Review

Outcomes Addressed by Whole-Body Electromyostimulation and Belt Electrode-Skeletal Muscle Electrical Stimulation Trials in Middle Aged to Older Adults – an Evidence Map

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Outcomes Addressed by Whole-Body Electromyostimulation and Belt Electrode-Skeletal Muscle Electrical Stimulation Trials in Middle Aged to Older Adults—An Evidence Map

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Abstract: Due to its time effective, joint friendly and highly customizable character whole-body-electromyostimulation (WB-EMS) is regarded as a feasible solution for a large variety of training issues particularly in the area of non-athletic application. To identify gaps in research and summarize prevalent evidence we conducted an evidence map on outcomes addressed by WB-EMS trials in middle-aged to older, non-athletic adults. Based on a comprehensive systematic search in five databases and two study registers according to PRISMA, 54 projects published in 80 articles were included. More than 90% of the studies reported outcomes related to the physical fitness or function domain. Body composition parameters were addressed by two thirds of the projects. Health-related outcomes addressed by WB-EMS included cancer/neoplasm (n=7), endocrine regulation (n=8), glucose metabolism (15), nervous system diseases (n=2), cardiovascular system diseases (n=22), non-specific chronic low back pain (n=4), osteopenia (n=5) and diseases of the renal system (n=12). Outcomes related to inflammation were addressed 18 times. Of importance, no studies reported clinically relevant adverse effects related to the WB-EMS intervention. In summary, while considerable evidence on outcomes related to fitness/function and body composition is prevalent, evidence gaps of WB-EMS research were particular evident for diseases of the nervous and cerebrovascular system.

Keywords: whole-body electrostimulation; electromyostimulation; health; fitness; function; health

1. Introduction

Whole-body electrostimulation (WB-EMS) "defined as simultaneous application of electric stimuli via at least six current channels or participation of all major muscle groups, with a current impulse effective to trigger muscular adaptations" [1] is an ever more popular training method. Due to its time effective, joint friendly, comprehensive and highly customizable character [1,2], WB-EMS might be an adequate solution for various training issues. In the last ten years a large number of articles on WB-EMS effects on various outcomes have been published. Apart from cross-sectional studies and studies on the acute effect of WB-EMS, the vast majority of studies focus on the effect of longitudinal training interventions on given outcomes. So far, a large variety of performance-, function-, fitness- and health-related outcomes in athletic and particularly in non-athletic cohorts have been addressed [3]. Restricting the results to middle-age to older adults, i.e. the dominant area of WB-EMS application [4], outcome domains addressed vary from muscle strength, endurance, flexibility, balance, body composition, chronic low-back pain, cardiometabolic, neoplasm, inflammation, bone mineral density, vascular endothelial function, left ventricular function, through to quality of life, disability, pain, and sleep quality - to list just a few.

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However, due to the rather stringent index of absolute or relative contraindications, a large variety of cohorts [5] and corresponding outcomes were not adequately addressed by WB-EMS trials. In diametral contrast, Belt Electrode-Skeletal Muscle Electrical Stimulation (B-SES), a neuromuscular electrostimulation (NMES) technique that stimulates large muscle areas (i.e. gluteals and lower extremities) and can thus be considered as closely related to WB-EMS, focuses predominately on severe diseases and conditions. Adding both NMES methods might increase the evidence for a wider applicability of WB-EMS on different outcomes. Considering further the limited resources for WB-EMS and B-SES research, it is important to identify and summarize prevalent evidence provided by WB-EMS and related techniques in order to align future research more efficiently. An evidence map [6] that listed the evidence, identify gaps, and provide results in a user-friendly format might be the appropriate tool to summarize research on WB-EMS and B-SES. The present evidence map thus aimed to provide an overview of study outcomes addressed by WB-EMS and closely related techniques in middle aged and older non-athletic people.

2. Methods

Our evidence map based on a systematic review of the literature. Two researchers (YHL, DS or WK) searched five electronic databases (Medline [PubMed], The Cochrane Central Register of Controlled Trials [CENTRAL], Cumulative Index to Nursing & Allied Health [CINAHL via Ebsco Host], SPORTDiscus (via Ebsco Host), Physiotherapy Evidence Database [PEDro]) and two study registers (Clinical trial.gov and the WHO's International Clinical Trials Registry Platform [ICTRP]) for scientific literature published from launch up to 6th March 2023 were searched without language restrictions. Strategies were developed applying free text words as no database-specific key words (e.g. MeSH, Thesaurus) were identified. We piloted our search and found a good balance for maximizing sensitivity and precision by (a) constructing the search around the term whole-body electromyostimulation only and (b) searching the title and abstract fields only in PubMed, CINAHL and SPORTDiscus, excluding Medline hits in CINAHL and by applying the 'Trials' filter in CENTRAL. To identify additional study reports, we manually searched Google Scholar on the same date as the medical databases. The full strategies can be found in Supplemental Table S1 (Supplement). Of note, our comprehensive search on WB-EMS and related technologies was considered as a database for varying review articles, to which more specified eligibility criteria were covered in the more dedicated articles.

Eligibility criteria

Study design

We included all types of longitudinal studies with an interventional study designs, [7], i.e. randomized or non-randomized clinical trials and intervention studies with or without control groups. We also accepted articles on the same project that focus on the same cohort but other outcomes. Only peer reviewed research was considered. Review articles, case reports, editorials, conference abstracts, letters, and all kind of thesis were not considered.

Population

Sedentary to non-athletic adult cohorts on average 45 years and older were included. Cohorts comprised of athletes or sport students were excluded but recreational sportsmen were accepted.

Comparators

Type or even presence of a control group was not considered as an eligibility criterion.

Intervention

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We only included studies that applied Whole-Body Electromyostimulation (WB-EMS [1]) or other kinds of electromyostimulation able to stimulate large muscle areas[1] simultaneously. Studies that applied local EMS or focus on single muscle groups were not considered.

Outcomes

In the present analysis, we included eligible studies independently of the outcomes addressed. This includes outcomes related to physical fitness/function, health-related outcomes and safety aspects. Special emphasis was placed on adverse effects of WB-EMS application. We defined "adverse event" as any untoward medical occurrence, unintended disease or injury. Muscular soreness, discomfort with the stimulation, or increased CK values without clinical relevance were not considered adverse effects.

Selection process

Titles, abstracts and full texts were independently screened by two reviewers (YHL, WK) according to the pre-specified eligibility criteria. Disagreements were solved by discussion or with the help of a third reviewer (DS). Reasons for excluding ineligible studies were recorded. In the case of missing data or doubtful information, authors were contacted for a maximum of three times within a six-week period.

Data management

Search results were downloaded and imported to Endnote. Duplicates were identified and excluded based on the method proposed by Bramer et al. [8]. Title and abstract screening as well as full-text screening was conducted using Endnote.

Data items

A Microsoft Excel table applied in former studies [9,10] and modified for the present research topic was used to extract relevant data of the included studies. One author (WK) extracted study, participant, and intervention characteristics, two other authors (YHL and SvS) checked and confirmed the results. The table was structured in several domains.

Publication characteristics include information related to the study type, first author, year and country of the publication while study characteristics listed, for example, number of study arms, sample size in WB-EMS and control group, comparator (i.e. predominately sedentary control group or active control) and methodological quality of the studies.

Intervention characteristics include (1) mode of application, i.e. isolated WB-EMS or WB-EMS with voluntary movements that should not relevantly affect outcomes versus superimposed WB-EMS or exercise added to WB-EMS. (2) WB-EMS system including the corresponding manufacturers. (3) Duration of the application (in months), training frequency (sessions/week), length of the session (in min) (4) Details of the impulse protocol (i.e. impulse type (mono / bipolar), impulse frequency (in Hz), impulse breadth (in µs), impulse intensity, impulse application (continuous or intermitted impulse), length of the impulse phase (in s) and (if applicable) intermitted impulse break (in s).

Due to the topic of the present evidence map, special emphasis was placed on outcome characteristics. Study endpoints were categorized in outcome domains (e.g. physical function/fitness) with subcategories (e.g. maximum strength, power) with specific regard to health-related outcomes. All adverse effects of the WB-EMS intervention were recorded independently of type (e.g. orthopedic, metabolic) or severity according to our definition listed above.

Diseases and conditions were classified according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10 GM [11]). We also recorded whether the outcome was defined as the primary/main study outcomes or as secondary/subordinate study endpoints by the authors. To properly address this issue we carefully checked the article but also the study registration and databases where applicable. When several primary outcomes were specified by a study or project (e.g.

[1] ≥50% of skeletal muscle mass

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[12], we accepted the first three outcomes as main study outcomes. In parallel, we accepted more than one primary outcome when the main outcome refers to a score composed of multiple outcomes (e.g. Sarcopenic Obesity).

Of importance, not completely in line with the character of the evidence map approach, we briefly address not only the number but also the results of projects/trials that reported adverse effects.

Quality assessment

Eligible studies were assessed for risk of bias by two independent reviewers (YHL and WK) using the Physiotherapy Evidence Database (PEDro) Scale Risk of Bias Tool [13] specifically dedicated to physiotherapy and/or exercise studies. In case of inconsistencies, a third independent reviewer (SvS) made the decision. Studies with >7 score points were classified as high, 5-7 score points moderate and <5 score points as low methodological quality studies respectively [14].

Data synthesis

Results are displayed for all studies in tables that display publication and study characteristics, exercise and stimulation characteristics and the cohort and participant characteristics of the included studies. To provide a quick overview, bubble charts with 4 dimensions were created with the y-axis indicating the number of studies of the given outcome category and the x-axis presenting the outcome categories and the color of the bubble represents if the given outcomes were addressed as core outcomes (i.e. primary outcome) or secondary/subordinate outcomes. In order to reliably estimate the latter aspect, two reviewers carefully checked the full text including methods, power calculations and statistical analysis but also study registration and online databases of the studies/projects – if available. Finally, the size of the bubble indicates the methodological quality according to PEDro. The largest size indicates at least one study of high methodological quality, the smallest size of the bubble chart represents at least one study of low methodological quality in the corresponding outcome category.

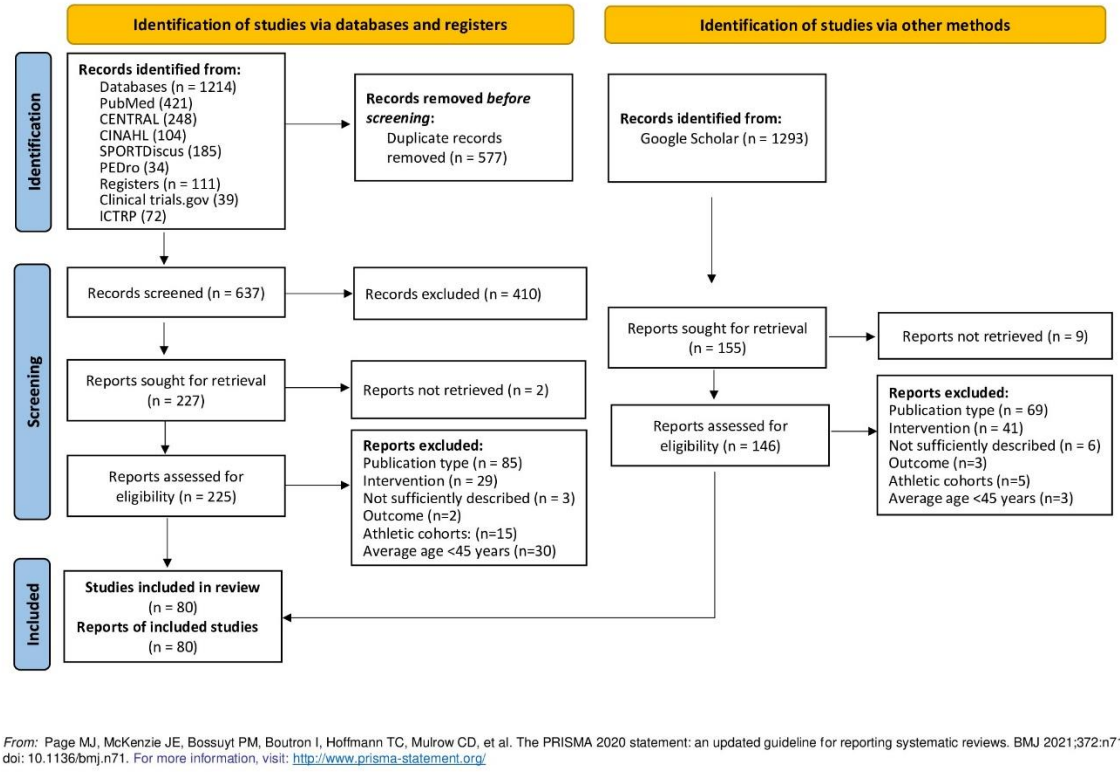

Figure 1. Flow diagram of search process according to PRISMA [15].

 doi:10.20944/preprints202403.0183.v1

3. Results

Of the 1103 records, 54 study projects published in 80 articles were ultimately included in the present evidence map (Figure 1) on outcomes addressed by WB-EMS studies with interventional [7] study designs [12,16–94].

Publication, study and participant characteristics

Table 1 displays publication and study characteristics of the included projects/trials. Based on the 54 projects, the majority of the projects were designed as RCTs (Table 1). Fifteen projects applied non-randomized controlled study designs, the remaining six trials (WB-EMS: n=2, B-SES: n=4) applied a single group design without control group [28,53,56,62,83,89] in an inpatient setting. The number of participants per study arm varies between three [64] and 96 [79]. Twenty projects were conducted in Germany, 17 in Japan (all B-SES), 4 in Korea, and 3 in Spain, Italy and the Czech Republic each. About three quarters of the studies were published during the last 5 years (Table 1). The methodological quality according to PEDro (Table 1) varies between 3 and 8 score points.

Most projects included all genders, 26% focus on female and four projects addressed male participants. The majority of the studies included cohorts largely independent of age. About half of the studies included participants 65 years and older, the youngest cohort was 49 years on average [21]. However, one study included also a few participants in their 20ies (e.g. [29]).

Most study cohorts (82%) were untrained (i.e. no frequent exercise prior to the study), six study cohorts can be considered as being moderately trained (1-2 sessions/week prior to the study) and one project included [37,38] well trained (>2 sessions/week prior to the study) participants. More than half of the cohorts were predominantly or exclusively overweight or obese (i.e. BMI mean ≥25 kg/m^2). Seven projects focused on healthy cohort while the majority (87%) of projects addressed cohorts with diseases or conditions.

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Table 1. Publication, study and participant characteristics of the included research project

	Author, project	year	country (code)	study-design	Number of study arms (n)	total sample size (n)	gender	age (years)	Body Mass Index
1	FitAging-Project; Amaro-Gahete et al. [16–20,24,26,33–35,60]	2019	ESP	RCT	4	80-89	m+w	53 ± 5	26.8
2	Bellia et al. [21]	2020	ITA	RCT	2	25	m+w	49±7	40.1
3	Blöckl et al. [22]	2022	GER	NRCT	2[2]	28	m+w	80±4	26.2
4	Bouty-Regard et al. [23]	2020	JPN	RCT	3	41	m+w	77±2	21.5
5	DiCagno et al. [25]	2023	ITA	RCT	3	24	m+w	72±6	n.g.
6	Evangelista et al. [27]	2021	BRA	RCT	2	30	m	75±7	n.g.
7	Fritzsche et al. [28]	2010	GER	No CG	1	15	m+w	56±16	26.8
8	Hamada et al. [29]	2023	JPN	NRCT	2	49	m+w	54±17	21.4
9	Homma et al. [30]	2022	JPN	RCT	2	27	m+w	79±6	22.0
10	Houdjijk et al. [31]	2022	NL	NRCT	4	75	m+w	45-75	31.8
11	Imaoka et al. [32]	2022	JPN	RCT	2	49	m+w	64±7	24.2
12	Kataoka et al. [36]	2019	JPN	RCT-	2	16	m+w	83±6	16.7
13	TEST I Project; Kemmler et al. [37,38,40]	2010	GER	RCT	2	30	w	65±6	26.0
14	TEST II-Project; Kemmler et al. [38–40]	2012	GER	RCT	2	28	m	69±3	28.1
15	TEST III-Project; Kemmler/von Stengel et al. [41–43,92]	2015	GER	RCT	2	76	m+w	>70	34.6
16	TEST III-Sub-Project; Kemmler et al. [43]	2013	GER	RCT	2	46	w	>70	22.1
17	Formosa-Project; Kemmler et al. [44,45,94]	2016	GER	RCT	3	75	w	77±4	25.1
18	FranSO-Project; Kemmler et al. [46–49,111].	2017	GER	RCT	3	100	m	77±5	26.1
19	Kim et al [50]	2020	KOR	RCT	2	25	w	71±3	30.9

 doi:10.20944/preprints202403.0183.v1

20	Konrad et al. [51]	2020	GER	NRCT	2	128	m+w	56±14	n.g.
21	Lukashevich et al. [52]	2020	BLR	RCT	3	52	w	45-65	n.g.
22	Matsumoto et al. [53]	2020	JPN	No CG	1	4	m+w	66±6	24.0
23	Matsuo et al. [54]	2022	JPN	NRCT	2	90	m+w	77±11	24.0
24	Micke et al. [55]	2021	GER	RCT	3	240	m+w	40-70	26.3
25	Mori 2020 et al. [56]	2020	JPN	NRCT	1	14	m	65±13	n.g.
26	Müllerova et al. [57]	2022	CZE	RCT	2	21	w	63±2	26.6
27	Nakamura et al. [58]	2019	JPN	RCT	2	94	m+w	76±12	21.0
28	Nakamura et al. [59]	2021	JPN	RCT	2	134	m+w	68±15	21.4
29	Nejad et al. [61]	2021	IRN	RCT	5	50	w	60-70	28.2
30	Noguchi et al. [62]	2017	JPN	No CG	1	8	m+w	69±10	n.g.
31	Nonoyama et al. [63]	2022	JPN	NRCT	2	42	m+w	72-84	24.4
32	Ochiai et al. [64]	2018	JPN	NRCT	2	6	m+w	60-90	n.g.
33	Leida-Project; Pano-Rodriguez et al. [65,66,73]	2020	ESP	RCT	2	34	w	61±4	26.5
34	Park 2021 et al. [68]	2021	Kor	RCT	2	34	w	70±4	27.5
35	Park et al. [67]	2021	Kor	RCT	3	81	w	61-79	24.4
36	Park et al [69]	2023	Kor	RCT	4	60	w	≥65	25.4
37	MetS-Project; Reljic el al. [70–72]	2022	GER	RCT	4	29-118	m+w	53±11	37.2
38	Sanchez-Infante et al. [75]	2020	ESP	RCT	2	28	w	40-60	25.5
39	Advanced cancer project; Schink et al. [76,77]	2018	GER	NRCT	2	131	m+w	60±13	25.2
40	Advanced cancer project; Schink et al. [78]	2018	GER	NRCT	2	31	m+w	55±15	25.4
41	Advanced cancer project; Richter et al. [74]	2019	GER	NRCT	2	75	m+w	59±13	25.5
42	Advanced cancer project; Schwappacher et al. [80]	2020	GER	NRCT	2	30	m+w	63±15	28.0
43	Advanced cancer project, Schwappacher et al. [79]	2021	GER	NRCT	2	12	m+w	62±9	26.8
44	Silvestri et al. [81]	2023	ITA	NRCT	2	52	m+w	43-81	24.6
45	Suzuki et al. [82]	2018	JPN	RCT	2	29	w	66±10	23.2
46	Suzuki. et al. [83]	2018	JPN	No CG	1	12	m+w	65±7	23.7

 doi:10.20944/preprints202403.0183.v1

47	Tanaka et al. [84,85]	2022	JPN	RCT	2	39	m+w	66±10	26.7
48	Teschler et al. [12]	2021	GER	NRCT	3	134	m+w	56±8	36.2
49	Tsurumi et al. [86]	2022	JPN	RCT	2	11	m+w	74±5	35.7
50	Vacoulikova et al. [88]	2021	CZE	RCT	3	21	m+w	60-65	22.7
51	Vacoulikova et al. [87]	2021	CZE	RCT	3	63	w	60-65	27.1
52	van Buuren et al. [90,91]	2014	GER	NRCT	3	60	w	61±11	27.0
53	van Buuren et al. [89]	2015	GER	No CG	1	15	m+w	62±4	29.7
54	Weissenfels et al. [93]	2018	GER	RCT	2	60	w	57±7	22.2

CG: control group; IS: Intervention study; m: men, n.a.: not applicable; NRCT: non-randomized controlled trial; RCT: randomized quality according to PEDro (maximum of 10 score points)

[1] due to the approach of calculating BMI by body length and mass in case of missing BMI we do not list the SD here; [2] training statu = 1 session per week, well-trained = 2-3 sessions per week;[3] Blöckl et al.: BMI refer to "frail cohort";[4] Houdjik et al: BMI refer to partic [5] according to PEDro.

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Intervention characteristics

Table 2 gives the intervention characteristics of the studies. Thirty-seven of the projects applied whole-body electromyostimulation (WB-EMS), 17 projects used Belt Electrode-Skeletal Muscle Electrical Stimulation (B-SES) that focuses on gluteal and/or lower extremity muscle stimulation applying 5-6 belt electrodes. Adjuvant or additional exercises (i.e. superimposed WB-EMS) with relevant effect on the primary study outcome or combined WB-EMS and conventional exercise programs were applied in about 20% of the projects. Nevertheless, apart from B-SES studies that focused on passive (i.e. without movements) EMS application, all WB-EMS studies conducted movements or exercises during the impulse phase[2].

The duration of the WB-EMS intervention varied considerably from 10 days [84] to 12 months [43,92]. Training frequency varied from 1 (e.g. [44,51,55] to 7 sessions/week (e.g. [58, 59, 64] of predominately 20-30 min duration/session. Only a few studies provided continuous impulse during the session [36, 86, 97], all the other trials exercised with intermitted WB-EMS protocols predominately with 4-6 s of impulse and 2-4 s of impulse break (Table 2). All but one sttudy [52] used low frequency impulse programs with impulse breadth of 200-400 µs. One project scheduled low impulse intensity [44,45,94], the remaining studies/projects reported moderate to high impulse intensities.

Apart from five projects that do not provide loss to follow-rates, the remaining projects/studies reported drop-out rates of 0% to 59%. Projects/Studies that displayed attendance rate (83%) reported an average rate of 92±8%.

[2] However, two studies [95, 96] additionally implemented a "passive" WB-EMS study arm

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Table 2. Intervention characteristics of the included research projects.

	Author	NEMS System	Isolated EMS?	Active mode?	Intervention length(months)	Sessions per week (n)	length of the session (min)	Impulse-frequency (Hz)	Impulse-width (µs)
1	FitAging-Project; Amaro-Gaehete et al. [16–20,24,26,33–35,60,112]	WB-EMS[1]	no	yes	3	2	20 or 32.5	15-20 or 35-75	200 - 40
2	Bellia et al. [21]	WB-EMS	yes	yes	6	2	20	15 or 85	400
3	Blöckl et al. [22]	WB-EMS	yes	yes	2	1-1.5	20	85	350
4	Bouty-Regard et al. [23]	B-SES[2]	yes	n.g.	3	2	20	20	250
5	DiCagno et al. [25]	WB-EMS	yes	yes	3	2	20	7 or 85	350
6	Evangelista et al. [27]	WB-EMS	no	yes	1.5	2	20	85	350
7	Fritzsche et al. [28]	WB-EMS	yes	yes	6	2	20	80	300
8	Hamada et al. [29]	B-SES	yes	yes	1	7(?)	20	20	250
9	Homma et al. [30]	B-SES	yes	no	3	3	40	20	250
10	Houdjijk et al. [31]	WB-EMS	yes	yes	4	2	20	85	350
11	Imaoka et al. [32]	B-SES	yes	no	0.5	5	20	20	250
12	Kataoka et al. [36]	B-SES	yes	no	3	3	20	4	250
13	TEST I Project; Kemmler et al. [37,38]	WB-EMS	yes	yes	3.5	2	20	7 or 85	350
14	TEST II-Project; Kemmler et al. [38,39]	WB-EMS	yes	yes	3.5	1.50	30	85	350
15	TEST-III-Project; Kemmler/von Stengel et al [40–42,92]	WB-EMS	yes	yes	12	1.50	20	85	350
16	TEST III-Sub-Project; Kemmler et al. [43]	WB-EMS	yes	yes	12	1.50	20	85	350
17	Formosa-Project Kemmler et al. [44,94]	WB-EMS	yes	yes	6	1	20	85	350
18	FranSO-Project; Kemmler et al. [46–49,111].	WB-EMS	yes	yes	4	1.50	20	85	350
19	Kim et al. [50]	WB-EMS	no	yes	2	3	40	85	350
20	Konrad et al. [51]	WB-EMS	yes	yes	1.5	1	20	85	350

 doi:10.20944/preprints202403.0183.v1

21	Lukashevich et al. [52]	WB-EMS	no	yes	0.66	4	20	Up to 25000	Up to 5000
22	Matsumoto et al. [53]	B-SES	yes	no	1	5	20	20	250
23	Matsuo et al. [54]	B-SES	yes	n.g.	0.5	5	20	20	250
24	Micke et al. [55]	WB-EMS	yes	yes	3	1	20	85	350
25	Mori 2020 et al. [56]	B-SES	yes	n.g.	1.5	2	30	20	250
26	Müllerova et al. [57]	WB-EMS	yes	yes	2.5	1	20	85	350
27	Nakamura et al. [58]	B-SES	yes	n.g.	0.5	7	20	20	250
28	Nakamura et al. [59]	B-SES	yes	n.g.	0.5	7	20	20	250
29	Nejad et al. [61]	WB-EMS	no	yes	3	3	20	15-33 or 35-75	200 and 400
30	Noguchi et al. [62]	B-SES	yes	n.g.	3	3	20	20	250
31	Nonoyama et al. [63]	B-SES	yes	n.g.	1.30	5	30	20	250
32	Ochiai et al. [64]	B-SES	yes	n.g.	1.10	7	20	20	250
33	Leida-Project; Pano-Rodriguez et al. [65,66,73]	WB-EMS	no	yes	2.5	2	40	7 or 55	150 to 350
34	Park 2021 et al. [68]	WB-EMS	no	yes	1.5	3	40	80	n.g.
35	Park et al. [67]	WB-EMS	no	yes	2	3	20	85	350
36	Park et al. [69]	WB-EMS	no	yes	2	3	45	4	n.g.
37	MetS-Project; Reljic el al. [70–72]	WB-EMS	yes	yes	3	2	20	85	350
38	Sanchez-Infante et al. [75]	WB-EMS	no	yes	2	1	20	10 or 85	350
39	Schink et al. [76,77]	WB-EMS	yes	yes	3	2	20	85	350
40	Schink et al. [78]	WB-EMS	yes	yes	3	2	20	85	350
41	Richter et al. [74]	WB-EMS	yes	yes	3	2	20	85	350
42	Schwappacher et al. [80]	WB-EMS	yes	yes	3	2	20	85	350
43	Schwappacher [79]	WB-EMS	yes	yes	3	2	20	85	350
44	Silvestri et al. [81]	WB-EMS	yes	yes	2	2	20	85	350
45	Suzuki et al. [82]	B-SES	yes	n.g.	2	3	20	20	250
46	Suzuki. et al. [83]	B-SES	yes	no	3	3	30	20	250
47	Tanaka et al. [84,85]	B-SES	yes	no	0.30	5	35	20	250

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48	Teschler et al. [12]	WB-EMS	yes	yes	1	1.50	20	85	350
49	Tsurumi et al. [86]	B-SES	yes	no	3	3	30	4	250
50	Vacoulikova et al. [88]	WB-EMS	yes	yes	2.5	1	20	85	350
51	Vacoulikova et al. [87]	WB-EMS	yes	yes	2.5	1	20	85	350
52	van Buuren et al. [90,91]	WB-EMS	yes	yes	2.5	2	20	80	350
53	van Buuren 2015 et al. [89]	WB-EMS	yes	yes	2.5	2	20	80	350
54	Weissenfels et al. [93]	WB-EMS	yes	yes	3	1	20	85	350

[1] WB-EMS: simultaneous application of electric stimuli via at least six current channels or participation of all major muscle groups, with a adaptations"[1]. In detail: large electrodes embedded in vest and cuffs were used to stimulate both thighs, upper arms, gluteals, lower and chest (stimulated area up to 2800 cm^2)

[2] B-SES: We are not aware of a dedicated definition of B.SES, however, B-SES focuses on the stimulation of gluteals and lower extremitie

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Outcomes: Physical function and fitness domain

More than 90% of the studies/projects included in the evidence map address physical function and fitness parameters however only a minority of the studies/projects defined physical function or fitness parameters as the core study outcome [12,29,30,32,36,44,49,52,53,66,69,76,85,88,97][3] (Figure 2)

Maximum strength

Maximum strength changes of the lower extremities [12,16,22,23,29,32,37,40,41,45,46,51,53,57,61,62,67,71,75,82,83,85,86], trunk [12,37,41,51,55,71,93] and upper extremities/hand[12,16,22,25,27,41,45,49,57,61–63,69,71,76,85] [4] were determined by many studies. About two thirds of the studies/projects applied isometric tests; functional tests were performed by seven studies and eight studies used isokinetic devices for strength assessments [16,22,45,46,57,67,75,83].

Power

The eligible studies determined changes in maximum power of the lower extremity by the 10s/3reps/5reps chair rise test [12,22,30,45,51,63,69,85,86], jump tests [45,51], leg press/leg extension devices [40,57] or functional tests [61,65].

Strength endurance

Changes in strength endurance of the lower extremities were determined by a 30 s sit to stand test [22,25,27,62,66,76,88], 2 min step test [61] or by an isokinetic leg extensor test [83]. Strength endurance of the trunk was determined by isometric or functional tests (e.g. front plank test) [16], upper extremity muscle endurance was determined by 30 s arm curl test [27,88]

Endurance

In summary, longitudinal intervention data on endurance parameters were reported by 18 trials/projects [12,16,25,27–30,40,61,62,66,69,76,85,86,88,89,91][5]. Most studies applied the 6 min (or 1 mile [61]) walking test [12,25,27,29,30,62,66,69,76,85,86,88]. Spiroergometry data was reported by [16,28,40,89,91].

Flexibility

Only a few studies/projects focus on flexibility changes [25,27,32,36,66,81,87] as an outcome. All authors focus on lower extremity flexibility, four of them [25,66,81,87] used the sit and reach test to determine flexibility of the hamstrings and lower back. Kataoka et al [36] considered ROM for hip flexion/abduction, knee flexion and extension as the primary study outcome in his cohort of bedridden elderly patients and Imaoka et al [32] focus on ankle dorsiflexion range in diabetes patients undergoing minor amputations. Three authors determined flexibility of trunk/upper extremity muscles by applying the back scratch test [27,66,87].

Balance

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[3] Some of these studies listed scores (i.e. Sarcopenie Z-Score) or test batteries (e.g. Senior Fitness Test battery) that included several fitness parameters as the primary or core study outcome.

[4] Maximum strength change was defined as primary outcome in the trials of Suzuki et al., Tanaka et al and Teschler et al. [12, 82, 85]

[5] Changes in endurance were defined as primary outcome by the trials of Homma et al. [30] and Teschler et al. [12].

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In summary, twelve authors [6] reported results of tests related to balance [22,25,30,51,62,63,66,75,82,85,86,88]. Six projects applied the balance tests included in the short physical performance battery (SPPB) [22,30,63,69,85,86][7], four trials used the timed up and go tests (TUG) [22,25,82,88] one study focused on the berg balance score [62]. Tests on balance platforms were conducted by two trials [51,81]. None of the studies considered balance as the primary study outcome.

Mobility, Agility

Apart from studies that applied the 4m (habitual) walking speed test included in the Short Physical Performance Battery (SPPB) [22,30,63,69,85,86] or the TUG-Test [22,25,82,88], only a few other studies listed parameters related to mobility and/or agility [22,25,44,49,52,58,66,76]. Habitual gait velocity was determined by [44,49,52,62,66,76]. Schink et al. [76] also focus on advanced gait parameters (e.g. stride time, swing time, variability. Blöckl et al. [22] used the choice stepping reaction test (CSRT) to assess agility and reaction time in his older cohort. Di Cagno et al. [25] applied a soda pop test in his cohort of Parkinson`s patients. None of the studies considered mobility, agility or coordination as the primary outcome.

Quality of life domain

In summary, 25 projects and 27 publications listed patient-reported changes in outcomes related to the quality of life (QoL) domain [12,22,25,28,30,32,34,39,46,51,52,55,58,59,63,64,67,69,71,77,81,82,84,90,93]. This included outcomes related to "Disability" [12,30,32,46,51,52,58,59,63,64,76,81] or frailty status [69].

Changes in overall pain [39,71,77], knee pain [67] and in particular low back pain [28,51,55,81,93] as determined by dedicated questionnaires/protocols were reported by the participants of nine studies. Five of the studies [51,55,67,81,93] considered knee or lower back pain reduction as the primary study outcome. Further, two of the studies [51,81] reported changes in disability related to back pain. Fatigue related to Parkinson`s disease [25] or advanced cancer [74,77] were reported by two research projects. In parallel, only two projects (FitAging, [34]; advanced cancer, [74,77] addressed insomnia/sleep quality as a secondary outcome. Of importance, none of the studies considered QoL parameters as the primary study outcome.

[6] Park et al. [69] only published data on short physical performance battery-score

[7] Changes in SPPB (…and 6MWT) was the primary study outcome of the trial of [30].

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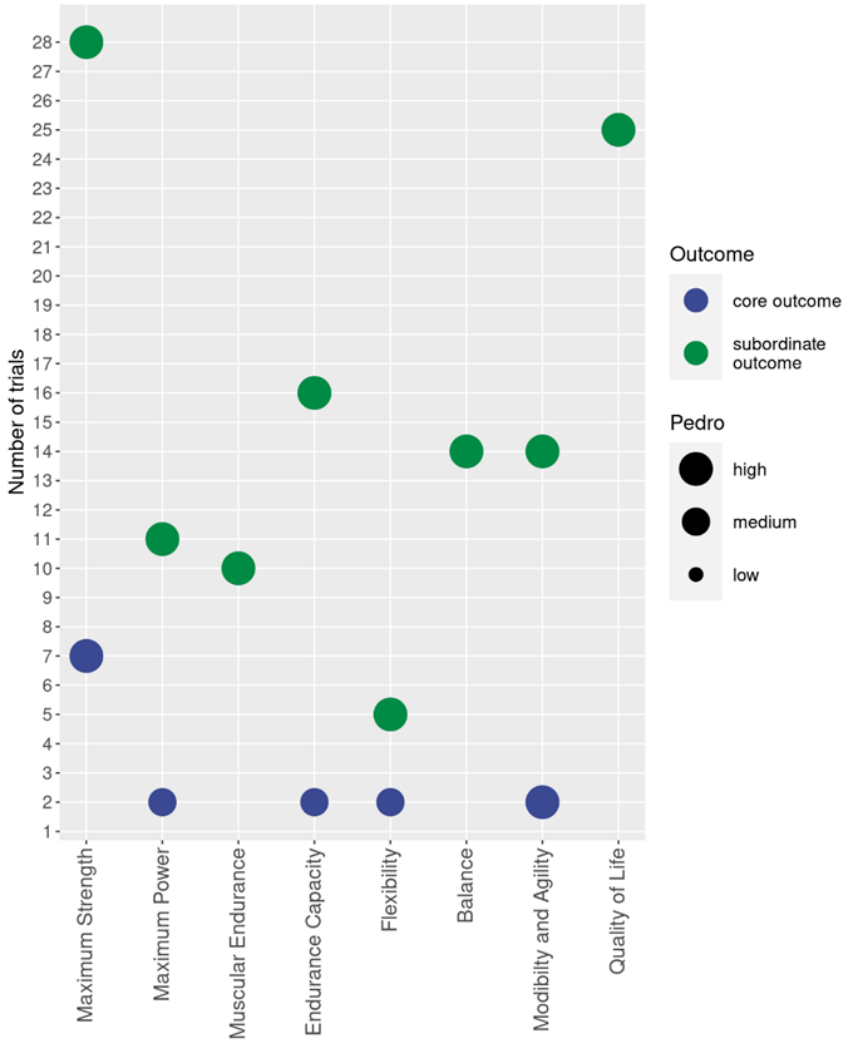

Figure 2. Physical fitness/function-related outcome addressed by WB-EMS. The y-axis presents the number of studies that focus on the corresponding cohort (x-axis). Different colors indicate whether the domain was considered a core (primary) or subordinate outcome. The size of the bubble indicates the methodological quality according to PEDro. The largest size indicates at least one study of high methodological quality in the domain. The smallest size of the bubble chart represents at least one study of low methodological quality in the domain.

Body composition and anthropometry

More than two thirds of the studies/projects reported changes body composition parameters as primary, secondary or tertiary outcome. Although difficult to conclude[8], about 14 studies considered changes in body composition and anthropometry at least as a core outcome [21,23,27,39,44,49,50,53,54,58,59,63,68,77] (Figure 3)

Lean body mass/fat free mass (LBM/FFM: [12,19,21,23,27,28,31,37,38,41,57,65,75] or/and muscle mass: [50,54,67–69,71,77,83] or/and appendicular skeletal muscle mass/skeletal muscle mass index (ASSM/SMI: [30,39,41,44,49,54,86]) were reported by 25 projects.

Total body fat changes [12,19,21,23,27,28,31,37,39,41,44,49,50,54,57,65,67–69,71,74,75,77,83,91] were reported by 25 projects.

[8] E.g. Kim et al. [50] listed "body composition" as the main outcome; Kemmler et al. [44, 49] applied Sarcopenic Obesity as the primary study outcome.

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Most studies/projects applied BIA [12,21,23,27,28,30,49,50,54,65,67–69,71,74,76–78,83,86,91] for the assessment of body composition. The minority of studies used DXA-technique, [19,31,39,44,57,75,92], one study [37] relied on the caliper method and a further study [53] determined changes in thigh and calf circumference.

Apart from total body fat, several studies determined trunk, abdominal, or visceral fat mass/rate by BIA [46,65], DXA [19,31,39,41] or CT [68] or, less sophisticated, by waist circumference [19,21,39,65,71,75,94].

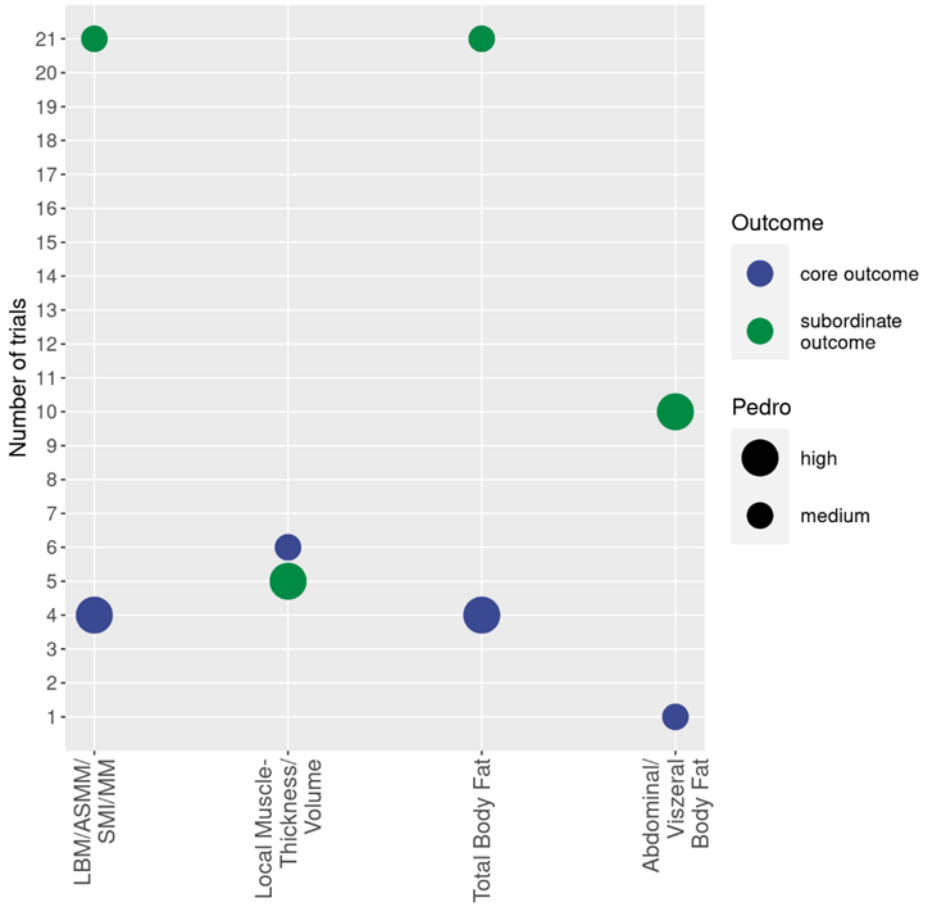

Figure 3. Body composition related outcome addressed by WB-EMS and classified according to the aspect whether the domain was considered a core (primary, blue color) or a subordinate outcome (green color).

Eleven studies focus on local muscle parameters (muscle thickness, cross-sectional area, cross-sectional volume) predominately at the mid-thigh/quadriceps site [23,27,29,46,54,58,59,63,68,83,86], calf [23] or upper arm [27] applying either ultrasound (US) [23,27,29,63,86], computed tomography (CT) [58,59,68] or magnetic resonance imaging (MRI)[46,83] techniques. Of relevance, five of the studies consider thigh muscle layer thickness (by US) as a primary outcome [23,54,58,59,63].

Resting metabolic rate. Two studies determine the basic or resting metabolic rate (RMR) by gas exchange parameters [20,37] as the gold standard procedure. One of them [37] considered EMR as the primary study outcome.

Health related outcomes

Apart from physical function and body composition parameters important for health, about 80% of the studies/projects addressed outcomes listed in the ICD 10. Of importance, some outcomes (e.g. TNFα; S-Klotho, creatine-kinase) refer to more than one ICD-10 classification, correspondingly the parameter might be listed several times (Figure 4)

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Neoplasm

Outcomes related to cancer and malignancies were addressed by 3 projects with 7 studies [50,67,74,77–80]. Kim et al [50] reported change in carcinoembryonic antigen (CEA), and together with Park et al. [67] determined inflammatory biomarkers including TNFα in general. The advanced cancer project [74,77–80] reported outcomes on dedicated cancer parameters e.g. malignant cell growth, proliferation and apoptosis or fatigue in a cohort of patients with advanced cancer.

Endocrine regulation

Thirteen studies of eight projects reported outcomes related to endocrine regulation. Three studies of the FitAging project determined WB-EMS effects on 1.25OH2D (Calcitriol) [24], testosterone, free Testosterone, Cortisol, Dehydroepiandrosteronesulfate (DHEA-S) [26] or S-Klotho [17], the latter as the primary project outcome. Di Cagno et al. [25] addressed neurotropic/growth factors (BDNF, FGF-21, NGF, proNGF)[9] and α-synuclein, which are particularly relevant outcomes in Parkinson patients. Apart from inflammatory markers also considered as hormones (e.g. Interferon γ (IFNγ), Interleukin 1 (IL1), Interleukin 6 (IL6), Tumor Nekrosis Factor (TNFα))[10], Reljic et al. and Kim et al listed WB-EMS effects on Adiponectin [70] and Resistin [50]in their obese cohorts. In parallel, Homma et al [30] addressed insulin-like growth factor 1 (IGF-1) and Irisin as a secondary study outcome in older hemodialysis patients. Schwappacher et al [80] reported changes in testosterone levels and neurotropic/growth factors (e.g. BDNF, IGFBP-3) in advanced cancer patients. Suzuki et al. [82] determined IGF-I, DHEA-S, adiponectin, and particularly relevant for his cohort of dialysis patients, atrial (ANP) and brain natriuretic peptide (BNP). Finally, Insulin was addressed by six studies/projects [18,21,69,70,82,83] that focus on obesity, the Metabolic Syndrome (MetS) or non-insulin-dependent (type II) diabetes mellitus (NIDDM).

Diabetes mellitus and the metabolic syndrome

Apart from the studies that determined Insulin [18,21,69,70,82,83] or Resistin levels [50,67] several other studies addressed glucose metabolism, the MetS or NIDDM with more dedicated outcomes or scores [18,21,31,40,47,69,72,82,83,86,89,94]. HbA1c results were reported by six studies [21,31,69,72,82,83,89]. HOMA and/or Quicki-Indices were reported by Amaro-Gahete et al. [18]; Bellia et al [21]; Park et al [69], Reljic et al. [72], and Suzuki et al. [83]. Three other studies calculated a metabolic risk [18]/Metabolic Syndrome Z-Score [72,94]. Parameters related to the MetS [21,72], or insulin resistance [31,83,86,89] were considered as primary or main outcome in six studies.

Diseases of the nervous system

Only two studies [25,52] addressed outcomes related to diseases of the nervous system. In a cohort of Parkinson patients, Di Cagno et al. [25] determined Parkinson Fatigue Score and neurotropic factors, growth factors (see above) and α-synuclein, biomarkers closely related to Parkinson`s disease. Lukashevich et al [52] applied the Modified Rankin-Scale, the Rivermead Mobility Index, Scandinavian Stroke Scale, functional tests and lower extremity kinematics in the early recovery phase after a cerebral infarction.

Cardiovascular diseases

A large number of studies/projects determined changes in outcomes related to cardiovascular diseases or conditions. Changes in blood pressure were reported by 12 studies [18,21,28,30,40,56,64,69,72,86,91,94]; apart from heart rate changes one author [60] focused on heart rate variability (HRV). Biomarkers of lipid metabolism including oxylipins and endocannabinoids [35] were addressed by 16 trials [12,18,21,23,31,35,40,47,50,69,72,73,82,83,86,94]. A further five authors

[9] brain derived neurotropic factor, Fibroblast growth factor-21, Nerve Growth Factor

[10] To avoid overlap, corresponding outcomes were given in the “inflammation” section.

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stated changes in hematologic and/or coagulation parameters [23,30,77,82,85] two further studies [82,85] assessed changes in brain-natriuretic peptide levels as a safety outcome. Changes in cardiorespiratory parameters as determined by spiroergometry were reported by five studies [18,28,61,89,91][11].

Mori et al. [56] and Park et al. [69] addressed vascular endothelial function of the lower extremities in dialysis patients [56] or pre-frail older women [69] via ultrasound imaging. Park et al. [69] and Ochai et al. [64] assessed WB-EMS/B-SES effects on arterial stiffness via ankle-brachial index (ABI) in prefrail older people [69] or patients with peripheral arterial disease (PAD) and severe ischemia of the lower extremities [64]. Finally, four studies focus on changes in left ventricular ejection fraction (LVEF) [85,89,91] and/or NT-pro-BNP [48,91] in older patients with acute or chronic heart failure [85,91], diabetes mellitus [89] or sarcopenic obesity [48]. In the latter cohort, Kemmler et al. [48] additionally addressed changes of CKMB and highly sensitive Troponin, pivotal biomarkers for the detection of cardiac injuries.

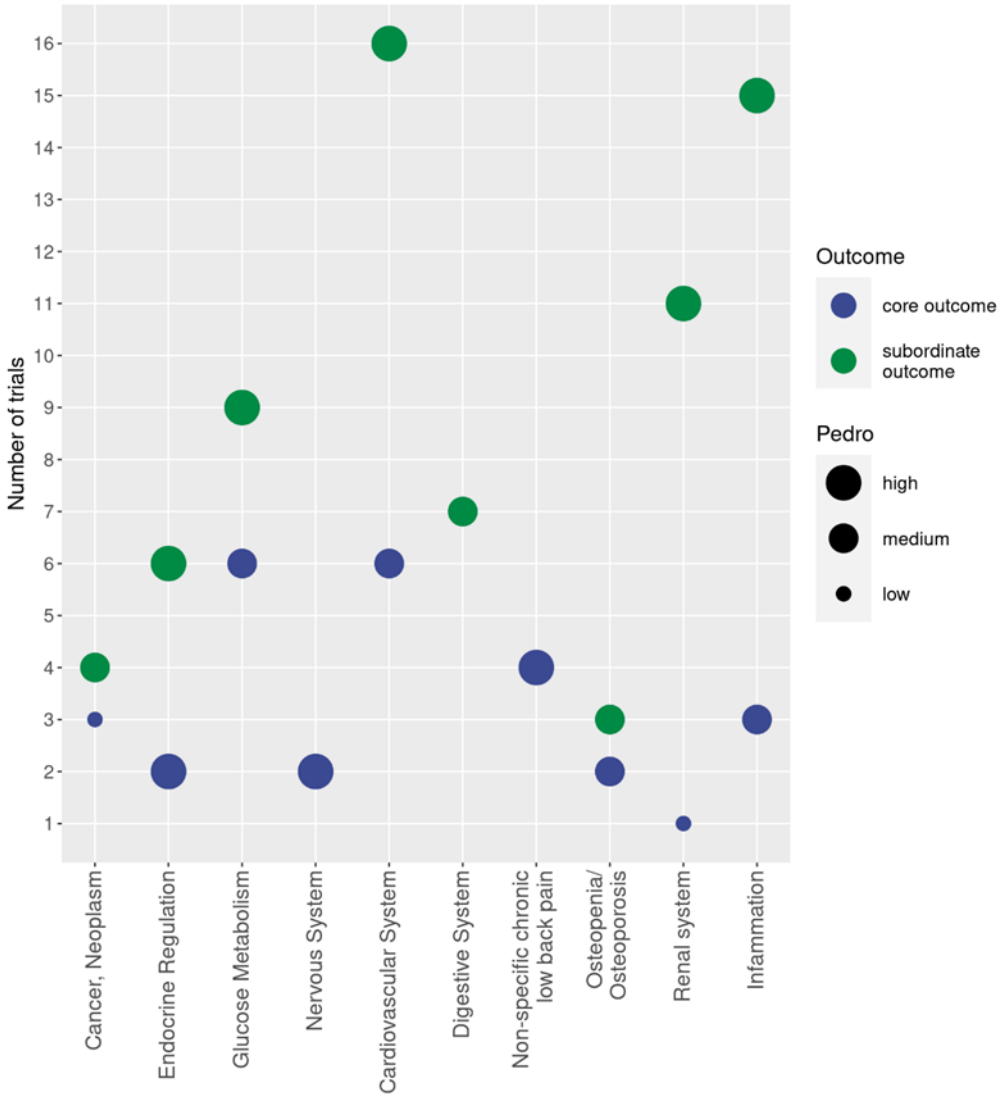

Figure 4. Health-related outcome addressed by WB-EMS and classified according to the aspect whether the domain was considered a core (primary) or a subordinate outcome.

Diseases of the respiratory system

[11] Although not explicitly stated, oxygen uptake can be considered the primary outcome of van Buuren et al. [91]

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Two studies [58,59] determined "days under mechanical ventilation" as secondary outcome in their cohorts of critically ill patients.

Diseases of the digestive system

The few studies that addressed this category [12,18,59,73,78] focus predominately on liver function determined by dedicated biomarkers [12,18,73] in healthy aged adults, or sarcopenic rehabilitation patients [12]. Nakamura et al. [59] focus on changes in diarrhea and vomiting events and gastric residual volume in his critically ill cohort (secondary outcome); appetite loss, constipation and diarrhea events as determined by questionnaire were secondary study outcomes in the advanced cancer project [74,77].

Diseases of the musculoskeletal system

One WB-EMS study [67] focused on osteoarthritis in older women with early knee Osteoarthritis applying the Knee Injury and Osteoarthritis Outcome Score (KOOS).

Non-specific chronic low back pain (NCLBP) was addressed by four trials [51,55,81,93] applying the visual analogue scale (VAS) [81] or the numeric rating scale (NRS10/11) [51,55,93] as a patient-reported outcome. Konrad et al [51] and Silvestri et al. [81] also applied the Oswestry Disability Index that focuses on low back pain and degenerative disc disease. Of importance, all of the studies clearly stated NCLBP as the primary study outcome.

Sarcopenia, recently included in the ICD-10 (M62.5), was addressed as a primary outcome by two studies [44,49]. At least three other studies [40,41,86] addressed morphometric (i.e. ASMM, SMI) and functional parameters (strength, power, muscle function) involved in the complex Sarcopenia diagnosis.

Outcomes related to exertional rhabdomyolysis were determined by several studies. Changes in creatine-kinase, myoglobin and other markers of muscle damage were also monitored by several other studies [12,22,23,28–30,48,50,71,73,78] predominately for safety aspects. In particular Blöckl et al. [22] and Schink et al [78] applied an advance protocol with multiple assessments during the WB-EMS intervention and [22] CK-levels drawn 48 and 72h post-exercise [12]. Outcomes related to rhabdomyolyses were main outcomes in one study/project [22].

Bone mineral density (BMD) or bone mineral content (BMC), i.e. outcomes specifically dedicated to Osteoporosis, were determined by five studies [19,57,75,87,92]. All studies applied dual energy x-ray absorptiometry (DXA) considered as the gold standard of bone densitometry and focus on middle aged to older women. Four studies determined whole body BMD, while von Stengel et al. [92] assessed BMD at the lumbar spine and femoral neck/total hip region of interest. Two studies considered BMD changes as the primary study outcome [92]. No study has so far focused on changes in markers of bone metabolism.

Diseases of the genitourinary system

Outcomes related with conditions or diseases related to the genitourinary system were addressed by several studies. Apart from outcomes on biomarkers of muscle status [12,22,23,30,48,53,71,73,78] also relevant for renal health, some studies additionally focus on outcomes related to renal function or failure [12,22,30,59,62,85]. Two studies that applied a combination of moderate (1.5 g/kg/d) [48] or high (1.8 g/kg/d) [59] protein intake and WB-EMS/B-SES in people with sarcopenic obesity or critically ill patient do not report relevant changes in blood urea nitrogen, creatinine, GFR, cystatin or other urea markers of protein metabolism and renal health. This result was confirmed by Tanaka et al. [85] that (comparable to the aforementioned studies that focus on the present outcome) observed no worsening of renal function or acute kidney injury in his cohort of frail patients with acute heart failure. Of importance, so far no eligible study on conventional WB-EMS or B-SES has focused on urinary incontinence as a study outcome.

[12] Data of Teschler et al. [98] indicate that CK and Myoglobin peaks occurred 48 to 72 h post-WB-EMS.

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Inflammation

Apart from creatine kinase (CK) as a marker of inflammation-induced muscle impairment [99], a large number of studies addressed outcomes related to inflammation predominately in older cohorts. C-reactive Protein (CRP) was determined by 12 studies/projects [23,29,30,32,50,53,59,62,67,70,78,82], highly sensitive CRP was assessed by three studies/projects [48,69,70]. IL-1 α was measured by Reljic et al [70], a further five studies [30,48,50,67,70] reported data on IL-6. TNFα results were listed by two studies [50,67]. Boutry-Regard et al [23] also addressed Transtyrethin, Fibrinogen, Orosomucoid as inflammatory outcomes; in parallel Reljic et al [70] reported data on Interferon γ (IFN γ) and Lipopolysaccharide-Binding Protein (LBP). Hematologic outcomes on inflammation were provided by two authors [32,59].

Adverse effects

While five studies failed to report adverse effects [56,57,59,62,86] and did not respond to our queries, no project/study listed relevant side effects related to the WB-EMS or B-SES application (Table 2). In detail, no study reported musculoskeletal adverse effects or injuries or negative effects on inflammatory, cardiovascular and cardiometabolic biomarkers or renal health, be it in cohorts with sarcopenia [12], sarcopenic obesity [48], advanced cancer [78], frailty [22], acute heart failure [85] or critical care patients [59]. Nevertheless, several studies reported changes in creatine-kinase, myoglobin and other markers of muscle damage [12,22,23,28–30,48,50,71,73,78], two of them [73,77] listed significant post-intervention CK increases. However, both studies reported changes far below the 5fold increase of resting CK levels considered as the threshold of rhabdomyolysis. While the clinical relevance of minor longitudinal CK changes is scarce, there is considerable evidence for severe rhabdomyolysis after too intense WB-EMS [100], particularly in novice applicants [98] Blöckl et al. [22] that closely monitor CK-kinetics (15min, 48h and 72h post EMS) after 1, 3 and 8 weeks reported CK-peaks consistently below 300 IE/l in frail older people. In contrast, Fritzsche et al. [28] reported one case of mild rhabdomyolysis (2770 IE/l CK) after acute WB-EMS in a patient with chronic heart failure, albeit without any clinical sign of rhabdomyolyses.

4. Discussion

The present evidence map aimed to identify and summarize WB-EMS application in middle aged and older people with respect to the study outcomes addressed. In summary, our results indicate the broad application of WB-EMS in several areas. Apart from physical fitness/function (Figure 2) and body composition (Figure 3) parameters expected to be addressed by a training technology with a comprehensive resistance exercise character [1,2], health-related outcomes were evaluated by the majority of studies/projects. We doubt that this finding might only be due to the advanced age of the cohort included in this review, since a twin study of this publication that focused on non-athletic adult cohorts addressed by WB-EMS [5] confirmed the high relevance of health-related topics in WB-EMS research. Reviewing this domain, a large variety of diseases and conditions have so far been addressed by longitudinal WB-EMS-trials (Figure 4); nevertheless, many health-related issues still have to be addressed. Considering the nature of WB-EMS i.e. the unique ability to stimulate large muscle areas simultaneously, not all health-related issues were similarly relevant for WB-EMS application and corresponding research, however. This particularly relates to local limitations (e.g. arthropathies, spondylopathies) and health issues in which the less elaborate local EMS might be the better option.

Summarizing general evidence for the different outcomes addressed by WB-EMS is a daunting task. This is particularly the case when it comes to the classification of outcomes in the present evidence map. We intended to strictly classify the outcomes of a trial into primary, secondary or subordinate study outcomes in order to categorize the methodologic relevance of the given outcome. However, many studies (a) do not specify a hierarchy of study outcomes, (b) listed a category of outcomes (i.e. “body composition”) as the primary study endpoint, (c) defined multiple parameters as primary endpoints or (d) focus on scores (e.g., MetS, Sarcopenic Z-score, SPPB) that combined

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multiple outcomes. Although we carefully checked articles, registers and online databases, we are aware that our categorization of core/primary vs. secondary/subordinate outcomes might be considered as not reliable in some cases. Another problem, albeit of lesser relevance for the present work, is the lack of a core outcome set (COS) that enables a pooled analysis of harmonized outcomes [101]. As an example, considering body composition, diverging outcomes largely based on the similar assessment (e.g. total or subtotal lean body mass (LBM), fat free mass (FFM), soft LBM or FFM, muscle mass, appendicular skeletal muscle mass, skeletal muscle mass index etc.) aggravate a joint analysis. Accordingly, for better comparability of study outcomes and data pooling, a COS with the minimum of the most important study endpoints under consideration of health conditions and population [101] should be defined at least for domains (i.e. physical fitness/function, body composition, safety aspects) frequently addressed in WB-EMS trials. A further problem important for the interpretation of the present evidence map is the aspect that outcome and cohorts do not match in all studies. This concerns, for example, the relevance on blood pressure outcomes in normotensive cohorts.

Nevertheless, we feel that several outcome domains were addressed with sufficient evidence. These are in particular the domains of physical fitness and function entailing the categories “maximum muscle strength”, “power”, “strength endurance”, “aerobic endurance”, “balance”, “mobility/agility”, and (with some restriction) “flexibility” - although more data on specific cohorts (e.g. stroke patients) is welcome. Correspondingly, sufficient evidence of WB-EMS application on outcomes related to body composition is provided so far. In detail however, muscle quality and local or overall fat distribution, for example, should be addressed with more emphasis by applying advanced technology [46,68].

Quality of life (QoL), also included in Figure 2, covers a large variety of outcomes differently addressed by the included trials. While sufficient evidence exists for self-reported pain episodes and disability outcomes, at least a few trials addressed other physiological aspects (e.g. [77]. Nevertheless, the mental health aspects of QoL in particular were rarely evaluated. However, due to the very individualized setting of WB-EMS it will be difficult to properly refer corresponding effects to WB-EMS effects per se and not to the close interaction between trainer and trainee.

As stated, health related outcomes were frequently addressed by WB-EMS trials in middle aged to older adults. In summary, we feel that sufficient evidence for the application of WB-EMS was provided for non-insulin dependent diabetes mellitus and the MetS, obesity, cardiovascular disease, renal health, sarcopenia, and in particular for unspecific chronic low back pain.

Five studies focus on BMD as determined by DXA, thus sufficient evidence for the application of WB-EMS in the area of osteopenia/osteoporosis should be evident. In detail however, only one study applied a sufficiently long intervention (>6 months [102]) and focused on a region of interest (e.g. lumbar spine, femoral neck [103]) specified for osteopenia/osteoporosis research [92].

Outcomes closely related to neoplasm/tumor/malignancies were predominately provided by the ongoing “advanced cancer project” in Erlangen, Germany [74,76–80]. Due to the palliative setting most of these studies however focus on physical function, QoL and body composition rather than dedicated biomarkers as primary outcomes. In parallel, endocrine regulation is also a complex cluster of diverging outcomes. So far, WB-EMS-induced changes of anabolic steroids (e.g. 1.25 OHD, Testosterone, DHEAS), growth factors (e.g. IGF-I), adipose tissue peptide hormones (e.g. Adiponectin, Resistin), myokines (e.g. BNDF, Irisin, IL-6) and their corresponding binding proteins (e.g. SHBG, IGFBP-3) have been evaluated by WB-EMS trials. However, none of the studies specifically focus on hormone deficiency conditions (e.g. hypogonadisms, post-menopause); thus the relevance of the results on the endocrine outcomes addressed remains limited. Considering that many studies focus on older patients, we suggest that changes in dedicated hormone profiles at least as explanatory outcomes for muscle and bone health should be addressed with more emphasis. Given the relevance of an exercise training technology able to trigger involuntary muscle contraction of large skeletal areas with dedicated stimulus intensity, the domain of diseases of the nervous system including paresis, paralysis, and spastic is particularly insufficiently addressed by WB-EMS. Although some evidence provided by local neuromuscular electromyostimulation (review in [104])

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might be transferable to WB-EMS, more studies should focus on outcomes related to the nervous system.

A highly relevant finding of the present work is the lack of relevant adverse effects, limited albeit by a few articles [56,57,59,62,86] that failed to report such effects. Of note, four of these five studies applied B-SES in vulnerable cohorts (e.g. critical care patients, end stage kidney disease) which might have aggravated the proper assignment of the undesired side effect to the EMS intervention.

While still many promising outcomes remain unaddressed by WB-EMS technology, some diseases or conditions considered as absolute WB-EMS contraindications for WB-EMS [105] were frequently addressed by the closely medically supervised trials. This particularly refers to non-insulin-dependent (type II) diabetes mellitus, tumor and cancer, outcome addressed by several studies predominantly in affected cohorts (e.g. [31,32,77,89]. Considering further the mandatory regulations on WB-EMS operation and trainer education provided by (German) federal authorities in 2019 [106,107], it might be justified to revise the present absolute contraindications [105] in the nearest future and so open WB-EMS application for cohorts in need of appropriate training methods. Of relevance however, WB-EMS for vulnerable cohorts still has to be applied in a closely supervised medically setting (i.e. medical WB-EMS [108]).

Some features of this evidence map might be confusing or hard to grasp for the reader. (1) First, in contrast to other types of literature reviews, evidence maps do not consider the intervention effect on the given outcome. This feature may be uncommon for the reader that potentially expect evidence for the effectiveness of WB-EMS on dedicated outcomes. However, considering the multitude of different outcomes along with the aspect that a systematic review that aimed to provide interpretable intervention effects have to adequately describe the cohort addressed and the intervention provided, indicate the sheer illegibility of such an approach. Applying a reasonable categorization and simple counting of eligible studies along with basic methodologic quality criteria in contrast enable a quick and comprehensive overview of outcomes addressed by WB-EMS and particularly current research gaps. Nevertheless, insight on the effectiveness of WB-EMS on various outcomes is crucial, however corresponding research should focus on single outcome domains (i.e. body composition) or single outcome categories (i.e. NCLBP). (2) Due to the large number of potentially eligible studies combined with (a) poor or confusing information provided, (b) difficulties in proper translation, (c) missing author response to our queries and (d) the approach of publishing several articles that reported overlapping outcomes of a project, we cannot be sure that we have identified all the eligible articles and properly classified their outcomes. (3) In order to provide a comprehensive overview on outcomes addressed by WB-EMS and related technologies, we included all types of interventional cohort studies, independent of randomization or the presence of a control group. (4) While WB-EMS and B-SES shared many features, some differences should be considered. First, B-SES focuses on hip and lower limb muscles, while WB-EMS addresses all main muscle groups including upper back, chest and upper extremities. Further, the included B-SES studies consistently focus on EMS application in a lying position and passive mode, while WB-EMS studies usually applied EMS in an upright position with adjuvant movements during the impulse phase. Finally, WB-EMS uses bipolar stimulation while B-SES relies on mono-polar impulses. (5) Another limitation already discussed refer to trials that failed to define a reliable hierarchy of outcomes. In summary, this reduces the plausibility of the analysis and contributes to publication bias. However, this limitation might be much more relevant when study effects were addressed. (6) Methodological quality was rated by the PEDro scale specifically dedicated to clinical physiotherapy and exercise studies. However, PEDro might not be perfectly applicable for non-randomized controlled trials, particularly those without control groups. Nevertheless, it is important to classify the contribution of the single studies for evidence and relevance of the domain. Rating of methodological quality is definitely a component of this process. (7) Finally, we based our criteria of “safety” on adverse effects reported by the studies. Apart from acute increases in CK post-exercise [28] that were comparably noted after heavy resistance exercise [109] and few drop-outs due to “discomfort with WB-EMS” (e.g. [49]) none of the included studies reported clinically relevant adverse effects. This does not necessarily indicate that WB-EMS is a “harmless” exercise technology for all cohorts. Undoubtedly, too intense stimulation

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intensity has resulted in severe rhabdomyolysis [98,100] particularly in novice users. Thus, it is important to respect guidelines [110] and the rather restrictive contraindications [105] on WB-EMS to ensure safe and effective application..

5. Conclusions

The present work provided evidence for the application of WB-EMS and the closely related B-SES technology to address a wide range of outcomes. While a large variety of musculoskeletal and cardiometabolic outcomes were sufficiently addressed by WB-EMS/B-SES research, particularly outcomes related to the domain of diseases of the nervous system have rarely been evaluated so far. Considering the character of WB-EMS as a highly supervised NMES technique that enables the simultaneous stimulation of large muscle groups with dedicated intensity, WB-EMS might be a promising option for favorably addressing outcomes related to neuronal diseases. The fact that none of the trials reported clinically relevant adverse effects should not obscure the fact that inappropriate (e.g. too intense or/and frequent) WB-EMS application will lead to severe adverse effects. Strict adherence to the guidelines for safe and effective WB-EMS application and corresponding contraindications should therefore be mandatory.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.: Table S1.

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References

1. Kemmler W., Kleinoder H., Fröhlich M. Editorial: Whole-Body Electromyostimulation: A Training Technology to Improve Health and Performance in Humans? *Frontiers in physiology.* **2020**, *11*, 523.
2. Kemmler W., Kleinoder H., Fröhlich M. Editorial: Whole-body electromyostimulation: A training technology to improve health and performance in humans? volume II. *Frontiers in physiology.* **2022**, *13*, 972011.
3. de Oliveira T. M. D., Felicio D. C., Filho J. E., et al. Effects of whole-body electromyostimulation on function, muscle mass, strength, social participation, and falls-efficacy in older people: A randomized trial protocol. *PLoS One.* **2021**, *16*, e0245809.
4. Eifler C. Marktsituation, Trends und Entwicklungen. In *Ganzkörper-EMS*, Kemmler, W., Fröhlich, M., Eifler, C. Eds.; Vol. Essentials Springer Spektrum, 2022.
5. Beier M., Schoene D., Kohl M., von Stengel S., Uder M., Kemmler W. Non-athletic cohorts enrolled in longitudinal whole-body electromyostimulation trials - An evidence map. *Sensors (Basel).* **2024**, *24*, 972.
6. Miake-Lye I. M., Hempel S., Shanman R., Shekelle P. G. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. *Syst Rev.* **2016**, *5*, 28.
7. Thiese M. S. Observational and interventional study design types; an overview. *Biochem Med (Zagreb).* **2014**, *24*, 199-210.

8. Bramer W. M., Giustini D., de Jonge G. B., Holland L., Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc.* **2016**, *104*, 240-243.
9. Mages M., Shojaa M., Kohl M., et al. Exercise Effects on Bone Mineral Density in Men. *Nutrients.* **2021**, *13*, 4244.
10. Mohebbi R., Shojaa M., Kohl M., et al. Exercise training and bone mineral density in postmenopausal women: An updated systematic review and meta-analysis of intervention studies with emphasis on potential moderators. *Osteo Int.* **2023**, *4*, 1145-1178.
11. ICD-10-GM. International Statistical Classification of Diseases and Related Health Problems, 10. Revision, German Modification. In *https://www.bfarm.de/EN/Code-systems/Classifications/ICD/ICD-10-GM/_node.html*, 2022.
12. Teschler M., Heimer M., Schmitz B., Kemmler W., Mooren F. C. Four weeks of electromyostimulation improves muscle function and strength in sarcopenic patients: a three-arm parallel randomized trial. *J Cachexia Sarcopenia Muscle.* **2021**, *12*, 843-854.
13. Maher C. G., Sherrington C., Herbert R. D., Moseley A. M., Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Physical therapy.* **2003**, *83*, 713-721.
14. Ribeiro de Avila V., Bento T., Gomes W., Leitao J., Fortuna de Sousa N. Functional Outcomes and Quality of Life After Ankle Fracture Surgically Treated: A Systematic Review. *J Sport Rehabil.* **2018**, *27*, 274-283.
15. Page M. J., McKenzie J. E., Bossuyt P. M., et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* **2021**, *372*, 71.
16. Amaro-Gahete F. J., De-la O. A., Jurado-Fasoli L., et al. Changes in Physical Fitness After 12 Weeks of Structured Concurrent Exercise Training, High Intensity Interval Training, or Whole-Body Electromyostimulation Training in Sedentary Middle-Aged Adults: A Randomized Controlled Trial. *Frontiers in physiology.* **2019**, *10*, 451.
17. Amaro-Gahete F. J., De-la O. A., Jurado-Fasoli L., et al. Exercise training increases the S-Klotho plasma levels in sedentary middle-aged adults: A randomised controlled trial. The FIT-AGEING study. *J Sports Sci.* **2019**, *37*, 2175-2183.
18. Amaro-Gahete F. J., De-la O. A., Jurado-Fasoli L., Martinez-Tellez B., Ruiz J. R., Castillo M. J. Exercise Training as a Treatment for Cardiometabolic Risk in Sedentary Adults: Are Physical Activity Guidelines the Best Way to Improve Cardiometabolic Health? The FIT-AGEING Randomized Controlled Trial. *J Clin Med.* **2019**, *8*,
19. Amaro-Gahete F. J., De-la O. A., Jurado-Fasoli L., Ruiz J. R., Castillo M. J., Gutierrez A. Effects of different exercise training programs on body composition: A randomized control trial. *Scand J Med Sci Sports.* **2019**, *29*, 968-979.
20. Amaro-Gahete F. J., De-la O. A., Jurado-Fasoli L., Sanchez-Delgado G., Ruiz J. R., Castillo M. J. Metabolic rate in sedentary adults, following different exercise training interventions: The FIT-AGEING randomized controlled trial. *Clin Nutr.* **2020**, *39*, 3230-3240.
21. Bellia A., Ruscello B., Bolognino R., et al. Whole-body Electromyostimulation plus Caloric Restriction in Metabolic Syndrome. *Int J Sports Med.* **2020**, *41*, 751-758.
22. Bloeckl J., Raps S., Weineck M., et al. Feasibility and Safety of Whole-Body Electromyostimulation in Frail Older People-A Pilot Trial. *Frontiers in physiology.* **2022**, *13*, 856681.
23. Boutry-Regard C., Vinyes-Pares G., Breuille D., Moritani T. Supplementation with Whey Protein, Omega-3 Fatty Acids and Polyphenols Combined with Electrical Muscle Stimulation Increases Muscle Strength in Elderly Adults with Limited Mobility: A Randomized Controlled Trial. *Nutrients.* **2020**, *12*, 1866.
24. De-la O. A., Jurado-Fasoli L., Castillo M. J., Gutierrez A., Amaro-Gahete F. J. Effect of Exercise Training on 1,25(OH)(2)D Levels: The FIT-AGEING Randomized Controlled Trial. *Sports Health.* **2022**, *14*, 518-526.
25. di Cagno A., Buonsenso A., Centorbi M., et al. Whole body-electromyostimulation effects on serum biomarkers, physical performances and fatigue in Parkinson's patients: A randomized controlled trial. *Front Aging Neurosci.* **2023**, *15*, 1086487.
26. Dote-Montero M., De-la O. A., Jurado-Fasoli L., Ruiz J. R., Castillo M. J., Amaro-Gahete F. J. The effects of three types of exercise training on steroid hormones in physically inactive middle-aged adults: a randomized controlled trial. *Eur J Appl Physiol.* **2021**, *121*, 2193-2206.
27. Evangelista A. L., Alonso A. C., Ritti-Dias R. M., et al. Effects of Whole Body Electrostimulation Associated With Body Weight Training on Functional Capacity and Body Composition in Inactive Older People. *Frontiers in physiology.* **2021**, *12*, 638936.
28. Fritzsche D., Fruend A., Schenk S., et al. Elektromyostimulation (EMS) bei kardiologischen Patienten. Wird das EMS-Training bedeutsam für die Sekundärprävention? *Herz.* **2010**, *35*, 34-40.

 doi:10.20944/preprints202403.0183.v1

29. Hamada R., Sato S., Miyasaka J., et al. Belt Electrode-Skeletal Muscle Electrical Stimulation During Early Hematopoietic Post-Transplantation To Prevent Skeletal Muscle Atrophy and Weakness. *Transplant Cell Ther.* **2023**, *29*, 51 e51-51 e57.
30. Homma M., Miura M., Hirayama Y., et al. Belt Electrode-Skeletal Muscle Electrical Stimulation in Older Hemodialysis Patients with Reduced Physical Activity: A Randomized Controlled Pilot Study. *J Clin Med.* **2022**, *11*, 622-630.
31. Houdijk A. P. J., Bos N., Verduin W. M., Hijdendaal M. M., Zwartkruis M. A. L. Visceral fat loss by whole-body electromyostimulation is attenuated in male and absent in female older Non-Insulin-Dependent diabetes patients. *Endocrinol Diabetes Metab.* **2022**, *5*, e377.
32. Imaoka S., Kudou G., Tsugiyama K., et al. Efficacy of Belt Electrode Skeletal Muscle Electrical Stimulation in the Postoperative Rest Period in Patients with Diabetes who Have Undergone minor Amputations: A Randomized Controlled Trial. *Int J Low Extrem Wounds.* **2022**, 15347346221077491.
33. Jurado-Fasoli L., Amaro-Gahete F. J., De-la O. A., Castillo M. J. Impact of different exercise training modalities on energy and nutrient intake and food consumption in sedentary middle-aged adults: a randomised controlled trial. *J Hum Nutr Diet.* **2020**, *33*, 86-97.
34. Jurado-Fasoli L., De-la O. A., Molina-Hidalgo C., Migueles J. H., Castillo M. J., Amaro-Gahete F. J. Exercise training improves sleep quality: A randomized controlled trial. *Eur J Clin Invest.* **2020**, *50*, e13202.
35. Jurado-Fasoli L., Yang W., Kohler I., et al. Effect of Different Exercise Training Modalities on Fasting Levels of Oxylipins and Endocannabinoids in Middle-Aged Sedentary Adults: A Randomized Controlled Trial. *Int J Sport Nutr Exerc Metab.* **2022**, *32*, 275-284.
36. Kataoka H., Nakashima S., Aoki H., et al. Electrical stimulation in addition to passive exercise has a small effect on spasticity and range of motion in bedridden elderly patients: A pilot randomized crossover study. *Health.* **2019**, *11*, 1072-1086.
37. Kemmler W., Schliffka R., Mayhew J. L., von Stengel S. Effects of Whole-Body-Electromyostimulation on Resting Metabolic Rate, Anthropometric and Neuromuscular Parameters in the Elderly. The Training and ElectroStimulation Trial (TEST). *J Strength Cond Res.* **2010**, *24*, 1880-1886.
38. Kemmler W., Teschler M., Von Stengel S. Effekt von Ganzkörper-Elektromyostimulation – „A series of studies“. *Osteologie* **2015**, *23*, 20-29.
39. Kemmler W., Birlauf A., von Stengel S. Einfluss von Ganzkörper-Elektromyostimulation auf das Metabolische Syndrom bei älteren Männern mit metabolischem Syndrom. *Dtsch Z Sportmed.* **2010**, *61*, 117-123.
40. Kemmler W., von Stengel S. Alternative Exercise Technologies to Fight against Sarcopenia at Old Age: A Series of Studies and Review. *J Aging Res.* **2012**, *2012*, 109013.
41. Kemmler W., Bebenek M., Engelke K., von Stengel S. Impact of whole-body electromyostimulation on body composition in elderly women at risk for sarcopenia: the Training and ElectroStimulation Trial (TEST-III). *Age.* **2014**, *36*, 395-406.
42. Kemmler W., Engelke K., Von Stengel S. Ganzkörper-Elektromyostimulation zur Prävention der Sarkopenie bei einem älteren Risikokollektiv. Die TEST-III Studie. *Dtsch Z Sportmed.* **2012**, *63*, 16-23.
43. Kemmler W., von Stengel S. Whole-body electromyostimulation as a means to impact muscle mass and abdominal body fat in lean, sedentary, older female adults: subanalysis of the TEST-III trial. *Clinical interventions in aging.* **2013**, *8*, 1353-1364.
44. Kemmler W., Teschler M., Weissenfels A., et al. Whole-body electromyostimulation to fight sarcopenic obesity in community-dwelling older women at risk. Resultsof the randomized controlled FORMOsA-sarcopenic obesity study. *Osteoporos Int.* **2016**, *27*, 3261-3270.
45. Kemmler W., von Stengel S., Teschler M., et al. Ganzkörper-Elektromyostimulation und Sarcopenic Obesity. Ergebnisse der randomisierten kontrollierten FORMOsASarcopenic Obesity Studie. *Osteologie.* **2016**, *25*, 204-211
46. Kemmler W., Grimm A., Bebenek M., Kohl M., von Stengel S. Effects of Combined Whole-Body Electromyostimulation and Protein Supplementation on Local and Overall Muscle/Fat Distribution in Older Men with Sarcopenic Obesity: The Randomized Controlled Franconia Sarcopenic Obesity (FranSO) Study. *Calcified tissue international.* **2018**, *103*, 266-277.
47. Kemmler W., Kohl M., Freiberger E., Sieber C., von Stengel S. Effect of whole-body electromyostimulation and / or protein supplementation on obesity and cardiometabolic risk in older men with sarcopenic obesity: the randomized controlled FranSO trial. *BMC geriatrics.* **2018**, *18*, 70.
48. Kemmler W., von Stengel S., Kohl M., et al. Safety of a Combined WB-EMS and High-Protein Diet Intervention in Sarcopenic Obese Elderly Men. *Clinical interventions in aging.* **2020**, *15*, 953-967.

49. Kemmler W., Weissenfels A., Teschler M., et al. Whole-body Electromyostimulation and protein supplementation favorably affect Sarcopenic Obesity in community-dwelling older men at risk. The Randomized Controlled FranSO Study. *Clinical interventions in aging.* **2017**, *12*, 1503-1513.
50. Kim J., Jee Y. EMS-effect of Exercises with Music on Fatness and Biomarkers of Obese Elderly Women. *Medicina (Kaunas).* **2020**, *56*, 156.
51. Konrad K. L., Baeyens J.-P., Birkenmaier C., et al. The effects of whole-body electromyostimulation (WB-EMS) in comparison to a multimodal treatment concept in patients with non-specific chronic back pain—A prospective clinical intervention study. *PloS one.* **2020**, *15*, e0236780.
52. Lukashevich U. A., Ponomarev, V.V., Tarasevich, M.I., Zhivolupov, S.A. . Functional reciprocal neuromuscular electric stimulation in adaptive kinesitherapy in post-stress patients. *Science & Healthcare.* **2020**, *22*, 80-88.
53. Matsumoto J. M., Y. Terabe, S. , Sakaki R. H., H. . Experience of Belt Electrode Skeletal Muscle Electrical Stimulation Method for Severe Lower Limb Ischemic Patients: A Case Report. *Physical Therapy in Clinical Practice, Research & Education.* **2020**, *27*, 81-85.
54. Matsuo K., Yoneki K., Tatsuki H., et al. Effect of Electrical Muscle Stimulation on the Reduction of Muscle Volume Loss in Acute Heart Failure Patients. *Int Heart J.* **2022**, *63*, 1141-1149.
55. Micke F., Weissenfels A., Wirtz N., et al. Similar Pain Intensity Reductions and Trunk Strength Improvements following Whole-Body Electromyostimulation vs. Whole-Body Vibration vs. Conventional Back-Strengthening Training in Chronic Non-specific Low Back Pain Patients: A 3-armed randomized controlled trial. *Frontiers in physiology.* **2021**, *13*, 664991.
56. Mori K., Tamura Y., Deguchi K., Miura Y., Yura, Y., T. K. Effect of belt electrode skeletal muscle electrical stimulation during hemodialysis on the endothelial function in hemodialysis patients [*透析患者に対する透析中のベルト電極式骨格筋電気刺激が血管内皮機能に及ぼす影響*] *Japanese Journal of Electrophysical Agents.* **2020**, *27*, 78-81.
57. Müllerová M., Vaculíková P., Potúčková A., Struhár I., Balousová D. N. Impact of Whole-Body Electromyostimulation and Resistance Training Programme on Strength Parameters and Body Composition in Group of Elderly Women at Risk of Sarcopenia. *Studia sportiva.* **2022**, *16*, 292-304.
58. Nakamura K., Kihata A., Naraba H., et al. Efficacy of belt electrode skeletal muscle electrical stimulation on reducing the rate of muscle volume loss in critically ill patients: A randomized controlled trial. *J Rehabil Med.* **2019**, *51*, 705-711.
59. Nakamura K., Nakano H., Naraba H., et al. High protein versus medium protein delivery under equal total energy delivery in critical care: A randomized controlled trial. *Clin Nutr.* **2021**, *40*, 796-803.
60. Navarro-Lomas G., Dote-Montero M., Alcantara J. M. A., Plaza-Florido A., Castillo M. J., Amaro-Gahete F. J. Different exercise training modalities similarly improve heart rate variability in sedentary middle-aged adults: the FIT-AGEING randomized controlled trial. *Eur J Appl Physiol.* **2022**, *122*, 1863-1874.
61. Nejad M. D., Nikbakht M., Ghanbarzadeh M., Ranjbar R. Effect of Concurrent Training Order With Electromyostimulation on Physical Performance in Young Elderly Women. *Archives of Rehabilitation.* **2021**, *21*, 508-525.
62. Noguchi Y., Hirano H., Mizutani C., Ito T., Kawamura N. Die Wirkung der elektrischen Stimulation der Skelettmuskulatur mit Gürtelelektroden während der Hämodialyse auf die körperliche Funktion von Hämodialysepatienten *[透析中ベルト電極式骨格筋電気刺激法が透析患者の身体機能に与える影響]*. *Journal of Dialysis Society.* **2018**, *51*, 87-91.
63. Nonoyama T., Shigemi H., Kubota M., Matsumine A., Shigemi K., Ishizuka T. Neuromuscular electrical stimulation in the intensive care unit prevents muscle atrophy in critically ill older patients: A retrospective cohort study. *Medicine (Baltimore).* **2022**, *101*, e29451.
64. Ochiai K., Tamura, Y., Ehara, K., Shimizu, R., Matushita, Y., Yasu, T. Bridging Therapy Using B-SES for Peripheral Arterial Disease Patients with Severe Lower Limb Ischemia. *Journal of Physical Therapy Science.* **2018**, *33*, 545-548.
65. Pano-Rodriguez A., Beltran-Garrido J. V., Hernandez-Gonzalez V., Nasarre-Nacenta N., Reverter-Masia J. Impact of Whole Body Electromyostimulation on Velocity, Power and Body Composition in Postmenopausal Women: A Randomized Controlled Trial. *Int J Environ Res Public Health.* **2020**, *17*, 4982.
66. Pano-Rodriguez A., Beltran-Garrido J. V., Hernandez-Gonzalez V., Reverter-Masia J. Effects of Whole-Body Electromyostimulation on Physical Fitness in Postmenopausal Women: A Randomized Controlled Trial. *Sensors (Basel).* **2020**, *20*,
67. Park S., Min S., Park S. H., Yoo J., Jee Y. S. Influence of Isometric Exercise Combined With Electromyostimulation on Inflammatory Cytokine Levels, Muscle Strength, and Knee Joint Function in Elderly Women With Early Knee Osteoarthritis. *Frontiers in physiology.* **2021**, *12*, 688260.

 doi:10.20944/preprints202403.0183.v1

68. Park S., Park J., Ham J. A., Jee Y. Effects of aerobic dance with electrical stimulant on body composition and radiological circumference of obese elderly women. *Gazzetta Medica Italiana Archivio per le Scienze Mediche.* **2021**, *180*, 000-000.
69. Park W., Lee J., Hong K., et al. Protein-Added Healthy Lunch-Boxes Combined with Exercise for Improving Physical Fitness and Vascular Function in Pre-Frail Older Women: A Community-Based Randomized Controlled Trial. *Clinical interventions in aging.* **2023**, *18*, 13-27.
70. Reljic D., Dieterich W., Herrmann H. J., Neurath M. F., Zopf Y. "HIIT the Inflammation": Comparative Effects of Low-Volume Interval Training and Resistance Exercises on Inflammatory Indices in Obese Metabolic Syndrome Patients Undergoing Caloric Restriction. *Nutrients.* **2022**, *14*,
71. Reljic D., Herrmann H. J., Neurath M. F., Zopf Y. Iron Beats Electricity: Resistance Training but Not Whole-Body Electromyostimulation Improves Cardiometabolic Health in Obese Metabolic Syndrome Patients during Caloric Restriction-A Randomized-Controlled Study. *Nutrients.* **2021**, *13*, 1640.
72. Reljic D., Konturek P. C., Herrmann H. J., Neurath M. F., Zopf Y. Effects of whole-body electromyostimulation exercise and caloric restriction on cardiometabolic risk profile and muscle strength in obese women with the metabolic syndrome: a pilot study. *J Physiol Pharmacol.* **2020**, *71*,
73. Reverter-Masia J., Pano-Rodriguez A., Beltran-Garrido J. V., Lecube A., Sánchez E., Hernández-González V. Effect of a Training Program on Hepatic Fat Content and Cardiometabolic Risk in Postmenopausal Women: The Randomized Controlled Trial. *Applied Sciences.* **2021**, *11*,
74. Richter H. Effect of electromyostimulation training and high-protein diet on gastrointestinal tumor patients in palliative and curative treatment settings. [Einfluss von Elektromyostimulationstraining und proteinreicher Ernährung auf gastrointestinale Tumorpatienten in palliativer und kurativer Behandlungssituation]. Friedrich-Alexander-University Erlangen-Nürnberg, Germany, Erlangen, 2019.
75. Sánchez-Infante J., Bravo-Sáncheza A., Abiánb P., Estebana P., Jimeneza J., Abián-Vicén J. The influence of whole-body electromyostimulation training in middle-aged women. *Isokinet Exerc Sci* **2020**, *1*, 1-9.
76. Schink K., Gassner H., Reljic D., et al. Assessment of gait parameters and physical function in patients with advanced cancer participating in a 12-week exercise and nutrition programme: A controlled clinical trial. *Eur J Cancer Care (Engl).* **2020**, *29*, e13199.
77. Schink K., Herrmann H. J., Schwappacher R., et al. Effects of whole-body electromyostimulation combined with individualized nutritional support on body composition in patients with advanced cancer: a controlled pilot trial. *BMC cancer.* **2018**, *18*, 886.
78. Schink K., Reljic D., Herrmann H. J., et al. Whole-Body Electromyostimulation Combined With Individualized Nutritional Support Improves Body Composition in Patients With Hematological Malignancies - A Pilot Study. *Frontiers in physiology.* **2018**, *9*, 1808.
79. Schwappacher R., Dieterich W., Reljic D., et al. Muscle-Derived Cytokines Reduce Growth, Viability and Migratory Activity of Pancreatic Cancer Cells. *Cancers (Basel).* **2021**, *13*, 3820.
80. Schwappacher R., Schink K., Sologub S., et al. Physical activity and advanced cancer: evidence of exercise-sensitive genes regulating prostate cancer cell proliferation and apoptosis. *J Physiol.* **2020**, *598*, 3871-3889.
81. Silvestri A., Ruscello B., Rosazza C., et al. Acute Effects of Whole-Body Electrostimulation Combined with Stretching on Lower Back Pain. *Int J Sports Med.* **2023**, *44*, 820-829.
82. Suzuki T., Ikeda M., Minami M., et al. Beneficial Effect of Intradialytic Electrical Muscle Stimulation in Hemodialysis Patients: A Randomized Controlled Trial. *Artif Organs.* **2018**, *42*, 899-910.
83. Suzuki Y., Suzuki H., Yato S., et al. Mittelfristige Auswirkungen der Elektrotherapie der Skeletmuskulatur mit Gürtelelektroden auf den Glukose und Fettstoffwechsel die Körperzusammensetzung, die Muskelkraft und die Muskelausdauer bei Patienten mit Typ-2 Diabetes [*型糖尿病患者における糖・脂質代謝および体組成, 筋力, 筋持久力に及ぼすベルト電極式骨格筋電気刺激療法の中期的効果*]. *Physical Therapy Science.* **2019**, *33*, 53-59.
84. Tanaka S., Kamiya K., Matsue Y., et al. Effects of electrical muscle stimulation on physical function in frail older patients with acute heart failure: a randomized controlled trial. *Eur J Prev Cardiol.* **2022**, *29*, e286-e288.
85. Tanaka S., Kamiya K., Matsue Y., et al. Efficacy and Safety of Acute Phase Intensive Electrical Muscle Stimulation in Frail Older Patients with Acute Heart Failure: Results from the ACTIVE-EMS Trial. *J Cardiovasc Dev Dis.* **2022**, *9*,
86. Tsurumi T., Tamura Y., Nakatani Y., et al. Neuromuscular Electrical Stimulation during Hemodialysis Suppresses Postprandial Hyperglycemia in Patients with End-Stage Diabetic Kidney Disease: A Crossover Controlled Trial. *J Clin Med.* **2022**, *11*, 6239.
87. Vaculikova P. P., A. Kotkova, M. Struhar, I. Balousova, D. N. Impact of Whole-Body Electromyostimulation and Resistance Training on Bone Mineral Density in women at risk for Osteopororosis. *IJPESS.* **2022**, 69-79.

88. Vaculikova P. P., A. Kotkova, M. Struhar, I. Balousova, D. Rozsypal, R. Impact of Whole-Body Electromyostimulation and Resistance Training on the Level of Functional Fitness in Elderly Women. *Studia Sportiva.* **2023**, *16*, 115-126.
89. van Buuren F., Horstkotte D., Mellwig K., et al. Electrical Myostimulation (EMS) Improves Glucose Metabolism and Oxygen Uptake in Type 2 Diabetes Mellitus Patients—Results from the EMS Study. *Diabetes Technol Ther.* **2015**, *17*, 413-419.
90. van Buuren F., Mellwig K. P., Frund A., et al. Electromyostimulation: Verbessserung von Lebensqualität, Sauerstoffaufnahme und linksventrikuläerer Funktion bei chronischer Herzinsuffizienz. *Rehabilitation.* **2014**, *53*, 321-326.
91. van Buuren F., Mellwig K. P., Prinz C., et al. Electrical myostimulation improves left ventricular function and peak oxygen consumption in patients with chronic heart failure: results from the exEMS study comparing different stimulation strategies. *Clinical research in cardiology : official journal of the German Cardiac Society.* **2013**, *102*, 523-534.
92. von Stengel S., Bebenek M., Engelke K., Kemmler W. Whole-Body Electromyostimulation to Fight Osteopenia in Elderly Females: The Randomized Controlled Training and Electrostimulation Trial (TEST-III). *Journal of osteoporosis.* **2015**, *2015*, 643520.
93. Weissenfels A., Teschler M., Willert S., et al. Effects of whole-body electromyostimulation on chronic nonspecific low back pain in adults: a randomized controlled study. *Journal of pain research.* **2018**, *11*, 1949-1957.
94. Wittmann K., Sieber C., von Stengel S., et al. Impact of whole body electromyostimulation on cardiometabolic risk factors in older women with sarcopenic obesity: the randomized controlled FORMOsA-sarcopenic obesity study. *Clinical interventions in aging.* **2016**, *11*, 1697-1706.
95. Özdal M., Bostanci Ö. Effects of whole-body electromyostimulation with and without voluntary muscular contractions on total and regional fat mass of women. *Archives of Applied Science Research.* **2016**, *8*, 75-79.
96. Stephan H., Wehmeier U. F., Forster T., Tomschi F., Hilberg T. Additional Active Movements Are Not Required for Strength Gains in the Untrained during Short-Term Whole-Body Electromyostimulation Training. *Healthcare (Basel).* **2023**, *11*, 741.
97. Evangelista A. L., Teixeira C. V. S., Barros B. M., et al. Does whole-body electrical muscle stimulation combined with strength training promote morphofunctional alterations? *Clinics (Sao Paulo).* **2019**, *74*, e1334.
98. Teschler M., Weissenfels A., Bebenek M., et al. Very high creatine kinase CK levels after WB_EMS. Are there implications for health. *Int J Clin Exp Med* **2016**, *9*, 22841-22850.
99. Bermejo I., Carnicero J., Garcia F., et al. POS1446 CREATINE KINASE COULD BE A MARKER OF CHRONIC INFLAMMATION-INDUCED SARCOPENIA IN FRAIL PATIENTS. *Annals of the Rheumatic Diseases* **2022**, *81*, 1067-1068.
100. Stollberger C., Finsterer J. Side effects of and contraindications for whole-body electro-myo-stimulation: a viewpoint. *BMJ Open Sport Exerc Med.* **2019**, *5*, e000619.
101. Kirkham J. J., Davis K., Altman D. G., et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. *PLoS Med.* **2017**, *14*, e1002447.
102. Eriksen E. F. Cellular mechanisms of bone remodeling. *Reviews in endocrine & metabolic disorders.* **2010**, *11*, 219-227.
103. WHO. *Assessment of osteoporotic fracture risk and its application to screening for postmenopausal osteoporosis.*; World Health Organization, Geneva, 1994.
104. Knutson J. S., Fu M. J., Sheffler L. R., Chae J. Neuromuscular Electrical Stimulation for Motor Restoration in Hemiplegia. *Phys Med Rehabil Clin N Am.* **2015**, *26*, 729-745.
105. Kemmler W., Weissenfels A., Willert S., et al. Recommended Contraindications for the Use of Non-Medical WB-Electromyostimulation. *Dtsch Z Sportmed.* **2019**, *70*, 278-281.
106. BMU. Regulation on Protection against Harmful Effects of Non-Ionizing Radiation in Human Applications (NiSV) *[Verordnung zum Schutz vor schädlichen Wirkungen nichtionisierender Strahlung bei der Anwendung am Menschen (NiSV)]*. Bundesministerium-für-Umwelt-Naturschutz-und-nukleare-Sicherheit: Bonn, 2019.
107. BMU. Requirements for the acquisition of expertise for applications of non-ionizing radiation sources on humans *[Anforderungen an den Erwerb der Fachkunde für Anwendungen nichtionisierender Strahlungsquellen am Menschen]*. Bundesministerium-für-Umwelt-Naturschutz-und-nukleare-Sicherheit: Bonn, 2020.
108. Berger J., Fröhlich M., Kemmler W. WB-EMS Market Development—Perspectives and Threats. *Int. J. Environ. Res. Public Health.* **2022**, *19*, 14211.
109. Koch A. J., Pereira R., Machado M. The creatine kinase response to resistance exercise. *Journal of musculoskeletal & neuronal interactions.* **2014**, *14*, 68-77.

 doi:10.20944/preprints202403.0183.v1

110. Kemmler W., Fröhlich M., Ludwig O., et al. Position statement and updated international guideline for safe and effective whole-body electromyostimulation training-the need for common sense in WB-EMS application. *Frontiers in physiology.* **2023**, *14*, 1174103.
111. Kemmler W., von Stengel S., Teschler M., et al. Ganzkörper-Elektromyostimulation, Sarkopenie und Adipositas. Ergebnisse der randomisierten kontrollierten "Franconia Sarcopenic Obesity Study" (FRANSO). *Osteoporose & Rheuma Aktuell.* **2017**, *15*, 12-18.
112. Amaro-Gahete F. J., De-la O. A., Sanchez-Delgado G., et al. Functional Exercise Training and Undulating Periodization Enhances the Effect of Whole-Body Electromyostimulation Training on Running Performance. *Frontiers in physiology.* **2018**, *9*, 720.