmorillonite + vitamin B VS No Berberine + montmorillonite + vitamin B-clinical cure rate



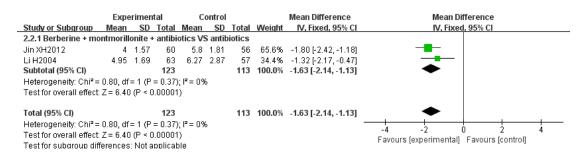
Appendix 7 Berberine + Bifidobacterium Lactobacillus triple viable + montmorillonite VS No Berberine + Bifidobacterium Lactobacillus triple viable + montmorillonite-clinical cure rate



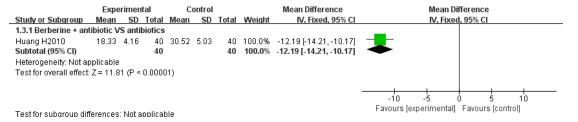
Appendix 8 Berberine + montmorillonite + anisodamine VS No Berberine + montmorillonite + anisodamine.-clinical cure rate



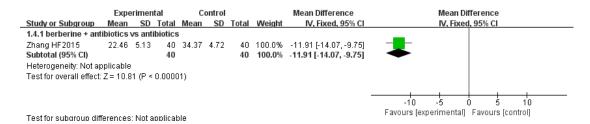
Appendix 9 Berberine vs no Berberine-the duration of diarrhea



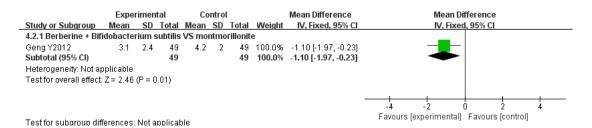
Appendix 10 Berberine+Montmorillonite versus No Berberine+Montmorillonite-the duration of diarrhea



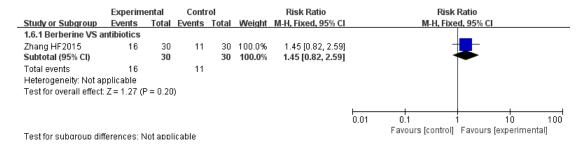
Appendix 11 Berberine vs no Berberine-stool frequency



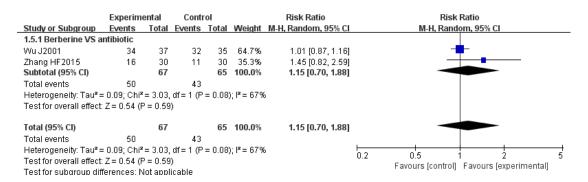
Appendix 12 Berberine vs no Berberine-faecal trait



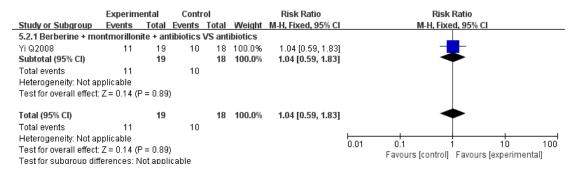
Appendix 13 Berberine + Bifidobacterium subtilis versus No Berberine + Bifidobacterium subtilis-stool frequency



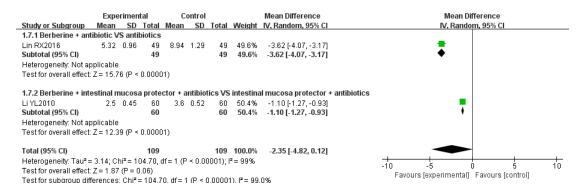
Appendix 14 Berberine vs no Berberine-stool routine examination



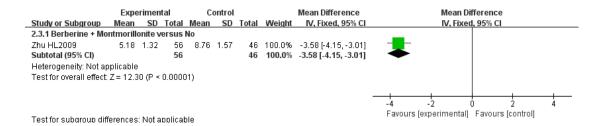
Appendix 15 Berberine vs no Berberine-stool bacterial culture



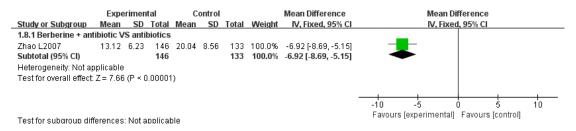
Appendix 16 Berberine + montmorillonite + vitamin B VS No Berberine + montmorillonite + vitamin B-Stool bacterial culture



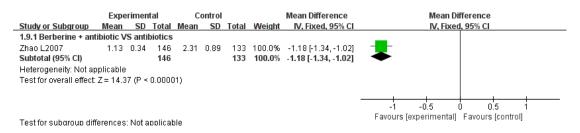
Appendix 17 Berberine vs no Berberine-the duration of hospitalization



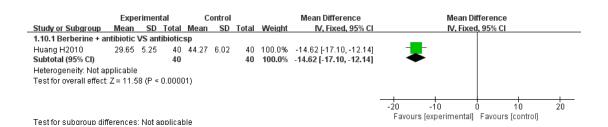
Appendix 18 Berberine+Montmorillonite versus No Berberine+Montmorillonite-the duration of hosilation



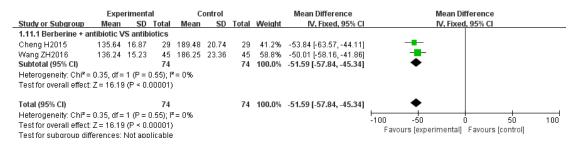
Appendix 19 Berberine vs no Berberine-the duration of heating



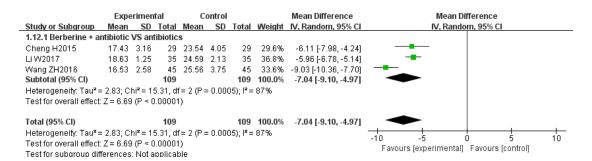
Appendix 20 Berberine vs no Berberine-the duration of vomiting



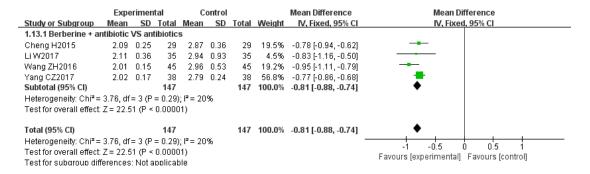
Appendix 21 Berberine vs no Berberine-the duration of systematic symptom



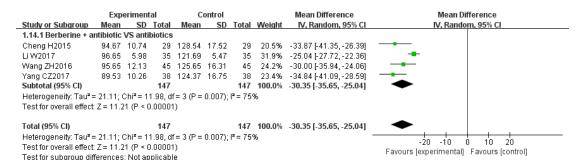
Appendix 22 Berberine vs no Berberine-Isoenzyme-CK



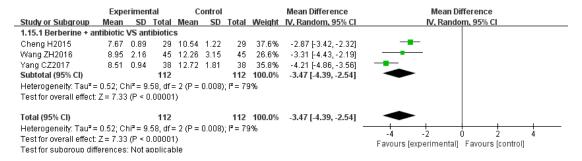
Appendix 23-Berberine vs no Berberine-Isoenzyme-CK-MB



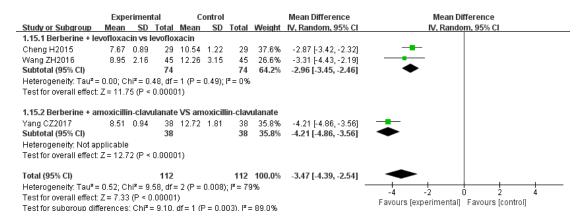
Appendix 24 Berberine vs no Berberine-Inflammatory factors-TNF- a



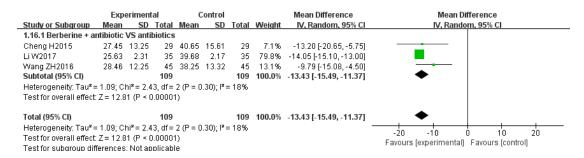
Appendix 25-Berberine vs no Berberine-Inflammatory factors-IL-6



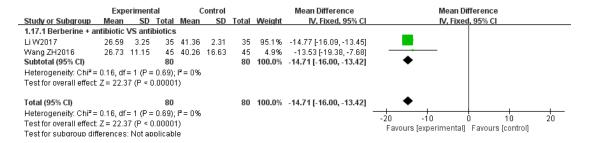
Appendix 26 Berberine vs no Berberine-Inflammatory factors-IL-10



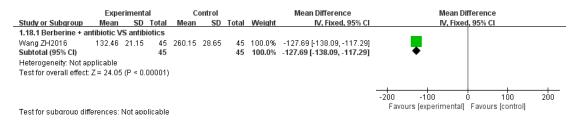
Appendix 27 Berberine vs no Berberine-Inflammatory factors-IL-10-subgroup analyses based on the type of antibiotic



Appendix 28 Berberine vs no Berberine-Myocardial enzyme-ALT



Appendix 29 Berberine vs no Berberine-Myocardial enzyme-AST



Appendix 30 Berberine vs no Berberine-Myocardial enzyme-LDH