BMJ Open Methadone maintenance treatment programme reduces criminal activity and improves social well-being of drug users in China: a systematic review and meta-analysis

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ABSTRACT

Objective: Methadone maintenance treatment (MMT) has been implemented in China since 2004 and has expanded into a nationwide programme. This study aims to evaluate changes in social functioning, family relations and drug-related criminal behaviour among MMT clients in China.

Design: Systematic review and meta-analysis. Methods: Both English and Chinese literature databases, including PubMed, Chongging VIP Chinese Science and Technology Journals Database (CQVIP), China National Knowledge Infrastructure (CNKI) and Wanfang Data, were comprehensively searched over the period 2004–2014 for studied indicators. Study selection, quality assessment and data extraction were conducted according to the PRISMA (preferred reporting items for systematic reviews and metaanalyses) Statement. Meta-analyses were conducted using Comprehensive Meta-Analysis Biostat software. Results: Thirty-eight articles were included in this review (1 in English and 37 in Chinese). The selfreported arrest rate decreased from 13.1% (95% CI 9.1% to 18.5%) at baseline to 3.4% (95% CI 1.5% to 7.7%) and 4.3% (95% CI 1.6% to 11.4%) after 6 and 12 months of MMT intervention, respectively. The rate of drug selling decreased from 7.6% (95% CI 3.8% to 14.8%) at baseline to 1.9% (95% CI 0.6% to 6.2%) and 3.0% (95% CI 1.0% to 8.9%) after 6 and 12 months of intervention, respectively. Similarly, the rates of selling sex for drugs and drug-related crime decreased from 5.3% (95% CI 2.4% to 11.1%) and 9.9% (95% CI 6.8% to 14.2%) at baseline to 1.1% (95% CI 0.5% to 2.3%) and 3.4% (95% CI 2.5% to 4.5%) at 6 months, then to 0.8% (95% CI 0.3% to 1.9%) and 3.4% (95% CI 0.8% to 13.1%) at 12 months after treatment initiation, respectively. In contrast, the rate of employment of clients and the proportion of clients having a good relationship with their family increased substantially from 26.4% (95% CI 22.9% to 30.1%) and 37.9% (95% CI 32.0% to 44.2%) to 41.6% (95% CI 36.6% to 48.0%) and 59.6% (95% CI 48.1% to 70.2%) at 6 months, then to 59.8% (95% CI 52.4% to 66.8%) and 75.0% (95% CI 69.0% to 80.2%) at 12 months after treatment initiation, respectively.

Strengths and limitations of this study

- This is the first study to review how methadone maintenance treatment (MMT) intervention can influence change in social functioning and family relations among drug users in MMT clinics in China.
- This study evaluated, through a meta-analysis of published literature since 2004 in China, changes in drug-related criminal behaviour and improvements in social functioning and family relations among drug users before and after initiating MMT interventions.
- The number of studies is limited and may lead to problems about representativeness of the large drug user population in China.

Conclusions: MMT has significantly reduced criminal activity, and improved employment rate and social wellbeing, of clients of the MMT programme. MMT is an effective measure to help drug users to resume societal and familial functions in China.

INTRODUCTION

Illicit drug misuse is a social and public **s**. health issue internationally. It not only increases the risk of transmission of diseases due to HIV and hepatitis C virus,^{1 2} but also increases drug-related criminal activity, family problems and healthcare expenditure.^{3 4} Heroin is the most common drug used among drug users in both developed and developing countries.^{5–7} Methadone maintenance treatment (MMT) has been found to be an effective harm-reduction programme for drug users.^{8–10} Methadone is a safe, low-cost and convenient generic drug for treatment of opioid dependence.^{11 12} It has effectively reduced drug-related mortality^{13–15} and drug-related crimes and helped drug users to resume social and familial functions.^{16–25}

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In 2004, eight outpatient MMT clinics were established in China.^{26 27} By 2012, these had expanded into a nationwide programme encompassing more than 756 clinics, covering 28 Chinese provinces. It has been shown that the eight pilot MMT clinics have significantly improved social functioning among MMT clients. The annual employment rate reportedly increased from 22.9% to 40.6% (p<0.01, compared with the baseline survey) and the proportion of clients with a harmonious relationship with their families increased from 49.6% to 65.8% (p<0.01) after MMT for 12 months. Self-reported criminal behaviour of clients also decreased from 20.7% to 3.8% (p<0.01).²⁴ Similar benefits of MMT have also been reported in other countries. For instance, the employment rate for MMT clients in Malaysia increased from 70.1% to 77.6% after 2 years of treatment.²⁸ A retrospective study in the UK also showed that the total number of convictions, theft and fraud convictions, and weeks spent in prison per year were reduced by (p=0.03), 39.3% 52.17% (p<0.001) and 82.8% (p=0.002), respectively.²⁹

Numerous studies have reported improvements in social and family well-being among MMT clients in China, but a systematic review that synthesises all these effects is lacking. Through a meta-analysis of published literature since 2004 in China, this study aimed to evaluate changes in drug-related criminal behaviour and improvements in social functioning and family relations among drug users before and after MMT intervention.

METHODS

Data sources

We conducted a systematic review of published peerreviewed research articles by searching the following databases: PubMed, Chongqing VIP Chinese Science and Technology Journals Database (CQVIP), China National Knowledge Infrastructure (CNKI) and Wanfang Data from January 2004 to October 2014. Keywords used in the database search were ('Methadone' OR 'Methadone maintenance treatment' OR 'Methadone maintenance therapy' OR 'Methadone maintenance' OR 'MMT') AND ('Crime' OR 'Criminal rates' OR 'Employment' OR 'Family relationship' OR 'Social functions') AND ('China' OR 'China mainland' OR 'Chinese'). We also performed a manual search of the reference lists of published articles. This review was reported according to the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statement issued in 2009.³⁰

Inclusion/exclusion criteria

Studies were eligible for inclusion in this systematic review if they met the following criteria: (1) articles published in Chinese or English; (2) study reported social functioning or family relations among clients in MMT programme at baseline and follow-up; (3) study characteristics, such as study location, investigation period, duration of intervention and sample size, were

reported. Pre- and post-intervention studies among MMT clients were also included. Exclusion criteria were: (1) review papers; (2) non-peer-reviewed local/government reports; (3) conference abstracts and presentations; (4) dissertations.

Study selection

Selected studies were evaluated by two independent investigators (H-MS, X-YL) according to the inclusion and exclusion criteria. Any disagreement between the investigators was resolved by discussion. If the same study data were published in both English and Chinese, the articles published in Chinese were excluded from this study. In cases where multiple studies were found to use the same data source, we selected the first published study for inclusion in the meta-analysis.

Quality assessment

Two independent investigators used a validated quality assessment tool for observational studies³¹ to assess the quality of studies. The following eight items were assessed to calculate a total quality score: (1) clear definition of the target population; (2) representativeness of probability sampling; (3) sample characteristics matching the overall population; (4) adequate response rate; (5) method of data collection; (6) reliability of survey measures/instruments; (7) validity of survey measures/ instruments; (8) appropriate statistical methods. Each item was scored 0 for 'No' and 1 for 'Yes'. The total quality score ranged from 0 to 8 (see online supplementary table S1).

Data extraction

Two independent investigators extracted the following information from all eligible studies: first author, year of publication, study location, investigation period, gender composition, age, sample size, duration of intervention, proportion of drug-related criminal activities (including drug trafficking, drug selling, robbery and theft to maintain drug habit), employment rate and relationship with family among clients on MMT at baseline and follow-up

Statistical analysis Meta-analysis software (V2.0; Biostat, Englewood N Jersey, USA). The offere 95% CIs were determined based on random-effects models. Heterogeneity tests were performed using the Cochran Q test (p<0.10 represents statistically significant heterogeneity) and I^2 statistic. Potential publication bias was measured by the Begg and Mazumdar rank correlation (p<0.05 represents statistically significant publication bias).

RESULTS

Trial flow/flow of included studies

According to our initial search strategies, 345 articles were identified from four electronic databases. We excluded 128 irrelevant articles after title screening. The remaining 217 abstracts were screened by two independent investigators (H-MS, X-YL), and 136 articles were excluded. The remaining 81 articles were eligible for full-text screening; of these, 43 were excluded. A total of 38 articles were therefore eligible and included in this review (1 in English, 37 in Chinese). Twenty-two studies reported changes in criminal activities (14 reported rate of arrest, 8 reported sale of drugs, 7 reported selling sex for drugs, and 12 reported rate of drug-related crime), and 37 studies reported changes in relationships with

family and friends (37 reported employment rate, 28 reported relationship with family and 11 reported relationship with friends) (figure 1).

Study characteristics

The sample size of MMT clients reported in the eligible studies ranged from 65 to 13 310 (median 320.5; IQR 120–651.5). A total of 30 239 participants were included in this review, and about 76.2% were male. The mean age of all MMT clients was 34.42 years (range 18–62 years). Of the 38 eligible articles, almost half of the studies (44.8%) were conducted in the provinces with high HIV prevalence (>20%),^{32 33} including Yunnan, Sichuan, Guangdong, Xinjiang, Guizhou and Guangxi. The follow-up period of MMT intervention ranged from

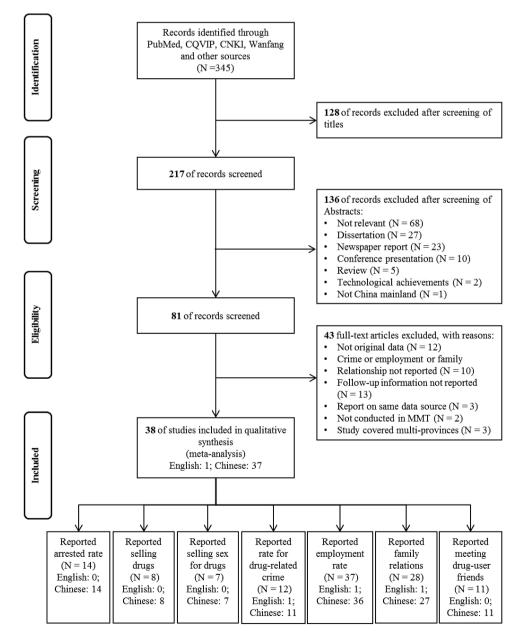


Figure 1 Flow chart for selection of studies. CNKI, China National Knowledge Infrastructure; CQVIP, Chongqing VIP Chinese Science and Technology Journals Database; MMT, methadone maintenance treatment.

6 to 48 months, and the majority were followed-up within 12 months (86.8%). Twenty studies were prospective cohort studies, and the others were retrospective.

Criminal activities

Criminal activity among MMT clients had significantly decreased after MMT intervention. The self-reported arrest rate decreased from 13.1% (95% CI 9.1% to 18.5%) at baseline (table 1 and figure 2A) to 3.4% (95% CI 1.5% to 7.7%), 4.3% (95% CI 1.6% to 11.4%) and 7.7% (95% CI 5.7% to 10.4%) at 6, 12 and 36 months follow-up. About 7.6% (95% CI 3.8% to 14.8%) of the clients had sold drugs before receiving the MMT intervention (table 1 and figure 2B). This rate had decreased to 1.9% (95% CI 0.6% to 6.2%) after 6 months, 3.0% (95% CI 1.0% to 8.9%) after 12 months and 1.0% (95% CI 0.1% to 6.6%) after 36 months. The proportion of clients selling sex for drugs decreased from 5.3% (2.4% to 11.1%) at baseline to 1.1% (0.5% to (2.3%) at 6 months and (0.8%) ((0.3%) to (1.9%) at 12 months (table 1 and figure 2C). The rate of drug-related crime also decreased from 9.9% (6.8% to 14.2%) at baseline to 3.4% (2.5% to 4.5%) at 6 months and 3.4% (0.8% to 13.1%) at 12 months (table 1 and figure 2D). Ten studies reported that the rate of drug-related crime decreased from 1.1-30.34% to 0.5-3.7%. In addition, six studies reported that the rate of selling sex for drugs decreased from 1.9-24.0% to 0.5-1.5% after the MMT intervention.

Social functioning

The rate of employment among clients improved after they had received MMT. The overall employment rate increased from 26.4% (95% CI 22.9% to 30.1%) at baseline (table 1 and figure 2E) to 41.6% (95% CI 36.6% to 48.0%) after 6 months of treatment, and further to 59.8% (95% CI 52.4% to 66.8%) after 12 months, but decreased slightly to 55.4% (95% CI 48.2% to 62.3%) after >12 months of treatment.

Family relations

Family relations among clients also improved after they had received MMT. In addition, only 37.9% (95% CI 32.0% to 44.2%) (table 1 and figure 2F) of drug users reported having a good relationship with their family before receiving MMT interventions; however, this rate increased significantly to 59.6% (95% CI 48.1% to 70.2%) after 6 months, 75.0% (95% CI 69.0% to 80.2%) after 12 months and 83.2% (95% CI 77.8% to 87.6%) after >12 months of treatment.

Contact with former drug-user friends

About 31.0% of clients (95% CI 25.7% to 36.8%) (table 1 and figure 2G) met their drug-user friends every day at baseline; however, the rate of daily contact with former drug-user friends decreased to 6.5% (95% CI 4.4% to 9.4%), 7.7% (95% CI 1.4% to 33.2%) and 1.0% (95% CI

Table 1 Comparison of social functioning and family relations before and after initiation of MMT	ations before and after initiation of	MMT		
		Post-intervention period		
	Baseline (admission to MMT) 6 months	6 months	12 months	>12 months
Arrest rate	13.1% (9.1% to 18.5%)	3.4% (1.5% to 7.7%)	4.3% (1.6% to 11.4%)	7.7% (5.7% to 10.4%)
Proportion selling drugs	6.5% (3.4% to 12.0%)	1.4% (0.5% to 3.9%)	3.0% (1.0% to 8.9%)	1.0% (0.1% to 6.6%)
Proportion selling sex for drugs	5.3% (2.4% to 11.1%)	1.1% (0.5% to 2.3%)	0.8% (0.3% to 1.9%)	1.0% (0.1% to 6.6%)
Rate of drug-related crime	9.9% (6.8% to 14.2%)	3.4% (2.5% to 4.5%)	3.4% (0.8% to 13.1%)	3.3% (2.1% to 5.3%)
Employment rate	26.1% (23.6% to 28.8%)	47.3% (40.9% to 53.8%)	54.7% (47.4% to 61.9%)	45.5% (37.2% to 54.1%)
Proportion with good family relations	39.7% (35.1% to 44.6%)	63.3% (54.7% to 71.1%)	72.1% (65.1% to 78.2%)	83.2% (77.8% to 87.6%)
Proportion in daily contact with former drug-user friends 25.3% (18.9% to 33.0%)	25.3% (18.9% to 33.0%)	4.0% (2.4% to 6.4%)	7.7% (1.4% to 33.2%)	1.0% (0.1% to 6.6%)
MMT, methadone maintenance treatment.				

Study	Event (n / N)	Event rate	Lower limit	Upper limit	Event rate and 95% CI	Weight (% (random)
01. Baseline						
Zhang HY 2013	9/334	0.027	0.014	0.051	—	6.66
Feng SQ 2010	12/371	0.032	0.018	0.056		6.96
Lu JJ 2010	8/185	0.043	0.022	0.084	• [] • •	6.50
Liu YJ 2007	9/130	0.069	0.036	0.128		6.61
Chen B 2011	8/102	0.078	0.040	0.149		6.45
Zhang HF 2009	11/120	0.092	0.051	0.158		6.81
Zhao YT 2009	8/65	0.123	0.063	0.227		6.38
Wei XL 2008	183 / 972	0.188	0.165	0.214		7.96
FuL P 2007	116/593	0.196	0.166	0.230		7.91
Tang YX 2013	24/120	0.200	0.138	0.281		7.36
Huang YJ 2012	31/150	0.207	0.149	0.279		7.50
Wang YZ 2008	51/237	0.215	0.167	0.272		7.71
Jiang A 2009	32/100	0.320	0.236	0.417		7.43
Tang XY 2008	87/196	0.444	0.376	0.514		7.77
Subtotal (95% CI)		0.131	0.091	0.185	~	
02. 6-month follow-	up					
Zhang HY 2013	0/187	0.003	0.000	0.041		5.67
Liu YJ 2007	1/130	0.008	0.001	0.053	—	8.07
Zhang HF 2009	3/120	0.025	0.008	0.075		11.26
Tang XY 2008	5/196	0.026	0.011	0.060		12.26
Wei XL 2008	18/667	0.027	0.017	0.042	The second secon	13.55
Zhao YT 2009	2/65	0.031	0.008	0.115	—	10.21
Huang YJ 2012	5/150	0.033	0.014	0.078		12.24
Tang YX 2013	10/120	0.083	0.045	0.148		13.07
Fu LP 2007	28/135	0.207	0.147	0.284		13.67
Subtotal (95% CI)		0.034	0.015	0.077	Image: A start and a start	
03. 12-month follow	-up					
Wang YZ 2008	6/237	0.025	0.011	0.055		31.58
Feng SQ 2010	10/371	0.027	0.015	0.049	—	34.20
Jiang A 2009	11/100	0.110	0.062	0.188		34.22
Subtotal (95% CI)		0.043	0.016	0.114	~	
04. >12-month follo	w-up					
Chen B 2011	1/102	0.010	0.001	0.066		25.12
Lu JJ 2010	3/185	0.016	0.005	0.049	—	74.88
Subtotal (95% CI)		0.014	0.005	0.037	👗 i	
Overall (95% CI)		0.077	0.057	0.104	•	
Test for heterogenity	: / ² =94.23%; p	<0.001			0% 10% 20% 30% 40%	50%

В	Study	Event (n / N)	Event rate	Lower limit	Upper limit	Event rate and 95% CI	Weight (%) (random)
	01. Baseline						
	Liu WY 2012	1/640	0.002	0.000	0.011		6.54
	Wei XL 2008	19/927	0.020	0.013	0.032		13.80
	Liu YJ 2007	6/130	0.046	0.021	0.099		12.09
	Zhang HF 2009	9/120	0.075	0.039	0.138		12.81
	Chen B 2011	10/102	0.098	0.054	0.173		12.94
	Fu LP 2007	77/593	0.130	0.105	0.159		14.46
	Huang YJ 2012	21/150	0.140	0.093	0.205		13.78
	Jiang A 2009	18/100	0.180	0.116	0.268		13.58
	Subtotal (95% CI)		0.065	0.034	0.120	<u> </u>	
	02. 6-month follow-u	q					
	Wei XL 2008	. 1/667	0.001	0.000	0.011		12.70
	Liu WY 2012	1/645	0.002	0.000	0.011		12.70
	Huang YJ 2012	3/150	0.020	0.006	0.060		17.98
	Liu YJ 2007	3/130	0.023	0.007	0.069		17.97
	Zhang HF 2009	3/120	0.025	0.008	0.075	- -	17.96
	Fu LP 2007	8/135	0.059	0.030	0.114		20.68
	Subtotal (95% Cl)		0.014	0.005	0.039	◆	
	03. 12-month follow	-up					
	Jiang A 2009	3/100	0.030	0.010	0.089		100.00
	Subtotal (95% Cl)		0.030	0.010	0.089		
	04. >12-month follow	v-up					
	Chen B 2011	1/102	0.010	0.001	0.066		100.00
	Subtotal (95% Cl)		0.010	0.001	0.066		
	Overall (95% CI)		0.036	0.022	0.058	•	
	Test for heterogenity: Publication bias: <i>p</i> =0		<0.001			0% 20%	40%

Figure 2 Changes in criminal activity, social well-being and family relations in Chinese clients at various intervention periods before and after initiation of methadone maintenance treatment (MMT): (A) rate of arrest by police; (B) rate of drug selling; (C) rate of selling sex for drugs; (D) rate of drug-related crime; (E) employment rate; (F) proportion having good relationship with family; (G) proportion having contact with former drug-user friends on a daily basis.

С	Study	Event (n / N)	Event rate	Lower limit	Upper limit	Event rate a	nd 95% Cl	Weight (%) (random)
	01. Baseline Feng SQ 2010	7/371	0.019	0.009	0.039	탅		13.98
	Chen GH 2008 Chen B 2011	12/554 4/102	0.022 0.039	0.012 0.015	0.038 0.100			14.71 12.78
	Fu LP 2007	25/593	0.042	0.029	0.062	-		15.28
	Huang YJ 2012	9/150	0.060	0.032	0.111			14.30
	Qu BW 2009	7/80	0.087	0.042	0.172			13.85
	Jiang A 2009 Subtotal (95% CI)	24 / 100	0.240 0.053	0.166 0.024	0.333 0.111			15.10
	02. 6-month follow- Chen GH 2009	•up 2 / 324	0.006	0.002	0.024	—		28.73
	Qu BW 2010	1/80	0.013	0.002	0.083	—		14.27
	Huang YJ 2013	2/150	0.013	0.003	0.052			28.52
	Fu LP 2008	2/135	0.015	0.004	0.057		i	28.48
	Subtotal (95% CI)		0.011	0.005	0.023			
	03. 12-month follow Feng SQ 2010	v-up 2/371	0.005	0.001	0.021	E.		40.11
	Jiang A 2009	1/100	0.010	0.001	0.068			19.96
	Fu LP 2009	2/197	0.010	0.003	0.040	—		39.92
	Subtotal (95% CI)		0.008	0.003	0.019	•		
	04. >12-month folio Chen B 2011	w-up 1 / 102	0.010	0.001	0.066			100.00
	Subtotal (95% CI)	17102	0.010	0.001	0.066			100.00
	Overall (95% CI)		0.016	0.010	0.026	•		
	Test for heterogenity Publication bias: p=		<0.001			0% 10% 2	20% 30%	40%
D	Study	Event (n / N)	Event rate	Lower limit	Upper limit	Event rate a	nd 95% Cl	Weight (%) (random)
	01. Baseline							
	Feng SQ 2010	4/371	0.011	0.004	0.028	D_		4.88
	Wei XL 2008	34/972	0.035	0.025	0.049			6.47
	Qu BW 2010 Chen B 2011	8 / 80 5 / 102	0.038 0.049	0.012 0.021	0.110 0.112			4.43 5.12
	Chen W 2010	719/13310	0.054	0.050	0.058			6.75
	Tang RH 2012b	72/784	0.092	0.074	0.114			6.61
	Chen GH 2008	54 / 554	0.097	0.075	0.125			6.56
	Tang RH 2012a Tang RH 2012c	38 / 382 54 / 533	0.099 0.101	0.073 0.078	0.134 0.130			6.48 6.56
	Fu LP 2007	69/593	0.116	0.093	0.130			6.60
	Tang RH 2012d	48/406	0.118	0.090	0.153	-0-		6.53
	Guo Y 2007	79/656	0.120	0.098	0.148	-0		6.62
	Tang RH 2012e Pang L 2007	76 / 457 121 / 585	0.166 0.207	0.135 0.176	0.203 0.242			6.61 6.66
	Chen W 2009	135 / 445	0.303	0.262	0.348			6.66
	Huang YJ 2012	46/150	0.307	0.238	0.385			6.46
	Subtotal (95% CI)		0.099	0.068	0.142			
	02. 6-month follow- Wei XL 2008	•up 4 / 667	0.006	0.002	0.016			6.60
	Qu BW 2010	1/80	0.013	0.002	0.083	—		2.11
	Guo Y 2007	5/233	0.021	0.009	0.051			7.60
	Chen W 2010 Pang L 2008	426 / 13310 22 / 609	0.032 0.036	0.029 0.024	0.035 0.054			21.70 15.38
	Chen GH 2008	12/324	0.037	0.024	0.064			12.24
	Tang RH 2012a	19/382	0.050	0.032	0.077	- - -		14.60
	Huang YJ 2013	8/150	0.053	0.027	0.103			9.90
	Fu LP 2007 Subtotal (95% CI)	8/135	0.059 0.034	0.030 0.025	0.114 0.045	- <u>-</u>		9.87
	02 12 month fall-					NOR 1		
	03. 12-month follow Feng SQ 2010	2/371	0.005	0.001	0.021			15.04
	Chen W 2009	7/445	0.016	0.008	0.033			16.69
	Fu LP 2007	4/197	0.020	0.008	0.053	—		16.14
	Chen W 2010	452 / 13310	0.034	0.031	0.037			17.45
	Tang RH 2012b Pang L 2009	29 / 784 178 / 468	0.037	0.026	0.053	L		17.27
	Subtotal (95% CI)	1/0/408	0.380 0.034	0.337 0.008	0.425 0.131			17.42
	04. >12-month follo	w-up						
	Chen B 2012	1/102	0.010	0.001	0.066			5.20
	Tang RH 2012e	10/457	0.022	0.012	0.040	D_		26.59
	Tang RH 2012d	15/406	0.037	0.022	0.060		1	31.27
	Tang RH 2012c Subtotal (95% CI)	26/533	0.049 0.033	0.033 0.021	0.071 0.053	—		36.94
	Overall (95% Cl)		0.045	0.037	0.056	*		
	Test for heterogenity Publication bias: p=		<0.001			0% 2	25%	50%

Figure 2 Continued.

Figure 2 Continued.

Study 01. Baseline Tang YX 2013 Wang YZ 2008 Hu WS 2010 Zhao YT 2009 Fan LR 2012 Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang RH 2012e Tang XY 2008 Zhang JY 2008 Zue LY 2006 Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012d Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2007 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2007 Tun Y 2012 Liu WY 2012 Zheng WX 2012 Liu JK 2009 Chen GH 2009 Chen GH 2008 Liu JK 2009 Chen GH 2008 Liu JK 2009 Chen GH 2008 Liu JK 2009 Chen GH 2008 Liu JK 2009 Chen GH 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	Event (n / N) 7 / 120 21 / 237 12 / 125 7 / 65 9 / 67 21 / 120 104 / 533 90 / 457 42 / 196 72 / 334 67 / 307 26 / 115 134 / 585 30 / 130 3128 / 13310 98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658 292 / 593	Event rate 0.058 0.099 0.108 0.175 0.197 0.216 0.216 0.218 0.229 0.231 0.243 0.244 0.272 0.283 0.286 0.287 0.304 0.361 0.364 0.364 0.369 0.405 0.413 0.492	Lower limit 0.028 0.055 0.052 0.0711 0.1164 0.163 0.162 0.175 0.176 0.159 0.197 0.166 0.228 0.202 0.170 0.214 0.223 0.242 0.242 0.223 0.221 0.226 0.223 0.210 0.251 0.265 0.228 0.223 0.210 0.251 0.265 0.269 0.278 0.311 0.335 0.325 0.325 0.310 0.423 0.423 0.423	Upper limit 0.117 0.132 0.209 0.238 0.254 0.231 0.236 0.275 0.263 0.263 0.268 0.311 0.265 0.311 0.265 0.311 0.265 0.311 0.287 0.335 0.287 0.335 0.287 0.335 0.311 0.304 0.315 0.376 0.376 0.376 0.312 0.342 0.353 0.431 0.414 0.478 0.478 0.493 0.478 0.493 0.493 0.493 0.493 0.495 0.495 0.478 0.493 0.493 0.495 0.478 0.493 0.493 0.493 0.495 0.478 0.493 0.493 0.493 0.495 0.478 0.493 0.493 0.493 0.495 0.478 0.493 0.493 0.493 0.495 0.478 0.493 0.493 0.493 0.493 0.478 0.493 0.493 0.493 0.493 0.493 0.478 0.493 0.	Event rate and 95% CI	Weight (%) (random) 1.60 2.39 1.99 1.55 1.73 2.32 2.99 2.96 2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.50 3.22 2.96 2.38 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 3.07 2.42 2.49 3.05 3.16 3.07 3.07 3.07 3.07 3.07 3.07 3.07 3.07
Tang YX 2013 Wang YZ 2008 Hu WS 2010 Zhao YT 2009 Fan LR 2012 Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang RH 2013 Zhang HY 2013 Zhang JY 2008 Zue LY 2006 Pang L 2007 Chen W 2010 Tang RH 2012d Oian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012d Oian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012d Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WP 2012 Zheng WX 2012 Liu WP 2012 Zheng WX 2012 Liu WP 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	$\begin{array}{c} 21 / 237 \\ 12 / 125 \\ 7 / 65 \\ 9 / 67 \\ 21 / 120 \\ 104 / 533 \\ 90 / 457 \\ 42 / 196 \\ 72 / 334 \\ 67 / 307 \\ 26 / 115 \\ 134 / 585 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 $	0.089 0.096 0.108 0.134 0.175 0.197 0.214 0.218 0.226 0.231 0.235 0.241 0.235 0.241 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.266 0.272 0.279 0.286 0.287 0.286 0.287 0.286 0.304 0.315 0.364 0.364 0.364 0.364 0.364 0.369 0.405 0.495	0.058 0.055 0.052 0.071 0.117 0.163 0.162 0.175 0.162 0.197 0.166 0.228 0.202 0.197 0.196 0.228 0.202 0.197 0.196 0.223 0.202 0.214 0.223 0.246 0.203 0.210 0.255 0.269 0.278 0.225 0.269 0.278 0.225 0.269 0.271 0.310 0.325 0.325 0.327 0.337 0.337 0.423	0.132 0.161 0.209 0.238 0.254 0.236 0.277 0.263 0.263 0.268 0.311 0.265 0.311 0.242 0.285 0.336 0.311 0.242 0.285 0.336 0.287 0.336 0.315 0.304 0.315 0.304 0.315 0.304 0.315 0.326 0.312 0.353 0.312 0.353 0.431 0.431 0.435	utophosephacephacephatephatephatephate	2.39 1.99 1.55 1.73 2.32 2.99 2.96 2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.03 2.62 2.96 3.03 2.62 2.96 3.03 3.07 3.07 2.42 2.49 3.05 3.16 3.07 3.07 3.07 3.07 3.07 3.14 3.03 2.51 2.81 2.40
Wang YZ 2008 Hu WS 2010 Zhao YT 2009 Fan LR 2012 Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang RH 2012c Tang XY 2008 Zhang HY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012d Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	$\begin{array}{c} 21 / 237 \\ 12 / 125 \\ 7 / 65 \\ 9 / 67 \\ 21 / 120 \\ 104 / 533 \\ 90 / 457 \\ 42 / 196 \\ 72 / 334 \\ 67 / 307 \\ 26 / 115 \\ 134 / 585 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 $	0.089 0.096 0.108 0.134 0.175 0.197 0.214 0.218 0.226 0.231 0.235 0.241 0.235 0.241 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.243 0.266 0.272 0.279 0.286 0.287 0.286 0.287 0.286 0.304 0.315 0.364 0.364 0.364 0.364 0.364 0.369 0.405 0.495	0.058 0.055 0.052 0.071 0.117 0.163 0.162 0.175 0.162 0.197 0.166 0.228 0.202 0.197 0.196 0.228 0.202 0.197 0.196 0.223 0.202 0.214 0.223 0.246 0.203 0.210 0.255 0.269 0.278 0.225 0.269 0.278 0.225 0.269 0.271 0.310 0.325 0.325 0.327 0.337 0.337 0.423	0.132 0.161 0.209 0.238 0.254 0.236 0.277 0.263 0.263 0.268 0.311 0.265 0.311 0.242 0.285 0.336 0.311 0.242 0.285 0.336 0.287 0.336 0.315 0.304 0.315 0.304 0.315 0.304 0.315 0.326 0.312 0.353 0.312 0.353 0.431 0.431 0.435		2.39 1.99 1.55 1.73 2.32 2.99 2.96 2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.03 2.62 2.96 3.03 2.62 2.96 3.03 3.07 3.07 2.42 2.49 3.05 3.16 3.07 3.07 3.07 3.07 3.07 3.14 3.03 2.51 2.81 2.40
Hu WS 2010 Zhao YT 2009 Fan LR 2012 Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang XY 2008 Zhang JY 2008 Zhang JY 2008 Vang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Huang YJ 2012 Tang RH 2012d Guo Y 2007 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu JW 2012 Liu JW 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu J 2010 Qu BW 2009 Han YB 2012 Fu L 2007 Subtotal (95% Cl)	$\begin{array}{c} 12 / 125 \\ 7 / 65 \\ 9 / 67 \\ 21 / 120 \\ 104 / 533 \\ 90 / 457 \\ 42 / 196 \\ 72 / 334 \\ 67 / 307 \\ 26 / 115 \\ 134 / 585 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 / 585 \\ 31 / 94 \\ 122 / 338 \\ 354 / 972 \\ 164 / 445 \\ 38 / 100 \\ 75 / 185 \\ 33 / 80 \\ 303 / 658 \\ \end{array}$	0.096 0.108 0.134 0.175 0.195 0.195 0.214 0.216 0.229 0.231 0.235 0.241 0.243 0.243 0.243 0.249 0.231 0.243 0.249 0.243 0.249 0.264 0.272 0.272 0.288 0.288 0.304 0.315 0.361 0.364 0.369 0.380 0.361 0.364 0.369 0.380 0.405 0.413 0.492	0.055 0.052 0.071 0.117 0.164 0.162 0.175 0.162 0.197 0.166 0.228 0.202 0.170 0.210 0.223 0.202 0.242 0.242 0.203 0.221 0.265 0.265 0.269 0.278 0.223 0.265 0.265 0.265 0.265 0.265 0.265 0.265 0.265 0.265 0.325 0.325 0.325 0.337 0.310 0.423	0.161 0.209 0.238 0.254 0.231 0.263 0.263 0.265 0.311 0.265 0.311 0.242 0.285 0.326 0.336 0.312 0.306 0.315 0.379 0.376 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.326 0.327 0.326 0.327 0.326 0.327 0.326 0.326 0.327 0.326 0.327 0.326 0.327 0.326 0.327 0.326 0.421 0.427 0.326 0.421 0.441 0.345 0.345 0.341 0.441 0.345 0.441 0.444 0.345 0.441 0.444 0.4479 0.4478 0.523	addaaaddaaaddaaaddaaaddaaddaaddaa	1.99 1.55 1.73 2.32 2.99 2.68 2.89 2.68 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 2.44 2.49 3.05 3.14 3.03 2.51 2.81 2.40
Zhao YT 2009 Fan LR 2012 Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang RH 2012e Tang XY 2008 Zhang JY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	7/65 9/67 21/120 104/533 90/457 42/196 72/334 67/307 26/115 134/585 30/130 3128/13310 98/406 25/103 134/538 39/150 101/382 213/784 183/656 28/99 32/112 159/554 404/1403 184/605 184/585 31/94 122/338 354/972 164/445 38/100 75/185 33/80 303/658	0.108 0.134 0.175 0.195 0.197 0.216 0.218 0.229 0.231 0.229 0.231 0.243 0.249 0.243 0.249 0.264 0.272 0.293 0.264 0.272 0.293 0.264 0.272 0.293 0.288 0.288 0.288 0.288 0.304 0.315 0.304 0.361 0.364 0.369 0.364 0.369 0.405 0.413 0.492	0.052 0.071 0.117 0.164 0.163 0.162 0.175 0.176 0.197 0.166 0.228 0.202 0.170 0.214 0.223 0.242 0.242 0.242 0.242 0.242 0.242 0.265 0.269 0.2265 0.269 0.242 0.311 0.325 0.325 0.325 0.337 0.310	0.209 0.238 0.254 0.231 0.236 0.263 0.263 0.265 0.311 0.265 0.311 0.265 0.385 0.285 0.335 0.285 0.336 0.336 0.311 0.305 0.336 0.311 0.315 0.379 0.376 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.326 0.311 0.326 0.326 0.311 0.326 0.326 0.325 0.335 0.326 0.335 0.326 0.326 0.325 0.336 0.326 0.325 0.336 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.336 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.326 0.335 0.336 0.335 0.336 0.336 0.335 0.336 0.335 0.336 0.335 0.336 0.335 0.326 0.335 0.336 0.336 0.336 0.336 0.336 0.336 0.336 0.336 0.336 0.326 0.336 0.326 0.336 0.336 0.326 0.336 0.326 0.336 0.326 0.336 0.326 0.341 0.444 0.479 0.444 0.479 0.444 0.479 0.444 0.479 0.444 0.479 0.4478 0.444 0.479		1.55 1.73 2.32 2.99 2.96 2.86 2.89 2.86 2.89 2.86 2.30 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.49 3.05 3.14 3.03 2.51 2.81 2.40
Fan LR 2012 Zhang HF 2009 Tang RH 2012e Tang RH 2012e Tang RH 2012e Tang XY 2008 Zhang HY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Chen W 2009 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	9 / 67 21 / 120 104 / 533 90 / 457 42 / 196 72 / 334 67 / 307 26 / 115 134 / 585 30 / 130 3128 / 13310 98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 605 184 / 685 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.134 0.175 0.197 0.214 0.218 0.226 0.231 0.235 0.241 0.235 0.243 0.243 0.243 0.249 0.264 0.272 0.279 0.264 0.272 0.279 0.286 0.287 0.286 0.287 0.288 0.286 0.287 0.288 0.304 0.315 0.364 0.364 0.364 0.364 0.364 0.369 0.405 0.492	0.071 0.117 0.163 0.162 0.175 0.176 0.159 0.197 0.166 0.228 0.202 0.701 0.214 0.223 0.246 0.203 0.210 0.225 0.203 0.210 0.225 0.265 0.265 0.265 0.265 0.265 0.265 0.265 0.228 0.227 0.311 0.355 0.325 0.320 0.337 0.310 0.423	0.238 0.254 0.236 0.236 0.277 0.268 0.311 0.242 0.285 0.336 0.311 0.242 0.285 0.336 0.315 0.394 0.315 0.304 0.315 0.304 0.315 0.326 0.312 0.326 0.312 0.353 0.312 0.353 0.431 0.431 0.435 0.435	,	1.73 2.32 2.99 2.96 2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Zhang HF 2009 Tang RH 2012c Tang RH 2012c Tang RY 2008 Zhang HY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu UW 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl)	$\begin{array}{c} 21 / 120 \\ 104 / 533 \\ 90 / 457 \\ 42 / 196 \\ 72 / 334 \\ 67 / 307 \\ 26 / 115 \\ 134 / 585 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 / 585 \\ 31 / 94 \\ 122 / 338 \\ 354 / 972 \\ 164 / 445 \\ 38 / 100 \\ 75 / 185 \\ 33 / 80 \\ 303 / 658 \\ \end{array}$	0.175 0.195 0.214 0.216 0.228 0.229 0.231 0.241 0.243 0.241 0.243 0.243 0.240 0.260 0.260 0.264 0.272 0.272 0.283 0.286 0.288 0.286 0.287 0.288 0.304 0.315 0.361 0.364 0.360 0.465	0.117 0.164 0.163 0.162 0.175 0.176 0.197 0.196 0.228 0.202 0.170 0.214 0.223 0.210 0.223 0.210 0.223 0.242 0.203 0.210 0.251 0.265 0.269 0.265 0.269 0.265 0.269 0.242 0.311 0.355 0.325 0.320 0.337 0.310 0.423	0.254 0.231 0.236 0.277 0.263 0.263 0.311 0.265 0.311 0.242 0.285 0.326 0.327 0.336 0.311 0.306 0.315 0.379 0.376 0.312 0.326 0.312 0.326 0.312 0.326 0.312 0.353		2.32 2.99 2.96 2.68 2.89 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Tang RH 2012c Tang RH 2012e Tang XY 2008 Zhang HY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Liu YJ 2007 Chen WV 2010 Tang RH 20122 Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen WY 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	$\begin{array}{c} 104 / 533 \\ 90 / 457 \\ 42 / 196 \\ 72 / 334 \\ 67 / 307 \\ 26 / 115 \\ 134 / 585 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 / 585 \\ 31 / 94 \\ 122 / 338 \\ 354 / 972 \\ 154 / 445 \\ 38 / 100 \\ 75 / 185 \\ 33 / 80 \\ 303 / 658 \end{array}$	0.195 0.197 0.214 0.216 0.218 0.229 0.231 0.243 0.243 0.243 0.249 0.264 0.272 0.272 0.272 0.283 0.264 0.272 0.283 0.286 0.287 0.288 0.288 0.288 0.288 0.288 0.288 0.288 0.304 0.315 0.361 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365 0.364 0.365	0.164 0.163 0.162 0.175 0.176 0.197 0.166 0.202 0.170 0.214 0.223 0.242 0.242 0.242 0.242 0.242 0.242 0.242 0.242 0.242 0.265 0.269 0.265 0.269 0.335 0.325 0.325 0.337 0.310	0.231 0.236 0.267 0.263 0.268 0.311 0.265 0.342 0.285 0.285 0.285 0.285 0.285 0.336 0.311 0.306 0.315 0.379 0.376 0.312 0.326 0.312 0.326 0.312 0.342 0.353 0.431 0.434 0.434 0.434 0.479 0.478		2.99 2.96 2.68 2.89 2.80 2.50 3.03 2.50 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.81 2.40
Tang RH 2012e Tang XY 2008 Zhang HY 2013 Zhang JY 2008 Xue LY 2006 Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Oian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JX 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang RH 2012L Zheng WX 2012 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu J 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	90 / 457 42 / 196 72 / 334 67 / 307 26 / 115 134 / 585 30 / 130 3128 / 13310 98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 364 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.197 0.214 0.216 0.218 0.226 0.231 0.235 0.241 0.243 0.243 0.243 0.249 0.264 0.272 0.279 0.286 0.287 0.286 0.287 0.288 0.287 0.288 0.304 0.361 0.364 0.361 0.364 0.360 0.364 0.369 0.389 0.405 0.443 0.492	0.163 0.162 0.175 0.176 0.197 0.197 0.197 0.228 0.228 0.223 0.242 0.242 0.242 0.243 0.242 0.265 0.265 0.269 0.278 0.242 0.311 0.325 0.325 0.337 0.310	0.236 0.277 0.263 0.311 0.268 0.311 0.242 0.285 0.335 0.287 0.336 0.311 0.304 0.315 0.376 0.326 0.312 0.342 0.353 0.341 0.342 0.353 0.431 0.431 0.439 0.395 0.414 0.395	addaddaddaddaddaddaddadda	2.96 2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.16 3.07 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.51 2.81 2.40
Tang XY 2008 Zhang HY 2013 Zhang J 2008 Xue LY 2006 Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI)	42 / 196 72 / 334 67 / 307 26 / 115 134 / 585 30 / 130 3128 / 13310 98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.214 0.216 0.226 0.229 0.235 0.241 0.243 0.243 0.243 0.249 0.260 0.264 0.279 0.283 0.260 0.264 0.279 0.283 0.286 0.287 0.288 0.304 0.305 0.361 0.364 0.369 0.380 0.364 0.369 0.364 0.369 0.364 0.369 0.361 0.369 0.361 0.369 0.369 0.369 0.361 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.369 0.361 0.369 0.361 0.369 0.361 0.369 0.361 0.369 0.361 0.369 0.361 0.364 0.369 0.361 0.369 0.361 0.364 0.369 0.361 0.364 0.369 0.361 0.364 0.364 0.364 0.365 0.364 0.364 0.364 0.365 0.364 0.364 0.369 0.364 0.364 0.369 0.364 0.369 0.364 0.369 0.364 0.369 0.364 0.369 0.364 0.369 0.369 0.364 0.3690	0.162 0.175 0.176 0.159 0.197 0.166 0.228 0.202 0.170 0.214 0.223 0.246 0.203 0.210 0.251 0.265 0.269 0.278 0.265 0.269 0.278 0.325 0.325 0.325 0.325 0.337 0.310	0.277 0.263 0.268 0.311 0.242 0.285 0.326 0.327 0.336 0.311 0.304 0.315 0.379 0.376 0.312 0.326 0.312 0.353 0.312 0.353 0.312 0.353 0.431 0.414 0.395 0.414 0.395	and a second	2.68 2.89 2.86 2.42 3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.49 3.05 3.14 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
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Pang L 2007 Liu YJ 2007 Chen W 2010 Tang RH 2012d Oian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Ou BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	$\begin{array}{c} 134 / 586 \\ 30 / 130 \\ 3128 / 13310 \\ 98 / 406 \\ 25 / 103 \\ 134 / 538 \\ 39 / 150 \\ 101 / 382 \\ 213 / 784 \\ 183 / 656 \\ 28 / 99 \\ 32 / 112 \\ 159 / 554 \\ 404 / 1403 \\ 184 / 605 \\ 184 / 585 \\ 31 / 94 \\ 122 / 338 \\ 354 / 972 \\ 164 / 445 \\ 38 / 100 \\ 75 / 185 \\ 33 / 80 \\ 303 / 658 \end{array}$	0.229 0.231 0.241 0.243 0.240 0.260 0.264 0.272 0.283 0.286 0.287 0.288 0.304 0.380 0.361 0.364 0.364 0.360 0.364 0.360 0.364 0.360 0.364 0.360 0.405 0.405	0.197 0.166 0.222 0.170 0.214 0.196 0.223 0.242 0.242 0.242 0.203 0.251 0.265 0.269 0.269 0.265 0.269 0.265 0.269 0.223 0.210 0.311 0.355 0.325 0.320 0.337 0.310	0.265 0.311 0.242 0.285 0.285 0.287 0.336 0.316 0.315 0.379 0.376 0.326 0.312 0.326 0.312 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.395	apoppoppoppoppoppoppoppop	3.03 2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 2.44 2.49 3.05 3.16 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.81 2.40
Liu ÝJ 2007 Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	$\begin{array}{c} 30 \ / \ 130 \\ 3128 \ / \ 13310 \\ 98 \ / \ 406 \\ 25 \ / \ 103 \\ 134 \ / \ 538 \\ 39 \ / \ 150 \\ 101 \ / \ 382 \\ 213 \ / \ 784 \\ 183 \ / \ 656 \\ 28 \ / \ 99 \\ 32 \ / \ 112 \\ 159 \ / \ 554 \\ 404 \ / \ 1403 \\ 184 \ / \ 605 \\ 184 \ / \ 585 \\ 31 \ / \ 94 \\ 122 \ / \ 338 \\ 354 \ / \ 972 \\ 154 \ / \ 445 \\ 38 \ / \ 100 \\ 75 \ / \ 185 \\ 33 \ / \ 80 \\ 303 \ / \ 658 \end{array}$	0.231 0.235 0.241 0.243 0.249 0.260 0.264 0.272 0.293 0.286 0.287 0.288 0.304 0.304 0.361 0.361 0.364 0.360 0.360 0.360 0.369 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.389 0.364 0.365	0.166 0.222 0.170 0.214 0.196 0.223 0.242 0.242 0.242 0.243 0.210 0.255 0.269 0.269 0.269 0.242 0.311 0.325 0.325 0.325 0.325 0.337 0.310	0.311 0.242 0.285 0.335 0.287 0.36 0.311 0.304 0.315 0.376 0.376 0.326 0.326 0.342 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478	hoppoppoppoppopp	2.50 3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Chen W 2010 Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	3128 / 13310 98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 685 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.235 0.241 0.243 0.260 0.264 0.272 0.279 0.288 0.286 0.287 0.288 0.304 0.315 0.364 0.364 0.364 0.369 0.389 0.369 0.405 0.492	0.228 0.202 0.170 0.214 0.214 0.246 0.246 0.203 0.210 0.251 0.265 0.265 0.265 0.278 0.242 0.311 0.335 0.325 0.325 0.325 0.325 0.337 0.310	0.242 0.285 0.335 0.287 0.336 0.311 0.304 0.315 0.376 0.326 0.326 0.342 0.353 0.431 0.431 0.495 0.495 0.414 0.395		3.22 2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Tang RH 2012d Qian YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	98 / 406 25 / 103 134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.241 0.243 0.260 0.260 0.264 0.279 0.283 0.286 0.287 0.288 0.304 0.380 0.361 0.364 0.369 0.380 0.369 0.380 0.405 0.413 0.492	0.202 0.170 0.214 0.196 0.223 0.242 0.242 0.203 0.251 0.265 0.269 0.278 0.242 0.311 0.325 0.325 0.325 0.320 0.337 0.310	0.285 0.335 0.287 0.336 0.311 0.304 0.315 0.379 0.376 0.326 0.312 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478		2.96 2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Qian [°] YH 2008 Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl)	$\begin{array}{c} 25 \ / \ 103 \\ 134 \ / \ 538 \\ 39 \ / \ 150 \\ 101 \ / \ 382 \\ 213 \ / \ 784 \\ 183 \ / \ 656 \\ 28 \ / \ 99 \\ 32 \ / \ 112 \\ 159 \ / \ 554 \\ 404 \ / \ 1403 \\ 184 \ / \ 605 \\ 184 \ / \ 585 \\ 31 \ / \ 94 \\ 122 \ / \ 338 \\ 354 \ / \ 972 \\ 164 \ / \ 445 \\ 38 \ / \ 100 \\ 75 \ / \ 185 \\ 33 \ / \ 80 \\ 303 \ / \ 658 \end{array}$	0.243 0.260 0.264 0.272 0.279 0.283 0.286 0.287 0.288 0.304 0.304 0.361 0.361 0.364 0.360 0.360 0.360 0.360 0.405 0.413 0.460	0.170 0.214 0.223 0.242 0.246 0.251 0.251 0.251 0.269 0.278 0.242 0.210 0.242 0.242 0.335 0.325 0.325 0.325 0.320 0.310 0.423	0.335 0.287 0.336 0.311 0.304 0.375 0.376 0.326 0.312 0.342 0.342 0.342 0.342 0.343 0.431 0.431 0.439 0.495 0.414 0.478 0.423		2.38 3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.81 2.40
Long ZY 2006 Huang YJ 2012 Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	134 / 538 39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 605 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.249 0.260 0.264 0.272 0.279 0.283 0.286 0.287 0.288 0.304 0.315 0.330 0.361 0.364 0.369 0.380 0.369 0.380 0.405 0.413 0.460	0.214 0.196 0.223 0.242 0.246 0.203 0.210 0.251 0.265 0.265 0.265 0.278 0.242 0.311 0.335 0.325 0.325 0.325 0.320 0.310 0.310 0.423	0.287 0.336 0.311 0.304 0.315 0.379 0.376 0.326 0.326 0.342 0.342 0.353 0.431 0.431 0.495 0.495 0.414 0.479 0.478		3.03 2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Huang YJ 2012 Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Liu WY 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	39 / 150 101 / 382 213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 605 184 / 685 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.260 0.264 0.272 0.283 0.286 0.287 0.288 0.304 0.315 0.304 0.364 0.369 0.369 0.369 0.380 0.405 0.413 0.460 0.492	0.196 0.223 0.242 0.246 0.203 0.210 0.265 0.269 0.278 0.269 0.278 0.242 0.311 0.335 0.325 0.325 0.310 0.310 0.423	0.336 0.311 0.304 0.315 0.379 0.376 0.326 0.312 0.342 0.353 0.312 0.342 0.353 0.312 0.342 0.353 0.414 0.395 0.414 0.395 0.414 0.478 0.478	hopophopophop	2.62 2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Tang RH 2012a Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	$\begin{array}{c} 101 \ / \ 382 \\ 213 \ / \ 784 \\ 183 \ / \ 656 \\ 28 \ / \ 99 \\ 32 \ / \ 112 \\ 159 \ / \ 554 \\ 404 \ / \ 1403 \\ 184 \ / \ 605 \\ 184 \ / \ 585 \\ 31 \ / \ 94 \\ 122 \ / \ 338 \\ 354 \ / \ 972 \\ 164 \ / \ 445 \\ 38 \ / \ 100 \\ 75 \ / \ 185 \\ 33 \ / \ 80 \\ 303 \ / \ 658 \end{array}$	0.264 0.272 0.283 0.286 0.287 0.288 0.304 0.315 0.330 0.361 0.369 0.369 0.369 0.369 0.380 0.405 0.413 0.460 0.492	0.223 0.242 0.246 0.203 0.210 0.251 0.265 0.269 0.278 0.242 0.315 0.325 0.325 0.325 0.310 0.310 0.423	0.311 0.304 0.315 0.376 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.419 0.418 0.478 0.478		2.96 3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.40
Tang RH 2012b Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu JK 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	213 / 784 183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.272 0.279 0.283 0.286 0.287 0.288 0.304 0.315 0.361 0.364 0.369 0.369 0.380 0.405 0.413 0.460 0.492	0.242 0.246 0.203 0.210 0.251 0.265 0.269 0.242 0.311 0.335 0.325 0.325 0.337 0.310 0.310 0.423	0.304 0.315 0.379 0.376 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.395 0.414 0.479 0.478 0.523		3.10 3.07 2.42 2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.40
Guo Y 2007 Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	183 / 656 28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.283 0.286 0.287 0.288 0.304 0.315 0.330 0.361 0.364 0.369 0.369 0.369 0.405 0.413 0.405 0.413	0.203 0.210 0.251 0.265 0.269 0.278 0.242 0.311 0.335 0.290 0.337 0.310 0.423	0.379 0.376 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		2.42 2.49 3.05 3.16 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Duan J 2008 Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	28 / 99 32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 184 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.286 0.287 0.288 0.304 0.315 0.361 0.361 0.369 0.380 0.405 0.405 0.413 0.460 0.492	0.210 0.251 0.265 0.269 0.278 0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.376 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.40
Liu JK 2009 Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	32 / 112 159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.286 0.287 0.288 0.304 0.315 0.361 0.361 0.369 0.380 0.405 0.405 0.413 0.460 0.492	0.210 0.251 0.265 0.269 0.278 0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.376 0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		2.49 3.05 3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.51 2.40
Chen GH 2008 Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	159 / 554 404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.287 0.288 0.304 0.315 0.330 0.361 0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.251 0.265 0.269 0.278 0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.326 0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		3.05 3.16 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Tang XJ 2012 Liu WY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	404 / 1403 184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.288 0.304 0.315 0.330 0.361 0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.265 0.269 0.278 0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.312 0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		3.16 3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Liu ŴY 2012 Zheng WX 2012 Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	184 / 605 184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.304 0.315 0.330 0.361 0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.269 0.278 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.342 0.353 0.431 0.414 0.395 0.414 0.479 0.478 0.523		3.07 3.07 2.44 2.97 3.14 3.03 2.51 2.81 2.40
Liu JB 2007 Yun Y 2014 Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Ou BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	184 / 585 31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.330 0.361 0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.278 0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.431 0.414 0.395 0.414 0.479 0.478 0.523		2.44 2.97 3.14 3.03 2.51 2.81 2.40
Yun Y 2014 Wei XI, 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	31 / 94 122 / 338 354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.330 0.361 0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.242 0.311 0.335 0.325 0.290 0.337 0.310 0.423	0.431 0.414 0.395 0.414 0.479 0.478 0.523		2.97 3.14 3.03 2.51 2.81 2.40
Wei XL 2008 Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	354 / 972 164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.364 0.369 0.380 0.405 0.413 0.460 0.492	0.335 0.325 0.290 0.337 0.310 0.423	0.395 0.414 0.479 0.478 0.523		3.14 3.03 2.51 2.81 2.40
Chen W 2009 Jiang A 2009 Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	164 / 445 38 / 100 75 / 185 33 / 80 303 / 658	0.369 0.380 0.405 0.413 0.460 0.492	0.325 0.290 0.337 0.310 0.423	0.414 0.479 0.478 0.523		3.03 2.51 2.81 2.40
Jiang A 2009 Lu JJ 2010 Ou BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	38 / 100 75 / 185 33 / 80 303 / 658	0.380 0.405 0.413 0.460 0.492	0.290 0.337 0.310 0.423	0.479 0.478 0.523		2.51 2.81 2.40
Lu JJ 2010 Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	75 / 185 33 / 80 303 / 658	0.405 0.413 0.460 0.492	0.337 0.310 0.423	0.478 0.523		2.81 2.40
Qu BW 2009 Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	33 / 80 303 / 658	0.413 0.460 0.492	0.310 0.423	0.523		2.40
Han YB 2012 Fu LP 2007 Subtotal (95% CI) 02. 6-month follow Liu YJ 2007	303 / 658	0.460 0.492	0.423			
Fu LP 2007 Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007		0.492		0.499		3.10
Subtotal (95% Cl) 02. 6-month follow Liu YJ 2007	292 / 593		0 450		<u> </u>	
02. 6-month follow Liu YJ 2007			0.452	0.533		3.09
Liu YJ 2007		0.261	0.236	0.288	•	
Liu YJ 2007						
	-up 33 / 130	0.254	0.186	0.336		4.35
	104 / 404	0.257	0.217	0.302		4.67
Tang RH 2012a	107 / 382	0.280	0.237	0.327		4.67
Zhang HF 2009	36 / 120	0.300	0.225	0.388	- T	4.36
Zhao YT 2009	20/65	0.308	0.208	0.429		4.03
Zhang HY 2013	62 / 187	0.332	0.268	0.402		4.53
Guo Y 2007	85/233	0.365	0.305	0.429		4.60
Chen GH 2008	137 / 324	0.423	0.370	0.477		4.67
Pang L 2007	263 / 609	0.432	0.393	0.472		4.74
Qian YH 2008	45/104	0.433	0.341	0.529		4.36
Liu JB 2007	45/94	0.479	0.380	0.579		4.33
Tang YX 2013	59 / 120	0.492	0.403	0.580	— <u>0</u> —	4.43
Tang XY 2008	99 / 196	0.505	0.435	0.575	-0	4.58
Fu LP 2007	68 / 134	0.507	0.423	0.591		4.47
Qu BW 2009	41 / 80	0.513	0.404	0.620		4.25
Wei XL 2008	343 / 667	0.514	0.476	0.552	- <u>-</u>	4.75
Han YB 2012	340 / 658	0.517	0.479	0.555		4.75
Zheng WX 2012	305 / 581	0.525	0.484	0.565		4.74
Chen W 2010	7467 / 13310	0.561	0.553	0.569	· · · · · · · · · · · · · · · · · · ·	4.83
Huang YJ 2012	98 / 150	0.653	0.574	0.725		4.47
Tang XJ 2012	902 / 1091	0.827	0.803	0.848		4.75
Liu WY 2012	536 / 648	0.827	0.796	0.854		4.69
Subtotal (95% CI)		0.473	0.409	0.538		
03. 12-month follow	w-up					
Tang RH 2012b	255 / 784	0.325	0.293	0.359		9.18
Wang YZ 2008	65 / 165	0.394	0.322	0.470		8.50
Pang L 2007	190 / 468	0.406	0.362	0.451	- - •	9.06
Fan LR 2012	51/124	0.411	0.328	0.500		8.25
Yun Y 2014	146 / 338	0.432	0.380	0.485		8.95
Jiang A 2009	50/100	0.500	0.403	0.597	— <u>i</u>)—	8.05
Xue LY 2006	59/115	0.513	0.422	0.603	— D —	8.21
Chen W 2009	243 / 445	0.546	0.500	0.592		9.06
Chen W 2010	7334 / 13310	0.551	0.543	0.559	i 🔝	9.39
Fu LP 2007	143 / 225	0.636	0.571	0.696		8.70
Duan J 2008	90 / 99	0.909	0.834	0.952		6.22
Liu JK 2009	102/112	0.911	0.842	0.951		— []- 6.44
Subtotal (95% CI)		0.547	0.474	0.619		
04. >12-month follo	ow-up					
Tang RH 2012c	177 / 533	0.332	0.293	0.373	- D -	17.42
Tang RH 2012e	176 / 457	0.385	0.342	0.431		17.35
Tang RH 2012d	158 / 406	0.389	0.343	0.437	- D - 1	17.24
Lu JJ 2010	95 / 185	0.514	0.442	0.585		16.21
Hu WS 2010	65/125	0.520	0.433	0.606		15.37
Zhang J 2008	136 / 220	0.618	0.552	0.680		16.42
Subtotal (95% CI)		0.455	0.372	0.541		
Overall (95% Cl)		0.344	0.320	0.368	•	
Test for heterogenit	y: / ² =98.79%; p<			-	· · · · · ·	
Publication bias: p=				(0% 25% 50% 75%	6 100%

F

Study	Event (n / N)	Event rate	Lower limit	Upper limit	Event rate and 95% CI	Weight (%) (random)
01. Baseline					I	
Tang YX 2013	1/120	0.008	0.001	0.057	—	0.82
Tang XY 2008	10/196	0.051	0.028	0.092	-	2.90
Hu WS 2010	18/125	0.144	0.093	0.217	- D - <u>_</u>	3.27
Wang YZ 2008	49/237	0.207	0.160	0.263	- <u></u> -	3.73
Yun Y 2014	78/338	0.231	0.189	0.279		3.86
Zhao YT 2009	15/65	0.231	0.144	0.348		3.06
Fu JH 2010	22/80	0.275	0.188	0.383		3.29
Qu BW 2009	26/80	0.325	0.232	0.435		3.36
Zhu YH 2012	71/212	0.335	0.275	0.401		3.79
Liu JB 2007 Pang L 2007	32 / 94 200 / 585	0.340 0.342	0.252 0.305	0.442 0.381		3.46 3.99
Guo Y 2007	238/656	0.363	0.327	0.400	—	4.01
Wei XL 2008	391 / 972	0.402	0.372	0.433		4.04
Fu LP 2007	241 / 599	0.402	0.364	0.442	- -	4.00
Fan LR 2012	51/124	0.411	0.328	0.500		3.63
Jiang A 2009	46/100	0.460	0.365	0.558		3.55
Chen GH 2008	266 / 554	0.480	0.439	0.522	- <u>-</u> -	4.00
Cai WB 2013	117 / 239	0.490	0.427	0.553		3.86
Liu WY 2012	318/639	0.498	0.459	0.536		4.01
Tang XJ 2012	737 / 1458	0.505	0.480	0.531		4.07
Huang YJ 2012	78/150	0.520	0.440 0.438	0.599		3.72
Qian YH 2008 Duan J 2008	55/103	0.534 0.535	0.438	0.628		3.56
Liu JK 2009	53 / 99 60 / 112	0.535	0.437	0.631 0.626		3.54 3.60
Zhang HY 2013	184 / 334	0.551	0.443	0.603		3.93
Zheng WX 2012	343 / 585	0.586	0.546	0.626		4.00
Chen B 2011	61 / 102	0.598	0.500	0.688		3.54
Liu YJ 2007	108 / 130	0.831	0.756	0.886		3.38
Subtotal (95% CI)		0.397	0.351	0.446	◆	
02. 6-month follow-	•					
Tang YX 2013	7/120	0.058	0.028	0.117		4.46
Tang XY 2008 Fu JH 2010	51/196	0.260	0.204	0.326		5.37 4.99
Qu BW 2009	19 / 68 39 / 80	0.279 0.488	0.186 0.380	0.397 0.596		5.17
Liu JB 2007	49/94	0.488	0.380	0.620		5.23
Zheng WX 2012	307 / 581	0.528	0.488	0.569		5.54
Guo Y 2007	135 / 233	0.579	0.515	0.641		5.45
Zhang HY 2013	117/187	0.626	0.554	0.692		5.40
Fu LP 2007	87/134	0.649	0.565	0.725		5.31
Zhao YT 2009	43 / 65	0.662	0.539	0.766		5.02
Chen GH 2008	244 / 324	0.753	0.703	0.797	- <u>-</u> -	5.45
Liu YJ 2007	98 / 130	0.754	0.673	0.820		5.24
Qian YH 2008	79/104	0.760	0.668	0.832		5.15
Cai WB 2013	178/234	0.761	0.702	0.811		5.39
Wei XL 2008 Huang YJ 2012	508/667	0.762	0.728 0.700	0.792 0.833		5.53 5.27
Liu WY 2012	116 / 150 508 / 643	0.773 0.790	0.757	0.833		5.52
Tang XJ 2012	864 / 1082	0.799	0.774	0.821		5.55
Zhu YH 2012	198/212	0.934	0.892	0.961	-	
Subtotal (95% CI)		0.633	0.547	0.711	-	
03. 12-month follow	/-up					
Yun Y 2014	184 / 338	0.544	0.491	0.597	+⊡- _	13.93
Pang L 2007	308 / 468	0.658	0.614	0.700		14.10
Fan LR 2012	87 / 124	0.702	0.615	0.776		12.29
Wang YZ 2008	116/165	0.703	0.629	0.768		12.82
Liu JK 2009	86/112	0.768	0.681	0.837		11.69
Duan J 2008	77/99	0.778	0.685	0.849		11.29 13.01
Fu LP 2007 Jiang A 2009	182 / 231 82 / 100	0.788 0.820	0.730 0.732	0.836 0.884		10.88
Subtotal (95% CI)	827100	0.820	0.752	0.884	-	10.88
04. >12-month follo						
Chen B 2011	84 / 102	0.824	0.737	0.886		46.88
Hu WS 2010	105 / 125	0.840	0.765	0.894		53.13
Subtotal (95% CI) Overall (95% CI)		0.832 0.578	0.778 0.544	0.876 0.612	~	
Test for heterogenity	·· (² -07.200/		2.2.1	2.0.2	0% 25% 50% 75% 1	 100%
Publication bias: p=0		~0.001			U/0 23/0 3U/0 13/0 1	0070

Figure 2 Continued.

0.1% to 6.6%) after 6, 12 and >12 months of intervention, respectively.

Quality assessment

All studies reported the study period, study location and sample size. All studies reached a total quality score of 3 or higher (out of a total of 8). The mean quality score

was 3.97, indicating a reasonably good quality for our selected studies (see online supplementary table S1).

DISCUSSION

To the best of our knowledge, this is the first study to review the effect of MMT on criminal activity, social

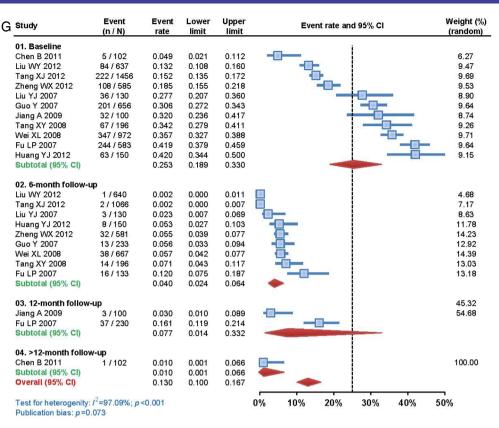


Figure 2 Continued.

functioning and family relations among MMT clients in China. Our findings indicate that MMT significantly decreased self-reported arrest rate, frequency of selling drugs, drug-related crime, selling sex for drugs, and likelihood of meeting former drug-user friends. In contrast, it improved employment rate and family relations. These findings are consistent with other international studies in England, Lithuania and Israel.^{34–37} In particular, a meta-analysis conducted by Marsch³⁸ showed that 85% of drug users who received MMT decreased drug-related crime. A systematic review conducted by Holloway et al^{89} also showed that criminal behaviour was reduced in MMT clients compared with non-MMT drug users. Despite these positive results, policy makers who have strong moral reservations about MMT would emphasise the physically dependent nature of methadone and ongoing spending of public funds on a population deemed 'socially evil' in many settings.⁴⁰ Further studies are necessary to evaluate other aspects of MMT, including structural barriers and cost-effectiveness of the programme, to help inform relevant policies in the future.

We have demonstrated improved employment rates and family relations among MMT clients in China. Consistently, a study conducted in the USA also indicated a significant improvement in employment outcomes with an integrated drug counselling and employment programme for MMT clients.⁴¹ In addition, a Swedish study showed that over 80% of people with severe heroin addiction obtained new jobs and were reintegrated into society after receiving MMT.⁴² In a separate study, Blix followed 345 heroin users for 24 years over the period 1966–1989 in Sweden; a 70–80% employment rate among MMT clients was reported.⁴² Interestingly, our meta-analysis indicated the best employment outcome at 12 months after treatment initiation, and the rate started to decline when treatment continued beyond 12 months. This finding is echoed by results of an early survey of the first eight pilot MMT clients are more likely to drop out of the treatment programme, which leads to a declining employment rate among those who keep going with treatment. Further, family relations of clients improved during the course of MMT. With reduced symptoms of addiction, clients are able to resume family duties and re-establish relationships with other family members.^{44 45}

Several limitations to this study should be noted. First, by the end of 2012, there were 756 MMT clinics in China, covering 28 Chinese provinces, but 13 provinces did not publish any reports on the related characteristics of social and familial relationships, and this limits our analysis in these regions. Second, only eight studies reported on clients who sold drugs, and this small number of studies may have resulted in information bias in our study. Third, owing to the small number of available studies, we pooled all study estimates beyond 12 months of follow-up in this analysis. Fourth, substantial heterogeneity existed between studies because of different study methodologies, method of recruitment and sampling sizes in different studies. Our meta-analyses

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CONCLUSIONS

The MMT programme in China has conclusively been shown to be effective in reducing criminal activity and improving employment outcome and social well-being of its clients. The MMT programme should not only focus on reducing drug misuse, but other advisory and intervention services, such as Voluntary Counselling and Testing of HIV, psychological therapy, and family intervention, should also be integrated into the programme.^{46 47} In parallel, clients should be encouraged to make use of rehabilitation facilities to improve their own awareness in order to safeguard their rights and interests. MMT may serve as a valuable opportunity to reduce drug-related harm among drug users and enable them to return to society as healthy and productive individuals.

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Contributors EPFC, LZ and XZ designed the study. H-MS and X-YL performed the data collection and provided the first draft of the manuscript. TL, YX, Y-HL and TT performed data analysis. LZ and EPFC assisted with data interpretation. EPFC, LZ and XZ provided critical revision for important intellectual content. All authors read and approved the final version of the manuscript.

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