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Tai Chi for Chronic Illness Management: Synthesizing Current Evidence from Meta-Analyses of Randomized Controlled Trials

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Running head: Tai Chi for Chronic Illness Management

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Abstract

An umbrella review of systematic reviews and meta-analyses of randomized controlled trials (RCTs) was conducted to evaluate the existing evidence of Tai Chi as a mind-body exercise for chronic illness management. MEDLINE/PubMed and Embase databases were searched from inception until 31st March 2019 for meta-analyses of at least two RCTs that investigated health outcomes associated with Tai Chi intervention. Evidence of significant outcomes (P-value <0.05) was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.

This review identified 45 meta-analyses of RCTs and calculated 142 summary estimates among adults living with 16 types of chronic illnesses. Statistically significant results (P-value <0.05) were identified for 81 of the 142 outcomes (57.0%), of which 45 estimates presenting 30 unique outcomes across 14 chronic illnesses were supported by high (n=1) or moderate (n=44) evidence. Moderate evidence suggests that Tai Chi intervention improved physical functions and disease-specific outcomes compared with non-active controls and cardiorespiratory fitness compared with active controls among adults with diverse chronic illnesses. Between-study heterogeneity and publication bias were observed in some meta-analyses.

Introduction

Tai Chi is an exercise that originated from China over 3000 years ago.[1] The practice of Tai Chi is characterized by slow, flowing physical movements that are coordinated with diaphragmatic breathing, musculoskeletal stretching and relaxation, kinesthetic body awareness, and meditative state of mind.[2] The energy cost of Tai Chi practice is 3.0 Metabolic Equivalents (METs), the same as that of dog walking, which is classified as a moderate-intensity exercise (3.0-6.0 METs).[3]

In the past twenty years, a few key interventional studies were conducted and demonstrated health benefits associated with Tai Chi in adults with Parkinson's disease,[4] fibromyalgia,[5, 6] osteoarthritis,[7] and chronic heart failure.[8] Studies of smaller scales were also carried out in other chronic illnesses.[9-14] Subsequently, over 2000 primary studies and 200 meta-analyses of Tai Chi trials have been published. However, most reviews focused on a single health condition and/or outcome and mixed active and non-active control groups. There is a lack of comprehensive overview to systematically evaluate the health benefits of Tai Chi in diverse populations with chronic physical and mental conditions.

To address the breadth of the literature, an increasing emphasis has been placed on the "umbrella review", which aims to synthesize existing systematic reviews with meta-analyses, to capture the breadth of intervention and outcome.[15, 16] In view of its potential role in chronic illness management, an overview of the breadth and validity of the current literature on Tai Chi associated health effects is needed. This umbrella review extracted data from published meta-analyses and determined the direction, magnitude, and significance of Tai Chi intervention associated effects on health outcomes among individuals with chronic illnesses, while evaluating the potential risk of biases of included studies.

Methods

This review was a priori registered (CRD42019129514) and executed following the PRISMA statement guideline.[17] Two reviewers (LZ and LY) independently searched electronic databases (MEDLINE/PubMed and Embase) from inception to 31st March 2019 (**Supplemental Methods**). We hand-searched the reference lists of eligible articles and other narrative overviews of systematic reviews/meta-analyses. Systematic reviews with meta-analyses that investigated the relationship of Tai Chi with any health outcome were included (for specific inclusion criteria, see **Supplemental Methods**).

Two reviewers (LZ and LY) independently performed two levels of data extraction (**Supplemental Methods**) including: lead author's name, year of publication, type of Tai Chi form, intervention dosage (weekly training frequency, length of each session, and intervention duration), adverse events, outcomes assessment, description on active and/or non-active control condition, type of metric (summary risk estimates: OR, RR, HR, SMD, MD) with the 95% CI, and the number of participants and/or cases for each study by interventions and controls.

Data analysis

For each meta-analysis, we estimated the summary effect size (e.g., Hedge's g) and its 95% CI through random-effects models.[18] We purposely reported studies using active control and non-active control comparison groups separately to illustrate the therapeutic effects of Tai Chi intervention with and without the presence of other disease management strategies.

Between-study inconsistency was estimated with the I^2 metric, with a value ≥50% indicative of high heterogeneity.[19] Additionally, we calculated the evidence of publication bias.[20]

Evidence from meta-analyses of RCTs was assessed in terms of the significance of the summary effect. With a P-value < 0.05, we evaluated the evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment.[21] The methodological quality of the included meta-analyses were assessed using the new Risk of Bias in Systematic Reviews (ROBIS) (**Supplemental Methods**).[22] All statistical analyses were conducted in Stata version 16.0 (StataCorp, Texas, USA).

Results

A total of 1407 articles were screened for title and abstract relevancy, and 262 full-texts were screened (**Figure 1**). After removing 207 articles, 45 meta-analyses (**eTable 1**) were included in the umbrella review. The median number of participants was 203 (range 38 to 865). The intervention doses, where reported, varied from 15 to 210 minutes each session, from once to seven times weekly. Although the intervention durations varied from 1 week to 24 months, 2% (11 out of 529) of RCTs had an intervention longer than 6 months, and 18.8% (99 out of 529) had a duration of 6 months. Among 142 unique estimates on the health effects of Tai Chi intervention, statistically significant results (P-value <0.05) were identified for 81 outcomes with very low to high evidence levels (for summary see **Table 1**, for GRADE assessment see **Table 2**).

Overall, Tai Chi interventions were conducted in 16 chronic illnesses, including Parkinson's disease (n=25), cancer (n=23), type-2 diabetes (n=18), osteoarthritis (n=17), heart failure (n=13), stroke (n=13), COPD (n=9), fibromyalgia (n=6), hypertension (n=4), multiple sclerosis (n=1), coronary heart disease (n=1), low back pain (n=1), and schizophrenia (n=6), clinical depression (n=2), mild cognitive impairment (n=2) and dementia (n=1). Data on adverse events were reported in 25 (55.6 %) meta-analyses, of which six suggested minor adverse events such as minor muscle soreness, foot and knee pain, ankle sprain and low back pain (**eTable 2**). No study reported serious adverse events nor negative effects resulting from Tai Chi intervention.

Neurological conditions

Among 25 summary estimates for Parkinson's disease, Tai Chi intervention showed statistically significant improvement in 8 health outcomes. When a non-active control group was employed, evidence was graded moderate in improving depression and mobility, and low for balance. Moderate evidence supported Tai Chi to improve disease specific symptoms (motor & non-motor symptoms assessed by unified Parkinson's disease rating scale) comparing with both non-active and active controls. Additionally, the improvement in physical functions (fall risk, rate of falls, balance) through Tai Chi intervention (vs. active controls) were supported by moderate evidence, while health-related quality of life presented low evidence. No significant association was found in walking related physical function, global or disease-specific quality of life or cognition (**eTable 3a**).

Thirteen outcomes were investigated among participants with stroke and eight outcomes showed significant improvement through Tai Chi (**eTable 3a**). Moderate evidence supported Tai Chi to improve four-limb and upper-limb function (vs. non-active controls) and improve activity of daily living (vs. active controls). Evidence was graded low for balance and depression, and non-significant for walking ability and sleep quality.

One meta-analysis included two Tai Chi RCTs in participants with multiple sclerosis and showed non-significant findings on fatigue (vs. active control).

Musculoskeletal conditions

For osteoarthritis, 12 outcomes were reported and eight were statistically significant. Notably, the evidence on Tai Chi intervention to improve osteoarthritis specific outcomes was generally graded moderate, including level of disability (vs. non-active control), severity of pain (vs. non-active and active control), and physical function measured by the Western Ontario and McMaster Universities Osteoarthritis Index, dominant/right knee flexion, cardiorespiratory fitness and fear of falling (vs. active control). Nevertheless, evidence on improving the level of disability and mobility (the Timed Up and Go test) was graded low, and non-significant for quality of life, depression, and other functional outcomes (vs. active control) (**eTable 3b**).

Four outcomes were investigated for fibromyalgia. Moderate evidence existed for improving fatigue (vs. non-active control) and sleep quality (vs. non-active and active controls). Low evidence supported Tai Chi in improving the severity of pain or depression.

For low back pain, moderate evidence supported Tai Chi in reducing the severity of pain compared with a non-active control group.

Cancer

Twenty-three summary estimates were generated in Tai Chi RCTs among cancer survivors covering 20 outcomes using active controls, one outcome using non-active controls, and one outcome using both comparison groups. Two RCTs included cancer of breast, lung, and prostate while others were conducted in breast cancer women only. A total of 12 outcomes reached statistical significance (P-values < 0.05). Moderate evidence supported Tai Chi to improve body mass index (BMI), fatigue, and serum cortisol level and interleukin-6 among cancer survivors vs. active control, while the remaining eight outcomes (physical function measures and depression) showed low levels of evidence (**eTable 3c**). No significant associations were found between Tai Chi intervention and bone health, insulin-like growth factor 1, wrist and elbow muscle strength, pain, fat mass percentage, quality of life, or pain, compared with active controls.

Type-2 diabetes

Among 12 outcomes that have been examined in Tai Chi RCTs of type-2 diabetes patients, seven outcomes showed significant improvements (**eTable 3d**). Notably, BMI, 2-hour postprandial blood glucose, hemoglobin A1c, fasting blood glucose, and total cholesterol have been examined in RCTs with both non-active and active controls, whilst fasting insulin and blood pressure were compared with non-active controls only. Among these outcomes, insulin resistance, BMI and 2-hour postprandial blood glucose presented moderate evidence, and others had low evidence.

Cardiopulmonary diseases

For Tai Chi RCTs of patients with heart failure, nine outcomes were evaluated and six showed significant improvement (**eTable 3e**). Of which, improvement in the 6-min walking test, cardiorespiratory fitness (VO_2 max) and diastolic blood pressure compared with active controls were supported by moderate evidence, yet evidence on serum B-type natriuretic peptide and quality of life was graded low. Moderate evidence supported that Tai Chi can improve heart left ventricular ejection fraction comparing with a non-active control, whilst the evidence was graded low comparing with an active control. Other outcomes (mobility [the Timed Get Up and Go test], serum N-terminal pro-brain natriuretic peptide and systolic blood pressure) were not significantly associated with Tai Chi vs. active controls.

Seven outcomes were evaluated in Tai Chi RCTs conducted in COPD patients (**eTable 3e**). Among four significantly improved functional outcomes comparing with non-active controls, lung function measured by forced vital capacity, 6-min walking test showed moderate evidence, whilst evidence on improvement in lung function measured by forced expiratory volume in 1s and dyspnea was low. Notably, the evidence supporting improved COPD-specific quality of life measured by St. George's respiratory questionnaire was graded high comparing with an active control group.

With respect to hypertension, four outcomes had been investigated using non-active controls (**eTable 3e**). Moderate evidence supported reductions in waist circumference and diastolic and systolic blood pressure. Although evidence was graded low, some benefits were also observed in reduced BMI through Tai Chi.

One outcome was investigated among patients with coronary heart disease, demonstrating moderate evidence in improved cardiorespiratory fitness (VO_2 max).

Cognitive and mental disorders

Several RCTs have been conducted to examine the effect of Tai Chi on schizophrenia specific outcomes including positive and negative emotions and discontinuation rate, with non-active and active comparison groups, respectively (**eTable 3f**). Negative emotion was the only significantly improved outcome when a non-active control was used, with low level of evidence. Nevertheless, compared with an active control group, moderate evidence supported that Tai Chi intervention improved global cognition for dementia patients, the severity of depression among the clinically depressed, and short-term memory among those with mild cognitive impairment.

Over half of meta-analyses scored low (n=29 out of 45) for risk of bias on ROBIS, and 16 scored unclear (**eTable 4**). A sizable portion of outcomes (13 out of 81) with moderate evidence were significant at P<0.00001.

Discussion

This umbrella review provides a broad overview of the existing evidence on Tai Chi for chronic illness management and a systematic evaluation of the methodological quality of available meta-analyses. The effect of Tai Chi intervention compared with non-active and/or active control groups has been investigated in 16 types of chronic illnesses and generated 142 summary estimates covering 79 unique outcomes. Eighty-one summary estimates showed nominal statistically significant results, of which 45 estimates across 14 chronic illnesses were supported by high (n=1) or moderate (n=44) evidence. Moderate evidence supports Tai Chi to improve cardiorespiratory fitness in heart failure and coronary heart disease comparing with conventional exercise; and to improve disease-specific outcomes in a range of mental health conditions. Substantial between-study heterogeneity and publication bias were observed in some meta-analyses, which downgraded the evidence to low.

Conventional exercises are characterized by their fitness targets, such as aerobic exercise to improve cardiorespiratory health, resistance training to improve certain muscles or muscle groups, and stretching to improve muscle stiffness and joint flexibility.[23] There is a strong research interest to understand whether health benefits differ by types of exercise.[24-26] To date, available evidence suggest the best gain is from combining both aerobics and resistance training.[26-28] Although it can be viewed as an alternative method of exercise, Tai Chi is unique in being multimodal or holistic, blending aerobics, resistance and stretch training.[29] Herein, we were able to make direct comparisons between Tai Chi and conventional exercise by including RCTs that used active control comparison groups. Despite mostly containing a mix of pharmacological and non-pharmacological strategies, the active control groups for eight significant outcomes used conventional exercise, supporting improvements in disease-specific quality of life for COPD, 2-hour postprandial blood glucose for type-2 diabetes, 6-min walking test for heart failure, balance, rate and risk of falls for Parkinson's disease, and daily activity ability for stroke.

Intriguing findings of this review included moderate evidence supporting Tai Chi to improve VO_2max for coronary heart disease (vs. active control [stretching]) and heart failure (vs. active control [medication + exercise]), improved 6 minutes-walk tests for COPD (vs. non-active control) and heart failure (vs. active control [aerobics exercise or walking]), and improved lung function for COPD (vs. non-active control). Being feasible and easy to standardize, the 6 minutes-walk test is considered one of the best compromises between test duration and ability to discriminate levels of cardiorespiratory fitness.[30] Cardiorespiratory fitness is not only critical for those with heart failure, COPD, and coronary artery disease, but it's also a strong predictor of mortality among the overall population.[31, 32] It is possible that Tai Chi improves these functions through the upper-extremity movements, which typically involve thoracic expansion and stretching to strengthen the diaphragmatic muscle. Additionally, abdominal breathing techniques in Tai Chi may reshape the breathing pattern to reduce the frequency of breath, keep the airways open longer,[33, 34] and activate the respiratory muscle.[35] Such changes may be associated with improved cardiorespiratory fitness.[36-41] As a low METs (3.0) exercise, whether Tai Chi can produce the same level of cardiorespiratory benefits as high impact aerobics exercise and its biological mechanisms need to be investigated and elucidated.

Tai Chi presents the potential to tackle a few rising health crises in recent years, including musculoskeletal pain[42, 43] and mental health.[44] These benefits may be attributable to the meditative character of Tai Chi.[45] Referred to as mindful exercise by the American College of Sports Medicine, a key component of Tai Chi is meditation, examining all dimensions of life, similar to the concept of mindfulness.[46] The practice of Tai Chi involves psychosomatic relaxation through abdominal breathing,[47] which may be effective in regulating stress-related mental symptoms.[48-50]Neutral spine alignment (erect posture), a signature move of Tai Chi, is the key to maintaining the center of gravity over the base of support, which may activate and strengthen core muscles, leading to reduced experiences of pain.[51, 52] With the development of imaging techniques, studies have begun to explore the effects of Tai Chi on brain structure and functioning.[13, 53-55]

Tai Chi has increasingly been used for stroke rehabilitation.[56] Yet, the duration of Tai Chi intervention was short (20.8% were 6 months or longer) in most studies with no long-term follow-up. Hence, the long-term effect of Tai Chi intervention is unknown. Another knowledge gap is the biological mechanisms through which Tai Chi may improve health outcomes. Few primary interventional studies incorporated kinetic measures of Tai Chi moves or relevant biological markers to elucidate biological pathways. Finally, the number of primary studies of Tai Chi intervention was generally small compared with RCTs of conventional exercise. One reason might be the need for experienced instructors and the perceived complexity of Tai Chi movements.[57] The recent development of several simplified, yet effective Tai Chi curriculums,[58-60] and the multi-media technology to deliver mobile intervention[61] may be adopted to overcome these barriers.

This umbrella review is strengthened by reanalyzing data from RCTs and comparing Tai Chi intervention to non-active and active control groups, respectively, which allows comparing Tai Chi with other established disease management strategies, rigorously evaluating the methodological quality and quality of evidence using a series of tools,[16, 21, 22] and including only RCTs to increase the confidence in the overall findings.

Nevertheless, there are several limitations. Firstly, the search strategy was limited to English-language title/abstract and thus might have missed publications in other languages. Secondly, given that this review is based on previously published meta-analyses, primary studies not included in published meta-analyses might have been missed. Finally, although this review restricted to meta-analyses of RCTs, rigorous assessment on the risk of bias using ROBIS indicated the risk was unclear for 16 out of 45 included meta-analyses.

Conclusions

Current evidence supports the benefits of Tai Chi in chronic illness management, particularly to improve cardiorespiratory fitness for COPD, coronary heart disease, or heart failure and improve physical functional and disease-specific outcomes for a range of chronic diseases. The number of meta-analyses on this topic increases continually. Rigorous trials with large sample size and longer duration are needed to inform the type, dose, frequency and duration of Tai Chi intervention for long-term chronic illness management.

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Table 1. Summary of Evidence Grading (GRADE)[a] for Meta-Analyses of Tai Chi Randomized Controlled Trials among Populations with Chronic Illnesses Diagnosis.

Disease/type of control group	Evidence Grade			
	High	**Moderate**	**Low**	**Very low**
Parkinson's disease				
Non-active		Severity of depression; Mobility; Unified Parkinson's Disease Rating Scale	Balance; Motor function	
Active		Balance; Rate of falls; Fall risk; Unified Parkinson's Disease Rating Scale	Quality of life	
Stroke				
Non-active		Physical function	Mobility, Activity of daily living; Physical function; Depression	Balance
Active		Activity of daily living		
Osteoarthritis				
Non-active		Physical function; Severity of pain; Level of disability		
Active		Flexion; Fear of falling; Cardiorespiratory fitness	Level of disability; Mobility	
Fibromyalgia				
Non-active		Sleep quality; Level of fatigue	Severity of depression	Severity of pain
Active		Sleep quality		
Low back pain				
Non-active		Severity of pain		
Cancer				
Active		Interleukin-6; Level of fatigue; Body mass index I; Cortisol level	Severity of depression; Physical function; Muscle strength	
Type-2 diabetes				
Non-active		2-hour postprandial blood glucose; Insulin resistance; Body mass index	Hemoglobin A1c; Systolic blood pressure; Fasting blood glucose; Total cholesterol	
Active		2-hour postprandial blood glucose; Body mass index	Hemoglobin A1c; Fasting blood glucose; Total cholesterol	
Heart failure				
Non-active		Heart left ventricular ejection fraction	Functional capacity; Serum B-type natriuretic peptide; Quality of life	
Active		Functional capacity; Diastolic blood pressure; Cardiorespiratory fitness	Quality of life	Heart left ventricular ejection fraction
COPD				
Non-active		Functional capacity; Lung function	Dyspnoea; Lung function	
Active	Quality of Life			
Hypertension				
Non-active		Systolic blood pressure; Diastolic blood pressure; Waist circumference	Body mass index	
Coronary heart disease				
Active		Cardiorespiratory fitness		
Schizophrenia				
Non-active			Negative symptoms	
Clinical depression				
Active		Severity of depression		
Mild cognitive impairment				
Active		Short-term memory		
Dementia				
Active		Global cognition		

[a]The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment includes limitations (study design), inconsistency (I^2>50%), indirectness (P [population], I[intervention] O[outcome measure] C[comparison]) impression (total sample size<500) and publication bias (small-study effects P>0.10).

Table 2: GRADE[a] Evidence for Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

						GRADE					
Author	**RCT (n)**	**Sample size (n)**	**Outcome**	**Effect size**	**I^2**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Publication bias**	**Overall**
Parkinson's disease (vs. non-active control)											
Song (2017)	2	66	Severity of depression	Moderate	0%	No	No	None	Yes	No	Moderate
Song (2017)	4	141	Mobility (Timed Up and Go Test)	Moderate	0%	No	No	None	Yes	No	Moderate
Song (2017)	4	168	Unified Parkinson's Disease Rating Scale	Moderate	0%	No	No	None	Yes	No	Moderate
Song (2017)	3	124	Balance	Large	58%	No	No	Yes	Yes	No	Low
Yang (2014)	4	146	Motor function	Moderate	63%	No	No	Yes	Yes	No	Low
Parkinson's disease (vs. active control)											
Ni (2014)	3	212	Balance (Berg Functional Reach test)	Large	49%	No	No	Not serious	Yes	No	Moderate
Winser (2018)	2	260	Rate of falls	Moderate	0%	No	No	None	Yes	No	Moderate
Lian (2017)	2	260	Fall risk	Small	0%	No	No	None	Yes	No	Moderate
Song (2017)	5	280	Unified Parkinson's Disease Rating Scale	Small	4%	No	No	Not serious	Yes	No	Moderate
Song (2017)	3	235	Balance	Small	0%	No	No	None	Yes	No	Moderate
Ni (2014)	4	259	Quality of life (Health related quality of life)	Large	86%	No	No	Yes	Yes	No	Low
Stroke (vs. non-active control)											
Lyu (2018)	2	100	Physical function (Fugl–Meyer Assessment all four limbs)	Large	0%	No	No	None	Yes	No	Moderate
Lyu (2018)	2	107	Physical function (Fugl–Meyer Assessment the upper-limb)	Large	7%	No	No	Not serious	Yes	No	Moderate
Lyu (2018)	7	382	Mobility (Timed Up and Go Test)	Large	75%	No	No	Yes	Yes	No	Low
Lyu (2018)	7	391	Activity of Daily Living	Large	93%	No	No	Yes	Yes	No	Low
Lyu (2018)	3	166	Physical function (Fugl–Meyer Assessment the lower limb)	Large	76%	No	No	Yes	Yes	No	Low
Zou (2018d)	5	357	Depression	Large	54%	No	No	Yes	Yes	No	Low
Zou (2018b)	9	432	Balance	Large	94%	No	No	Yes	Yes	Yes	Very low
Li (2018)	12	856	Activity of Daily Living	Large	94%	No	No	Yes	No	No	Moderate
Osteoarthritis (vs. non-active control)											
Fernandopulle (2017)	2	140	Physical function (WOMAC)	Large	0%	No	No	None	Yes	No	Moderate
Escalante (2010)	6	259	Severity of pain	Moderate	2%	No	No	not serious	Yes	No	Moderate
Hall (2017)	4	243	Level of disability	Moderate	0%	No	No	None	Yes	No	Moderate

						GRADE					
Author	RCT (n)	Sample size (n)	Outcome	Effect size	I²	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Overall
Osteoarthritis (vs. active control)											
Zou (2019b)	2	86	Flexion -Dominant/right knee (proprioception)	Large	0%	No	No	None	Yes	No	Moderate
Chang (2016)	2	134	Fear of Falling	Moderate	0%	No	No	None	Yes	No	Moderate
Escalante (2011)	2	68	Cardiorespiratory fitness	Moderate	0%	No	No	None	Yes	No	Moderate
Kong (2016)	5	183	Severity of pain	Moderate	33%	No	No	Not serious	Yes	No	Moderate
Hall (2017)	5	187	Level of disability	Large	90%	No	No	Yes	Yes	No	Low
Chen (2016)	3	166	Mobility (Timed Up and Go Test)	Moderate	0%	No	No	None	Yes	Yes	Low
Fibromyalgia (vs. non-active control)											
Cheng (2019)	3	203	Sleep quality	Moderate	0%	No	No	None	Yes	No	Moderate
Cheng (2019)	4	307	Level of fatigue	Moderate	39%	No	No	Not serious	Yes	No	Moderate
Cheng (2019)	3	209	Severity of depression	Small	64%	No	No	Yes	Yes	No	Low
Cheng (2019)	3	190	Severity of pain	Large	78%	No	No	Yes	Yes	No	Very low
Fibromyalgia (vs. active control)											
Raman (2013)	3	245	Sleep quality	Small	7%	No	No	Not serious	Yes	No	Moderate
Low back pain (vs. non-active control)											
Kong (2016)	3	385	Severity of pain	Large	45%	No	No	Not serious	Yes	No	Moderate
Cancer (vs. active control)											
Ni (2019)	2	38	Interleukin-6	Large	0%	No	No	None	Yes	No	Moderate
Song (2018)	5	289	Level of fatigue	Moderate	24%	No	No	Not serious	Yes	No	Moderate
Tao (2016)	3	148	Body mass index	Small	2%	No	No	Not serious	Yes	No	Moderate
Ni (2019)	2	73	Cortisol level	Trivial	0%	No	No	None	Yes	No	Moderate
Chen (2016)	2	88	Severity of depression	Large	50%	No	No	Yes	Yes	No	Low
Ni (2019)	5	465	Physical function (upper limb function)	Large	87%	No	No	Yes	Not serious	No	Low
Pan (2015)	3	63	Physical function (elbow extension)	Large	0%	No	No	None	Yes	Yes	Low
Pan (2015)	3	63	Muscle strength (handgrip strength)	Moderate	0%	No	No	None	Yes	Yes	Low
Pan (2015)	3	63	Physical function (elbow flexion)	Moderate	0%	No	No	None	Yes	Yes	Low
Pan (2015)	3	63	Physical function (horizontal abduction)	Moderate	0%	No	No	None	Yes	Yes	Low
Pan (2015)	3	63	Physical function (abduction)	Moderate	0%	No	No	None	Yes	Yes	Low
Ni (2019)	4	330	Muscle strength (upper limb)	Small	38%	No	No	Not serious	Yes	Yes	Low
Type-2 diabetes (vs. non-active control)											
Chao (2018)	5	162	2- hour postprandial blood glucose	Large	0%	No	No	None	Yes	No	Moderate

						GRADE					
Author	**RCT (n)**	**Sample size (n)**	**Outcome**	**Effect size**	**I²**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Publication bias**	**Overall**
Zhou (2019)	4	268	Insulin resistance	Large	0%	No	No	None	Yes	No	Moderate
Zhou (2019)	5	244	Body mass index	Large	0%	No	No	None	Yes	No	Moderate
Zhou (2019)	11	451	Hemoglobin A1c	Large	90%	No	No	Yes	Not serious	No	Low
Zhou (2019)	4	190	Systolic blood pressure	Large	66%	No	No	Yes	Yes	No	Low
Zhou (2019)	17	586	Fasting blood glucose	Moderate	51%	No	No	Yes	No	Yes	Low
Zhou (2019)	8	424	Total cholesterol	Moderate	70%	No	No	Yes	Not serious	No	Low
Type-2 diabetes (vs. active control)											
Chao (2018)	3	84	2 hour postprandial blood glucose	Moderate	0%	No	No	None	Yes	No	Moderate
Xia (2019)	6	296	Body mass index	Moderate	31%	No	No	Not serious	Yes	No	Moderate
Xia (2019)	9	527	Hemoglobin A1c	Moderate	84%	No	No	Yes	No	Yes	Low
Xia (2019)	12	606	Fasting blood glucose	Moderate	79%	No	No	Yes	No	Yes	Low
Xia (2019)	5	270	Total cholesterol	Small	60%	No	No	Yes	Yes	No	Low
Heart failure (vs. non-active control)											
Gu (2017)	5	503	Heart left ventricular ejection fraction	Large	97%	No	No	Not serious	No	No	Moderate
Gu (2017)	8	651	Functional capacity	Large	89%	No	No	Yes	No	Yes	Low
Gu (2017)	3	253	Serum B-type natriuretic peptide	Large	89%	No	No	Yes	Yes	No	Low
Gu (2017)	3	382	Quality of life	Large	99%	No	No	Yes	Yes	No	Low
Heart failure (vs. active control)											
Gu (2017)	2	72	Function capability	Large	0%	No	No	None	Yes	No	Moderate
Ren (2017)	2	68	Diastolic blood pressure	Large	0%	No	No	None	Yes	No	Moderate
Ren (2017)	2	90	Cardiorespiratory fitness (VO2 max)	Large	0%	No	No	None	Yes	No	Moderate
Gu (2017)	5	216	Quality of life	Large	75%	No	No	Yes	Yes	No	Low
Ren (2017)	5	396	Left ventricular ejection fraction	Large	98%	No	No	Yes	Yes	Yes	Very low
COPD (vs. non-active control)											
Guo (2016)	8	573	Functional capacity (6-mins walking test)	Large	89%	No	No	Yes	No	No	Moderate
Guo (2016)	3	389	Lung function (forced vital capacity/FVC)	Small	13%	No	No	Not serious	Yes	No	Moderate
Yan (2013b)	3	328	Dyspnoea	Large	38%	No	No	Not serious	Yes	Yes	Low
Guo (2016)	6	524	Lung function (forced expiratory volume in 1s/FEV1)	Trivial	64%	No	No	Yes	No	Yes	Low
COPD (vs. active control)											
Wu (2014)	5	535	Quality of Life	Large	0%	No	No	None	No	No	High

						GRADE					
Author	**RCT (n)**	**Sample size (n)**	**Outcome**	**Effect size**	**I²**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Publication bias**	**Overall**
Hypertension (vs. non-active control)											
Wang (2013)	10	879	Systolic blood pressure	Large	99%	No	No	Yes	No	No	Moderate
Wang (2017)	10	879	Diastolic blood pressure	Large	99%	No	No	Yes	No	No	Moderate
Lian (2017)	3	375	Waist circumference	Moderate	0%	No	No	None	Yes	No	Moderate
Lian (2017)	4	451	Body mass index	Small	58%	No	No	Yes	Not serious	No	Low
Coronary heart disease (vs. active control)											
Yang (2017)	2	102	Cardiorespiratory fitness (VO2 max)	Large	0%	No	No	None	Yes	No	Moderate
Schizophrenia (vs. non-active control)											
Zheng (2016)	3	240	Negative symptoms	Large	82%	No	No	Yes	Yes	No	Low
Clinical depression (vs. active control)											
Zou (2018c)	2	100	Severity of depression	Moderate	0%	No	No	None	Yes	No	Moderate
Mild cognitive impairment (vs. active control)											
Zou (2019a)	2	106	Short-term memory	Moderate	0%	No	No	None	Yes	No	Moderate
Dementia (vs. active control)											
Wu (2019)	3	218	Global cognition (MMSE)	Large	0%	No	No	None	YEs	No	Moderate

[a]The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment includes risk of bias (study design), indirectness (P [population], I[intervention] O[outcome measure] C[comparison]), inconsistency (I^2>50%), imprecision (total sample size<500) and publication bias (small-study effects P>0.10).

Supplementary Content

Supplemental methods:

Full search terms in the electronic database.

Full search keys in title and abstract: (“meta-analysis" or “meta-an” or “systematic review”) AND ((“tai chi” or “taiji” or “qi gong” or “qigong”) OR ((“mindful” or “mind-body” or “mind body” or “mind and body” or “meditative” or “meditation”) AND (“therapy” or “exercise” or “movement or “intervention”))).

Specific inclusion criteria.

(1) Systematic reviews with meta-analyses containing sufficient data (as defined later) for a meta-analysis measuring one or more types of Tai Chi with a self-report (e.g. quality of life questionnaire) or objective health outcome (e.g. physical function, serum biomarkers);

(2) Studies had to report these outcomes as odds ratio [OR], relative risk [RR], hazard ratio [HR], standardized mean difference [SMD] or mean difference [MD] along with 95% confidence intervals [CIs] and sample size;

(3) Studies included at least one non-active control group and/or active control group vs. Tai Chi intervention conducted in a population with chronic illness, and provided pre-post measures on study outcomes;

(4) Studies had to report pre-post measures on study outcomes from at least 2 RCTs;

(5) Studies published in any language but having at least the abstract published in English.

Two-levels data extraction.

The first-level extraction was conducted on each included meta-analysis to identify numbers of population-outcome-control-specific outcomes, extracting information on EndNote identification number, journal, first author name, and year of publication, the number of included studies and the total number of participants, the inclusion criteria for studied population or type of participants, outcome assessment, and the number of active and/or non-active control. An active control is a group that received more than “do nothing” or “minimal intervention” (e.g., psychosocial support therapy, attention control, other types of exercise, rehabilitation). If two or more meta-analyses examined the same association (population-outcome-control-specific estimate), we included the largest in terms of RCTs for the next level data extraction. During the second-level extraction, the following data were extraction: lead author's name, year of publication, type of Tai Chi form, intervention dosage (weekly training frequency, length of each session, and intervention duration), adverse event, outcomes assessment, description on active and/or non-active control condition, type of metric (summary risk estimates: OR, RR, HR, SMD, MD) with the 95% CI, and the number of participants and/or cases for each study by interventions and controls.

Grading of the evidence and risk of bias (quality) assessment.

Evidence from meta-analyses of RCTs was assessed in terms of the significance of the summary effect, using a P-value < 0.05 as the threshold for statistical significance. When the P-value for effect size estimate by the random effect model is < 0.05, we evaluated the evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment including limitations (study design), inconsistency (I^2>50%), indirectness (P [population], I[intervention] O[outcome measure] C[comparison]) impression (total sample size<500) and publication bias (small-study effects P>0.10). Outcomes with a P-value < 0.05 and a moderate/high GRADE assessment was classified as strong evidence.

Finally We assessed the methodological quality of the included meta-analyses using the new Risk of Bias in Systematic Reviews (ROBIS) evaluation tool to assess the quality of the methods employed in systematic reviews.[31] The ROBIS includes four different domains: 1) study eligibility criteria; 2) identification and selection of studies; 3) data collection and study appraisal; 4) synthesis and findings.

Supplemental eTables:

eTable 1: An Overview of Included Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

eTable 2: Adverse Event (AE) Reporting in Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

eTable 3a: Tai Chi and health outcomes of patients with neurological condition

eTable 3b: Tai Chi and health outcomes of patients with musculoskeletal conditions

eTable 3c: Tai Chi and health outcomes of patients with cancer

eTable 3d: Tai Chi and health outcomes of patients with type 2-diabetes

eTable 3e: Tai Chi and health outcomes of patients with cardiopulmonary diseases

eTable 3f: Tai Chi and health outcomes of patients with cognitive and mental disorders

eTable 4: ROBIS quality assessment in Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

eTable 1: An Overview of Included Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

ID	Author	Year of publication	
1	Chang	2016	Wang WD, Chen S, Lee CL, et al. The Effects of Tai Chi Chuan on Improving Mind-Body Health for Knee Osteoarthritis Patients: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med* 2016;2016:1813979.
2	Chao	2018	Chao M, Wang C, Dong X, et al. The Effects of Tai Chi on Type 2 Diabetes Mellitus: A Meta-Analysis. *J Diabetes Res* 2018;2018:7350567.
3	Chen	2016	Chen YW, Hunt MA, Campbell KL, et al. The effect of Tai Chi on four chronic conditions-cancer, osteoarthritis, heart failure and chronic obstructive pulmonary disease: a systematic review and meta-analyses. *Br J Sports Med* 2016;50(7):397-407.
4	Cheng	2019	Cheng CA, Chiu YW, Wu D, et al. Effectiveness of Tai Chi on fibromyalgia patients: A meta-analysis of randomized controlled trials. *Complementary therapies in medicine* 2019;46:1-8.
5	Escalante	2010	Escalante Y, Saavedra JM, Garcia-Hermoso A, et al. Physical exercise and reduction of pain in adults with lower limb osteoarthritis: a systematic review. *J Back Musculoskelet Rehabil* 2010;23(4):175-86.
6	Escalante	2011	Escalante Y, Garcia-Hermoso A, Saavedra JM. Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review. *J Sci Med Sport* 2011;14(3):190-8.
7	Fernandopulle	2017	Fernandopulle S, Perry M, Manlapaz D, et al. Effect of Land-Based Generic Physical Activity Interventions on Pain, Physical Function, and Physical Performance in Hip and Knee Osteoarthritis: A Systematic Review and Meta-Analysis. *Am J Phys Med Rehabil* 2017;96(11):773-92.
8	Gu	2017	Gu Q, Wu SJ, Zheng Y, et al. Tai Chi Exercise for Patients with Chronic Heart Failure: A Meta-analysis of Randomized Controlled Trials. *Am J Phys Med Rehabil* 2017;96(10):706-16.
9	Guo	2016	Guo JB, Chen BL, Lu YM, et al. Tai Chi for improving cardiopulmonary function and quality of life in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Clin Rehabil* 2016;30(8):750-64.
10	Hall	2017	Hall A, Copsey B, Richmond H, et al. Effectiveness of Tai Chi for Chronic Musculoskeletal Pain Conditions: Updated Systematic Review and Meta-Analysis. *Phys Ther* 2017;97(2):227-38.
11	Kong	2016	Kong LJ, Lauche R, Klose P, et al. Tai Chi for Chronic Pain Conditions: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Sci Rep* 2016;6:25325.
12	Li	2018	Li GY, Wang W, Liu GL, et al. Effects of Tai Chi on balance and gait in stroke survivors: A systematic meta-analysis of randomized controlled trials. *Journal of rehabilitation medicine* 2018;50(7):582-88.
13	Lian	2017	Lian Z, Yang L, Bian Y, et al. Effects of Tai chi on adults with essential hypertension in China: A systematic review and meta-analysis. *European Journal of Integrative Medicine* 2017;12:153-62.
14	Lyu	2018	Lyu D, Lyu X, Zhang Y, et al. Tai Chi for Stroke Rehabilitation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Front Physiol* 2018;9:983.
15	Ni	2014	Ni X, Liu S, Lu F, et al. Efficacy and safety of Tai Chi for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2014;9(6):e99377.
16	Ni	2019	Ni X, Chan RJ, Yates P, et al. The effects of Tai Chi on quality of life of cancer survivors: a systematic review and meta-analysis. *Supportive care in cancer* 2019;27(10):3701-16.

17	Pan	2013	Pan L, Guo Y, Yan J. Effects of Tai Chi training on exercise capacity and quality of life in patients with chronic heart failure: A meta-analysis. *European Journal of Heart Failure* 2013;15(3):316-23. d
18	Pan	2015	Pan Y, Yang K, Shi X, et al. Tai chi chuan exercise for patients with breast cancer: a systematic review and meta-analysis. *Evid Based Complement Alternat Med* 2015;2015:535237.
19	Raman	2013	Raman G, Zhang Y, Minichiello VJ, et al. Tai Chi Improves Sleep Quality in Healthy Adults and Patients with Chronic Conditions: A Systematic Review and Meta-analysis. *J Sleep Disord Ther* 2013;2(6)
20	Ren	2017	Ren X, Li Y, Yang X, et al. The Effects of Tai Chi Training in Patients with Heart Failure: A Systematic Review and Meta-Analysis. *Front Physiol* 2017;8:989.
21	Song	2017	Song R, Grabowska W, Park M, et al. The impact of Tai Chi and Qigong mind-body exercises on motor and non-motor function and quality of life in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism Relat Disord* 2017;41:3-13.
22	Song	2018	Song S, Yu J, Ruan Y, et al. Ameliorative effects of Tai Chi on cancer-related fatigue: a meta-analysis of randomized controlled trials. *Supportive care in cancer* 2018;26(7):2091-102.
23	Tao	2016	Tao WW, Jiang H, Tao XM, et al. Effects of Acupuncture, Tuina, Tai Chi, Qigong, and Traditional Chinese Medicine Five-Element Music Therapy on Symptom Management and Quality of Life for Cancer Patients: A Meta-Analysis. *Journal of pain and symptom management* 2016;51(4):728-47.
24	Wang	2013	Wang J, Feng B, Yang X, et al. Tai chi for essential hypertension. *Evid Based Complement Alternat Med* 2013;2013:215254.
25	Winser	2018	Winser SJ, Tsang WW, Krishnamurthy K, et al. Does Tai Chi improve balance and reduce falls incidence in neurological disorders? A systematic review and meta-analysis. *Clin Rehabil* 2018;32(9):1157-68.
26	Wu	2014	Wu W, Liu X, Wang L, et al. Effects of Tai Chi on exercise capacity and health-related quality of life in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2014;9:1253-63.
27	Wu	2019	Wu C, Yi Q, Zheng X, et al. Effects of Mind-Body Exercises on Cognitive Function in Older Adults: A Meta-Analysis. *Journal of the American Geriatrics Society* 2019;67(4):749-758.
28	Xia	2019	Xia TW, Yang Y, Li WH, et al. Different training durations and styles of tai chi for glucose control in patients with type 2 diabetes: a systematic review and meta-analysis of controlled trials. *BMC Complement Altern Med* 2019;19(1):63.
29	Xiang	2017	Xiang Y, Lu L, Chen X, et al. Does Tai Chi relieve fatigue? A systematic review and meta-analysis of randomized controlled trials. *PLoS One* 2017;12(4):e0174872.
30	Yan	2013a	Yan JH, Gu WJ, Sun J, et al. Efficacy of Tai Chi on pain, stiffness and function in patients with osteoarthritis: a meta-analysis. *PLoS One* 2013;8(4):e61672.
31	Yan	2013b	Yan JH, Guo YZ, Yao HM, et al. Effects of Tai Chi in patients with chronic obstructive pulmonary disease: preliminary evidence. *PLoS One* 2013;8(4):e61806.
32	Yan	2014	Yan JH, Pan L, Zhang XM, et al. Lack of efficacy of Tai Chi in improving quality of life in breast cancer survivors: a systematic review and meta-analysis. *Asian Pac J Cancer Prev* 2014;15(8):3715-20.
33	Yang	2014	Yang Y, Li XY, Gong L, et al. Tai Chi for improvement of motor function, balance and gait in Parkinson's disease: a systematic review and meta-analysis. *PLoS One* 2014;9(7):e102942.

34	Yang	2015	Yang Y, Qiu WQ, Hao YL, et al. The efficacy of traditional Chinese Medical Exercise for Parkinson's disease: a systematic review and meta-analysis. *PLoS One* 2015;10(4):e0122469.
35	Yang	2017	Yang YL, Wang YH, Wang SR, et al. The Effect of Tai Chi on Cardiorespiratory Fitness for Coronary Disease Rehabilitation: A Systematic Review and Meta-Analysis. *Front Physiol* 2017;8:1091.
36	Zeng	2014	Zeng Y, Luo T, Xie H, et al. Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses. *Complementary therapies in medicine* 2014;22(1):173-86.
37	Zheng	2016	Zheng W, Li Q, Lin J, et al. Tai Chi for Schizophrenia: A Systematic Review. *Shanghai Arch Psychiatry* 2016;28(4):185-94.
38	Zhou	2015	Zhou J, Yin T, Gao Q, et al. A Meta-Analysis on the Efficacy of Tai Chi in Patients with Parkinson's Disease between 2008 and 2014. *Evid Based Complement Alternat Med* 2015;2015:593263.
39	Zhou	2019	Zhou Z, Zhou R, Li K, et al. Effects of tai chi on physiology, balance and quality of life in patients with type 2 diabetes: A systematic review and meta-analysis. *Journal of rehabilitation medicine* 2019;51(6):405-17.
40	Zou	2018a	Zou L, Sasaki JE, Zeng N, et al. A Systematic Review With Meta-Analysis of Mindful Exercises on Rehabilitative Outcomes Among Post-stroke Patients. *Arch Phys Med Rehabil* 2018;99(11):2355-64.
41	Zou	2018b	Zou L, Yeung A, Li C, et al. Effects of Mind(-)Body Movements on Balance Function in Stroke Survivors: A Meta-Analysis of Randomized Controlled Trials. *Int J Environ Res Public Health* 2018;15(6)
42	Zou	2018c	Zou L, Yeung A, Li C, et al. Effects of Meditative Movements on Major Depressive Disorder: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Clin Med* 2018;7(8)
43	Zou	2018d	Zou L, Yeung A, Zeng N, et al. Effects of Mind-Body Exercises for Mood and Functional Capabilities in Patients with Stroke: An Analytical Review of Randomized Controlled Trials. *Int J Environ Res Public Health* 2018;15(4)
44	Zou	2019a	Zou L, Loprinzi PD, Yeung AS, et al. The Beneficial Effects of Mind-Body Exercises for People With Mild Cognitive Impairment: a Systematic Review With Meta-analysis. *Archives of physical medicine and rehabilitation* 2019;100(8):1556-73.
45	Zou	2019b	Zou L, Han J, Li C, et al. Effects of Tai Chi on Lower Limb Proprioception in Adults Aged Over 55: A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil* 2019;100(6):1102-1113.

eTable 2: Adverse Event (AE) Reporting in Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

ID	Author	Year of publication	Meta-analyses reported AE (Yes/ No)	Primary studies reported AE (Yes/No)	AE Occurrence (Yes/ No)	Notes
1	Chang	2016	Yes	Yes	Yes	Iincreased knee pain (n=1).
2	Chao	2018	No	N/A	N/A	
3	Chen	2016	No	N/A	N/A	
4	Cheng	2019	No	N/A	N/A	
5	Escalante	2010	No	N/A	N/A	
6	Escalante	2011	No	N/A	N/A	
7	Fernandopulle	2017	Yes	Yes	No	
8	Gu	2017	No	N/A	N/A	
9	Guo	2016	No	N/A	N/A	
10	Hall	2017	No	N/A	N/A	
11	Kong	2016	Yes	Yes	Yes	Small initial increase in back pain symptoms that were alleviated by the third or fourth week (n=3); iincreased upper back pain that was alleviated once the upper extremity posture had been corrected (n=1); minor muscle soreness, foot and knee pain at the commencement of the intervention (n = NR).
12	Li	2018	Yes	Yes	No	
13	Lian	2017	Yes	Yes	No	
14	Lyu	2018	Yes	No	N/A	
15	Ni	2014	Yes	Yes	No	
16	Ni	2019	Yes	No	N/A	
17	Pan	2013	Yes	No	N/A	
18	Pan	2015	No	N/A	N/A	
19	Raman	2013	No	N/A	N/A	
20	Ren	2017	No	N/A	N/A	
21	Song	2017	Yes	Yes	No	
22	Song	2018	No	N/A	N/A	
23	Tao	2016	No	N/A	N/A	
24	Wang	2013	Yes	No	N/A	
25	Winser	2018	No	N/A	N/A	

26	Wu	2014	No	N/A	N/A	
27	Wu	2019	Yes	Yes	Yes	Minor musculoskeletal injury (wrist: n=1; ankle: n=1).
28	Xia	2019	Yes	No	N/A	
29	Xiang	2017	Yes	No	N/A	
30	Yan	2013a	Yes	Yes	No	
31	Yan	2013b	Yes	Yes	No	
32	Yan	2014	yes	No	N/A	
33	Yang	2014	Yes	Yes	Yes	Ankle sprain (n=4); low back pain (n=1); and muscle soreness (n=1)
34	Yang	2015	Yes	Yes	Yes	Back pain and ankle sprain (n =NR)
35	Yang	2017	Yes	Yes	Yes	Dyspnea (n=2); muscle pain (n=5); and fatigue (n=6).
36	Zeng	2014	No	No	N/A	
37	Zheng	2016	No	N/A	N/A	
38	Zhou	2015	No	N/A	N/A	
39	Zhou	2019	No	N/A	N/A	
40	Zou	2018a	Yes	No	N/A	
41	Zou	2018b	Yes	Yes	No	
42	Zou	2018c	Yes	Yes	No	
43	Zou	2018d	No	N/A	N/A	
44	Zou	2019a	Yes	Yes	No	
45	Zou	2019b	Yes	Yes	No	

Note: AE = adverse event; N/A = not applicable; NR: not reported

eTable 3a: Tai Chi and health outcomes of patients with neurological condition

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		Parkinson's disease (vs. non-active control)					
Song (2017)	2	66	Severity of depression	Hedge's g = -.62 (-1.14 to -.09)	.022	Moderate	0%
Song (2017)	4	141	Mobility (Timed Up and Go Test)	Hedge's g = -.55 (-.88 to -.22)	.001	Moderate	0%
Song (2017)	4	168	Unified Parkinson's Disease Rating Scale	Hedge's g = -.64 (-.95 to -.33)	<.001	Moderate	0%
Song (2017)	3	124	Balance	Hedge's g = .88 (.24 to 1.52)	.007	Low	58%
Yang (2014)	4	146	Motor function	SMD = -.65 (-1.26 to -.04)	.038	Low	63%
Ni (2014)	2	50	Gait velocity	MD = -.03 (-.59 to .53)	.922	N.A	0%
Ni (2014)	2	50	Stride length	MD = 0 (-.56 to .56)	.999	N.A	0%
Song (2017)	2	43	Cognition	Hedge's g = -.22 (-.85 to .4)	.477	N.A	0%
Song (2017)	2	48	Functional capacity (6-min walking test)	Hedge's g = -.53 (-1.11 to .04)	.067	N.A	0%
Winser (2018)	2	260	Rate of falls	MD = .18 (-.08 to .43)	.174	N.A	0%
Yang (2014)	2	46	Balance-Tandem Stance Test	SMD = .43 (-.64 to 1.5)	.433	N.A	68%
Yang (2015)	2	51	Quality of life (Parkinson's disease questionnaires 39)	SMD = .06 (-1.93 to 2.05)	.952	N.A	90%
Yang (2015)	2	50	Physical function (step length)	SMD = -.01 (-.57 to .56)	.985	N.A	0%
Zhou (2015)	3	71	Quality of life (total score)	SMD = -.16 (-1.46 to 1.13)	.803	N.A	84%
		Parkinson's disease (vs. active control)					
Ni (2014)	3	212	Balance (Berg Functional Reach test)	MD = 3.5 (2.3 to 4.71)	<.000001	Moderate	49%
Winser (2018)	2	260	Rate of falls	MD = .51 (.22 to .8)	.001	Moderate	0%
Lian (2017)	2	260	Fall risk	Odds ratio = .53 (.32 to .88)	.014	Moderate	0%
Song (2017)	5	280	Unified Parkinson's Disease Rating Scale	Hedge's g = -.42 (-.67 to -.17)	.001	Moderate	4%
Song (2017)	3	235	Balance	Hedge's g = .48 (.21 to .75)	.001	Moderate	0%
Ni (2014)	4	259	Quality of life (Health related quality of life)	MD = -.97 (-1.75 to -.2)	.014	Low	86%
Ni (2014)	3	216	Stride length	MD = .49 (-.13 to 1.11)	.121	N.A	74%
Ni (2014)	3	216	Gait velocity	MD = .36 (-.46 to 1.18)	.389	N.A	85%
Ni (2014)	3	212	Mobility (Timed Up and Go Test)	MD = -.54 (-1.34 to .26)	.187	N.A	38%
Yang (2014)	4	301	Motor function	SMD = -.69 (-1.43 to .05)	.067	N.A	84%
Yang (2015)	3	78	Quality of life (Parkinson's disease questionnaire-39)	SMD = .08 (-1.79 to 1.94)	.935	N.A	94%
		Stroke (vs. non-active control)					
Lyn (2018)	2	100	Physical function (Fugl–Meyer Assessment all four limbs)	MD = 4.48 (1.89 to 7.07)	.001	Moderate	0%

Lyn (2018)	2	107	Physical function (Fugl–Meyer Assessment the upper-limb)	MD = 8.27 (4.69 to 11.84)	<.000001	Moderate	7%
Lyn (2018)	7	382	Mobility (Timed Up and Go Test)	MD = 1.15 (.56 to 1.75)	<.001	Low	75%
Lyn (2018)	7	391	Activity of daily living	MD = 10.18 (5.09 to 15.28)	<.001	Low	93%
Lyn (2018)	3	166	Physical function (Fugl–Meyer Assessment the lower limb)	MD = 2.76 (.95 to 4.56)	.003	Low	76%
Zou (2018d)	5	357	Depression	Hedge's g = -1 (-1.35 to -.65)	<.000001	Low	54%
Zou (2018b)	9	432	Balance	Hedge's g = 2.03 (.99 to 3.07)	<.001	Very low	94%
Zou (2018a)	2	88	Gait speed	SMD = .59 (-.12 to 1.31)	.104	N.A	56%
		Stroke (vs. active control)					
Li (2018)	12	856	Activity of daily living	SMD = 1.2 (.56 to 1.85)	<.001	Moderate	94%
Li (2018)	3	155	Sleep quality	SMD = -.58 (-1.78 to .61)	.339	N.A	0%
Li (2018)	4	251	Mobility (Timed Up and Go Test)	SMD = 1.71 (-.27 to 3.69)	.091	N.A	97%
Zou (2018a)	2	145	Gait speed	SMD = .16 (-.2 to .52)	.394	N.A	0%
Zou (2018b)	4	279	Balance	Hedge's g = .48 (-.09 to 1.05)	.098	N.A	84%
		Multiple sclerosis (vs. active control)					
Xiang (2017)	2	103	Level of fatigue	SMD = -.77 (-1.75 to .22)	.128	N.A	79%

*N.A.: not applicable; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 3b: Tai Chi and health outcomes of patients with musculoskeletal conditions

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		Osteoarthritis (vs. non-active control)					
Fernandopulle (2017)	2	140	Physical function (WOMAC)	MD = -10.81 (-15.91 to -5.71)	<.001	Moderate	0%
Escalante (2010)	6	259	Severity of pain	Cohen d = .67 (.41 to .93)	<.000001	Moderate	2%
Hall (2017)	4	243	Level of disability	SMD = -.67 (-.93 to -.41)	<.000001	Moderate	0%
Yan (2013)	3	156	Stiffness (WOMAC)	SMD = -.3 (-.79 to .18)	.222	N.A	54%
		Osteoarthritis (vs. active control)					
Zou (2019b)	2	86	Flexion -Dominant/right knee (proprioception)	SMD = -1.12 (-1.58 to -.66)	<.000001	Moderate	0%
Chang (2016)	2	134	Fear of Falling	SMD = -.63 (-.98 to -.28)	<.001	Moderate	0%
Escalante (2011)	2	68	Cardiorespiratory fitness	Cohen d = .7 (.21 to 1.19)	.005	Moderate	0%
Kong (2016)	5	183	Severity of pain	SMD = -.62 (-1 to -.25)	.001	Moderate	33%
Hall (2017)	5	187	Level of disability	SMD = -1.19 (-2.27 to -.12)	.030	Low	90%
Chen (2016)	3	166	Mobility (Timed Up and Go Test)	SMD = .56 (.09 to 1.04)	0.019	Low	0%
Chang (2016)	5	206	Stiffness (WOMAC)	SMD = -.2 (-.7 to .31)	.446	N.A	66%
Chang (2016)	2	53	Cardiopulmonary function (Stair climb test)	SMD = -.63 (-1.82 to .56)	.300	N.A	71%
Chang (2016)	4	161	Physical function (WOMAC)	SMD = -.13 (-.6 to .33)	.569	N.A	46%
Chang (2016)	2	53	Functional capacity (6-min walking test)	SMD = .06 (-1.57 to 1.69)	.943	N.A	84%
Chen (2016)	2	137	Quality of life	SMD = .24 (-.11 to .59)	.186	N.A	5%
Chen (2016)	3	151	Severity of depression	SMD = .31 (-.3 to .92)	.324	N.A	61%
Chen (2016)	2	79	Knee extensor strength	SMD = .26 (-.19 to .7)	.259	N.A	0%
		Fibromyalgia (vs. non-active control)					
Cheng (2019)	3	203	Sleep quality	SMD = -.51 (-.73 to -.3)	<.000001	Moderate	0%
Cheng (2019)	4	307	Level of fatigue	SMD = -.6 (-.91 to -.3)	<.001	Moderate	39%
Cheng (2019)	3	209	Severity of depression	SMD = -.49 (-.98 to -.01)	.044	Low	64%
Cheng (2019)	3	190	Severity of pain	SMD = -.88 (-1.58 to -.18)	.013	Very low	78%
		Fibromyalgia (vs. active control)					
Raman (2013)	3	245	Sleep quality	SMD = .4 (.13 to .68)	.004	Moderate	7%
Kong (2016)	2	164	Severity of pain	SMD = -.52 (-1.09 to .05)	.072	N.A	68%
		Low back pain (vs. non-active control)					
Kong (2016)	3	385	Severity of pain	SMD = -.81 (-1.1 to -.52)	<.000001	Moderate	45%

*N.A.: not applicable; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 3c: Tai Chi and health outcomes of patients with cancer

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		vs. non-active control					
Song (2017)	2	105	Level of fatigue	SMD = -.24 (-.91 to .44)	.488	N.A	78%
Tao (2017)	2	217	Vital capacity (objective measure)	SMD = 365.21 (-134.97 to 865.4)	.152	N.A	94%
		vs. active control					
Ni (2019)	2	38	Interleukin-6	MD = 2.21 (.74 to 3.68)	.003	Moderate	0%
Song (2018)	5	289	Level of fatigue	SMD = -.58 (-.85 to -.31)	<.001	Moderate	24%
Tao (2016)	3	148	Body mass index	SMD = -.37 (-.71 to -.03)	.031	Moderate	2%
Ni (2019)	2	73	Cortisol level	MD = -.09 (-.16 to -.02)	.011	Moderate	0%
Chen (2016)	2	88	Severity of depression (self-reported)	SMD = -.97 (-1.9 to -.04)	.040	Low	50%
Ni (2019)	5	465	Physical function (upper limb function)	SMD = 1.19 (.64 to 1.75)	<.001	Low	87%
Pan (2015)	3	63	Physical function (elbow extension)	SMD = 1.29 (.74 to 1.84)	<.000001	Low	0%
Pan (2015)	3	63	Muscle strength (handgrip strength)	SMD = .61 (.1 to 1.12)	.019	Low	0%
Pan (2015)	3	63	Physical function (elbow flexion)	SMD = .76 (.24 to 1.27)	.004	Low	0%
Pan (2015)	3	63	Physical function (horizontal abduction)	SMD = .77 (.25 to 1.29)	.003	Low	0%
Pan (2015)	3	63	Physical function (abduction)	SMD = .58 (.08 to 1.09)	.024	Low	0%
Ni (2019)	4	330	Muscle strength (upper limb)	SMD = .44 (.15 to .74)	.003	Low	38%
Chen (2016)	3	91	Quality of life (self-reported)	SMD = -.17 (-.82 to .49)	.618	N.A	48%
Pan (2015)	2	38	Insulin-like growth factor 1	SMD = -1.11 (-2.3 to .09)	.069	N.A	65%
Pan (2015)	3	102	Severity of pain (self-reported)	SMD = -.05 (-.42 to .32)	.787	N.A	0%
Yan (2014)	3	226	Bone mineral density	SMD = .67 (-.13 to 1.47)	.101	N.A	0%
Yan (2014)	2	205	Muscle strength (wrist)	SMD = .59 (-.14 to 1.33)	.113	N.A	0%
Yan (2014)	2	205	Muscle strength (elbow)	SMD = .58 (-.4 to 1.56)	.249	N.A	11%
Yan (2014)	2	205	Bone mineral density (L2-4)	SMD = .1 (-.1 to .3)	.322	N.A	93%
Yan (2014)	2	205	Bone mineral density (femur)	SMD = .02 (-.01 to .05)	.219	N.A	28%
Zeng (2014)	2	40	Body composition (fat mass percentage)	MD = -.67 (-2.44 to 1.09)	.453	N.A	0%

*N.A.: not applicable; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 3d: Tai Chi and health outcomes of patients with type 2-diabetes

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		vs. non-active control					
Chao (2018)	5	162	2- hour postprandial blood glucose	MD = -2.07 (-2.89 to -1.26)	<.000001	Moderate	0%
Zhou (2019)	4	268	Insulin resistance	WMD = -.83 (-1.37 to -.28)	.003	Moderate	0%
Zhou (2019)	5	244	Body mass index	WMD = -1.61 (-2.42 to -.8)	<.001	Moderate	0%
Zhou (2019)	11	451	Hemoglobin A1c	WMD = -.94 (-1.4 to -.49)	<.001	Low	90%
Zhou (2019)	4	190	Systolic blood pressure	WMD = -9.36 (-18.23 to -.48)	.039	Low	66%
Zhou (2019)	17	586	Fasting blood glucose	WMD = -.69 (-.95 to -.43)	<.000001	Low	51%
Zhou (2019)	8	424	Total cholesterol	WMD = -.65 (-1.06 to -.23)	.002	Low	70%
Xia (2019)	2	73	Triglycerides	SMD = -.17 (-.56 to .22)	.405	N.A	0%
Zhou (2019)	4	190	Diastolic blood pressure	WMD = -3.47 (-7.39 to .44)	.082	N.A	18%
Zhou (2019)	7	400	Fasting insulin	WMD = -.35 (-.82 to .11)	.133	N.A	74%
		vs. active control					
Chao (2018)	3	84	2 hour postprandial blood glucose	MD = -.62 (-1.08 to -.15)	.009	Moderate	0%
Xia (2019)	6	296	Body mass index	SMD = -.61 (-.93 to -.28)	<.001	Moderate	31%
Xia (2019)	9	527	Hemoglobin A1c	SMD = -.68 (-1.18 to -.18)	.008	Low	84%
Xia (2019)	12	606	Fasting blood glucose	SMD = -.51 (-.9 to -.12)	.010	Low	79%
Xia (2019)	5	270	Total cholesterol	SMD = -.41 (-.77 to -.05)	.024	Low	60%
Xia (2019)	5	270	Low-density lipoprotein cholesterol	SMD = -.56 (-1.21 to .09)	.091	N.A	84%
Xia (2019)	5	270	High-density lipoprotein cholesterol	SMD = .04 (-.01 to .1)	.139	N.A	0%
Xia (2019)	6	286	Triglycerides	SMD = -.15 (-.41 to .11)	.263	N.A	59%

*N.A.: not applicable; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 3e: Tai Chi and health outcomes of patients with cardiopulmonary diseases

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		Heart failure (vs. non-active control)					
Gu (2017)	5	503	Heart left ventricular ejection fraction	MD = 8.21 (2.72 to 13.71)	.003	Moderate	97%
Gu (2017)	8	651	Functional capacity (6-min walking test)	MD = 50.53 (28.49 to 72.56)	<.000001	Low	89%
Gu (2017)	3	253	Serum B-type natriuretic peptide	MD = -2.42 (-4.46 to -.39)	.020	Low	89%
Gu (2017)	3	382	Quality of life	MD = -7.01 (-12.25 to -1.77)	.009	Low	99%
Pan (2013)	2	90	N-terminal pro-brain natriuretic peptide	MD = -61.16 (-179.27 to 56.95)	.310	N.A	76%
		Heart failure (vs. active control)					
Gu (2017)	2	72	Function capability (6-min walking test)	MD = 55.66 (17.99 to 93.33)	.004	Moderate	0%
Ren (2017)	2	68	Diastolic blood pressure	SMD = 5.96 (.94 to 10.99)	.020	Moderate	0%
Ren (2017)	2	90	Cardiorespiratory fitness (VO2 max)	SMD = 1.32 (.09 to 2.56)	.036	Moderate	0%
Gu (2017)	5	216	Quality of life	MD = -14.07 (-22.63 to -5.51)	.001	Low	75%
Ren (2017)	5	396	Left ventricular ejection fraction	SMD = 11.67 (8.76 to 14.59)	<.000001	Very low	98%
Ren (2017)	2	68	Systolic blood pressure	SMD = 14.69 (-3.86 to 33.24)	.121	N.A	75%
Ren (2017)	2	116	Mobility (Timed Get Up and Go Test)	SMD = -.19 (-.78 to .4)	.53	N.A	0%
Ren (2017)	3	176	Serum B-type natriuretic peptide	SMD = -.94 (-2.2 to .32)	.145	N.A	92%
		COPD (vs. non-active control)					
Guo (2016)	8	573	Functional capacity (6-mins walking test)	MD = 25.77 (4.9 to 46.64)	.016	Moderate	89%
Guo (2016)	3	389	Lung function (forced vital capacity/FVC)	MD = .2 (.04 to .36)	.012	Moderate	13%
Yan (2013)	3	328	Dyspnoea	SMD = -.86 (-1.44 to -.28)	.004	Low	38%
Guo (2016)	6	524	Lung function (forced expiratory volume in 1s/FEV1)	MD = .1 (.01 to .19)	.039	Low	64%
Guo (2016)	6	320	Lung function (FEV1/FVC)	MD = 1.36 (-2.22 to 4.95)	.456	N.A	81%
Guo (2016)	2	329	Oxygen saturation	MD = -.28 (-1.22 to .66)	.557	N.A	0%
		COPD (vs. active control)					
Wu (2014)	5	535	Quality of Life	MD = -3.52 (-6.06 to -.97)	.007	High	0%
Chen (2016)	3	367	Dyspnoea	SMD = .51 (-.13 to 1.15)	.118	N.A	75%
Wu (2014)	4	465	Functional capacity (6-min walking test)	MD = 13.67 (-1.06 to 28.4)	.069	N.A	64%
		Hypertension (vs. non-active control)					
Wang (2013)	10	879	Systolic blood pressure	MD = -14.21 (-17.68 to -10.75)	<.000001	Moderate	99%
Wang (2017)	10	879	Diastolic blood pressure	MD = -6.6 (-8.41 to -4.79)	<.000001	Moderate	99%
Lian (2017)	3	375	Waist circumference	SMD = -.53 (-.74 to -.33)	<.000001	Moderate	0%

Lian (2017)	4	451	Body mass index	SMD = -.39 (-.73 to -.05)	.023	Low	58%
	Coronary heart disease (vs. active control)						
Yang (2017)	2	102	Cardiorespiratory fitness (VO2 max)	SMD = 4.82 (3.65 to 5.99)	<.000001	Moderate	0%

*N..A.: not applicable; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 3f: Tai Chi and health outcomes of patients with cognitive and mental disorders

Author	RCT (n)	Sample size (n)	Outcome	Summary estimate (95% CI)*	P value	GRADE	I²
		Schizophrenia (vs. non-active control)					
Zheng (2016)	3	240	Negative symptoms	SMD = -.91 (-1.6 to -.22)	.010	Low	82%
Zheng (2016)	3	240	Positive symptoms	SMD = -.3 (-.72 to .12)	.166	N.A	62%
Zheng (2016)	2	130	Discontinuation rate	Risk ratio = .92 (.27 to 3.11)	.895	N.A	0%
		Schizophrenia (vs. active control)					
Zheng (2016)	2	151	Positive symptoms	SMD = .23 (-.11 to .56)	.188	N.A	0%
Zheng (2016)	2	204	Discontinuation rate	Risk ratio = .31 (.06 to 1.53)	.150	N.A	0%
Zheng (2016)	3	211	Negative symptoms	SMD = -.86 (-2.13 to .41)	.186	N.A	94%
		Clinical depression (vs. non-active control)					
Zou (2018c)	2	75	Severity of depression	SMD = -.36 (-.88 to .16)	.177	N.A	1%
		Clinical depression (vs. active control)					
Zou (2018c)	2	100	Severity of depression	SMD = -.68 (-1.11 to -.26)	.002	Moderate	0%
		Mild cognitive impairment (vs. active control)					
Zou (2019a)	2	106	Short-term memory	SMD = .51 (.12 to .9)	.010	Moderate	0%
Zou (2019a)	3	367	Executive function	SMD = -.3 (-.69 to .09)	.131	N.A	57%
		Dementia (vs. active control)					
Wu (2019)	3	218	Global cognition (MMSE)	MD = 2.9 (2.22 to 3.58)	<.000001	Moderate	0%

*N.A.: not applicable; MD: mean difference; SMD: standard mean difference; *No study reported effect estimate that favored control groups.*

eTable 4: ROBIS quality assessment in Meta-Analyses of Tai Chi Randomized Controlled Trials among Study Populations with Diagnosed Chronic Illnesses

ID	Author Name	Year of publication	1. Concerns regarding specification of study eligibility criteria	2. Concerns regarding methods used to identify and/or select studies	3. Concerns regarding methods used to collect data and appraise studies	4. Concerns regarding the synthesis and findings	Risk of bias in the review RISK: LOW/HIGH/UNCLEAR Rationale for risk:
1	Chang	2016	High	Low	High	Unclear	Unclear
2	Chao	2018	Low	Low	Low	Low	Low
3	Chen	2016	Low	Low	Low	Low	Low
4	Cheng	2019	Low	Unclear	Low	High	Unclear
5	Escalante	2010	Low	Unclear	Unclear	Unclear	Unclear
6	Escalante	2011	Low	Unclear	Unclear	High	Unclear
7	Fernandopulle	2017	Low	Unclear	Low	Low	Low
8	Gu	2017	Low	High	Low	Low	Low
9	Guo	2016	Low	Low	Low	Low	Low
10	Hall	2017	Low	High	Low	Low	Low
11	Kong	2016	High	Low	Low	Low	Low
12	Li	2018	Low	Low	Low	High	Low
13	Lian	2017	Low	High	Low	Low	Low
14	Lyu	2018	Low	Low	Unclear	Low	Low
15	Ni	2014	Low	Low	Low	Low	Low
16	Ni	2019	Low	Unclear	Low	Low	Low
17	Pan	2013	High	Low	Unclear	Low	Unclear
18	Pan	2015	Low	Low	Low	Unclear	Low
19	Raman	2013	Low	Unclear	Unclear	Unclear	Unclear
20	Ren	2017	Low	Unclear	Low	Unclear	Unclear
21	Song	2017	High	Unclear	Low	Low	Unclear
22	Song	2018	Low	Low	Low	Low	Low
23	Tao	2016	Low	Unclear	Low	Unclear	Unclear
24	Wang	2013	Low	Low	Unclear	High	Unclear
25	Winser	2018	Low	Unclear	Low	Low	Low
26	Wu	2014	Low	Unclear	Low	Unclear	Unclear
27	Wu	2019	Unclear	Unclear	Low	Unclear	Unclear

28	Xia	2019	Low	Low	Low	Unclear	Low
29	Xiang	2017	Low	Low	Low	Low	Low
30	Yan	2013a	Low	Low	Low	Low	Low
31	Yan	2013b	Low	Low	Low	Unclear	Low
32	Yan	2014	Low	Low	Low	Unclear	Low
33	Yang	2014	Low	Low	Low	High	Low
34	Yang	2015	Low	Unclear	Low	High	Unclear
35	Yang	2017	Low	Unclear	Low	Low	Low
36	Zeng	2014	Low	Low	Low	High	Low
37	Zheng	2016	Low	Low	Low	Low	Low
38	Zhou	2015	Unclear	Unclear	Low	High	Unclear
39	Zhou	2019	Unclear	Low	Low	Unclear	Unclear
40	Zou	2018a	Low	Low	Low	Low	Low
41	Zou	2018b	Low	Unclear	Low	Low	Low
42	Zou	2018c	Low	Low	Low	Low	Low
43	Zou	2018d	Low	Low	Low	Low	Low
44	Zou	2019a	Low	Low	Low	Low	Low
45	Zou	2019b	Low	Unclear	Unclear	High	Unclear