

Appendix table 1 Characteristics of excluded studies(ordered by study ID)

Study	Reason for exclusion
Ding 1985	No relevant result
Fan 1986	Not a RCT
Guo 1990	Not a RCT
Han 2013	Not a RCT
He 1988	Not a RCT
Huang 1959	Not a RCT
Li 1986	Not a RCT
Li 2004	Preventive study
Liang 1986	Preventive study
Ma 1996	Not a RCT
Sun 2008	Not a RCT
Suolang 2008	Not a RCT
Wang 1983	Preventive study
Wang 1988	Not a RCT
Wang 1989	Preventive study
Wu 1991	Preventive study
Yang 2009	Not a RCT
Yang 2010	Not a RCT
Yi 2006	Not a RCT
Yu 2016	Not a RCT
Zhang 1989	Not a RCT
Zhang 1996	No relevant result
Zhang 2006	Not a RCT
Zhang 2009	Not a RCT
Zhong 1986	Not a RCT
Zhou 1998	Not a RCT

Appendix table 2 Characteristics of included trials

Study	Case No.		Age		Intervention	Control	Follow-up (months)	Outcome	
	I	C	I	C					
Niu 1981 ²²	27	29	6~13	6~13	Se + VE: Se tablet 2mg/week +VE 15mg/day	Placebo/week	12	Improvement of lesions on X-ray	metaphyseal
YSSG 1982 ²³	166	159	3~13	3~13	Se tablet, 1 mg/week (3-10 yrs), 2 mg/week (11-13 yrs)	Placebo/week	12	Improvement of lesions on X-ray	metaphyseal
Wang 1983 ²⁴	47	42	5~15	5~15	Se + VC: Se tablet 2mg/week +VE 15mg/day	No treatment	11	Improvement of lesions on X-ray	metaphyseal
Cui 1984 ^{25*}	30	30/30	7~19	7~19	Se tablet, 1 mg/week (7-10 yrs), 2 mg/week (11-19 yrs)	①VC 200 mg 3 times/day; ②Placebo/week	6~12	Improvement of lesions on X-ray	metaphyseal
Niu 1984 ²⁶	56	59	6~13	6~13	Se tablet first week: 1.0 mg/day (< 10 yrs), 2.0 mg/day (> 11 yrs); after: 1.0 mg/week (< 10 yrs), 2.0 mg/week (> 11 yrs)	Placebo/week	24	Improvement of lesions on X-ray Repairing rate at the distal end of phalanges in hands on X-ray films	metaphyseal
Guo 1985 ²⁷	50	50	5~15	5~15	Se tablet, 1 mg/week (<5 yrs), 2 mg/week (>5 yrs)	Placebo/week	12	Improvement of lesions on X-ray	metaphyseal

Study	Case No.		Age		Intervention	Control	Follow-up (months)	Outcome	
	I	C	I	C					
Guo 1986 ^{28*}	60/60	60	5~14	5~14	①Se tablet, 0.5mg/week (<7 yrs), 1 mg/week (>8 yrs); ②Se yeast, 0.5mg/week (<7 yrs), 1 mg/week (>8 yrs);	Placebo/week	13	Improvement of metaphyseal lesions on X-ray	metaphyseal
Niu 1986 ²⁹	285	277	6~13	6~13	Se tablet, 1 mg/week (<10 yrs), 2 mg/week (>10 yrs)	Placebo/week	12~24	Improvement of metaphyseal lesions on X-ray Repairing rate at the distal end of phalanges in hands on X-ray films	metaphyseal
Wu 1986 ³⁰	171	177	5~16	5~16	Se tablet, 1 mg/week (< 10 yrs), 2 mg/week (> 10 yrs)	Placebo/week	12	Improvement of metaphyseal lesions on X-ray	metaphyseal
Deng 1988 ³¹	43	46	2~13	2~13	Se tablet, no details	No treatment	36	Improvement of metaphyseal lesions on X-ray Repairing rate at the distal end of phalanges in hands on X-ray films	metaphyseal

Study	Case No.		Age		Intervention	Control	Follow-up (months)	Outcome
	I	C	I	C				
Niu 1990 ³²	210	228	6~13	6~13	Se tablet, first week: 0.5 mg/day (< 5 yrs), 1.0 mg/day (6-10 yrs), 2.0 mg/day (> 11 yrs); after: 1.0 mg/month (< 5 yrs), 2.0 mg/month (6-10 yrs), 4.0 mg/month (> 11 yrs)	Placebo/month	12	Improvement of metaphyseal lesions on X-ray
Zhou 1991 ^{33#}	25/30	35/29	4~12	4~12	①Se + VC: Se tablet 1mg/10day+ VC 100mg/day; ②Se salt (sodium selenite: salt = 1:60,000) /10day	③VC, 300mg/day; ④No treatment	12	Improvement of metaphyseal lesions on X-ray
Moreno-Reyes 2003 ³⁴	113	95	10±0.28	10±0.3	Se tablet, 1 mg/week	Placebo/week	12	Improvement of metaphyseal lesions on X-ray Repairing rate at the distal end of phalanges in hands on X-ray films
Chen 2003 ^{35*}	50/50	50	6~11	6~11	①Se tablet 1mg/week; ② Se + VC: Se tablet 1mg/week+ VC 300 mg 2 times/day	VC 300mg bid	12	Improvement of metaphyseal lesions on X-ray

Study	Case No.		Age		Intervention	Control	Follow-up (months)	Outcome
	I	C	I	C				
Cai 2005 ³⁶	31	31	7~13	7~13	Se tablet, 2mg/10 days (7-10 yrs), 3 mg/10 days (11-13 yrs)	No treatment	18	Improvement of metaphyseal lesions on X-ray Repairing rate at the distal end of phalanges in hands on X-ray films

I= intervention, C = control, YSSG = Yongshou scientific survey group of Kashin-Beck Disease, yrs = years, Se = Sodium selenite, Se salt =selenium salt, VC = vitamin C, Se + VC = the combination of sodium selenite with vitamin C ; Se + VE = the combination of sodium selenite with vitamin E, Se yeast = selenium enriched yeast. * Three arms study, # Four arms study

Appendix table 3 Risk of Bias of Included Studies

Study	Balanced allocation	Allocation concealment	Blinding	Completeness of outcome	Selective outcome reporting	Other Bias	overall assessment*
Niu 1981 ²²	Unclear	Unclear	Double-blind	Low	Low	Low	Unclear
YSSG 1982 ²³	Unclear	Unclear	Double-blind	Low, No dropout	Low	Low	Unclear
Wang 1983 ²⁴	unclear	unclear	Double-blind	High, dropouts >20%	Low	High, no ITT analysis	High
Cui 1984 ²⁵	unclear	unclear	Double-blind	High, dropouts >20%	Low	High, no ITT analysis	High
Niu 1984 ²⁶	Unclear	Unclear	Double-blind	Low, No dropout	Low	High, no ITT analysis	High
Guo 1985 ²⁷	Unclear	Unclear	Not Used	High, dropouts >20%	Low	High, no ITT analysis	High
Guo 1986 ²⁸	Unclear	Unclear	Unclear	High, dropouts >20%	Low	High, no ITT analysis	High
Niu 1986 ²⁹	Unclear	Unclear	Double-blind	Low, No dropout	Low	Low	Unclear

Wu 1986 ³⁰	Unclear	Unclear	Double-blind	Unclear, No dropout < 20%	Low	High, no ITT analysis	High
Deng 1988 ³¹	Unclear	Unclear	Unclear	Low, drop out < 10%	Low	High, no ITT analysis	High
Niu 1990 ³²	Unclear	Unclear	Single-blind	Low, No dropout	Low	Low	Unclear
Zhou 1991 ³³	Unclear	Unclear	Unclear	Low, No dropout	Low	Low	Unclear
Moreno-Reyes 2003 ³⁴	Unclear	Unclear	Double-blind	Unclear, No dropout < 20%	Low	High no ITT analysis	High
Chen 2003 ³⁵	Unclear	Unclear	Unclear	High, dropouts > 20%	Low	High, no ITT analysis	High
Cai 2005 ³⁶	Unclear	Unclear	Not Used	Low, No dropout	Low	Low	Unclear

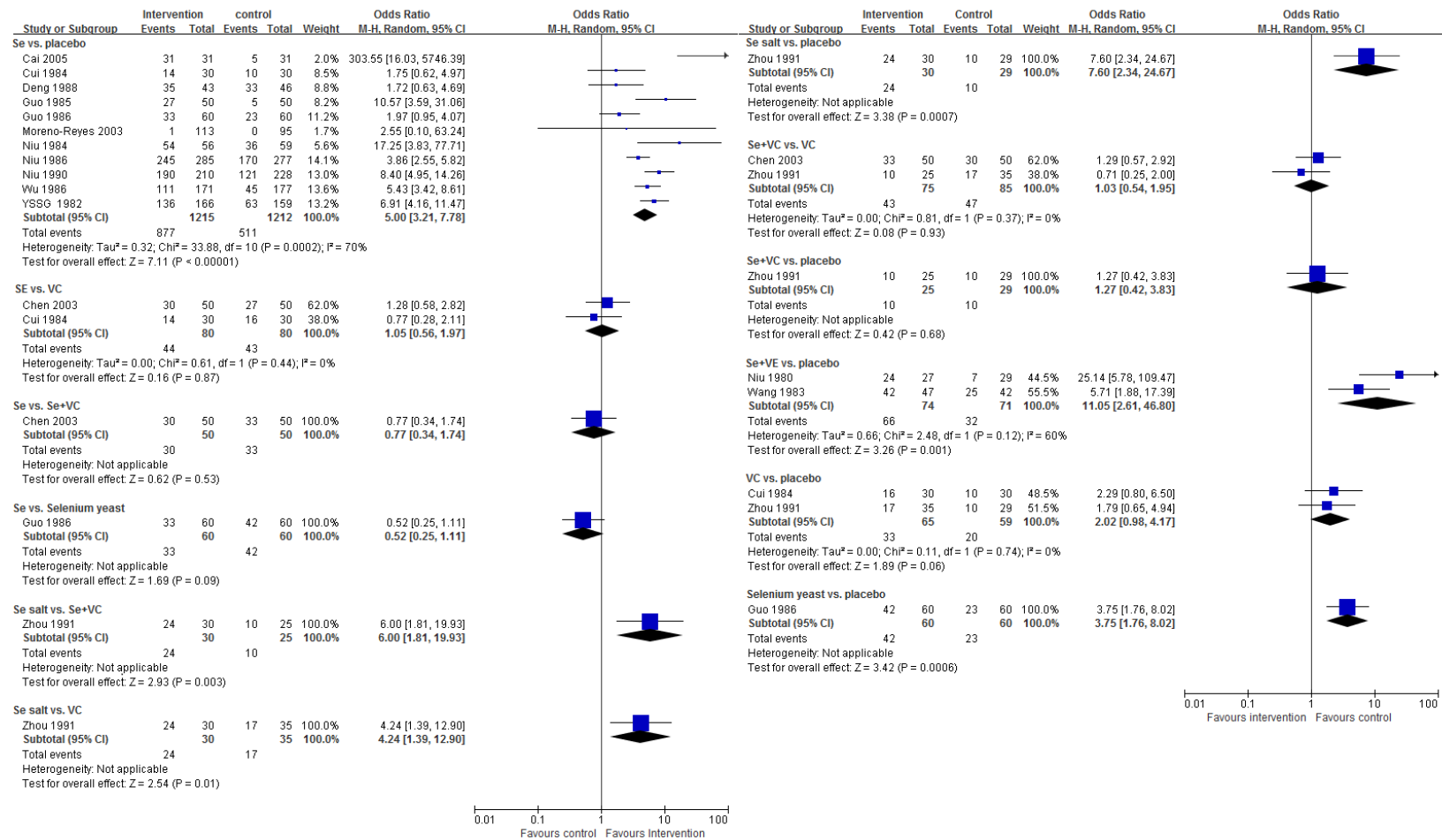
*: Overall Score: Low risk of bias = no bias detected in any domain; Unclear risk of bias = one category or more is potentially at risk of bias; High risk of bias = one category or more is at high risk of bias.

ITT = intention to treat

Appendix table 4 Data from included studies

Author	Treatment	Group 1		Group 2			Group 3			Group 4		
		Case No.	Total No.	Treatment	Case No.	Total No.	Treatment	Case No.	Total No.	Treatment	Case No.	Total No.
Niu 1981 ²²	Se +VE	24	27	Placebo	7	29						
YSSG 1982 ²³	Se	136	166	Placebo	63	159						
Wang 1983 ²⁴	Se+VE	42	47	Placebo	25	42						
Cui 1984 ²⁵	Se	14	30	VC	16	30	Placebo	10	30			
Niu 1984 ²⁶	Se	54	56	Placebo	36	59						
Guo 1985 ²⁷	Se	27	50	Placebo	5	50						
Guo 1986 ²⁸	Se	33	60	Se yeast	42	60	Placebo	23	60			
Niu 1986 ²⁹	Se	245	285	Placebo	170	277						
Wu 1986 ³⁰	Se	111	171	Placebo	45	177						
Deng 1988 ³¹	Se	35	43	Placebo	33	46						
Niu 1990 ³²	Se	190	210	Placebo	121	228						
Zhou 1991 ³³	Se salt	24	30	VC	17	35	Se+ VC	10	25	Placebo	10	29
Moreno-Reyes 2003 ³⁴	Se	1	113	Placebo	0	95						
Chen 2003 ³⁵	Se	30	50	VC	27	50	Placebo	33	50			
Cai 2005 ³⁶	Se	31	31	Placebo	5	31						

Se = Sodium selenite, Se salt =selenium salt, VC = vitamin C, Se + VC = the combination of sodium selenite with vitamin C ; Se + VE = the combination of sodium selenite with vitamin E, Se yeast = selenium enriched yeast.



Appendix figure: Forest plot for intervention-control pairwise meta-analyses of repairing rate of metaphyseal lesions on X-ray films.