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# Problems of scientific methodology related to placebo control in *Qigong* studies: A systematic review

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ABSTRACT

*Introduction:* *Qigong* is widespread in the West and used for preventive care, stress-induced conditions, emotional and vegetative symptoms like migraine and hypertension, as well as for better coordination in the elderly and quality of life enhancement in severe disease such as cancer. Adequate controls for *Qigong* research are lacking, compromising the level of efficacy evidence. Adequate *Qigong* placebo control exercises should match clear and standardized criteria.

*Methods:* Three computerized databases were assessed in January 2018 (Scopus, Web of Science and MEDLINE on PubMed) using the following keywords or their combinations: (*Qigong* OR *Qi Gong* OR *Gong Qi* OR *Chi Kung* OR *Kung Chi* OR *Kiko* OR *Ki Gong* OR *Ki Kong*) AND placebo. In addition, all reference lists were scanned for further relevant articles. Literature was examined for the effects of *Qigong* as compared to a control intervention.

*Results:* 110 articles were found, 78 of which were excluded after examining the title and abstract, and 16 because they were duplicates. Four more articles were found by searching in the bibliographies of published papers. A total of 20 studies were included in this systematic review. We found that, to the best of our knowledge, no criteria for placebo controls have been published in peer-reviewed journals so far.

*Conclusion:* Placebo controls should be developed by the usage of vegetative functional assessments such as heart rate variability, thermography, and electrophysiological measurements, thus excluding major vegetative effects of the exercise, as well as by the usage of psychometric tests and other quantitative evaluations.



## 1. Introduction

*Qigong* (QG) is a therapeutic technique of traditional Chinese medicine, which is used as a preventive care method, currently paid for by the social security systems of some Western countries such as Germany. Most national health care systems, however, require objective scientific proof of efficacy for reimbursement of a therapy. *Qigong* attracts a growing number of practitioners making these scientific proofs more and more urgent.

To scientifically evaluate *Qigong*, it is necessary to develop study designs including suitable placebo controls. We were interested in whether such controls exist. Validating the respective studies and the existing literature, and based on hypotheses about the functional features of *Qigong* and involved parameters, we developed five criteria for a placebo *Qigong*.

*Qigong* was developed from the background of Traditional Chinese Medicine (TCM), including the application of meridians and acupoint theory, the regulation of *qi*, attaching importance to the concept of holism, and treatment differentiation based on different

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signs and symptoms. TCM hypothesizes that the meridian system is the path to transport *qi* and blood (*xue*), connecting the Zang-fu organs, surface, and different parts of the body. These practices allow the activation of the body's muscles and tendons, the breath control, and the nourishment of the mind or *shen* through resting meditation. These exercises are thought to stimulate the meridians and collaterals, promote the circulation of *qi* and blood, and regulate the internal organs to strengthen the overall state of health (Jiang and Zou, 2013). According to TCM, health is present when the *qi* of the body is flowing smoothly and there is a sufficiency but not an excess (Cassidy, 2002). According to Porkert, *qi* could be defined as 'immaterial energy with qualification and direction' (Porkert and Hempen, 1995), or according to the Heidelberg Model of TCM as a 'vegetative capacity to function of a tissue or organ which may cause the sensation of pressure tearing or flow' (Greten, 2008a; Greten, 2013a; J Greten, 2004).

A contemporary understanding of TCM considers it to be an ancient model of systems biology, which develops its own type of diagnosis. In Western terms, this can be called a vegetative functional diagnosis (H. J. Greten, 2011a, 2011b; Greten, 2013b; Greten, 2008a; Greten, 2008b; Johannes Greten, 2007). This diagnosis has been precisely analysed and defined and shown to be the basis of optimal treatment results (Duarte et al., 2013; Karner et al., 2013; Maimer et al., 2013; Nishimura et al., 2013; Schröder et al., 2007; Schroeder et al., 2008; Seca et al., 2016). Thus, acupuncture as the best-known treatment modality of TCM can be understood as a systematic application of vegetative reflexology with both peripheral and central nervous effects that, traditionally, is based on a Chinese medical (vegetative functional) diagnosis. As well as acupuncture, we hypothesize that also *Qigong* is based on such peripheral and central nervous effects, stimulated by related reflexological mechanisms.

There are three primary types of *Qigong* training: Martial, Medical and Spiritual (Johnson et al., 2000). Within each one, *Qigong* can be practised with active (*Dong Gong*) and passive (*Ling Gong*) exercises, both embracing a wide variety of lineages and styles. Active *Qigong* involves movement aimed to stimulate acupoints and channels, as well as to strengthen internal organs, whereas passive *Qigong* is focused on the meditative aspect of the practice, which can be performed sitting, lying or standing, in order to cultivate and store the *qi*, stimulating the internal body and clearing the mind (Tse, 1996). Some popular systems of active *Qigong* are, for example, the *Ba Duan Jin*, which means literally 'Eight Pieces of Silk Brocade', the *Xi Sui Jing*, known as the 'Bone Marrow Cleansing', and the *Wu Qin Xi*, known as 'The Five Animal Frolics' (Cohen, 1999). Within the passive *Qigong* practice, some styles are based on static postures without the dynamic component that might be understood, according to the western point of view, as physical exercise. A good example of this type of *Qigong* is the *Zhan Zhuang* system, which is recognised in the West as the 'holding the tree' posture. This practice is similar to the 'White Ball' *Qigong* exercise, according to the Heidelberg Model of TCM (H. Greten, 2009; Matos et al., 2015). Generally, *Qigong* and other related techniques can be described as concentrative breathing and motion exercises that have mental, emotional (Rodrigues et al., 2018; Sertel et al., 2010) and vegetative (L. Matos et al., 2012; Matos et al., 2015) effects, which are the major predecessor of the autogenic training of western medicine (Greten, 2013b). From a western perspective, it could be hypothesized that *Qigong*, like other meditation techniques, elicits the relaxation response and alleviates the dysregulation of the hypothalamic-pituitary-adrenal axis (Benson et al., 1974; Wang et al., 2013). In the context of the underlying diagnosis, the exercises can also be regarded as traditional vegetative biofeedback exercises, that work via self-perception ('awareness'), the building-up of a positive sense of the body (positive inner object) by a process of becoming vegetatively balanced.

For the induction of vegetative effects associated with the autonomic nervous system regulation, breath control seems to be crucial, as special movements can stretch or relax the so-called meridians of Chinese Medicine (Johannes Greten, 2007). According to Western research, they may be regarded as vegetative reflex organs, consisting of special skin areas (acupoints) with increased nerve fibres and mast cells (MC). Mast cells are widely distributed in the connective tissue, particularly in sub-epithelial regions, surrounding blood vessels, nerves, smooth muscle cells, mucous glands, and hair follicles, being found predominantly at the interface between the host and the external environment (da Silva et al., 2014). They play an important role in inducing the inflammatory cascade. The physical stimulation at acupoints deform collagen fibres by stress and promote the activation of the surrounding MCs, which immediately release a large number of mediators, among them histamine, into the nearby extracellular space via degranulation (Ding et al., 2013; Fong and Crane, 2018). These substances increase blood vessel permeability and act on the surrounding peripheral nerve endings generating a positive biofeedback signal by neurotransmitters (Ding et al., 2013). Therefore, by stretching and relaxing these fibres it is believed that MC degranulation occurs, leading to depolarization in vegetative reflex patterns (Ding et al., 2013; Zhang et al., 2008). Indeed, during acupuncture and close to the needle, the injured fascia, which is composed of collagen fibres, elastic fibres, fibroblasts, adipocytes, and MC, bound to the needles as shown by electro-microscopical analysis of the needle after removal (Kimura et al., 1992). Langevin showed that an acupuncture needle can cause the connective tissue to twist in the acupoints, thereby inducing signal transduction along the meridians at the cellular level (Langevin et al., 2002; Langevin and Yandow, 2002). This makes clear how related (the diagnosis-dependent) acupuncture effects occur and *Qigong* exercises act, and how this therapy has vegetative features.

Another special feature of these exercises is the systematic enhancement of self-perception, frequently including the induction of guided imagination. For instance, in the so-called 'White Ball' *Qigong* (H. Greten, 2009), an imaginary white rice paper ball is held between the hands, which leads to the induction of almost paraesthetic sensations in the hands, traditionally called the *qi* sensation or *Ba Chu*. This sensation is believed to be essential for the effectiveness of the exercises, just like the '*de qi*' is essential for acupuncture effects, which supports our hypothesis of *Qigong* being a vegetative functional therapy.

The beneficial effects of *Qigong* on mood, anxiety, depression and general psychological well-being are well known (P.-S. Chang et al., 2018; Johansson et al., 2011; Osypiuk et al., 2020; Wang et al., 2013; J.-j. Wu et al., 2019), and the inherent emotional manifestations may functionally be related to vegetative functions. According to the Portuguese neuroscientist António Damásio, deep emotional states and their balance are expressed by the same centres that regulate vegetative homeostasis. This author even defines emotions to be a part of the vegetative balance in man (Damasio, 1999). In other words: vegetative balance fosters emotional stability and balance.

In the last decades, several clinical studies using *Qigong* have shown that significant effects can be induced in vegetatively-induced symptoms like migraine, hypertension, the frequency of falling in the elderly, quality of life of cancer patients (Sertel et al., 2010) and even pain (Bai et al., 2015). To support the process of integration of *Qigong* into Western medical health care systems, the related therapeutic effects should be quantified by objectively measurable physical parameters, and adequate controls should be available. We suggest that adequate control exercises should match

the following criteria (Gerdesmeyer et al., 2017; Gupta and Verma, 2013; Peters, 2001):

1) placebos should have no major vegetative effects on the participants;
2) placebo exercises should be as similar as possible to the true exercise (verum) in physical movements to induce comparable suggestive effects, to induce similar circulatory activation and energy consumption;
3) placebo control exercise should show minimal mental or emotional effects on the psychological features examined (target symptoms);
4) a description of the verum and control exercises sufficient to confirm results by others should be published prior or along with the study data;
5) the features 1 to 4 should be ideally shown before the studies, to allow prospective trials to be done. We would summarise this idea under the name placebo.

Although in the majority of the studies the term *Qigong* was formally introduced (K. W. Chen et al., 2009; W.-h. Wu et al., 1999), it is not certain whether the usage of this term was adequate for the respective interventions. The concept of placebo was developed in pharmacology to differentiate between specific (therapeutic) and non-specific effects of a drug (Shepherd, 1993), and it has not yet been clarified which components of the *Qigong* intervention are therapeutic, and which ones are not.

For these reasons we performed a systematic literature review of *Qigong* studies to find out if the effects of *Qigong* were quantified by objectively measurable physical parameters, as well as if adequate controls, integrating a placebo component based on the above mentioned five criteria were present in the selected studies. Therefore, we aim to reach an objective conclusion regarding the current state of the literature and to determine what has been reported about the therapeutic and medical value of this system of exercises in the treatment of specific symptoms. The aim is to strengthen the importance of well-designed placebo controls, required to examining hypotheses regarding either the theory and/or mechanism of *Qigong* efficacy while used in the daily context of clinical practice. Furthermore, we hope to reveal where further research is still necessary.

## 2. Methods

The literature was examined for the effects of *Qigong* as compared to a control intervention. The systematic review was completed following the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Moher et al., 2009). The PRISMA flow diagram of this systematic review is shown in Fig. 1.

### 2.1. Data sources

The two first authors of this paper performed searches in 3 computerized databases: Scopus, Web of Science and MEDLINE on PubMed Scopus (since inception to January 16th, 2018) using the following keywords or their combinations: (*Qigong* OR *Qi Gong* OR *Gong Qi* OR *Chi Kung* OR *Kung Chi* OR *Kiko* OR *Ki Gong* OR *Ki Kong*) AND placebo. Besides, all reference lists were scanned for further relevant articles. Literature was examined for the effects of *Qigong* as compared to a control intervention.

### 2.2. Study inclusion and exclusion criteria

Inclusion criteria were: randomised controlled trial; the presence of a control group; internal *Qigong* or *qi* training (as opposed to external *Qigong*); objective parameters as outcome measures. Studies testing external *Qigong*, *qi* therapy or *qi* emission were excluded.

In order to clarify these terms, internal *Qigong* comprises the exercises and practices of self-regulation and external *Qigong*, also known as *qi* emission, external *qi* requires the *Qigong* practitioner to manipulate at a distance the patient's *qi* by focusing on the energetic properties of the patients' channels, collaterals, and points, as well as internal organs (Johnson et al., 2000).

Only papers published in English or, at least, with the abstract in English were included.

### 2.3. Quality assessment

The quality of the included studies could be evaluated by using validated assessment tools such as the Physiotherapy Evidence-Based Database (PEDro) scale or the Jadad quality criteria. This study considered the Jadad score (Jadad et al., 1996) modified by White and Ernst for acupuncture trials (White and Ernst, 1999). This scale was chosen for its brevity and simplicity, widespread use, versatility and reliability in different settings, and because it was shown to be adaptable for a TCM intervention (Augestad et al., 2012; Olivo et al., 2008). Indeed, TCM is a system of sensations and findings designed to establish the functional vegetative state of a person, which can be treated by Chinese pharmacotherapy, acupuncture, Chinese manual therapy (*Tuina*), *Qigong* or dietetics. Although the practical application of these therapeutics seems to be quite different from each other, they do share the same principles while evaluating the vegetative functional tendencies and the diagnostically relevant signs of a person. Those indicate the functional state of a body island (body region) and correlate with the functional properties of a meridian (H. J. Greten, 2014; Liang Liu and Liu, 2011; Stump, 2011).

Briefly, for a total of 5 points, 1 point was given for each of the following conditions: randomised study; appropriate method of randomization; subjects blinded to intervention; evaluator blinded to intervention; description of withdrawals and dropouts. Subject blinding was assumed when the control intervention was indistinguishable from *Qigong*, even if the word 'blinding' did not occur in the report. Trials with 4 or 5 points were considered to be of high quality.

## 3. Results

The database search yielded 110 articles (36 from Web of Science, 42 from Scopus and 32 from Medline), 78 of which were excluded based on the examination of the title and abstract, and 16 because they were duplicates. Four additional articles were found by searching in the bibliographies of the published papers.

A total of 20 studies were included in the systematic review. The papers retrieved have been summarized in Table 1.

The studies were of heterogeneous quality. Sample sizes varied from 14 to 176, with 8 studies with $n > 100$ and 8 studies with $n < 50$. Only 4 papers (Burini et al., 2006; Campo et al., 2014; Cheung et al., 2005; X. Liu et al., 2011) had a Jadad score of 4, due to the blinding of the investigator/analyser, and none had a score of 5, because of the difficulty of blinding patients due to the nature of the intervention.

Regarding the *Qigong* intervention, 17/20 studies reported the type of *Qigong* that was used. Of these, 3/17 described the names of the individual *Qigong* exercises (Campo et al., 2014; Loh et al., 2014; Tsang et al., 2013), and 8/17 described in detail how to perform the exercise (Chan et al., 2013; C. Chang et al., 2013; X. Chen et al., 2016; Cheung et al., 2005; Rendant et al., 2011; Tsang et al., 2013; von

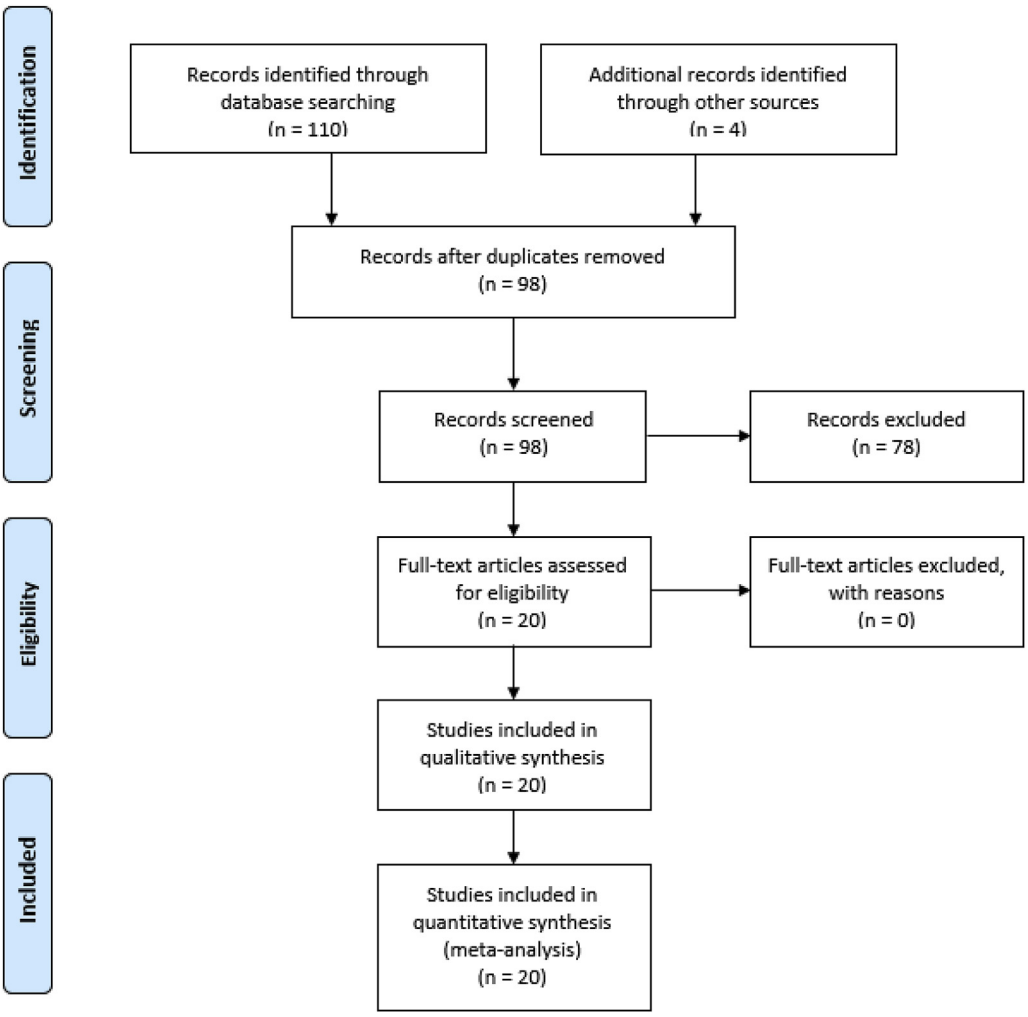


**Fig. 1.** PRISMA flow diagram.

Trott et al., 2009; Yeh and Chung, 2016). In particular, Tsang et al. (2013) illustrated 2 movements (over 10) in the standing and sitting positions with photographs. None of these studies describes the diagnostic process, or the basic principles and specific therapeutic ideas behind the application of these *qi* exercises.

Regarding the outcome measures, 4 studies reported only objective physical parameters (blood pressure, serum cortisol, etc.) (X. Chen et al., 2016; Lee et al., 2003; X. Liu et al., 2011; Sun et al., 2014), 8 studies reported only subjective data (like pain questionnaires and quality of life assessments) (Blödt et al., 2015; Chan et al., 2013; Gaitan-Sierra and Hyland, 2014; Loh et al., 2014; Putiri and Gillham, 2012; Rendant et al., 2011; von Trott et al., 2009; Yeh and Chung, 2016), and 8 studies reported both objective and subjective data (Burini et al., 2006; Campo et al., 2014; C. Chang et al., 2013; Cheung et al., 2005; Ho et al., 2012; Lee et al., 2004; Teut et al., 2016; Tsang et al., 2013).

Regarding the type of control used, 9 studies used different types of physical exercise, such as aerobic training, non-aerobic stretching, dancing and exercise therapy; 3 studies used reading, 3 studies used common medical care, 3 studies used waiting list control (see Table 2). Two studies used a placebo or sham *Qigong* as a control, which was very similar to the *Qigong* intervention, but without the concept of 'moving *qi*' (Lee et al., 2004), meditation and healing sounds (X. Liu et al., 2011).

## 4. Discussion

The gold standard to verify the effectiveness of a new intervention is to test it in a prospective, randomised and controlled trial (Kaufman, 2015; Misra, 2012). Therefore, the new intervention is assessed against a placebo control, with a randomised distribution of participants in the two groups, using carefully defined outcome measures, which must be collected before and after the treatment. Within this framework, the placebo should reproduce some non-specific aspects of the intervention, to verify if the intervention has specific effects. Nevertheless, in our review, the control options of the included studies remain somewhat unclear regarding the aspects they aim to represent in comparison to the verum *Qigong* groups.

From the 20 studies included in this review, only four of them had a Jadad score of 4, but none had a score of 5, which might be due to the difficulty of blinding patients to the intervention with *Qigong*. The studies examined in this review used different types of control, such as physical exercise or reading (see Table 2). One might speculate that physical exercise may have been used to mimic the non-specific effects of posture and movement within the exercises, while reading and discussion may have been used to the non-specific effects of concentration and focusing. There was no type of control based on the breathing element and no evaluation of

**Table 1**
Characteristics of the included studies.

| Author, year | Participants, sample size | Disease | Intervention | Control | Outcome measures | Results |
|---|---|---|---|---|---|---|
| Blödtet al. (2015) | 127 patients | Chronic low back pain. | 12 weekly 90-min QG sessions over 3 months. | 12 weekly 60-min therapy sessions over 3 months. | 1) Pain intensity in the last seven days (VAS 0–100) after 3 months; 2) Roland-Morris disability, health-related quality of life, self-efficacy, sleep quality, suspected adverse reactions and serious adverse events. Follow-up was measured after 6 and 12 months. | No significant difference in the primary and secondary outcomes. |
| Burini et al. (2006) | 26 PD patients under stable medication. | Advanced Parkinson's disease. | AT1+QG2: 20 aerobic training sessions followed by 20 QG sessions with 2 months interval between the interventions. | QG1+AT2: the same treatments performed with an inverted. | Unified Parkinson's Disease Rating Scale (UPDRS), Brown's Disability Scale (BDS), 6 Min Walking Test (6MWT), Borg scale for breathlessness, Beck Depression Inventory (BDI) and Parkinson's Disease Questionnaire-39 items (PDQ-39), Spirometry test and maximum cardiopulmonary exercise test (CPET). All measures immediately before and after each treatment phase. | Significant increase in 6MWT and a larger decrease in Borg score after aerobic training. Significant improvement in cardiorespiratory parameters after aerobic training. |
| Gaitan-Sierra et al. (2014) | 80 healthy undergraduate psychology students. | No disease. Healthy volunteers seeking for well-being improvement. | 5-day QG intervention | Comparison between hand position (high vs low) and type of mental focus (body focus vs positive focus). | Expectancy, intrinsic motivation and perceived effort were evaluated. Mood change was assessed by the Positive and Negative Affect Schedule (PANAS) and perceived benefit from the intervention was measured using a single item on a 7-point scale. | The high hand position improved negative affect and was reported more intrinsically motivating but was unrelated to perceived effort. Positive focus produced better positive affect. For all groups combined, intrinsic motivation and effort predicted all three outcomes. The association between expectancy and perceived benefit was mediated via intrinsic motivation and perceived effort. |
| Campo et al. (2014) | 40 older fatigued and sedentary prostate cancer survivors (11 dropped out). | Prostate cancer survivors. | Biweekly 60-min QG sessions for 12 weeks. | Biweekly 60-min an a-aerobic stretching sessions for 12 weeks. | 1) Feasibility (retention & class attendance rates) and fatigue (FACIT-Fatigue); 2) distress (Brief Symptom Inventory-18, BSI-18). | QG group had significantly higher class attendance rates and significant improvement in the FACIT-Fatigue and distress scores. |
| Chan et al. (2013) | 137 patients (17 dropped out). | Chronic Fatigue Syndrome-like Illness. | 10 120-min sessions of QG training for 5 weeks (Wu Xing Ping Heng Gong) and 12 weeks of home-based QG self-practice. | Waiting list control group. | Chalder Fatigue Scale, Hospital Anxiety and Depression Scale. | In the QG group significant improvement of depression score and total physical and mental fatigue score. No effect of QG on anxiety. |
| Chang et al. (2013) | 67 adolescents. | | Weekly 45-min Laughing QG sessions for 8 weeks. | Reading or doing homework for the same time. | Rosenberg Self-Esteem Scale, Chinese Humor in the Face Scale, salivary cortisol, blood pressure, heart rate, heart rate variability. | Mood states and humor improved in the QG group. Cortisol decreased in QG group. Significant differences in HRV (HF, LF and LF/HF ratios) in the control group. |
| Chen et al. (2016) | 78 hypertensive patients > 18 years old. | Essential hypertension. | "One-minute" QG exercise for 5 days. | 1-min reading session for 5 days. | Blood pressure. | Not completely randomised and low post-hoc power of the study. Significant increase of DBP on day 2 in QG group. |
| Cheung et al. (2005) | 88 hypertensive patients (18–75 years old). | Essential hypertension. | Two 2-h training classes of Guolin QG per week for 4 weeks, then monthly for another 12 weeks. | Two 2-h training classes of exercise per week for 4 weeks, then monthly for another 12 weeks. | Blood pressure SF-36, Beck Anxiety and Depression Inventory scores. | HR, BMI, waist circumference, cholesterol, renin and 24h urinary albumin excretion significantly decreased in both groups after 16 weeks. General health, bodily pain, social functioning and depression also improved in both groups. No significant differences between QG and exercise. |
| Lee et al. (2003) | 28 volunteers | | 1) Chun Do Sun Bop Qi-training (1h); 2) Chun Soo Qi-therapy. | 1) Placebo training (same movements without gathering or moving Qi); 2) placebo Qi-therapy. | White blood cell, Neutrophil, Lymphocyte and Monocyte concentration, NK Cell number. | Qi training increased WBC and lymphocytes after 2 h. Qi training and sham training decreased NK cells. |
| Lee et al. (2004) | 32 men (20–40 years old) | | 3 lessons of 60-min Chun Do Sun Bup QG. | Sham QG (same movements without gathering or moving Qi).<br>Usual medical care. | Anxiety STAI-X1 Plasma Cortisol, ACTH, Aldosterone. | Verum QG group caused a significant decrease in anxiety and ACTH vs sham QG. |

(*continued on next page*)

**Table 1** (*continued*)

| Author, year | Participants, sample size | Disease | Intervention | Control | Outcome measures | Results |
|---|---|---|---|---|---|---|
| Liu et al. (2011) | 41 diabetic patients (25 women, 5 drooped out) | Diabetes control. | 3 QG training sessions per week for 12 weeks + usual medical care. | | HbA1c, insulin resistance, fasting and 2-h blood glucose and insulin bodyweight waist circumference, leg strength. | Significant improvement in QG group for HbA1c, insulin resistance, fasting blood insulin, weight, waist circumference, leg strength; QG intervention was a significant predictor of reduced weight. |
| Liu et al., 2012 | 14 subjects (2 dropped out) | Fibromyalgia | Weekly healing sounds QG, 20-min sessions for 6 weeks. | Six Sham QG 20-min sessions for 6 weeks. With same movements but without meditation and healing sounds. | SMPQ, MFI-20, PSQI, FQI. | Verum QG significantly better in all outcome measures. |
| Loh et al. (2014) | 95 women CG: 32 | Breast cancer survivors. | Weekly 90-min sessions of Zhi Neng QG trial for 8 weeks. | 1) Weekly 90-min sessions of exercise (line dancing); 2) Usual care. | QoL, distress, fatigue. | Significant improvement of QoL in QG group vs exercise and vs usual care. |
| Putiri et al. (2012) | 32 diabetic adults (19 women). | Diabetes mellitus. | Weekly 60-min Yi Ren Medical QG (YRMQ) sessions for 12 weeks. | 1) Weekly 60-min Progressive Resistance Training (PRT) sessions; 2) Standard care. | Perceived Stress Scale (PSC) Beck Depression Inventory. | YRMQ decreased stress scores by 29% PRT decreased stress scores by 18% and depression scores by 50% No change in the untreated group. |
| Rendant et al. (2011) | 123 patients 20 −60 yo (88% women). | Chronic neck pain. | 18 90-min sessions of Neiyang QG over 6 months. | 1) 18 sessions of exercise therapy over 6 months; 2) Waiting list. | 1) VAS for neck pain in the last 7 days; 2) Neck Pain and Disability Scale (NPAS), SF-36, general sense of perceived self-efficacy (GSF). | 1) pain improved by VAS in QG vs waiting list group at 6 months; 2) secondary outcomes better in QG group vs control; No differences between QG and exercise therapy for primary and secondary outcomes. |
| Sun et al. (2014) | 32 diabetic adults (9 dropped out). | Diabetes mellitus | Weekly 60-min Yi Ren Medical QG (YRMQ) sessions. | 1) Weekly 60-min Progressive Resistance Training (PRT) sessions; 2) Standard care. | Fasting blood glucose and insulin, HOMA-IR, body mass index (BMI). | BMI decreased in both YRMQ and PRT groups compared to control. HOMA-IR improved in YRMQ group vs PRT group. |
| Teut et al. (2016) | 176 older adults > 65 years old. | Chronic low back pain. | 1) 12 90-min QG sessions over 3 months; 2) 24 45-min Viniyoga Yoga sessions over 3 months. | No intervention. | 1) over the past 7 days: average of group pain intensity; 2) at 3 and 6 months: average pain intensity over the past 7 days with VAS, back function, risk of falls, SF-36, Geriatric Depression Scale, body self-efficacy 3- at 6 months; pain intensity from the FRI, pain medication use, frequency of falls, the handgrip strength test, credibility and treatment satisfaction, and adverse events. | No significant differences. |
| Tsang et al. (2013) | 134 frail elders >60 years old (18 dropped out). | Psychosocial, cognitive, physical and physiological functioning of frail elders. | 24 60-min sessions of "Yan Chai Yi Jin Ten-Section Brocades" QG over 12 weeks. | 24 60-min sessions of newspaper reading and discussion over 12 weeks (2/week). | Geriatric Depression Scale (GDS), Perceived Benefit Questionnaire (PBQ), Lowenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G), handgrip strength, Timed Up and Go Test, heart rate, blood pressure, FVC, FEV1. | The experimental participants had a significantly higher level of self-perceived benefits on physical health (increase by 5.7%), activities of daily living (increase by 3.9%), and overall health status (increase by 6.9%). |
| Von Trott et al. (2009) | 117 patients >55 yo (95% women). | Chronic neck pain. | 24 45-min sessions of Dantian QG over 3 months. | 1) 24 sessions of Exercise therapy (ET) over 3 months (2/ week); 2) Waiting list (WL). | 1) VAS; 2) Neck Pain and Disability Scale (NPAS), SF-36, general scale of depression (ADS). | No significant differences between QG vs ET and QG vs WL after 3 months. |
| Yeh et al. (2016) | 108 patients (6 dropped out). | Non-Hodgkin's lymphoma and Chemotherapy. | 20-min Chan-Chuang QG sessions twice daily for 21 days during chemotherapy. | Usual care. | ECOG-PSR for performance with fatigue intensity section, Verran and Snyder-Halpern Sleep Scale. | The average fatigue, worse fatigue, and overall sleep quality significantly decreased over time in the QG group. |

vegetative changes.

However, the studies comparing *Qigong* with physical exercise showed that in 3/9 cases there are no differences between the interventions, while *Qigong* is better than exercise in 4/9 cases, and exercise is better than *Qigong* in 2/9 cases (see Table 2). The inconsistency of these comparisons may be because physical exercise is not an inert placebo, as it has well-characterized physiological and neurovegetative effects (Franconi and Robinson, 2015; Laing et al., 2011). Furthermore, a placebo for *Qigong* should also include some other features like the duration of the exercise, or changes in physiological values (like caloric turnover, blood pressure, and heart rate variability) as an expression of the sympathetic

**Table 2**
Type of control used in the selected studies and overall outcome comparison with verum Qigong.

| Author, year | Type of Control | Results |
|---|---|---|
| Blödt et al. (2015) | Exercise therapy. | No significant differences. |
| Burini et al. (2006) | QG1+ aerobic training sessions. | Aerobic training better. |
| Gaitan-Sierra et al. (2014) | Comparison between hand position (high vs low) and type of mental focus (body focus vs positive focus). | Therapeutic benefit is related to a motivational concordance and positive focus. |
| Campo et al. (2014) | Non-aerobic stretching. | QG group better. |
| Chan et al. (2013) | Waiting list control group. | Significant improvements in QG group. |
| Chang et al. (2013) | Reading or doing homework for the same time. | Significant improvements in QG group and significant differences in HRV in control. |
| Chen et al. (2016) | Reading. | QG group is worse. |
| Cheung et al. (2005) | Exercise. | No significant differences between QG and exercise. |
| Lee et al. (2003) | Placebo training (same movements without gathering or moving Qi) and placebo Qi-therapy. | Qi training increased WBC and lymphocytes. Qi training and sham training decreased NK cells. |
| Lee et al. (2004) | Sham QG (same movements without gathering or moving Qi). | Verum QG group better. |
| Liu et al. (2011) | Usual medical care. | Significant improvement in QG group. |
| Liu et al., 2012 | Sham QG with same movements but without meditation and healing sounds. | Verum QG significantly better. |
| Loh et al. (2014) | Exercise (line dancing). | Significant improvement of QoL in QG group. |
| Putiri et al. (2012) | Progressive Resistance Training (PRT) sessions. | QG group better. |
| Rendant et al. (2011) | Exercise therapy and waiting list. | QG group better than control; No differences between QG and exercise therapy. |
| Sun et al. (2014) | Progressive Resistance Training (PRT) sessions and standard care. | BMI decreased in both YRMQ and PRT groups compared to control. HOMA-IR improved in YRMQ group vs PRT group. |
| Teut et al. (2016) | No intervention. | No significant differences. |
| Tsang et al. (2013) | Newspaper reading and discussion. | QG group better. |
| Von Trott et al. (2009) | Exercise therapy (ET) and waiting list (WL). | No significant differences between QG vs ET and QG vs WL. |
| Yeh et al. (2016) | Usual care. | QG group better. |

and parasympathetic balance, which should be equivalent to the intervention. It, therefore, appears that placebo should be developed based on these findings, before judging on possible therapeutic medical effects of *Qigong*. Also, reading and waiting list controls do not resemble *Qigong* and are therefore inadequate to detect a specific effect of the *Qigong* intervention, such as the increase of the microcirculation in the fingers and hands, the changes in the electrical properties of acupoints or even the perception of the '*ba chu*' sensations (L. Matos et al., 2012; L. C. Matos et al., 2019).

Two studies compared *Qigong* with a control using the same movements of the *Qigong* intervention, but without meditation and healing sounds (X. Liu et al., 2011) and without 'gathering' or 'moving' *qi*, terms that were not further explained or defined in the studies (Lee et al., 2004). From these two studies, only the one performed by X. Liu et al. (2011) had a Jadad score of 4. In both studies, the group doing verum *Qigong* did significantly better on the outcome measures. Although these results were never reproduced, they could suggest that the imagination/focusing part is a specific aspect of the intervention, and future studies on *Qigong* should take this into account while designing the placebo. Only in 8 papers (Chan et al., 2013; C. Chang et al., 2013; X. Chen et al., 2016; Cheung et al., 2005; Rendant et al., 2011; Tsang et al., 2013; von Trott et al., 2009; Yeh and Chung, 2016), the intervention was described, and only in some studies, it was properly done. The description of the *Qigong* intervention is important, but it is overlooked by many authors, and that makes the study non-reproducible and, more importantly, non-transferrable into clinical practice.

*Qigong* has been traditionally used for health purposes, and particular forms of *Qigong* are used because of their specific effects on health and disease (Lee et al., 2011; Lui and Qiang, 2010). Some *Qigong* exercises are used for the preservation of health and quality of life, while other 'medical *Qigong*' exercises are for special indications like back pain or cancer, just to mention a few. The choice of exercises according to the symptom or disease seems to be relevant in this field of research. As shown in acupuncture, the traditional way of allocation is by a traditional Chinese medical diagnosis. Similarly, due to the therapeutic nature of *Qigong*, studies are prone to follow the same methodology, by referring to some diagnostic hypotheses and principles while choosing the type of exercise.

In other areas of TCM, like acupuncture, good reporting of published studies has been facilitated due to the existence of the STRICTA recommendations (MacPherson et al., 2002), however, even so, there has been little evidence of the significant impact of these recommendations over time (Lizhou Liu et al., 2015). Nevertheless, STRICTA guidelines seem to be a useful starting point to promote standardization while reporting interventions in clinical trials involving *Qigong*. The checklist of six key items might be adaptable to *Qigong* as follows: Item 1. *Qigong* rationale (system of *Qigong* chosen and reasoning beyond the selection); Item 2. Details of *Qigong* exercise (clear description of the exercise involving biodynamics, breathing and mind focus); Item 3. Treatment regimen (frequency and duration of the intervention); Item 4. Other components of treatment (details of other interventions administered to the *Qigong* group (e.g. moxibustion, cupping, herbs, lifestyle advice). Setting and context of treatment, including instructions to practitioners, and information and explanations to patients); Item 5. Practitioner background (qualification or professional affiliation, years in *Qigong* practice, other relevant experience); Item 6. Control or comparator interventions (rationale and precise description of the control or comparator) (MacPherson et al., 2010).

### 4.1. Limitations

One of the major limitations of this study is the use of the word 'placebo' as a search strategy. The option for this word limited the output of the main search. For example, several randomised controlled trials are using one of the most popular *Qigong* systems as the main intervention, *Ba Duan Jin*, but none of the selected studies in this review considered it, because those studies did not consider a placebo control, according to the criteria previously described as a reasonable standard in *Qigong* studies. Indeed, this review aimed to find out if there is any type of placebo control respecting the criteria established as essential to increase research quality standards (Gupta and Verma, 2013; Kaufman, 2015; Peters, 2001). Therefore, the adopted limiting strategy seemed to be reasonable, even if much of the selected studies had controls other than placebos. Nevertheless, other words could have been used in the search, together or as an alternative to 'placebo', such as 'sham *Qigong*' or 'fake *Qigong*'. The research team believe that by doing this, the output of this review would be richer notwithstanding the main conclusion would be the same. Moreover, further studies should pay special attention to research exploring the nature of placebos, as well as to the tendency towards the development of pragmatic randomised trials (Dal-Ré et al., 2018; Munnangi and Angus, 2019; Norwegian Knowledge Centre for the Health Services, 2006).

## 5. Conclusions

In summary, this review points towards the low overall quality of the evaluated studies, and, in consequence, the meta-analyses based on such low-quality studies should be considered with prudence.

In the included studies: 1) the principal features of therapy and intervention were often not clearly communicated; 2) 12 studies showed objective physical measurements with partly contradictory results; 3) even if the keyword placebo was used for the literature search, only 2 papers reported a control that can be considered a placebo *Qigong*.

It is also suggested that both diagnostic and therapeutic principles should be defined and communicated wherever possible. Moreover, this review proposes criteria for the technical definition of placebo *Qigong* and showed that no such placebo controls have been published in peer-reviewed journals so far. Indeed, this might be common to other practices that do share some theoretical and practical aspects, such as yoga. In both cases, further studies should assess attitudes and expectations from therapy in both verum and control groups.

According to this study, placebo controls for *Qigong* should be developed by the usage of vegetative functional assessments such as heart rate variability, thermography, and electrophysiological measurements, thus excluding major vegetative effects by the exercise, as well as by the usage of psychometric tests and other quantitative evaluations. Only with these criteria, the rigour of research can be raised while examining hypotheses regarding either the theory and/or mechanisms of *Qigong* clinical efficacy.

## CRediT authorship contribution statement

**Mário Gonçalves:** Conceptualization, Methodology, Formal analysis, Data curation, Writing - original draft. **Luís Carlos Matos:** Conceptualization, Methodology, Formal analysis, Data curation, Writing - original draft. **Leonel Duarte:** Methodology, Formal analysis, Data curation. **Jorge Machado:** Formal analysis, Data curation, Writing - review & editing. **Henry Johannes Greten:** Formal analysis, Data curation, Writing - review & editing. **Giovanna Franconi:** Formal analysis, Data curation, Writing - review & editing.

## Declaration of competing interest

The authors certify that there is no conflict of interest with any financial organisation regarding the material discussed in the manuscript Professor Henry Johannes Greten is the founder of the Heidelberg model of TCM. He teaches this model in the Master's degree of TCM at the Institute of Biomedical Sciences Abel Salazar of the University of Porto and uses it in his daily-based clinical practice.

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