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# Effects of Neuromuscular Electrical Stimulation on Quadriceps Muscle Strength and Mass in Healthy Young and Older Adults: A Scoping Review

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## Abstract

**Objective.** Although neuromuscular electrical stimulation (NMES) has been used as a safe and relevant complement to voluntary resistance training, its effectiveness in increasing quadriceps femoris muscle strength and mass in healthy young and older adults has not been determined. The aim of this scoping review was to assess the effects of NMES on quadriceps muscle strength and mass in healthy young and older adults.

**Methods.** CENTRAL, Pedro, MEDLINE, and PubMed were searched from inception to September 2019. Randomized controlled trials (RCTs) that compared NMES with control group or voluntary resistance training for healthy young and older adults were included. Study characteristics, primary and secondary outcome parameters, and details of the NMES intervention were extracted by 2 reviewers. Only studies for which full text was available in English were included.

**Results.** Thirty-two RCTs including 796 healthy participants were identified as being eligible for young adults, and 5 RCTs including 123 healthy participants were identified as being eligible for older adults. The available evidence strongly suggests that NMES improves quadriceps muscle strength compared with a control group in young adults, but its efficacy seems lower than that of voluntary resistance training. The available limited evidence regarding the effects of NMES on quadriceps muscle mass compared with control in young adults is inconclusive, with 3 RCTs showing positive effects and 3 RCTs not showing positive effects. The very limited available evidence from 5 RCTs in older adults suggests that NMES might be beneficial for increasing quadriceps muscle strength and mass.

**Conclusion.** Overall, the evidence indicates that NMES is an efficacious method for increasing quadriceps muscle strength in young adults, whereas its impact on muscle mass requires further investigations. In addition, the effectiveness of NMES needs to be confirmed in older adults on the basis of more high-quality RCTs with larger sample sizes.

**Impact.** This scoping review of 37 RCTs including 919 people is the first study, to the authors' knowledge, to show that the use of NMES increases quadriceps muscle strength in young adults and might improve quadriceps muscle strength compared with control interventions in older adults. In both young and older adults, the effects of NMES on quadriceps muscle mass are still unclear.

**Keywords:** Exercise Training, Muscle Atrophy, Neuromuscular Electrical Stimulation, Physical Therapy, Scoping Review

## Introduction

Neuromuscular electrical stimulation (NMES) consists of delivering preprogrammed trains of stimuli to muscles via surface electrodes positioned on the skin, with the ultimate goal to generate strong muscle contractions. There is now compelling evidence that NMES is a relevant and legal complement to voluntary resistance training protocols for muscle strength and mass improvement in healthy humans.<sup>1</sup> It has recently been shown that anabolic signaling pathways related to skeletal muscle hypertrophy were upregulated after NMES training protocols in a dose-dependent manner.<sup>2</sup> Moreover, we have previously showed that NMES is an effective method for increasing muscle strength and mass in healthy young humans.<sup>3</sup> These findings clearly show that NMES training can be used as a safe strategy to increase muscle strength and mass. However, NMES application through the skin leads to activation of nociceptive receptors, thereby inevitably inducing discomfort or pain sensations. As a consequence, NMES training protocols are usually performed at submaximal intensity (<60% of the maximum voluntary contraction [MVC]) so that NMES has been considered as less effective than voluntary resistance training with high loads for inducing strength gains.<sup>4</sup> Despite the previous meta-analyses evaluating the effectiveness of NMES for increasing muscle strength in young adults,<sup>4</sup> there has been a rapid increase in NMES training trials over the past decade that justifies an update. In addition, the potential hypertrophic effects of NMES have never been reviewed in healthy young adults.

Skeletal muscle mass and strength decline with age in a process termed sarcopenia. Longitudinal studies showed that muscle strength loss occurs faster than muscle atrophy in older adults.<sup>5</sup> Although voluntary resistance training has been considered as the best strategy for increasing skeletal muscle strength and mass,<sup>6</sup> older adults may be reluctant to perform voluntary resistance exercise, particularly those with poor mobility and motivation or pain.<sup>7,8</sup> In this regard, studies have shown that fewer than 15% of older people are willing to participate in resistance training programs.<sup>7,9,10</sup> These limiting factors highlight a need for alternatives to voluntary resistance training to reduce the deleterious consequences of sarcopenia.<sup>11</sup> On that basis, NMES could be an attractive strategy for minimizing muscle weakness and atrophy in older people, especially for targeting the quadriceps muscle, which is the primary locomotor muscle for daily living activities. Indeed, quadriceps muscle weakness is an important risk factor in the development of major health issues, including falls, bone fractures, disability, and mortality in the older populations.<sup>12</sup> Interestingly, NMES can be easily self-administered at home or at the bedside, thereby providing potential physical therapy for older people who are reluctant or unable to participate in voluntary resistance programs. Although NMES has been shown to be an effective strategy for limiting muscle weakness in adults with advanced progressive disease,<sup>13</sup> the impact of NMES training on quadriceps muscle strength and mass in healthy older adults remains unclear.

The aim of this scoping review was to synthesize the existing literature relative to the effects of NMES training on quadriceps muscle strength and mass in healthy young and older adults.

## Methods

A scoping review was chosen as the most appropriate form of review for studying the effects of NMES training on

quadriceps muscle strength and mass in healthy young and older adults at this time. The main intention was to identify gaps in knowledge as well as possible future directions. Moreover, the present review is reported in line with the 5-stage framework outlined by Arksey and O'Malley,<sup>14</sup> which aimed to make scoping reviews "rigorous and transparent" as well as repeatable to improve methodological rigor. This review was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses for Scoping Reviews checklist.<sup>15</sup>

## Research Question

This scoping review aimed to answer the following questions: (1) what are the effects of NMES versus control intervention on quadriceps muscle strength and mass in healthy young and older adults? and (2) what are the effects of NMES versus voluntary resistance training on quadriceps muscle strength and mass in healthy young and older adults?

## Data Sources and Searches

Four online databases (CENTRAL, Pedro, MEDLINE, and PubMed) were searched systematically from the earliest date available until September 2019, without language restriction. A broad range of keywords related to NMES ("neuromuscular electrical stimulation" or "electrical stimulation" or "electrostimulation" or "electromyostimulation") outcomes (cross-sectional area or muscle hypertrophy or muscle mass or muscle size or fiber size or magnetic resonance imaging or computed tomography or tomography or X-ray or strength or muscle force), study design (randomized controlled trial or RCT or clinical trial), and their synonyms were used (Suppl. Appendix 1). The clinical trial registry and WHO International Clinical Trial Registry Platform (<https://clinicaltrials.gov/>; <https://www.who.int/ictrp/search/en/>) were also searched for unpublished trials. Backward (reference lists) and forward (citation) tracking of the eligible articles was also conducted to identify any relevant papers. The search was finalized on September 18, 2019.

## Study Selection

Two reviewers (M.A., F.M.) independently screened the article titles and abstracts to identify relevant studies; then, they obtained full text of relevant articles. M.A. and F.M. read the full texts and assessed their content using predetermined criteria. In cases of disagreements or ambiguous issues, consensus was reached through discussion and consultation with a third reviewer, J.G.

In the present scoping review, we excluded trials that randomly assigned 1 limb of an individual to receive intervention while the other limb was considered as control. To find all relevant studies, references of included articles and reviews were cross-checked. All studies that fulfilled the following criteria were included in this scoping review.

## Type of Studies

Only randomized, controlled, and parallel trials (RCTs) were eligible for inclusion considering no publication date or publication status restrictions.

## Participants

Healthy young (>18 years to <60 years) and older adults (age >60 years) were eligible.

## Intervention and Comparators

We included RCTs comparing a form of NMES (whether called neuromuscular electrical stimulation or electrical stimulation) applied over the muscle belly compared with either a control procedure (sham, or no treatment) or voluntary resistance exercise. We included studies for which outcomes were available before (ie, pre-intervention) and after (ie, post-intervention) the procedure to evaluate treatment effectiveness.

Exclusion criteria included training protocols with NMES applied over the nerve trunk, magnetic stimulation, or whole-body electrical stimulation. NMES interventions were not limited to stimulation frequency, duty cycle, or stimulation intensity. Studies were excluded that included participants with chronic disease (eg, stroke, brain injury, spinal cord injury, cerebral palsy, cancer, chronic obstructive pulmonary disease, and heart failure), who underwent an orthopedic procedure (eg, knee ligament surgery), and who were professional or recreational athletes.

## Outcomes

Primary outcomes were pre- and post-intervention assessment of quadriceps muscle strength (one-repetition maximum [1RM], isokinetic maximal voluntary strength) and secondary outcome was quadriceps muscle mass/size (measured by validated outcome tools such as anthropometry, magnetic resonance imaging, ultrasound, computerized tomography,<sup>10</sup> or biopsy) between intervention and comparator groups.

## Quality Assessment

The quality of studies was independently assessed by 2 reviewers (M.A., F.M.) using the Cochrane Risk of Bias tool.<sup>16</sup> The tool consists of 7 domains (sequence generation, concealment of allocation, blinding, incomplete outcome data, selective outcome reporting, and other risks of bias), and each of the domains was rated as low, high or unclear risk of bias. If there were differences in the authors' ratings, it was resolved via discussion. Although risk of bias usually pertains to meta-analysis studies for evaluating the effectiveness of interventions, this analysis was performed to take into account that all the included studies were RCTs and therefore to enhance the methodology of the present scoping review.<sup>17</sup>

## Data Extraction

In the present scoping review, data were extracted and collated in Microsoft Excel (Microsoft, Redmond, WA, USA) for "sifting, charting, and sorting."<sup>14</sup> M.A. and F.M. first extracted all predetermined relevant variables, including study characteristics (number of participants randomized to control or interventions, age, first author, gender, and trial design), details of the NMES intervention (pulse duration, frequency, duty cycle, stimulation intensity, training duration, and session/week), and primary and secondary outcome parameters. Importantly, when multiple time points were assessed in a study, baseline and last time point were used for the scoping review. If raw data were not available in table or text, data were extracted using Web Plot Digitizer from figures. In addition, when several variables were available for quadriceps muscle strength (eg, isokinetic at different speeds), the mean change from baseline and respective SD were considered separately and then combined using the Cochrane calculator. SDs were calculated when not reported for pre- to-post correlation coefficient. Because this calculation needs an estimate of pre-post correlation coefficients, we conservatively applied

correlation coefficients of 0.5, as previously reported.<sup>18</sup>

$$\Delta SD = \sqrt{SD_{baseline}^2 + SD_{final}^2 - (2 \times corr \times SD_{baseline} \times SD_{final})}$$

## Data Analysis

Descriptive data from included studies were extracted under the coding categories and were analyzed quantitatively through summary counts. Data were organized, synthesized, tabulated, and summarized narratively in the text.

## Role of the Funding Source

The funders played no role in the design, conduct, or reporting of this study.

## Results

### Study Identification

A total of 3026 records were identified in our literature searches after duplicates were removed. By screening titles and/or abstracts, 2929 citations were excluded. Of 97 full-text articles obtained, 60 were excluded; the corresponding reasons are mentioned in [Supplemental Appendix 2](#). Finally, 37 studies involving healthy participants were included for analysis ([Fig. 1](#)).

### Description of Included Studies and Characteristics of Intervention

The characteristics of the included studies and their protocols are presented in [Tables 1 and 2](#). Thirty-seven studies involving 919 healthy participants were included in the present scoping review. Of them, 32 RCTs including 796 healthy participants were identified as being eligible for young adults, and 5 RCTs including 123 healthy participants were identified as being eligible for older adults. Publication dates ranged from 1982 to 2018, sample size ranged from 5 to 23 participants, and the mean age ranged from 18 to 85 years.

Of 919 included participants, 491 were part of a control or comparison group (resistance exercise training) and the remaining 428 were part of a NMES training program. Duration of interventions ranged from 3 to 16 weeks, with an average of 3 sessions per week (range of 2–6 sessions). Seven studies used NMES in combination with additional interventions (isometric exercise,<sup>19</sup> stair climbing,<sup>20</sup> voluntary contraction,<sup>21</sup> weight training with plyometric exercise,<sup>22</sup> strength training,<sup>23</sup> eccentric training,<sup>24</sup> and cycling<sup>25</sup>) compared with the same additional intervention. Regarding the stimulation parameters, stimulation frequency ranged from 20 Hz to 150 Hz for pulsed current and 2000 Hz to 5000 Hz for Russian current, and pulse duration varied from 100 to 600  $\mu$ s. Most included studies reported that stimulation intensity was gradually increased throughout the training session to a level of maximally tolerated intensity according to the pain threshold of each participant. Studies also quantified the electrically evoked force level expressed as a percentage of MVC force. The training intensity for NMES ranged from 20% to 134% MVC and from 36% to 40% MVC in young and older adults, respectively. The training intensity for voluntary resistance training ranged from 20% to 100% MVC in young adults and from 40% to 90% MVC in older adults.

### Risk of Bias Quality Assessment

The overall methodological quality of the included studies was considered as poor to moderate with an average score of 3.1

**Table 1.** Characteristics of Included RCTs for Young Adults<sup>a</sup>

Reference	Participants and Groups Allocation	Group Design	Training Protocol	Frequency	Current Characteristics	Intensity	Pulse Duration	Outcome Measure
Romero et al, 1982 <sup>40</sup>	Experimental group: n = 9; age = 22 ± 1 Control group: n = 9; age = 24 ± 3 gender: female	Experimental group: NMES Control group: no exercise	5 wk × 2 sessions/wk	2000 Hz	Russian current	50 mA	Not reported	MVC
Laughman et al, 1982 <sup>38</sup>	Experimental group: n = 20 Control groups: Group 1. n = 19 Group 2. n = 19 age = 21–39 gender: female/male	Experimental group: NMES Control groups: Group 1. isometric exercise Group 2. no exercise	5 wk × 5 sessions/wk	2500 Hz	Russian current	30% MVC	Not reported	MVC
McMiken et al, 1983 <sup>51</sup>	Experimental group: n = 8 Control group: n = 7 age = 19–27 gender: female/male	Experimental group: NMES Control group: isometric exercise	3 wk × 4 sessions/wk	75 Hz	Pulsed current	80% MVC	100 μs	MVC
Kramer et al, 1983 <sup>42</sup>	Experimental group: n = 10 Control groups: Group 1. n = 10 Group 2. n = 10 age = 21 gender: female	Experimental group: NMES Control groups: Group 1. voluntary exercise Group 2. no exercise	4–5 wk × 2–3 sessions/wk	2500 Hz	Russian current	Maximally tolerated	500 μs	MVC
Singer et al, 1983 <sup>48</sup>	Experimental group: n = 5; age = 35 ± 2 Control groups: Group 1. n = 5; age = 30 Group 2. n = 5; age = 31 gender: male	Experimental group: NMES Control groups: Group 1. no exercise Group 2. isometric exercise	4 wk × 3 sessions/wk	Not reported	Russian current	Maximally tolerated (80 mA)	Not reported	MVC
Currier et al, 1983 <sup>28</sup>	Experimental group: n = 8; age = 21 ± 2 Control groups: Group 1. n = 9; age = 25 ± 4 Group 2. n = 8; age = 23 ± 4 gender: female/male	Experimental group: NMES Control groups: Group 1. no exercise Group 2. maximal voluntary isometric contractions training	5 wk × 3 sessions/wk	2500 Hz	Russian current	60% pretest MVC or more	10 μs	MVC
Mohr et al, 1984 <sup>45</sup>	Experimental group: n = 6 Control groups: Group 1. n = 5 Group 2. n = 6 age = 21–29 gender: female	Experimental group: NMES Control groups: Group 1. isometric exercise Group 2. no exercise	3 wk × 5 sessions/wk	50 Hz	Pulsed current	Maximally tolerated	17–28 μs	MVC
Selkowitz et al, 1984 <sup>41</sup>	Experimental group: n = 12 Control group: n = 12 age = 18–32 gender: female/male	Experimental group: NMES Control group: no exercise	4 wk × 3 sessions/wk	2200 Hz	Russian current	91% MVC	450 μs	MVC
Fahey et al, 1985 <sup>30</sup>	Experimental group: Group 1. n = 9; age = 28 ± 4 gender: female Group 2. n = 9; age = 26 ± 3 gender: male Control groups: Group 1. n = 9; age = 26 ± 3 gender: female Group 2. n = 9; age = 29 ± 3 gender: male	Experimental group: NMES group gender: female/male Control group: no exercise gender: female/male	6 wk × 3 sessions/wk	50 Hz	Pulsed current	Maximally tolerated	Not reported	MVC

(Continued)



**Table 1.** Continued

Reference	Participants and Groups Allocation	Group Design	Training Protocol	Frequency	Current Characteristics	Intensity	Pulse Duration	Outcome Measure
Hartsell et al, 1986 <sup>19</sup>	Experimental groups: Group 1. n = 6 Group 2. n = 6 Control group: n = 4 age = 18–35 gender: male	Experimental groups: Group 1. monopolar NMES + isometric exercise Group 2. bipolar NMES + isometric exercise Control group: isometric exercise	6 wk × 5 sessions/wk	65 Hz	Pulsed current	Maximally tolerated	2 ms	MVC
Kubiak et al, 1987 <sup>36</sup>	Experimental group: n = 10 Control groups: Group 1. n = 10 Group 2. n = 9 age = 18–30 gender: female/male	Experimental group: NMES Control groups: Group 1. isometric exercise Group 2. no exercise	5 wk × 3 sessions/wk	50 Hz	Pulsed current	45% MVC	Not reported	MVC
Lai et al, 1988 <sup>37</sup>	Experimental groups: Group 1. n = 8; age = 25 ± 3 Group 2. n = 8; age = 27 ± 3 Control group: n = 8; age = 23 ± 3 gender: female/male	Experimental groups: Group 1. low-intensity NMES Group 2. high-intensity NMES Control group: no exercise	3 wk × 5 sessions/wk	50 Hz	Pulsed current	25% MVC 50% MVC	200 μs	MVC
Hortobagyi et al, 1998 <sup>34</sup>	Experimental group: n = 8; age = 26 ± 7 Control groups: Group 1. n = 8; age = 23 ± 2 Group 2. n = 6; age = 24 ± 3 gender: female	Experimental group: NMES Control groups: Group 1. voluntary exercise Group 2. no exercise	6 wk × 4 sessions/wk	2500 Hz	Russian current	Maximally tolerated	Not reported	MVC
Hortobagyi et al, 1999 <sup>57</sup>	Experimental group: n = 8 Control group: n = 8 age = 25 ± 4. gender: female	Experimental group: NMES Control group: voluntary exercise	6 wk × 4–6 sessions/wk	2500 Hz	Russian current	Maximally tolerated	Not reported	MVC
Pérez et al, 2002 <sup>49</sup>	Experimental group: n = 10; age = 22 Control group: n = 5; age = 22 gender: male	Experimental group: NMES Control group: no exercise	6 wk × 3 sessions/wk	45–60 Hz	Pulsed current	Maximally tolerated	300 μs	Fiber CSA
Bircan et al, 2002 <sup>26</sup>	Experimental groups: Group 1. n = 10 Group 2. n = 10 Control group: n = 10; age = NR gender: female/male	Experimental groups: Group 1. NMES with bipolar interferential current Group 2. NMES with low-frequency current Control group: no exercise	3 wk × 5 sessions/wk	80 Hz	Pulsed current	Maximally tolerated	100 μs	MVC
Porcari et al, 2002 <sup>46</sup>	Experimental group: n = 16; age = 19 ± 1 Control group: n = 11; age = 20 ± 1 gender: female	Experimental group: NMES Control group: concurrent sham stimulation sessions	8 wk × 3 sessions/wk	45–150 Hz	Pulsed current	Maximum tolerated	Not reported	MVC
Parker et al, 2003 <sup>39</sup>	Experimental group: n = 9 Control group: n = 9; age = 23 ± 3 gender: female/male	Experimental group: NMES Control group: no exercise	4 wk × 2–3 sessions/wk	5000 Hz	Russian current	63%–69% MVC	200 μs	MVC
Lategan et al, 2004 <sup>43</sup>	Experimental group: n = 5; age = 22 Control group: n = 10; age = 22 gender: female/male	Experimental group: NMES Control group: no exercise	5 wk × 3 sessions/wk	50 Hz	Pulsed current	39% MVC	100 μs	MVC

(Continued)

Table 1. Continued

Reference	Participants and Groups Allocation	Group Design	Training Protocol	Frequency	Current Characteristics	Intensity	Pulse Duration	Outcome Measure
Herrero et al, 2006 <sup>32</sup>	Experimental group: n = 10; age = 19 ± 1 Control group: n = 10; age = 21 ± 1 gender: male	Experimental group: NMES Control group: no exercise	4 wk × 4 sessions/wk	120 Hz	Pulsed current	Maximally tolerated	400 µs	MVC
Gondin et al, 2005 <sup>31</sup>	Experimental group: n = 12; age = 23 ± 5 Control group: n = 8; age = 24 ± 2 gender: male	Experimental group: NMES Control group: no exercise	8 wk × 4 sessions/wk	75 Hz	Pulsed current	68% MVC	400 µs	MVC muscle CSA
Bezerra et al, 2009 <sup>21</sup>	Experimental group: n = 11; age = 23 ± 4 Control group: n = 10; age = 26.0 ± 5 gender: NR	Experimental group: NMES + voluntary contraction group Control group: voluntary contraction group	6 wk × 3 sessions/wk	100 Hz	Pulsed current	Maximally tolerated	400 µs	MVC muscle CSA
Baskan et al, 2010 <sup>50</sup>	Experimental group: n = 10 Control group: n = 10; age = 21 ± 1 gender: NR	Experimental group: NMES Control group: maximum voluntary isometric contraction group	6 wk × 3 sessions/wk	2500 Hz	Russian current	Maximally tolerated	Not reported	MVC
Zory et al, 2010 <sup>47</sup>	Experimental group: n = 12; age = 24 ± 3 Control group: n = 8; age = 25 ± 4 gender: male	Experimental group: NMES Control group: no exercise	4 wk × 4 sessions/wk	75 Hz	Pulsed current	Maximally tolerated	400 µs	MVC
Herrero et al, 2010 <sup>22</sup>	Experimental group: n = 11; age = 21 ± 3 Control group: n = 8; age = 21 ± 2 gender: male	Experimental group: NMES + weight + plyometric Control group: weight + plyometric	4 wk × 2 sessions/wk	120 Hz	Pulsed current	Maximally tolerated	400 µs	MVC
Draz et al, 2014 <sup>29</sup>	Experimental group: n = 20 age = 22 ± 4 Control groups: Group 1. n = 20; age = 23 ± 3 Group 2. n = 20; age = 22 ± 4 gender: male	Experimental group: NMES Control groups: Group 1. isokinetic contraction training Group 2. control group	4 wk × 3 sessions/wk	2500 Hz	Russian current	Maximally tolerated	200 µs	MVC
Altug et al, 2015 <sup>44</sup>	Experimental group: n = 13 age = 21 ± 1 Control group: n = 12; age = 22 ± 2 gender: NR	Experimental group: NMES Control group: no exercise	4 wk × 3 sessions/wk	2500 Hz	Russian current	Maximally tolerated	Not reported	MVC
Abulhasan et al, 2016 <sup>23</sup>	Experimental group: n = 10 Control group: n = 10 age: male = 20 ± 4; female = 19 ± 1 gender: female/male	Experimental group: NMES + strength training Control group: strength training	3 wk × 5 sessions/wk	50 Hz	Pulsed current	75%–134% MVC	400 µs	1RM muscle CSA
Bousetta et al, 2016 <sup>27</sup>	Experimental groups: Group 1. n = 8; age = 22 ± 1 Group 2. n = 8; age = 21 ± 1 Control group: n = 8; age = 21 ± 2 gender: male	Experimental groups: Group 1. NMES morning training Group 2. NMES evening training Control group: no exercise	4 wk × 3 sessions/wk	100 Hz	Pulsed current	Maximally tolerated	400 µs	1RM
Kadri et al, 2017 <sup>35</sup>	Experimental group: n = 12 age = 22.7 ± 2.7 Control groups: Group 1. n = 12; age = 22 ± 1 Group 2. n = 12; age = 23 ± 1 gender: male	Experimental group: NMES Control groups: Group 1. voluntary training Group 2. no exercise	8 wk × 3 sessions/wk	50 Hz	Pulsed current	20% MVC	380 µs	MVC
Da Silva et al, 2018 <sup>24</sup>	Experimental group: n = 13; age = 25 ± 5 Control group: n = 15; age = 25 ± 5 gender: female/male	Experimental group: NMES + eccentric training Control group: eccentric training	6 wk × 2 sessions/wk,	80 Hz	Pulsed current	Maximally tolerated	400 µs	MVC muscle CSA
Mathes et al, 2017 <sup>25</sup>	Experimental group: n = 11 Control group: n = 10; age = 23 ± 5 gender: male	Experimental group: NMES + cycling Control group: cycling	4 wk × 5 sessions/wk	80 Hz	Pulsed current	Maximally tolerated	400 µs	Force

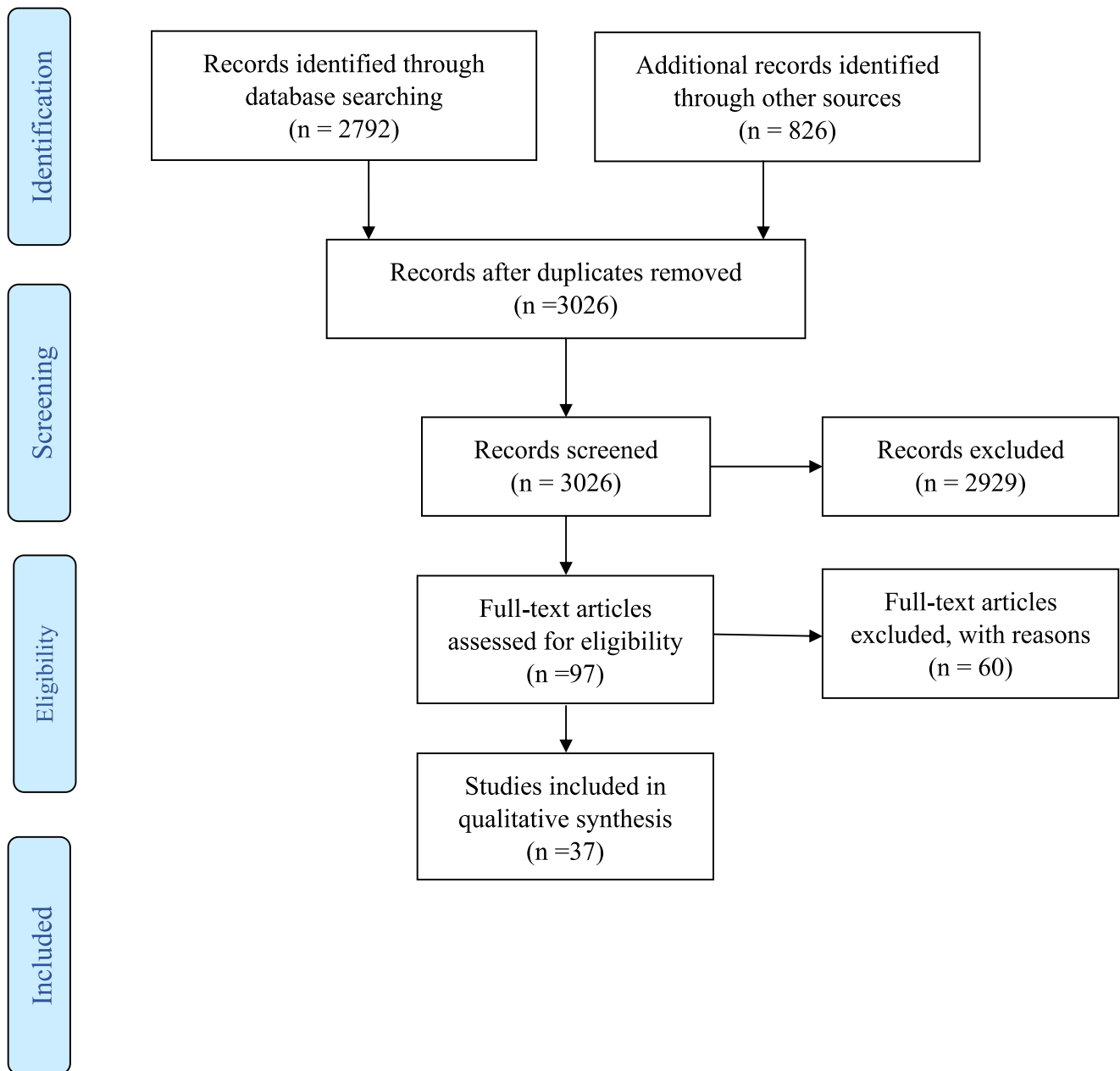
<sup>a</sup> CSA = cross-sectional area; MVC = maximum voluntary contraction; NMES = neuromuscular electrical stimulation; NR = not reported; RCT = randomized controlled trial.

**Table 2.** Characteristics of included RCTs for older adults<sup>a</sup>

Study	Participants and Group Allocations	Group Design	Training Protocol	Frequency	Current Characteristics	Intensity	Pulse Duration ( $\mu$ s)	Outcome Measure
Caggiano et al, 1994 <sup>55</sup>	Experimental group: n = 11 Control group: n = 7 age: 72 $\pm$ 4 gender: male	Experimental group: NMES Control group: submaximal VIC	4 wk $\times$ 3 sessions/wk	25–50 Hz	Pulsed current	38%–45% MVC	100–113 $\mu$ s	MVC
Paillard et al, 2004 <sup>20</sup>	Experimental group: n = 10; age: 67 $\pm$ 3 Control group: n = 11; age = 67 $\pm$ 3 gender: female	Experimental group: NMES + stair-climbing Control group: stair-climbing	6 wk $\times$ 4 sessions/wk	20 Hz	Pulsed current	Maximal tolerated	350 $\mu$ s	MVC
Benavent-Caballer et al, 2014 <sup>54</sup>	Experimental group: n = 22; age = 83 $\pm$ 4 Control groups: Group 1. n = 23; age = 84 $\pm$ 6 Group 2. n = 22; age = 85 $\pm$ 5 gender: female/male	Experimental group: NMES Control group: no exercise voluntary contraction	16 wk $\times$ 3 sessions/wk	50 Hz	Pulsed current	40% MVC	400 $\mu$ s	Rectus femoris CSA
Zampieri et al, 2016 <sup>56</sup>	Experimental group: n = 10 age = 71 $\pm$ 7 Control group: n = 7; age = 70 $\pm$ 3 gender: female/male	Experimental group: NMES Control group: leg press	9 wk $\times$ 3 sessions/wk	60 Hz	Pulsed current	40% MVC	Not reported	MVC Fiber CSA
Filippo et al, 2016 <sup>53</sup>	Experimental group: n = 14 Control group: n = 8 age = 70 $\pm$ 2 gender: male	Experimental group: NMES Control group: no exercise	8 wk $\times$ 3 sessions/wk	75 Hz	Pulsed current	Maximally tolerated	400 $\mu$ s	MVC

<sup>a</sup> CSA = cross-sectional area; MVC = maximum voluntary contraction; NMES = neuromuscular electrical stimulation; RCT = randomized controlled trial; VIC = voluntary isometric contractions.





**Figure 1.** PRISMA flow diagram of study selection.

out of 7 on the Cochrane risk of bias tool. In this review, although all the 37 included studies have declared randomization, only 6 of them described the randomization process, and an unclear risk of bias was considered in the remaining 31 studies. Although blinding is desirable, it was hard to apply in these trials because no study mentioned blinding of participants and personnel, and only 5 of the included studies reported blinding of outcome assessors. Finally, selective reporting bias in a majority of studies was considered as low risk. The results of the risk of bias assessment are provided in Figure 2.

### Young Adults

#### NMES Versus Control Intervention: Quadriceps Muscle Strength

Twenty-eight RCTs involving 647 participants (333 of whom received NMES treatment, and the 314 remaining served as control) assessed quadriceps muscle strength in young adults using a dynamometer or 1RM by free weights. Among them, 22 RCTs (78.6%)<sup>19,21,23,24,26-43</sup> reported a significant improvement of quadriceps muscle strength after NMES, while 6 RCTs (21.4%)<sup>25,44-48</sup> reported non-significant changes. Changes in quadriceps muscle strength after

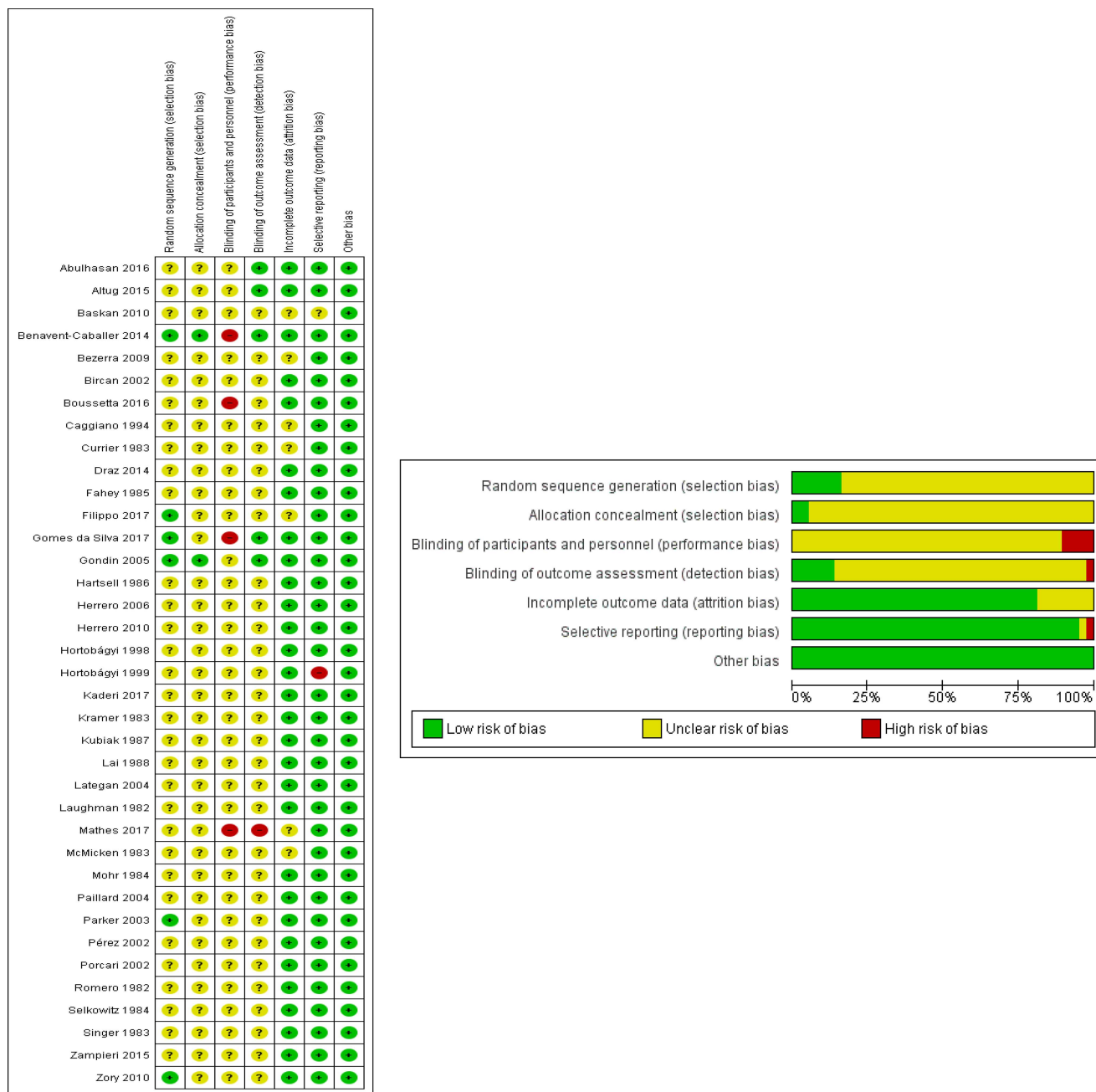


Figure 2. Results of the risk of bias assessment.

NMES ranged from +0.74%<sup>45</sup> to +48.5%,<sup>37</sup> with a mean improvement of approximately 14.5%. The corresponding NMES training intensity ranged from 20%<sup>35</sup> to 134%<sup>23</sup> MVC. NMES training duration ranged from 3<sup>23,37,45</sup> to 8<sup>31,35,46</sup> weeks, with an average of 3 sessions per week. NMES was performed in combination with an additional intervention, including isometric exercise,<sup>19,21</sup> knee extension,<sup>24,44</sup> plyometric training,<sup>32</sup> and cycling<sup>26</sup> in 6 studies.

**NMES Versus Control Intervention: Quadriceps Muscle Mass**

Six RCTs involving 124 participants (66 of whom received NMES treatment, and the 58 remaining served as control) assessed the effects of NMES on muscle mass using anthropometry,<sup>32</sup> ultrasonography,<sup>23,24,31</sup> histology,<sup>49</sup> and MRI.<sup>21</sup>

Among them, 3 RCTs (50%)<sup>31,32,49</sup> reported significant increase in quadriceps muscle mass after NMES, whereas 3 RCTs (50%)<sup>21,23,24</sup> failed to observe significant changes. Changes in quadriceps muscle mass after NMES ranged from +3%<sup>21</sup> to +14%,<sup>49</sup> with a mean improvement of approximately 6.7%. The corresponding NMES training intensity ranged from 68%<sup>31</sup> to 134%<sup>23</sup> MVC. In those 3 RCTs that reported a non-significant increase in quadriceps muscle mass, NMES was performed in combination with an additional intervention, including isometric<sup>21</sup> and dynamic exercises.<sup>23,24</sup> Interestingly, the training duration ranged from 4<sup>32</sup> to 8<sup>31</sup> weeks with an average of 4 sessions per week (66 NMES training sessions in total) in RCTs showing significant muscle hypertrophy, whereas the training duration ranged from 3<sup>23</sup> to 6<sup>21,24</sup> weeks with an average of 3 sessions per

week (45 NMES training session in total) in RCTs showing no significant changes in muscle mass.

#### NMES Versus Voluntary Resistance Training: Quadriceps Muscle Strength

Eleven RCTs with 247 participants (125 of whom received NMES treatment, while the 122 performed voluntary resistance training) compared quadriceps muscle strength in young adults using a dynamometer. Among them, 9 RCTs (81.8%)<sup>28,29,34–36,38,42,50,51</sup> reported that NMES and voluntary resistance training improved quadriceps muscle strength, whereas 2 RCTs (18.2%)<sup>45,52</sup> reported non-significant changes in quadriceps strength after NMES training. Changes in quadriceps muscle strength in NMES groups ranged from +0.74%<sup>45</sup> to +36%<sup>34</sup> with a mean improvement of 15.3%. Changes in quadriceps muscle strength ranged from +9.2%<sup>42</sup> to +54%<sup>34</sup> after voluntary resistance training, with a mean improvement of approximately 21.8%. The training intensity for NMES ranged from 20%<sup>35</sup> to 80%<sup>51</sup> MVC. Also, the training intensity for voluntary resistance training ranged from 20%<sup>35</sup> to 100% MVC.<sup>29,34,36,38,42</sup> The training duration for both NMES and voluntary resistance training ranged from 3 weeks<sup>45,51</sup> to 6 weeks,<sup>34,50</sup> with an average of 3 sessions a week. In all RCTs except 1,<sup>29</sup> which used isokinetic exercise, isometric contractions were always performed during voluntary resistance training program.

#### NMES Versus Voluntary Resistance Training: Quadriceps Muscle Mass

A single RCT reported larger but non-significant changes in a cross-sectional area (assessed by anthropometry) after NMES compared with voluntary resistance training.<sup>50</sup> NMES involved 10 repetitions of 10-second contractions with 50-second rest periods between, with Russian current (2500 Hz) for 3 sessions per week for 6 weeks at a stimulation intensity eliciting tetanic contractions. The voluntary resistance training group performed maximal voluntary isometric knee extensions (10 repetitions of 10 seconds, with 50-second relaxing periods in between) with 3 sessions per week for 6 weeks.

#### Older Adults

##### NMES Versus Control Intervention: Quadriceps Muscle Strength

Two RCTs with 43 participants (25 NMES vs 15 control) assessed quadriceps muscle strength in older adults using a dynamometer and reported a significant improvement of quadriceps muscle strength after NMES. Changes in quadriceps muscle strength after NMES ranged from +18.7%<sup>20</sup> to +20%<sup>53</sup> with a mean improvement of approximately 19.5%. The corresponding NMES training intensity in both RCTs was determined according to each individual maximally tolerable intensity. NMES training duration ranged from 6<sup>20</sup> to 8<sup>53</sup> weeks, with an average of 3 sessions per week.

##### NMES Versus Control Intervention: Quadriceps Muscle Mass

A single RCT with 55 participants (22 NMES vs 23 control) assessed quadriceps muscle mass in older adults using ultrasonography.<sup>54</sup> This high-quality RCT (risk of bias score = 6) reported a significant increase in rectus femoris muscle cross-sectional area (ie, +30%, measured by ultrasonography) after

NMES compared with control. NMES involved 15 stimulation trains delivered at 50 Hz, with a training intensity reaching 40% MVC. The training program included 3 sessions per week for 16 weeks.

#### NMES Versus Voluntary Resistance Training: Quadriceps Muscle Strength

Two RCTs with 35 participants (21 of whom received NMES treatment, and 14 performed voluntary resistance training) assessed quadriceps muscle strength by dynamometer. These 2 RCTs reported a significant improvement of quadriceps muscle strength after both NMES and voluntary resistance training. Changes in quadriceps muscle strength ranged from +8.5%<sup>55</sup> to +10.7%<sup>56</sup> after NMES, with a mean improvement of approximately 9.6%. Changes in quadriceps muscle strength ranged from +9.7%<sup>55</sup> to +10.4%<sup>56</sup> after voluntary resistance training, with a mean improvement of approximately 10%. The training intensity ranged from 36%<sup>56</sup> to 40%<sup>55</sup> MVC for NMES and from 42%<sup>55</sup> to 90%<sup>56</sup> MVC for the voluntary resistance training protocols. The training duration ranged from 4 weeks<sup>55</sup> to 9 weeks,<sup>56</sup> with an average of 3 sessions per week.

#### NMES Versus Voluntary Resistance Training: Quadriceps Muscle Mass

Two RCTs involving 62 participants (32 of whom received NMES treatment and 30 performed voluntary resistance training) assessed the effects of NMES on quadriceps muscle mass in older adults using biopsy<sup>56</sup> and ultrasonography.<sup>54</sup> These 2 RCTs reported a significant increase in quadriceps muscle mass after NMES, and this parameter was either increased<sup>54</sup> or unchanged<sup>56</sup> after voluntary resistance training. Changes in quadriceps muscle mass after NMES were +33%<sup>54</sup> in rectus femoris and 7%<sup>56</sup> in vastus lateralis, with a mean increase of 20%. Changes in quadriceps muscle mass voluntary resistance training were +12%<sup>54</sup> in rectus femoris and -5%<sup>56</sup> in vastus lateralis, with a mean increase of 3.5%. The corresponding NMES training intensity ranged from 36%<sup>56</sup> to 40%<sup>54</sup> MVC and from 40%<sup>54</sup> to 90%<sup>56</sup> MVC for voluntary resistance training. The training duration ranged from 9 weeks<sup>56</sup> to 16 weeks,<sup>54</sup> with an average of 3 sessions per week.

## Discussion

This is the first scoping review, aimed at determining the effectiveness of NMES training on quadriceps muscle strength and mass compared with control and resistance training interventions in both healthy young and older adults. The available evidence indicates that NMES is a relevant method for increasing quadriceps muscle strength in young adults, but its efficacy seems lower than voluntary resistance training. In addition, the effects of NMES on quadriceps muscle mass are still unclear in young adults. Finally, although evidence is emerging that NMES might be attractive for increasing quadriceps muscle strength and mass in older adults, the effectiveness of NMES needs to be confirmed in more high-quality RCTs with larger sample sizes.

In the present scoping review, we followed the Cochrane guidelines for risk of bias assessment for RCT studies. The overall methodological quality of the included studies was considered poor to moderate, with an average score of 3.1 out of 7 on the Cochrane risk of bias tool. In this scoping

review, all the included studies have declared randomization; however, most of them did not report the generation of random sequence. Although blinding is desirable, the trials did not report blinding of personnel and/or participants, and they seldom reported assessor blinding and allocation concealment. The sample sizes were also small in the majority of studies included in this review.

### Young Adults

Although more data, new analyses, and quality of the evidence using Cochrane risk of bias tool were included in the present work, the overall conclusion is similar to a previous systematic review and meta-analysis published almost 15 years ago.<sup>4</sup> The available evidence from 22 RCTs shows that NMES is beneficial for improving quadriceps muscle strength in young adults compared with control. Thus, NMES can be considered as effective training for young adults who seek to increase quadriceps muscle strength. It should, however, be pointed out that there was a large variability among the included studies in terms of NMES training duration (ie, range = 3–8 weeks) and training intensity (range = 20%–134% MVC). This could explain why NMES-induced quadriceps strength gains widely differ among studies (range = +0.74%<sup>45</sup> to +48.5%,<sup>37</sup> mean strength gains of approximately 14.5%), even though further studies are warranted to determine the optimal training dose and intensity on quadriceps strength improvement.

The available evidence from 11 RCTs that compared NMES versus voluntary resistance training strongly suggests that these 2 training modalities are efficient for improving quadriceps muscle strength in young adults. Our findings indicate that NMES training is not more (or less) effective than resistance exercise training for increasing quadriceps muscle strength in young adults. Indeed, of 11 included studies in this review, it turns out that NMES-induced strength gains (approximately 15%) seem lower than the strength improvement obtained after voluntary resistance training (approximately 22%), although no statistical analysis was performed. This is in agreement with the previous meta-analysis.<sup>4</sup> It should, however, be pointed out that the training intensity ranged from 20% to 80% MVC for NMES, whereas this variable reached 100% MVC for voluntary resistance training. This could explain why NMES-induced quadriceps strength gains seem lower than those obtained after voluntary resistance training, even though further studies are needed to objectively determine the contribution of this factor on quadriceps muscle strength improvement.

This is the first scoping review, to our knowledge, focusing on the potential hypertrophic effects of NMES in young adults. The evidence regarding the effectiveness of NMES for increasing quadriceps muscle mass in young adults compared with control is inconclusive. Indeed, 3 RCTs<sup>31,32,49</sup> showed beneficial effects of NMES on quadriceps muscle mass with a mean increase reaching approximately 7% (range = +3%<sup>21</sup> to +14%<sup>49</sup>). On the contrary, 3 RCTs reported a non-significant increase in quadriceps muscle mass after NMES performed in combination with voluntary exercise.<sup>21,23,24</sup> It is noteworthy that a lower number of training sessions was performed in the 3 RCTs showing no quadriceps muscle hypertrophy compared with the 3 RCTs in which a significant increase in quadriceps muscle mass was observed (ie, 45 vs 66 sessions, respectively), thereby indicating the need for investigating the effects of NMES training dose on quadriceps muscle mass. It should also be pointed out that

we judged the quality of the evidence for muscle mass to be low to extremely low, and RCTs mostly involved small sample sizes, with only 124 young adults (66 participants for NMES intervention and 58 participants as control group) and no more than 13 participants in the NMES intervention group. The divergent findings regarding the effectiveness of NMES for increasing quadriceps muscle mass in young adults may be due to the differences in sample sizes, intervention protocols, and diversity of measuring instruments and different tools and strategies for muscle mass assessment. So far, only a single RCT<sup>50</sup> examined the effectiveness of NMES compared with isometric resistance training for increasing quadriceps muscle mass in young adults. Although a larger change in quadriceps muscle cross-sectional area was reported after NMES, this difference was not statistically significant compared with voluntary resistance training. Overall, although NMES can upregulate anabolic/muscle remodeling signaling pathways,<sup>58</sup> further studies are needed to carefully investigate its effectiveness on skeletal muscle hypertrophy. Taken together, the present scoping review suggests that NMES remains an interesting training modality for young adults but cannot be considered as a surrogate to voluntary resistance training.

### Older Adults

Despite the widespread use of NMES in young adults, the evidence regarding the effectiveness of NMES on quadriceps muscle strength and mass in healthy older adults remains anecdotal as illustrated by the paucity of NMES studies (ie, only 2 RCTs) performed in this population. The very limited available evidence from 2 RCTs<sup>20,53</sup> involving 43 participants (25 NMES vs 15 control) in older adults suggests that NMES might be beneficial for quadriceps muscle strength improvement (approximately 20%). This seems to be consistent with a recent systematic review<sup>59</sup> evaluating the effects of NMES training on lower limb muscle function in elderly. The very limited available evidence from 2 RCTs<sup>55,56</sup> comparing NMES with voluntary resistance training program in older adults suggest that NMES-induced strength gains (approximately 9.6%) seem similar to those observed after voluntary resistance training (approximately 10%). Although the training intensity during NMES was submaximal (ie, <40% MVC) in these 2 RCTs, likely due to discomfort or pain sensations, and was either similar<sup>55</sup> or much lower<sup>56</sup> than that reached during voluntary resistance training protocols, the latter training modality was not superior to the former for increasing quadriceps muscle strength. Overall, the very limited available evidence from only 2 RCTs suggests that NMES training might be relevant for increasing quadriceps muscle strength in older adults who are reluctant to perform voluntary resistance exercise.<sup>7,8</sup> However, additional RCTs are needed to carefully investigate the potential strengthening effects of NMES in this population.

The available evidence regarding the effectiveness of NMES training for increasing quadriceps muscle mass in older adults compared with either control or voluntary resistance training intervention is also limited. So far, a single study<sup>54</sup> showed up to a nearly 30% increase in rectus femoris muscle cross-sectional area after NMES compared with a control intervention. From the 2 included RCTs, quadriceps muscle mass increased after 16 weeks of either NMES or resistance training protocols,<sup>54</sup> whereas myofiber size was either slightly



increased after NMES or significantly decreased after voluntary training.<sup>56</sup> These results could also be explained by the small sample size and the small number of published RCTs assessing muscle mass in older adults. It is noteworthy that, because skeletal muscle mass begins to decline around the age of 40 to 50 years,<sup>60</sup> even a modest increase in muscle mass might be very important in this population. Also, considering the specificity of motor unit recruitment associated with NMES,<sup>61</sup> this training modality could be relevant to target type II muscle fibers that appear to be more vulnerable and more susceptible to atrophy than type I fibers.<sup>62,63</sup> Overall, there have been very few RCTs on the effect of NMES on quadriceps muscle strength and mass in older adults, and the previous findings must be cautiously interpreted. Overall, more high-quality RCTs should be performed to determine whether and to what extent NMES could be a relevant strategy for minimizing the deleterious effects of sarcopenia. This should include NMES training characteristics similar to those used in young adults to assess potential age-dependent NMES effectiveness for increasing quadriceps muscle strength and mass.

### Limitations

There are some limitations in this scoping review. First, the majority of included studies had low to moderate quality and small sample size as outlined in the discussion. In addition, only 1 study meeting the inclusion criteria examined the effect of NMES on muscle mass compared with control in older adults. Second, because of the sex difference in electrical excitability responses and therefore requirement of different current doses to optimize treatment effectiveness,<sup>64,65</sup> it would be important to determine whether the effectiveness of NMES is sex dependent. Third, evaluating the effectiveness of NMES on quadriceps muscle function (eg, walking distance, endurance capacity, etc) was beyond the scope of the present scoping review and should be addressed in future studies. Fourth, studies involving professional or recreational athletes were excluded from the present scoping review, thereby potentially limiting the interpretation of the comparison between NMES and voluntary training programs. Fifth, the present scoping review focuses on healthy older adults, but growing evidence is emerging that illustrates MES is an efficacious tool for increasing quadriceps muscle strength and mass in individuals with chronic disease.<sup>66,67</sup> Finally, this scoping review demonstrates that the currently available evidence regarding the effectiveness of NMES on quadriceps muscle strength and mass in healthy young and older adults is too sparse and heterogeneous to apply meta-analysis. There are, however, some relevant RCT data that in combination with future research have the potential to yield more definitive conclusions in this field.

This scoping review suggests that NMES is a relevant method for increasing quadriceps muscle strength in young adults, but its efficacy for inducing muscle hypertrophy is still unclear. In the same way, the effects of NMES on both quadriceps muscle strength and mass remain to be carefully investigated in healthy older adults. The current literature is strongly limited by studies of poor to moderate quality. Overall, more high-quality RCTs with larger sample sizes are required to assess the effectiveness of NMES, especially in older adults.

### Author Contributions

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### Systematic Review Registration

This systematic review was registered in PROSPERO, the International Prospective Register of Systematic Reviews (ref. no. CRD42020151204).

### Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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