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

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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

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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 $\geq 50\%$ 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

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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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Tables

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	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

Author	RCT (n)	Sample size (n)	Outcome	Effect size	I²	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

								GRADE			
Author	RCT (n)	Sample size (n)	Outcome	Effect size	I²	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Overall
Hall (2017)	4	243	Level of disability	Moderate	0%	No	No	None	Yes	No	Moderate
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

Author	RCT (n)	Sample size (n)	Outcome	Effect size	I²	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Overall
								GRADE			
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
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

						GRADE					
Author	RCT (n)	Sample size (n)	Outcome	Effect size	I²	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Overall
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
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 (I²>50%), imprecision (total sample size<500) and publication bias (small-study effects P>0.10).