



The additive effect of neuromuscular electrical stimulation and resistance training on muscle mass and strength

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Received: 5 October 2024 / Accepted: 23 December 2024

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Abstract

Purpose To compare strength and muscle mass development between conventional resistance training (RT) and a combined resistance training with neuromuscular electrical stimulation group (RT + NMES).

Methods Searches of EBSCO, GoogleScholar, PubMed, and ResearchGate were conducted for studies that met the inclusion criteria of being a randomized controlled trial comparing RT in isolation with NMES and RT being done simultaneously. Effect sizes were calculated as the standard mean difference (SMD) and meta-analyses were computed using random effects models. Thirteen studies were included in the analyses.

Results When comparing strength gain, there was a favorable effect towards superimposed training (SMD: 0.31; 95% CI 0.13–0.49; $p=0.02$; $I^2=73.05\%$) with similar results seen for muscle mass (SMD: 0.26; 95% CI 0.04–0.49; $p=0.02$; $I^2=21.45\%$).

Conclusion Use of NMES during RT results in greater gains in strength and muscle mass compared to RT performed in isolation. Incorporation of NMES into RT protocols may represent a more effective strategy to improve muscle strength and muscle mass. Future studies should explore whether use of NMES concurrently with RT may have additive effects on metabolic and/or cardiovascular health.

Communicated by Michael I Lindinger.

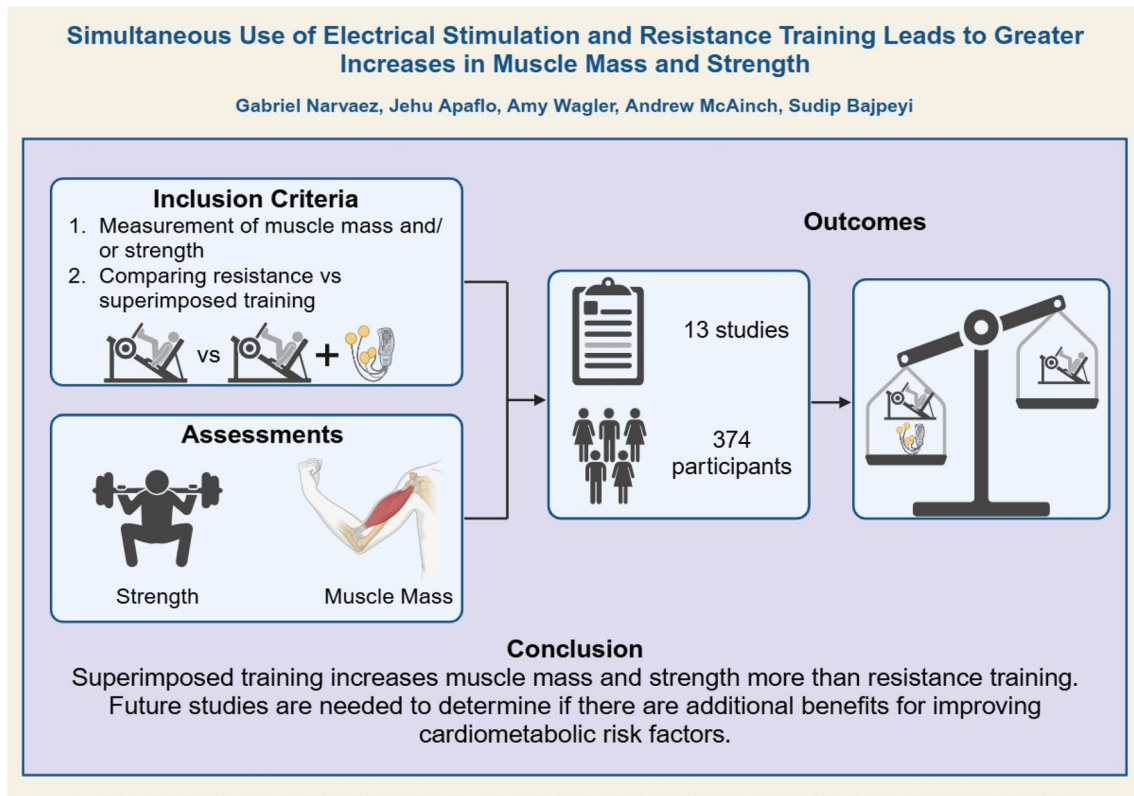
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Graphical Abstract



Keywords Electrical stimulation · Muscular strength · NMES · Strength training

Introduction

Resistance training (RT) defined as dynamic or static muscular contractions against external resistance (Philips 2007), has long been shown to improve body composition (Candow and Burke 2007; Fyfe et al. 2022; Grgic et al. 2022), increase muscular strength (Fyfe et al. 2022; Currier et al. 2023; Grgic et al. 2022) and is recommended for all ages (Grgic et al. 2020; Stricker et al. 2020; Fragala et al. 2019; McQuilliam et al. 2020; Lesinski et al. 2020). Similarly, the use of neuromuscular electrical stimulation (NMES) has also been shown to increase strength and muscle mass in upper and lower body musculature (Mukherjee et al. 2023; Porcari et al. 2002; Corso et al. 2006; Jandova et al. 2020). NMES presents a cost effective, noninvasive, alternative strategy to induce involuntary muscle contractions (Dehail et al. 2008), whereas traditional resistance training utilizes voluntary muscle contractions. Analogous to the action potential mechanism involved in voluntary muscle contraction, the electrical current from NMES stimulates motor axons and/or intramuscular nerve endings (Hultman et al. 1983; Gobbo et al. 2014), causing changes to the

muscle membrane potential, which in turn causes calcium to be released, activating the signaling cascade that leads to skeletal muscle contraction (Silverthorn 2020). Notably, NMES has a unique form of motor unit recruitment that appears to be random and nonselective in nature (Bickel et al. 2011; Maffiuletti 2010), whereas resistance training recruits smaller motor units, increasing in size until enough motor units are recruited for the force generated for muscle contraction (Henneman et al. 1965). Given the altered motor unit recruitment seen with NMES, it is possible that proportionally, a relatively larger number of large motor units may be recruited at any given quantity of force compared to voluntary contractions. This is due to larger diameter axons being excited easily from electrical stimuli with NMES, even at low intensities (Maffiuletti 2010). Moreover, engaging larger motor units, which are generally composed of highly glycolytic type II fibers can be challenging with voluntary exercise among orthopedic patients who might not be capable of performing high-load resistance training due to injury or a recent surgical operation (Hainaut and Duchateau 1992; Silverthorn et al. 2020; Maffiuletti 2010). Therefore, combining voluntary exercise with NMES could offer a potential

advantage in improving strength and/or muscle mass in comparison to conventional voluntary exercise.

While a recent meta-analysis comparing NMES to resistance training has shown similar improvements in muscle strength, a small but not statistically significant effect favoring superimposed NMES on RT was noted (Happ and Behringer 2022). The authors determined that statistical power was limited in this study due to the small sample size, and further study was needed. To our knowledge, there are no systematic review and meta-analysis studies to date that evaluate the effectiveness of using NMES with RT. To address this gap, this systematic review and meta-analysis aimed to assess the effects of superimposed NMES on resistance training induced increases in muscle strength and muscle mass compared to conventional RT.

Methods

Electronic search strategy and eligibility criteria

This meta-analysis and systematic review was performed in accordance with the Cochrane Collaboration (Higgins et al. 2022) and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Page et al. 2021). The protocol of the study was registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42022341872). Randomized controlled trials and intervention studies performed in humans that examined the effect of superimposing NMES on RT-induced muscle contractions as it relates to muscle strength and muscle mass were included. A computerized search was performed on EBSCO, GoogleScholar, PubMed, and ResearchGate to identify potential literature. The following keywords were initially used across the aforementioned databases: “neuromuscular electrical stimulation” OR “NMES” OR “electrical stimulation” AND “resistance training” OR “strength training” OR “weight training” AND “muscular strength” OR “strength” AND “muscle mass” OR “mass” OR “body composition.” References of selected studies were also reviewed to identify additional studies that could be included that were not found with the search terms. The search was not restricted to any geographical location or sex but was restricted to those without any neurological or muscular impairments, studies published in English or with an English translation available, and studies conducted in humans. The electronic search was performed without a date limitation.

Study selection

In accordance with AMSTAR 2 recommendations (Shea et al. 2017), two researchers (G.N. and J.A.) independently located and reviewed the title and abstract of the prospective

articles to confirm that the following inclusion criteria were met for the systematic review: (1) studies contain both RT and a superimposed group, (2) NMES was administered over the skin, (3) muscle strength, muscle mass and/or body composition were evaluated as an outcome, (4) there were no neurological or muscular impairments in the participants, (5) original data was reported in the studies, (6) studies were conducted in humans, (7) studies were randomized controlled trials and (8) studies were published in English or had an English translation available. Studies that met the inclusion criteria for the systematic review were considered for inclusion in the meta-analysis if they met the following additional criteria: articles clearly presented the pre- and post-intervention data with the mean and standard deviation or standard error of mean values. All reviewers reviewed the selected articles for any discrepancies in inclusion criteria and after articles were identified based on the initial inclusion criteria, a full-text review of all articles was performed preceding data extraction.

Data collection and extraction

Authors independently extracted relevant data which included the following: (1) author name, (2) age of participants, (3) description of the study population, (4) sex distribution, (5) study duration, (6) days of training performed per week, (7) NMES protocol, (8) RT protocol, and (9) methods used to assess muscle strength and muscle mass. The meta-analysis was limited to analyzing the effects of superimposing NMES onto RT for muscle strength and muscle mass using longitudinal studies that met the inclusion criteria ($n = 13$).

Risk of bias and quality assessment

Reviewers independently assessed the risk of bias for the studies included in the meta-analysis using Cochrane Collaboration’s Risk of Bias Tool (RoB2) (Higgins et al. 2022). Studies were assessed for the following criteria: (1) random sequence generation, (2) allocation concealment, (3) blinding participants, (4) blinding of outcome assessment, (5) incomplete data reporting, and (6) selective reporting.

Statistical analyses

The meta-analyses were performed to determine the effect of superimposing NMES on RT-induced muscular contractions on muscle strength and muscle mass, the primary outcome measures of this study. Continuous outcomes were reported as the mean difference (MD) and standardized mean difference (SMD) from pre- to post-intervention with a 95% confidence interval (95% CI). Random effects meta-analysis models were used to analyze data in R (version 4.2.2).

Statistical heterogeneity among studies was assessed using I^2 Statistics. I^2 values of 25–50% were considered indicative of low heterogeneity, 50–75% were considered moderate heterogeneity, and values above 75% were considered to have a high degree of heterogeneity (Deeks et al. 2019). Sensitivity analyses were performed using a Q test for moderators in the random effect meta-analysis model to determine if the various parameters of the resistance training and/or NMES protocols were associated with the muscular strength and muscle mass outcomes. A p -value of <0.05 was considered statistically significant for all statistical tests.

Results

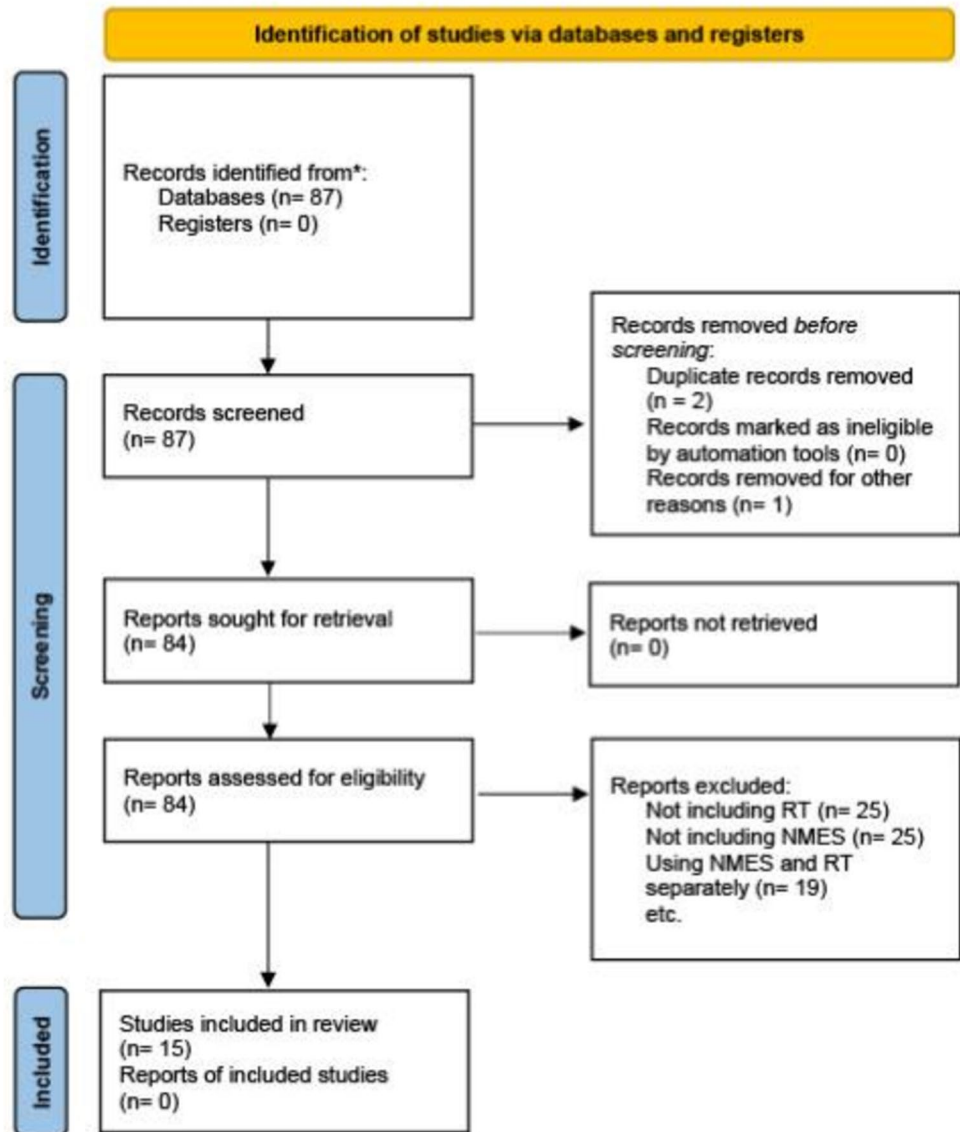
Compliance with Ethical standards

Given this article was a review of published studies, ethical approval was not required.

Study selection

The PRISMA flow diagram provides details of the database search results along with the exclusion reasoning (Fig. 1) Of the 87 studies that were originally identified as meeting the inclusion criteria, three studies were excluded due to either being a duplicate or a response to an article without original research. Of the remaining 84 studies, 69 were removed after a full-text assessment as those studies compared NMES

Fig. 1 Flow diagram of the search strategy



and RT without having a superimposed group, not including RT, or not including NMES. The remaining 15 studies met the inclusion criteria for systematic review, while two were excluded from the meta-analysis due to not stating both the mean and standard deviation or standard error of mean for pre- and post-intervention measurements, leading to 13 studies being included in the meta-analysis.

Population characteristics

Population characteristics of the reviewed studies are detailed in Table 1. The 15 studies in this systematic review were conducted in healthy adults ($n=12$), teenagers ($n=1$), and elderly ($n=2$). In terms of physical activity, the studies included sedentary ($n=5$), active ($n=9$), and one study did not provide information on physical activity levels. Data from these studies consisted of 488 total participants (age ranging from 16 to 84) with sample sizes varying from 15 to 89. Among the included studies, seven studies had both male and female study participants, four studies reported only male participants, three studies reported only female participants, and one study did not specify the sex of their participants (Evangelista et al. 2019). The thirteen randomized controlled trials included in the meta-analysis consisted of 374 healthy participants with 198 being male and 121 being female and sample sizes varying from 10 to 48. Of the participants in the meta-analysis, 172 were allocated to the superimposed NMES and RT group and 165 were allocated to the RT group with one study not describing the distribution of study participants (Abulhasan et al. 2016). Some studies also included an inactive control and/or NMES-only group; however, these groups were excluded from the analyses.

Study designs and primary outcome measurement methods

Study characteristics and training protocols are summarized in Table 1. Studies reported one or more measurements of muscular strength ($n=14$) included one repetition max (Evangelista et al. 2019; Abulhasan et al. 2016), isokinetic dynamometer (Burkett et al. 1998; Da Silva et al. 2018; Iwasaki et al. 2006; Park et al. 2016, 2021), hand dynamometer (Jang and Park 2021; Benavent-Caballer et al. 2014), force transducer (Ludwig et al. 2020), load cell (Herrero et al. 2010) and maximum voluntary contraction (Dormann et al. 2019; Micke et al. 2018; Wirtz et al. 2016). Studies reported one or more measures of muscle mass ($n=7$), included muscle thickness determined by ultrasound (Micke et al. 2018; Abulhasan et al. 2016; Da Silva et al. 2018; Matos et al. 2022; Benavent-Caballer et al. 2014), skeletal muscle mass determined by bioelectrical impedance analysis (Jang and Park 2021; Park et al. 2021), magnetic resonance imaging

(Park et al. 2021) and circumference measurements performed with a tape measure (Park et al. 2021; Jang and Park 2021). Of the thirteen studies included in the meta-analysis, 12 studies reported pre- and post-intervention muscle strength (Benavent-Caballer et al. 2014; Dormann et al. 2019; Evangelista et al. 2019; Da Silva et al. 2018; Herrero et al. 2010; Iwasaki et al. 2006; Jang and Park 2021; Ludwig et al. 2020; Micke et al. 2018; Park et al. 2016, 2021; Wirtz et al. 2016) and 6 studies reported pre- and post-intervention muscle mass (Evangelista et al. 2019; Park et al. 2021; Da Silva et al. 2018; Benavent-Caballer et al. 2014; Jang and Park 2021; Matos et al. 2022).

Overview of the neuromuscular electrical stimulation protocols

NMES protocols of the included studies are outlined in Table 1 including intervention duration, number of sessions, time per training session, frequency, pulse width, and intensity. NMES frequencies of less than 50 Hz are considered low frequency (Hultman and Spriet 1986; Jabbour et al. 2015; Hamada et al. 2003), while frequencies of 50 Hz or greater are considered high frequency (Bergstrom and Hultman 1988; Erickson et al. 2017; Johnson et al. 2003; Laufer and Elboim 2008). Along with the protocols, studies that used low (Iwasaki et al. 2006; Jang and Park 2021) and high frequencies (Evangelista et al. 2019; Wirtz et al. 2016; Park et al. 2021, 2016; Dormann et al. 2019; Ludwig et al. 2020; Micke et al. 2018; Da Silva et al. 2018; Herrero et al. 2010; Benavent-Caballer et al. 2014; Abulhasan et al. 2016) were also identified. Two studies did not provide details on NMES protocol (Burkett et al. 1998; Matos et al. 2022). Pulse width was consistent with available protocols ranging from 300 to 400 μ s. While most studies used the NMES intensity at participant's maximum tolerable level ($n=8$) (Abulhasan et al. 2016; Wirtz et al. 2016; Dormann et al. 2019; Park et al. 2016; Micke et al. 2018; Da Silva et al. 2018; Herrero et al. 2010; Benavent-Caballer et al. 2014), two protocols used ratings of perceived exertion (RPE) (Evangelista et al. 2019; Ludwig et al. 2020), one study provided a numerical value for intensity in milliamps (Jang and Park 2021), one reported intensity in volts (Iwasaki et al. 2006), and four studies did not provide information on NMES intensity (Burkett et al. 1998; Park et al. 2021; Matos et al. 2022; Jang and Park 2021). Most study intervention lengths ranged from 4 to 12 weeks (Evangelista et al. 2019; Burkett et al. 1998; Iwasaki et al. 2006; Wirtz et al. 2016; Park et al. 2021; Dormann et al. 2019; Ludwig et al. 2020; Da Silva et al. 2018; Herrero et al. 2010; Benavent-Caballer et al. 2014; Matos et al. 2022; Jang and Park 2021) while two studies reported 2 weeks intervention length (Abulhasan et al. 2016; Park et al. 2016) and one study conducted an intervention for 16 weeks (Benavent-Caballer et al. 2014).

Table 1 Characteristics of the included studies

Author	I.G	N	Population	Age (yrs)	Weight (kg)	Frequency (Hz)	Pulse width (µs)	NMES intensity	Contraction:Rest (sec)	Length (mins)	Super-imposed application	Sets	Reps	Tempo	Intensity	Intervention	Muscle group trained	Strength outcome	Mass Outcome
*Abulhasan et al.	RT	M-14 F-16	Active	19±1 20±4		50	400	Max threshold	N/A		Continuous	3	8 to Fail		80% IRM	5× over 2 weeks	Quadriceps	=	=
*Burkett et al.	RT RT+	5 5	Active Male	23.6±9.26 22.5±4.04	73.5±9.75 70.8±6.25				N/A		Synchronized	3	10		MR	3x/wk for 9 weeks	Quadriceps	=	Not measured
Benavent-Caballer et al.	RT RT+	22 (M-7 F-15) 22 (M-8 F-14)	Elderly	85.5±4.7 83.6±3.6	65.1±11.3 63.6±11.1	50	400	Adjusted to tolerance	3:2	35	Synchronized	3	15	2:2:1:3	40% IRM	3x/wk for 16 weeks	Quadriceps	=	RT+↑
Dormann et al.	RT RT+	11 11	Active Female	20.5±1.8 20.4±2.8	62.0±4.7 65.5±10.7	85	350	70% Pain threshold	3-5:0:0-5	35	Synchronized	3	10, 8, 5, 8 s	2:1:2, 2:0:2, 0.5:0:0.5	RPE>16	2x/wk for 4 weeks	Hamstrings	=	Not measured
Evangelista et al.	RT RT+	23 25	Active Untrained	25.1±3.2 25.5±6.1	78.1±15.3 78.1±7.5	85	350	RPE 5-6 7-8	Continuous	20	Continuous	3	8 to 12		MR	2x/wk for 8 weeks	Quadriceps	RT+↑	RT+↑
Gomes da Silva et al.	RT RT+	15 (M-8 F-7) 13 (M-8 F-5)	Healthy Active	25.0±4.90 25.23±4.62	69.47±11.85 66.61±11.02	80	400	Max tolerable	5:5		Synchronized	1-3	10	4:5:1:0	100% IRM	2x/wk for 6 weeks	Quadriceps	=	=
Herrero et al.	RT RT+	8 11	Sedentary Male	20.9±2.5 21.4±2.9	79.0±8.4 80.2±4.8	120		Max tolerable	1:1		Synchronized	8	10	1:0.5:1:1	70% MVC	4x/wk for 4 weeks	Quadriceps	RT+↑	Not measured
Iwasaki et al.	RT RT+	8 8	Sedentary Male	21.8 22.3	64.79±9.11 61.40±10.51	20		50.46±9.01 V 44.79±9.22 V	2.4:4:7.6 ms		Synchronized	10	10		65-70% IRM	3x/wk for 6 weeks	Quadriceps	RT↑	Not measured
Jang et al.	RT RT+	10 9	Elderly Female	73.3±4.50 73.22±4.76	53.72±5.40 53.69±8.62	35	300	10-12 mA	Continuous	20	Continuous	1 2	10			3x/wk for 4 weeks	Quadriceps	=	=
Ludwig et al.	RT RT+	12 18	Teen Athlete Male	16.42±0.90 16.28±0.67	70.84±6.08 67.25±5.30	85	350	RPE 6-7	4:4	20	Synchronized	1	15 60 s	1:0:1:0		1x/wk for 10 weeks	Quadriceps	RT+↑	Not measured
Matos et al.	RT RT+	10 10	Trained Male	25.3±4.03 23.8±3.43	73.5±5.13 75.6±9.23				N/A	24	Synchronized w/ Eccentric	3	10		100% IORM 60% 10 RM	2x/wk for 8 weeks	Biceps	Not measured	=
Micke et al.	RT RT+	9 9	Trained Males	22.8±2.5 28.8±3.0	77.6±9.0 80.2±6.6	85	350	70% Pain threshold	3-5:0:0-5		Synchronized	3	10, 8, 5, 10 s	2:0:2:1, 2:0:2:0, 3:0:1:1, 1:0:3:0	RPE>16	2x/wk for 8 weeks	Quadriceps	RT+↑	Not measured
Park et al.	RT RT+	12 11	Female	25.2±5.7 23.5±4.2	67.9±10.5 65.1±5.8	80			5:3	20	Continuous	1	20, 60 s			3x/wk for 6 weeks	Hamstrings	=	=

Table 1 (continued)

Author	I.G	N	Population	Age (yrs)	Weight (kg)	Frequency (Hz)	Pulse width (µs)	NMES intensity	Contraction:Rest (sec)	Length (mins)	Superimposed application	Sets	Reps	Tempo	Intensity	Intervention	Muscle group trained	Strength outcome	Mass Outcome
Park et al.	RT	10	Sedentary Male	24.5 25.0	69.1 ± 7.6 71.1 ± 5.2	100	300	Max tolerable	10:20		Synchronized	2	10	0:0:1–2:8–9	5x/wk for 2 weeks	Back extensors	=	Not measured	
Wirtz et al.	RT	10	Athlete Male	21.9 ± 1.6 22.1 ± 1.9	78.3 ± 4.4 83.7 ± 8.9	85	350	70% Pain threshold	N/A		Synchronized	1–3	10	2:1:2:1	50% 100% IORM	2x/wk for 6 weeks	Hamstrings	=	Not measured

* Studies excluded from the meta-analysis; † significantly greater improvement; = no difference between group

IRM 1 repetition maximum, IORM 10 repetition maximum, cm centimeters, Hz Hertz, IG intervention group, kg kilograms, MVC maximum voluntary contraction, MR maximal repetitions, µs microseconds, mA milliamps, ms milliseconds, min minutes, N/A not available, RPE rating of perceived exertion, RT+ superimposed group, RT resistance training group, Repts repetitions, sec seconds, Tempo eccentric:isometric:concentric:isometric, V volts, yrs years

Overview of the resistance training protocols

Resistance training protocols are also outlined in Table 1 including the number of sets, repetitions per set, intensity, rest between each set, intervention duration, and number of training sessions. The number of sets and repetitions were generally consistent among studies. Most studies utilized three sets per exercise (Evangelista et al. 2019; Burkett et al. 1998; Wirtz et al. 2016; Dormann et al. 2019; Micke et al. 2018; Benavent-Caballer et al. 2014; Matos et al. 2022) while two studies used as low as one set (Park et al. 2021; Ludwig et al. 2020) and one study used as many as ten sets (Iwasaki et al. 2006). Most studies used repetitions per set in the 8–12 range which is commonly recommended for general strength training (ACSM 2021), while two studies used sets of 15 repetitions (Ludwig et al. 2020; Benavent-Caballer et al. 2014) and one study used as high as 20 repetitions per set (Park et al. 2021). Like the NMES protocols, the intensity of resistance training was inconsistent among the included studies. While many studies utilized values based on a percentage of 1 repetition max (Abulhasan et al. 2016; Iwasaki et al. 2006; Da Silva et al. 2018; Benavent-Caballer et al. 2014), other studies also used RPE (Dormann et al. 2019; Micke et al. 2018), repetition maximum (Evangelista et al. 2019; Burkett et al. 1998), and 10 repetition max (Wirtz et al. 2016; Matos et al. 2022). Several studies did not report on resistance training intensity (Park et al. 2021, 2016; Ludwig et al. 2020; Jang and Park 2021). While half of the studies either did not report or did not control for repetition tempo, eight studies did include tempo in their protocols (Wirtz et al. 2016; Dormann et al. 2019; Park et al. 2016; Ludwig et al. 2020; Micke et al. 2018; Da Silva et al. 2018; Herrero et al. 2010; Benavent-Caballer et al. 2014).

Overview of the superimposed NMES protocol with resistance training

Specific protocols for using NMES with RT are outlined in Table 1. Of the fifteen included studies, ten studies had NMES synchronized with the RT (Burkett et al. 1998; Wirtz et al. 2016; Dormann et al. 2019; Park et al. 2016, 2021; Ludwig et al. 2020; Micke et al. 2018; Da Silva et al. 2018; Herrero et al. 2010; Benavent-Caballer et al. 2014), one study used a synchronized protocol but in the antagonist muscle instead of the agonist muscle (i.e. hamstring stimulation during knee extension and quadricep stimulation during knee flexion) (Iwasaki et al. 2006), one study used a synchronized protocol with synchronization only during the eccentric phase of each repetition (Matos et al. 2022), and three studies had the NMES running continuously during training (Abulhasan et al. 2016; Evangelista et al. 2019; Jang and Park 2021).

Risk of bias

Assessment of quality and risk of bias are displayed in Fig. 2. Using the Cochrane Collaborations' Risk of Bias (RoB) tool (Higgins et al. 2022) 13.3% of studies presented with low risk, 66.7% moderate risk, and 20% high risk with an overall rating of moderate to low risk. A substantial portion of the risk is due to many studies not blinding the participants or persons delivering the intervention to which group the participants were allocated, along with not calculating sample size leading to many studies having a moderate risk of bias in deviation from the intended intervention. However, in the case of NMES, it is near impossible to blind participants as to which method of stimulation they are receiving as it will be noticed and result in blinding failure. Three studies were classified as high risk due to lack of randomization of study participants, in one study due to logistical concerns as they were teenagers who took public transportation and needed to be scheduled into similar time blocks and had unequal sample sizes between groups (Ludwig et al. 2020), with the remaining two having measurement of outcome bias as they trained the lower body but reported strength of the upper body using a handheld grip strength dynamometer (Benavent-Caballer et al. 2014; Jang and Park 2021).

Outcome of the included studies

The effect of superimposed NMES on RT-induced muscular strength

A summary of the extracted data for muscle strength is shown in Fig. 3. The meta-analysis for muscle strength is based on standardized mean difference (SMD) from 12 studies with a pooled standard deviation used in

the analysis. Each study compared the improvement in strength in NMES + RT and conventional RT groups. The SMD across all studies was 0.31 (95% CI 0.13, 0.49) with a p -value of 0.02 and an I^2 heterogeneity value of 73.05%. This was substantiated by the systematic review with four of the studies finding significant differences in favor of the superimposed group (Evangelista et al. 2019; Ludwig et al. 2020; Micke et al. 2018; Herrero et al. 2010) and one additional study demonstrating that while there was no significant difference, a medium effect size in favor of superimposed training was found (Park et al. 2016).

The effect of superimposed NMES on RT training induced muscle mass

Among the studies included in the systematic review and meta-analysis, 6 studies investigated the effect of superimposing NMES on RT regarding muscle mass. A summary of the extracted data for muscle mass is depicted in Fig. 4. The meta-analysis for muscle mass is based on the SMD from 6 studies with a pooled standard deviation used in the analysis. Each study compared muscle mass increases in NMES + RT and resistance training groups. The SMD of the 6 studies was 0.26 (95% CI 0.03, 0.49) with a p -value of 0.02 and an I^2 heterogeneity value of 21.45%. The meta-analysis on muscle mass was also substantiated by the systematic review with two studies demonstrating a significant difference favoring the superimposed group (Evangelista et al. 2019; Benavent-Caballer et al. 2014). Additionally, to determine if there were any influencing factors from either the RT or the NMES protocols on muscle strength and muscle mass, a sensitivity analysis was performed.

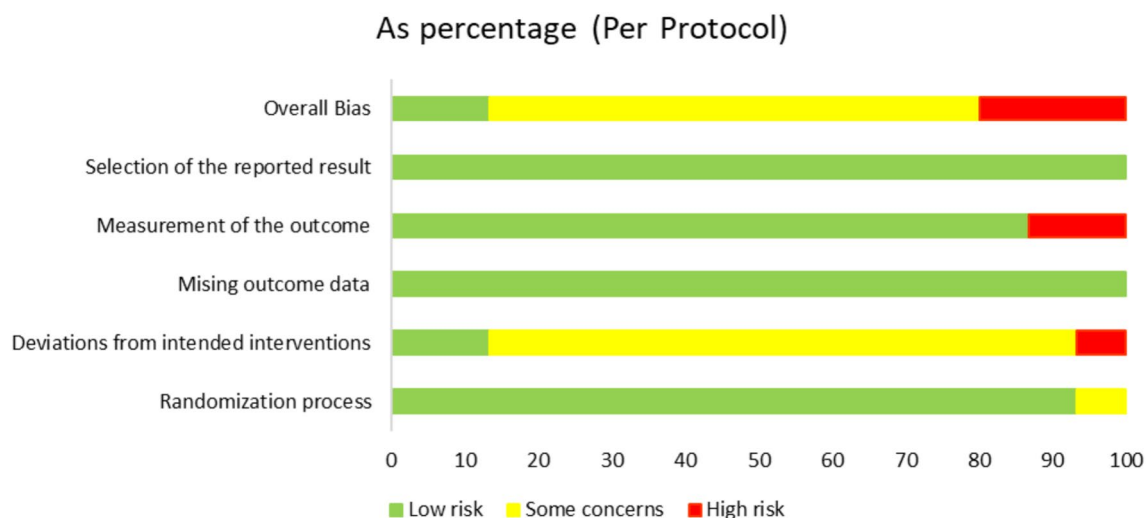


Fig. 2 Risk of bias for studies included in the meta-analyses

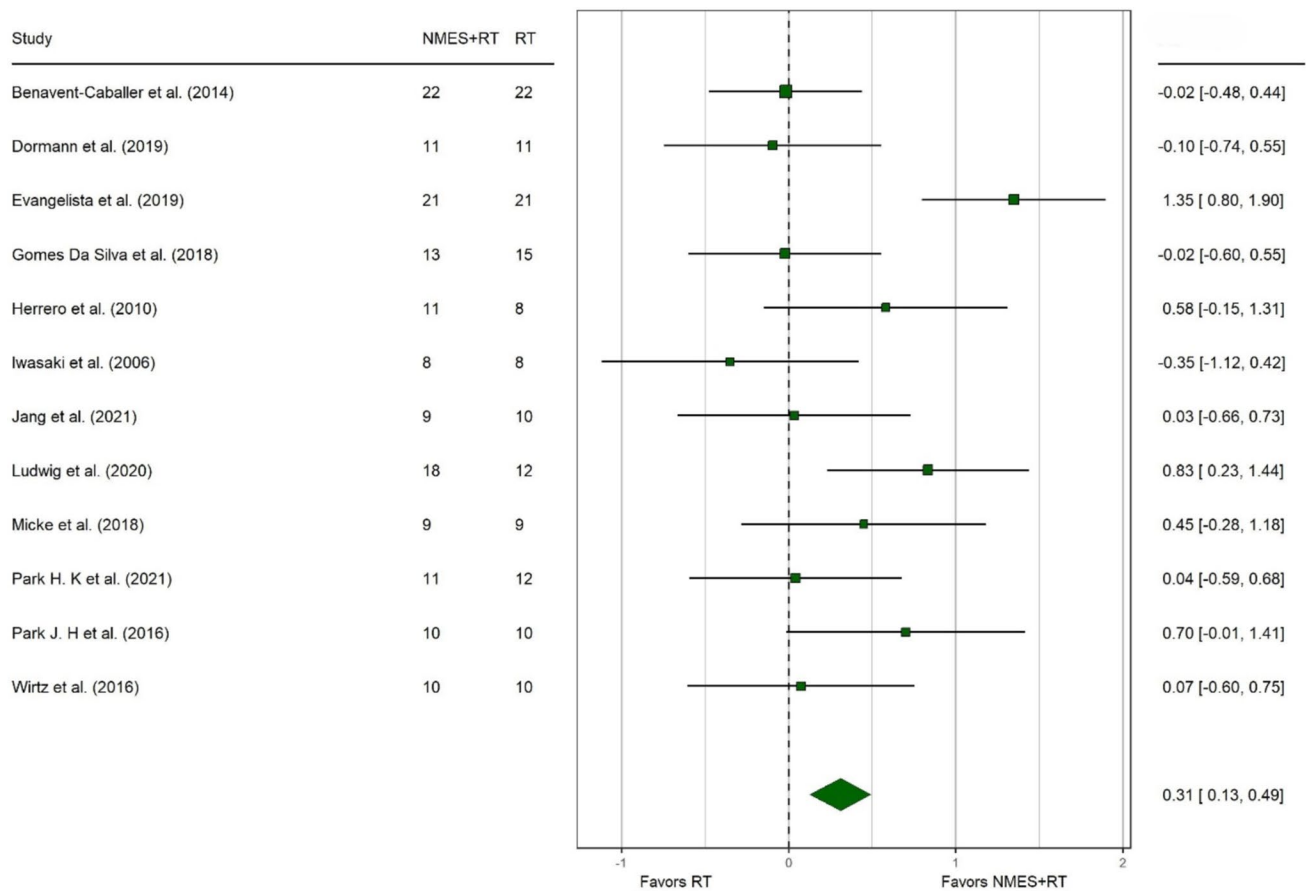


Fig. 3 Forest plot depicting the standard mean difference for muscular strength in NMES+RT and RT groups. Studies favoring RT are in the negative range and those favoring NMES +RT are in the positive range. Data presented are mean difference \pm 95% confidence intervals

Sensitivity analysis of the effect of superimposed NMES on RT-induced muscular strength

There are many variables that were seen to influence the gain in muscular strength. For the RT variables, number of sets ($p=0.02$) and repetitions per set ($p=0.01$) were found to be associated with the increase in muscular strength. For NMES, the frequency ($p<0.01$) was associated with increased muscular strength. For the overall training protocol, sessions per week ($p<0.01$), total number of sessions ($p=0.03$), and time of training per week ($p=0.03$) were positively associated with muscular strength. Other factors measured but did not have an influence on muscular strength include NMES pulse width ($p=0.40$), time per session ($p=0.20$), and intervention duration (0.10).

Sensitivity analysis of the effect of superimposed NMES on RT training-induced muscle mass

The above-mentioned variables were also assessed to determine if there were influences on the increase in muscle mass.

None of the variable were found to have an association with increases in muscle mass ($p>0.05$).

Discussion

The purpose of this systematic review and meta-analysis was to determine the effect of superimposing NMES on RT-induced adaptations in muscle strength and muscle mass. Based on the meta-analysis performed, we conclude that superimposing NMES on RT results in greater increases in both muscle strength and muscle mass compared to conventional RT.

RT has long been recommended for improving muscle strength and muscle mass. NMES is commonly used in therapeutic and rehabilitative settings to prevent the loss of muscle strength and muscle mass during immobilization and physical inactivity (Hainaut and Duchateau 1992; Stevens-Lapsley et al. 2012; Vaz et al. 2013). NMES is also practical and convenient to use due to the cost, portability and minimal equipment and effort required to receive the benefits associated with it. Unlike RT, the strength gains associated

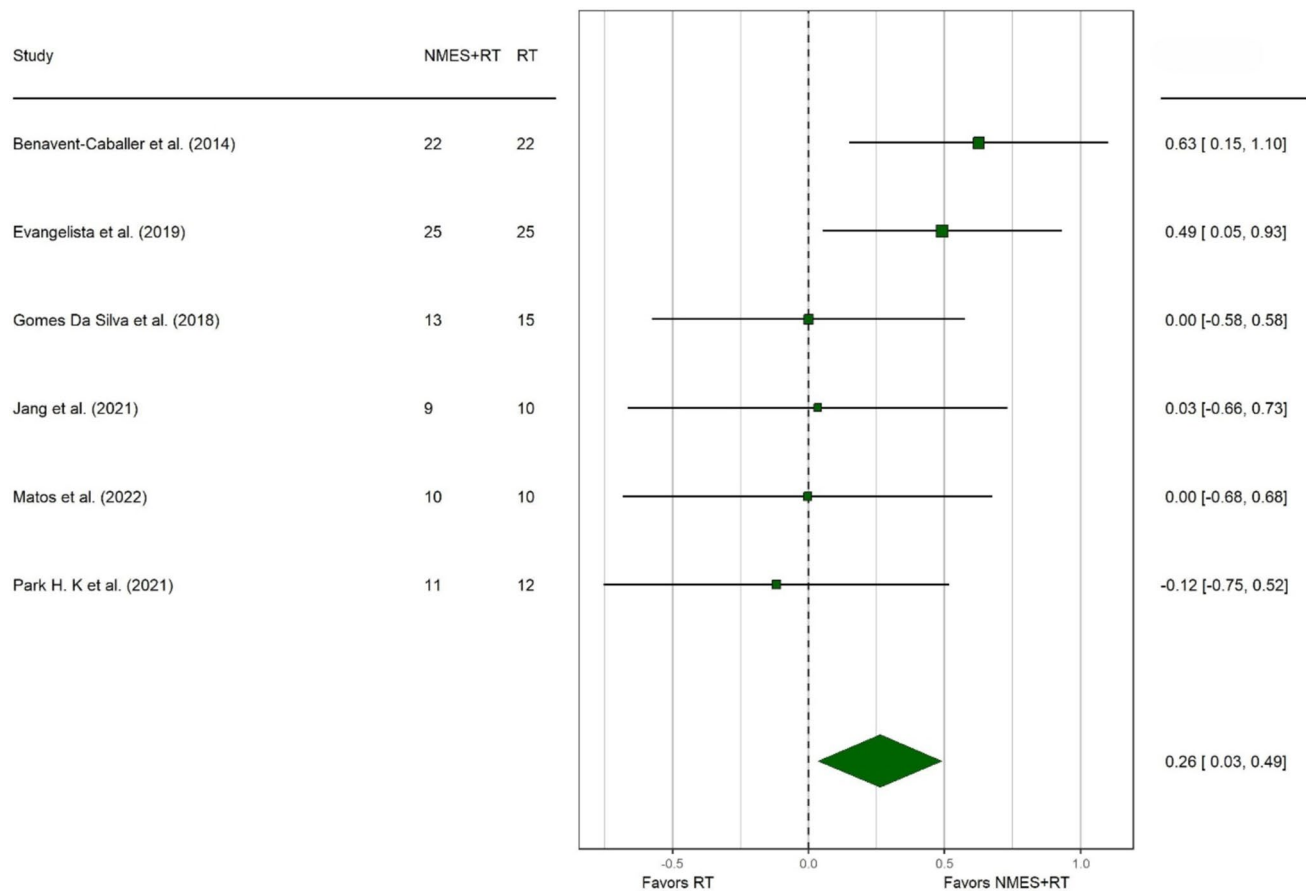


Fig. 4 Forest plot depicting the standard mean difference for muscle mass in NMES + RT and RT groups. Studies favoring RT are in the negative range and those favoring NMES + RT are in the positive range. Data presented are mean difference \pm 95% confidence intervals

with NMES may be attributed to synchronous motor unit depolarization instead of the oscillation of muscle fibers seen in voluntary contractions and constant, higher intensity firing rates of the motor units leading to more force production (Dehail et al. 2008). Previous research has shown that use of NMES can prevent the loss of muscle strength in the quadriceps for patients recovering from knee arthroplasty and offset the detrimental effects of osteoarthritis on quadriceps strength and muscle mass in patients unable to perform conventional RT due to pain and joint stiffness (Stevens-Lapsley et al. 2012; Vaz et al. 2013). Although both NMES and RT have been shown to increase muscle strength and mass when used alone, whether there is an additive effect of NMES being used with RT remained unknown.

This is the first systematic review and meta-analysis that has investigated whether the addition of NMES to a RT intervention leads to greater gains in muscle strength compared to RT performed alone. The results indicate a significantly greater increase in muscle strength when NMES is superimposed on RT compared to RT performed alone. When examining days of training per week and the length of intervention, most studies were similar regarding the total

number of training sessions. However, in the studies favoring superimposed training (Evangelista et al. 2019; Park et al. 2016; Ludwig et al. 2020; Micke et al. 2018; Herrero et al. 2010), frequencies of the NMES protocols ranged from 85 to 120 Hz while the studies that reported no greater gain with superimposed NMES (Abulhasan et al. 2016; Burkett et al. 1998; Wirtz et al. 2016; Park et al. 2021; Dormann et al. 2019; Da Silva et al. 2018; Benavent-Caballer et al. 2014; Jang and Park 2021) used NMES frequencies ranging from 20 to 85 Hz. This was further substantiated by the sensitivity analysis showing a positive association between NMES frequency and increases in muscular strength. Therefore, high-frequency NMES may be necessary for greater gains in muscle strength with superimposed NMES. This could be due to the force-frequency relationship in which increasing frequency is shown to increase force output (Binder-Macleod et al. 1995; Gregory et al. 2007). One important factor to consider is the positioning of the electrodes in relation to nerve endings. Applying stimulation at the motor point of the target muscle will elicit motor branch excitation while suboptimal positioning would require higher intensities while also exciting afferent fibers leading to an increased

pain sensation (Gobbo et al. 2014, 2011). Also, the contraction and rest times of each NMES contraction should be noted. Of the studies that included detailed NMES protocols, each contraction lasted a relatively short period of time (< 30 s). This is important due to high-frequency fatigue associated with NMES (Moritani et al. 1985). When performed for 30 s or longer, NMES causes significant fatigue and decreased force output (Moritani et al. 1985). Next, most studies favoring superimposed training were conducted in active or athletic populations (Evangelista et al. 2019; Ludwig et al. 2020; Micke et al. 2018). More physically active participants may be better able to tolerate NMES due to superior muscular coordination compared to the untrained participants leading to the electrical stimulation potentially being more effective (Gondin et al. 2011). Among the studies that did not show a greater gain in muscle strength by superimposing NMES, two studies measured strength in different muscle groups than the muscle group trained during the intervention (Benavent-Caballer et al. 2014; Jang and Park 2021). These studies measured grip strength using a handheld dynamometer while training the lower body. It is possible that strength measurements focused on the lower body may have demonstrated different results due to the principle of specificity (ACSM 2021). Taken together, the existing evidence suggests that superimposing NMES on RT can be beneficial in causing significantly greater increases in muscle strength than RT performed alone.

The results of the systematic review and meta-analysis also demonstrate that superimposing NMES on RT results in greater increases in muscle mass than RT performed alone. Studies that demonstrated greater increases in muscle mass with superimposed NMES (Evangelista et al. 2019; Benavent-Caballer et al. 2014) used 8–16 week training interventions; whereas the training duration was only 2–8 weeks in studies that did not result in greater increases in muscle mass with superimposed NMES (Park et al. 2021; Da Silva et al. 2018; Matos et al. 2022; Jang and Park 2021). Therefore, it may be possible that a minimum of 8 weeks of training duration is necessary to see significant improvement in muscle mass between the two modes of exercise as is generally expected when training for muscle hypertrophy (Abe et al. 2000; Damas et al. 2018). This was substantiated by the sensitivity analyses. While intervention duration was not related to increased muscle mass or strength ($p > 0.05$), sessions per week, total number of sessions, and time of training per week all were ($p < 0.05$). It is likely that overall volume of exercise may be a factor in the greater increases found. It should also be noted that no studies controlled the participants' diet. Having a sufficient intake of protein has been shown to significantly increase muscle strength, fat-free mass, as well as muscle cross-sectional area through increasing muscle protein synthesis and inhibiting muscle protein

breakdown, yielding a net positive muscle protein balance (Morton et al. 2018; van Loon and Gibala 2011). Due to this lack of control, the role diet could have played in the included studies remains unknown.

Limitations

There are limitations to these analyses that must be noted. The primary outcome measures reported in each study were used and provide the main conclusion of the study results. Given some of the studies reported multiple variables that are indicative of muscle strength and mass, analyses based on only one variable may be considered a limitation of this study. While there were significantly greater gains in muscle mass and strength favoring superimposed training, the majority of studies examined the lower body musculature via either the quadriceps or hamstrings, while only two studies examined the upper body with muscles including the back extensors (Park et al. 2016) and biceps (Matos et al. 2022). A greater amount of muscle groups trained with superimposed stimulation are needed to determine the effects on whole-body muscle mass and strength. Next, the muscle mass analysis was limited by a small sample size as only 6 studies investigated the effect of superimposed training compared to resistance training for muscle mass development. While there were significantly greater increases in muscle mass, more studies are needed to provide a better understanding on the effect of superimposing NMES during resistance training for muscle mass. Also, the effectiveness of NMES is related to training intensity (Maffiuletti 2010). Given that force evoked from NMES was not measured in any of the included studies, there is no way of knowing how much force NMES was accounting for during the training protocols. Also, most studies used NMES in synchronization with sets of exercise. However, some NMES protocols were continuous in which NMES would be administered at the given contraction/rest time regardless of it came on during a set or during the rest period between sets. Of the studies using continuous NMES, there were conflicting results with 1 study finding significant differences favoring superimposed training while the others did not. The mode of superimposing NMES may have also been a factor in the overall results and should be considered.

In conclusion, the effects of superimposed training compared to conventional resistance training indicate greater gains in muscle mass and strength following at least eight weeks of high-frequency electrical stimulation (≥ 85 Hz). If one is looking to maximize the effectiveness of a resistance training protocol, using NMES simultaneously during training sessions leads to better gains. Whether there are additional benefits for other factors such as glycemic control remains unknown and requires further study.

Author contribution SB conceived of the study, GN and JA did the initial search and selected articles for the study. SB reviewed the search results. AW analyzed the data and created figures. All authors contributed to the writing and revision of the article and approved the submitted version.

Funding This work was supported by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health under award number R01DK132430 (SB).

Data availability The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

Declarations

Conflict of interest There are no conflicts of interests to note. The results of the study are presented clearly, honestly, with no fabrication, falsification, or manipulation of data.

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