Energy consumption and cost during walking with different modalities of assistance after stroke: a systematic review and meta-analysis

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Purpose: To estimate pooled rates of gross and net energy consumption (ml/kg/min and J/kg/min) and energy cost (ml/kg/m and J/kg/m) during level surface walking with different assistance modalities post-stroke.

Materials and Methods: Four databases were searched using keywords related to stroke, walking, and energy requirements. Three independent reviewers screened 3296 records and included 42 studies in quantitative analysis.

Results: Pooled rates without significant important heterogeneity were identified for: gross energy consumption during unassisted overground walking at comfortable walking speed (10.55 ml/kg/min; 95% CI [9.93–11.16]), gross energy consumption during treadmill walking with rigid exoskeleton assistance (7.08 ml/kg/min; 95% CI [6.52–7.65]), gross energy cost during unassisted overground walking in patients with chronic stroke (0.24 ml/kg/m; 95% CI [0.28–0.48]), gross energy cost during unassisted treadmill walking in patients with subacute stroke (0.45 ml/kg/m; 95% CI 0.45–0.45), and net energy cost during overground walking with assistive devices and orthoses in patients with chronic stroke (4.12 J/kg/m, 95% CI [3.55–4.69]).

Conclusions: Walking, unassisted and with the use of assistive devices and lower limb orthoses, induces low- to moderate-intensity exercise as recommended by exercise guidelines for stroke survivors. Future studies should explore whether bodyweight-supported or robot-assisted walking can also reach moderate-intensity.

Introduction

Post-stroke, the energy requirements of walking are altered [1]. Some patients spend up to three times more energy per unit of distance than able-bodied subjects [2,3]. Such energy requirements potentially limit a patient’s ability to be physically active and engage in rehabilitation or activities of daily living.

The energy requirements of walking can be assessed by respiratory gas analysis [4]. After a few minutes of submaximal walking at constant workload, the amount of oxygen consumption reaches a plateau and achieves a steady-state condition. At this point, the oxygen consumption measured expresses the energy consumption required for walking – expressed in millilitres oxygen per kilogram bodyweight per minute (ml/kg/min), or converted to Joules per kilogram bodyweight per minute (J/kg/min).

Since energy consumption depends on the walking speed (e.g., comfortable walking speed [CWS] or maximal walking speed [MWS]) [5,6], another common expression is energy cost. Energy cost refers to the amount of oxygen consumed per distance walked, and is obtained by dividing energy consumption by walking speed (ml/kg/m or J/kg/m) [1]. Both outcomes can be expressed as gross (total amount) or net (amount above resting level) measures.

In 2016, Kramer et al. [3] published a meta-analysis (29 studies till 2014 with 501 participants) reporting post-stroke energy consumption and cost during self-selected, comfortable walking. Pooled data showed a mean energy consumption of 11.29 ml/kg/min (95% CI 9.70–12.87) and a mean energy cost of 0.64 ml/kg/m (95% CI 0.44–0.85) during overground walking 1–6 months post-stroke (two studies, n = 19) – a three and a half times higher cost than that of healthy controls at self-selected speed (mean difference 0.47 ml/kg/m, 95% CI 0.29–0.66) [3].

During treadmill walking over 6 months post-stroke, a lower
mean oxygen cost was found (0.43 ml/kg/m, 95% CI 0.36–0.49, four studies, n = 74) [3]. Unfortunately, such overview is only available for unassisted walking after stroke (only a habitual ankle-foot orthosis [AFO] was allowed). However, patients with stroke use various devices besides an AFO to assist walking during activities of daily living or rehabilitation – such as assistive devices [7], lower limb orthoses, bodyweight support (BWS) systems [8], and walking robots [9]. Assistive devices, like parallel bars, canes, and walkers, improve balance and stability during walking, and reduce the load on weight-bearing structures [7,10]. These devices are often used in combination with lower limb orthoses. The most common type seen post-stroke is an AFO, which offers important benefits with regard to speed [11], balance [12], and knee and ankle kinematics [12]. To assist walking in severely impaired patients who cannot walk, BWS systems and walking robots are used. Depending on the impairment level, two types of robots are used: “exoskeletons” (moving the patient’s hip, knee and/or ankle joints) and “end-effectors” (moving the patient’s feet, placed on footplates) [9].

To the best of our knowledge, there is no overview of the energy requirements of assisted walking after stroke. An overview of the energy consumption according to the type of assistance could help clinicians choosing which type may be used to meet exercise guidelines for stroke survivors. Stroke guidelines recommend exercising large-muscle activities, such as walking, 3–5 times per week for 20–60 min at moderate intensity (between 10.5 and 21.5 ml/kg/min) [13,14]. Another goal of gait rehabilitation is to teach patients to walk safely in an energy efficient manner – or in other words to decrease their energy cost of walking. An overview of the energy cost of walking according to the type of assistance can help clinicians to choose which type may improve their patients’ walking economy.

This systematic review aims to answer two questions: (1) How much energy do patients with stroke consume according to the type of assistance during steady-state level surface walking (gross and net values in ml/kg/min and J/kg/min)? (2) Which assistance modality is the most energy efficient for steady-state level surface walking after stroke (gross and net values in ml/kg/m and J/kg/m)? This meta-analysis provides objective estimates of the exercise intensity of walking after stroke, rather than observation by clinicians or subjective reports by patients.

Methods

Protocol and registration

The Cochrane Handbook and PRISMA guidelines were followed for the methodology and reporting of this review [15,16]. Protocol details were registered prospectively on PROSPERO (CRD42016052932).

Eligibility criteria

Studies were included if:

1. Studies were published in English, French, or Dutch since 1997. This cut-off point (i.e., last 20 years) was chosen because new-generation respiratory gas analysis systems are more accurate and sensitive [17].

2. Studies were cross-sectional studies, (non-)randomized controlled trials, uncontrolled clinical trials, case-control studies, validity studies or reliability studies. Only baseline or first session data were extracted of studies testing a training or experimental intervention (e.g., novel AFO) and studies investigating test–retest reliability.

3. Studies included subacute (2 weeks to 3 months post-stroke) and/or chronic (over 3 months post-stroke) patients with stroke with residual lower limb disabilities (e.g., motor impairment, hemiplegia, spasticity, or muscle weakness described in the eligibility criteria or baseline patient characteristics).

4. Energy requirements were measured by respiratory gas analysis, under steady-state conditions, and during submaximal level surface walking at constant workload (unassisted or with any assistance modality).

Studies were excluded if:

1. Studies were narrative or systematic reviews, overview of reviews, protocols [labelled “wrong study design”] or meeting abstracts [labelled “wrong publication type”].

2. The presence of residual physical disabilities was not defined in the eligibility criteria or could not be defined based on description of patient characteristics [labelled “wrong population”].

3. A mixed neurological population was included (e.g., a combination of patients with stroke and multiple sclerosis) and data items of interest (see data collection process) were not presented for patients with stroke separately [labelled “wrong population”].

4. Energy requirements were only measured during uphill or backward walking, running, stair climbing, jumping or walking with incremental load; or measured after a training intervention [labelled “wrong intervention”].

5. Energy requirements were based on total walking time (pre-steady-state plus steady-state period), or steady-state conditions were unclear (e.g., not mentioned which period of walking was analysed) [labelled “wrong outcome”].

6. Study data of interest were reported in multiple publications [labelled “duplicate data”]. Only the publication reporting the largest sample size or most data items of interest was included.

Information sources and search

PubMed, Web of Science, Embase and the Cochrane Central Register of Controlled Trials were searched from inception to 20 August 2018 (N.L., S.D.B.). Keywords related to stroke, walking, and energy consumption and cost were used (Supplementary Tables S1–S4). Reference lists of related systematic and narrative reviews were screened for missing studies [1,3,18].

Study selection

Three independent review authors (N.L., S.D.B., N.D.) checked eligibility. Using Rayyan – a web application for the rapid exploring and filtering of eligible studies for systematic reviews (Qatar Computing Research Institute, Doha, Qatar) – authors screened titles and abstracts of all identified records in a blinded standardized manner. Irrelevant records were excluded. Full texts of remaining records were obtained and screened. Disagreements were resolved by consensus. A fourth independent review author (E.S.) was consulted if consensus was not reached.

Data collection process and data items

A data collection table was developed, pilot-tested on three randomly-selected included studies and refined accordingly. Two review authors (S.D.B., N.D.) extracted data from included studies. A third review author (N.L.) double-checked all extracted data. If the required data were absent or reported insufficiently in the
publication, authors were individually contacted by email. In total, 29 authors were contacted about 35 manuscripts [5,19–53].

From each included study, information was extracted on (1) patient characteristics (number, age, sex, time post-stroke, functional ambulation category [FAC], Berg Balance Scale, Lower Extremity Fugl-Meyer Assessment); (2) assistance modality (description, settings); (3) walking intervention (walking surface, walking speed, walking duration); and (4) gross and net oxygen consumption [mL/kg/min and J/kg/min] and cost [mL/kg/m and J/kg/m] (mean, SD, SE, sample size). If FAC scores were not reported, we assessed the score retrospectively based on reported eligibility criteria (FAC 0: cannot walk or needs help from two or more persons, FAC 1: needs continuous manual support to carry weight, FAC 2: needs manual support to help with balance and coordination, FAC 3: needs verbal supervision, FAC 4: can walk independently on level surfaces, FAC 5: can walk independently on all surfaces) [54]. If energy consumption and cost were only reported graphically, and we received no author response, mean and SD (or SE) were estimated based on the graphs.

Risk of bias assessment
Criteria for assessing risk of bias in the included studies were based on the Cochrane Collaboration’s tool [15] and the Methods Guide for Comparative Effectiveness Reviews [55] (Supplementary Table S5). Applicable domains (sampling, performance, detection, attrition and reporting bias) were rated “high,” “low,” or “unclear” at the population and outcome level of interest for this systematic review. Two independent review authors rated the risk of bias (N. L. and E.S.). Disagreements were resolved by consensus.

Summary measures and planned methods of analysis
Primary measures were pooled mean and 95% confidence interval (CI) of the energy consumption and cost rates during walking with different assistance modalities (classified according to type of walking surface). Random effects model meta-analyses were performed using the generic inverse variance method to calculate pooled means (DerSimonian and Laird model, Review Manager, Version 5.3). A random effects model was chosen because we assumed that the true effect may vary across studies due to differences in study population or walking intervention. A meta-analysis was conducted when the same construct was examined in at least two studies.

To include multiple independent groups of studies with a parallel group design in a meta-analysis – when more than one group was applicable to the review question (e.g., intervention and control group) – groups were entered as though it were separate studies [56]. To include multiple measures of studies with a crossover design in a meta-analysis – when more than one walking intervention was applicable to the review question (e.g., walking with 80 and 100% robotic guidance) – a summary mean and SE were calculated [56]. Calculations are described in Supplementary Formula S1. By using summary means and SEs (instead of treating each walking intervention as though it were a separate study), we avoided assigning more weight to studies with multiple walking interventions than to studies with only one. Treating the data as it would provide independent information, when in fact the data come from the same set of participants, would underestimate the error and overestimate the precision of the pooled mean. Because correlations between pairs of walking interventions were unknown, we used Pearson correlations of 0.5 (moderate positive correlation) and performed sensitivity analyses to assess the effect of higher correlations (0.7 and 0.9).

Inconsistency across studies due to heterogeneity was quantified by the I² statistic. I² values over 50% were classified as important presence of heterogeneity [57]. Statistical significance of heterogeneity was based on the Chi-squared test’s p-value (p-value < 0.05). When a meta-analysis demonstrated significant and important presence of heterogeneity (I² > 50% and Chi² test’s p-value < 0.05), subgroup analyses were planned for the time after stroke (“2 weeks to 3 months,” “over 3 months,” or “mixed”) and type of speed (“CWS,” “MWS,” “imposed walking speed,” or “mixed walking speed”). The category “mixed walking speed” was added because the use of summary means and SEs prevented the assignment of data to separate subgroups.

Results
Study selection
Our total search yielded 4296 records, including 1000 duplicate records. Title and abstract of 3296 records were screened and 3192 records were excluded. Of the remaining 104 full texts, 57 studies were excluded due to reasons related to publication type, population, intervention, outcome, and duplicate data (Figure 1). In total, 47 studies were included [2,4,5,19,22,23,25–53,58–66], of which 42 were used in quantitative synthesis [2,4,5,19,22,23,25–39,41–44,46–48,50,53,58–66].

Characteristics of included studies
Patient characteristics
In total, 937 patients with stroke (521 males, 309 females, and 107 unknown) were included (age [pooled mean ± standard deviation]: 58 ± 11 years). Four studies included subacute patients (n = 158, 1.9 ± 0.1 months post-stroke), 35 studies chronic patients (n = 701, 3.6 ± 3.7 years post-stroke), and 8 studies both subacute and chronic patients (n = 78, 0.6 ± 0.1 years post-stroke). In five studies, mean FAC was below 3 (manual contact required during walking). In 35 studies, mean FAC was greater than or equal to 4 (ambulatory independent). Table 1 lists detailed information.

Assistance modalities
The identified assistance modalities were classified into: unassisted walking (overground and on a treadmill), walking with assistive devices and/or lower limb orthoses (overground and on a treadmill), walking with BWS (on a treadmill), walking with rigid exoskeleton assistance (on a treadmill), walking with soft exoskeleton assistance (overground), and walking with end-effector assistance (on foot plates). None of the studies reported energy consumption or cost during overground walking with BWS. The categories assistive devices and lower limb orthotics were combined, because most studies did not distinguish between these modalities. In one study – assigned to the category assistive devices and/or lower limb orthoses – one participant (6%) received 15% BWS in addition to handrail support [33].

Walking interventions
Walking durations ranged from 3 to 18 min. Participants walked at CWS (0.15–1.15 m/s), MWS (0.63–1.19 m/s), or imposed speeds (fast [0.85–1.39 m/s], percentage of CWS [0.29–0.97 m/s], or arbitrary [0.28–0.56 m/s]).
Outcome measures
The following outcomes were identified: gross energy consumption in ml/kg/min (28 studies, \(n = 531\)), net oxygen consumption in ml/kg/min (1 study, \(n = 7\)), gross energy cost in ml/kg/m (17 studies, \(n = 391\)), gross energy cost in J/kg/m (1 study, \(n = 15\)), net energy cost in ml/kg/m (3 studies, \(n = 36\)), and net energy cost in J/kg/m (8 studies, \(n = 97\)). None of the studies reported gross or net energy consumption in J/kg/min.

For 6 studies, missing data items of interest were provided by email [22,31,32,38,46,48]; for 11 studies data items of interest were missing (no author response). Six of these 11 studies reported the data items of interest graphically. Results of these studies were estimated based on the graph [5,19,27,34,36,47]. The remaining five studies could not be included in quantitative analyses and are not further discussed in quantitative synthesis below [40,45,49,51,52].

Risk of bias assessment
Risk of sampling bias was high in 31 studies (66%, recruitment in only one centre or recruitment of a specific target population), and unclear in the remaining (Table 2; Supplementary Table S3). Risk of performance bias was unclear in 33 studies (70%, insufficient reporting of food, alcohol, nicotine or caffeine intake, or activity restrictions prior to the measurements), and high in 6 studies (13%, order of the different walking interventions was not randomized or insufficient rest between measurements). Risk of detection bias was low in all studies. Risk of attrition bias was low in 32 studies (68%), unclear in 11 studies (23%, insufficient reporting), and high in 4 studies (9%, missing outcome data likely related to true outcome or to influence results). Risk of reporting bias was unclear in 46 studies (98%, no mentioning of pre-registered protocol), and high in one study (2%, results not listed as stated in the method section).

Quantitative synthesis of results per outcome
Results below are based on Pearson’s correlation coefficients of 0.5. Changing coefficients made no trivial difference (Supplementary Tables S6–S8).

Gross energy consumption in ml/kg/min
Pooled results were reported in Figure 2. Important significant between-study heterogeneity was found in all walking modalities, except treadmill walking with rigid exoskeleton assistance (\(I^2=49\%, p = 0.14\)). Subgroup analysis based on type of speed removed heterogeneity for unassisted overground walking at CWS (11.08 ml/kg/min, 95% CI 10.03 to 12.13, \(I^2=0\%, p = 0.97\)). For most other walking modalities, subgroup analysis was not applicable because the subgroups contained only a single study or a single subgroup contained all studies (Table 3).

A single study reported gross energy consumption rates during treadmill walking with BWS (\(n = 9\), crossover design) [60]. The study reported a mean of 9.42 ml/kg/min (95% CI 8.42–10.42) at CWS, and a mean of 9.88 ml/kg/min (95% CI 8.53–11.23) at MWS.

Net energy consumption in ml/kg/min
A single study reported net energy consumption rates during unassisted overground walking (\(n = 7\), crossover design) [34]. The study reported a mean of 8.07 ml/kg/min (95% CI 6.70–9.44) at CWS, and a mean of 10.64 ml/kg/min (95% CI 8.35–12.93) at MWS.

Gross energy cost in ml/kg/m
Pooled results were reported in Figure 3. Important between-study heterogeneity was found in all walking modalities. Subgroup analysis based on time after stroke removed heterogeneity for unassisted overground walking in the chronic stage after stroke (0.24 ml/kg/m, 95% CI 0.22–0.26, \(I^2=0\%, p = 1.00\)) and unassisted treadmill walking in the subacute stage after stroke (0.45 ml/kg/m, 95% CI 0.45–0.45, \(I^2=0\%, p = 1.00\)). For 3 out of 4 walking modalities, subgroup analysis based on type of speed was not applicable because the subgroups contained only a
Table 1. Characteristics of included studies examining energy consumption (ml/kg/min or J/kg/min) or cost (ml/kg/m or J/kg/m) during walking with different assistance modalities after stroke.

| Authors (year) | N | Male/ Female | Age (years) | Time since stroke (months) | FAC (0–5) | BBS (5/6) | FMA-LE (0–1) | Modality of assistance | Description of assistance | Walking surface | Speed (m/s) | Type of speed | Duration (min) |
|----------------|---|---------------|-------------|----------------------------|-----------|-----------|-------------|--------------------|-------------------------|----------------|-------------|--------------|----------------|
| Awad (2016) [19] | 14 | 8/6 | 61 (6) | 18 (13) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | TM | 0.73 (0.30) | OG CWS | 5 |
| | 15 | 11/4 | 63 (5) | 32 (27) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | TM | 0.76 (0.35) | OG CWS | 5 |
| | 16 | 9/7 | 55 (6) | 21 (30) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | TM | 0.63 (0.32) | OG CWS | 5 |
| Awad (2017) [20] | 7 | 3/4 | 45 (9) | 38 (26) | ≥4 | n/a | n/a | Unassisted | Soft exoskeleton | | TM | 0.97 (0.29) | OG CWS | 8 |
| Boyne (2016) [22] | 11 | 7/4 | 59 (9) | 46 (35) | 4.4 (0.9) | n/a | 24.2 (4.8) | Assistive devices and/or lower limb orthoses | | | TM | 0.63 (0.42) | TM CWS | 5 |
| | 5 | 3/2 | 57 (12) | 76 (24) | 4.6 (0.9) | n/a | 23.2 (7.3) | Assistive devices and/or lower limb orthoses | | | TM | 0.74 (0.31) | TM CWS | 5 |
| Bregman (2010) [23] | 4 | 2/2 | 53 (13) | 67 (28) | n/a | 49.8 (6.3) | n/a | Assistive devices and/or lower limb orthoses | | | TM | 0.63 (0.42) | TM CWS | 5 |
| Brouwer (2009) [58] | 10 | 6/4 | 65 (10) | 71 (49) | 4 | n/a | n/a | Unassisted | | | TM | 0.97 (0.18) | OG CWS | 120% |
| Carver (2011) [59] | 12 | 5/7 | 60 (8) | 96 (48) | ≥4 | 46.0 (9.0) | n/a | Unassisted | Without assistive walking devices | | TM | 0.84 (0.28) | OG CWS | 6 |
| Chantraine (2005) [25] | 6 | 3/3 | 55 (18) | 79 (33) | 5 | n/a | n/a | Unassisted | | | TM | 0.77 (0.29) | OG CWS | 6 |
| Danielsson (2000) [60] | 9 | 6/3 | 56 (8) | 17 (7) | 4.1 (0.8) | n/a | 20.9 (7.1) | Unassisted | | | TM | 0.81 (0.03) | OG CWS | 6 |
| Danielsson (2004) [61] | 10 | 8/2 | 52 (10) | 23 (26) | ≥4 | n/a | 19.9 (2.1) | Unassisted | | | TM | 0.77 (0.29) | OG CWS | 6 |
| Danielsson (2007) [62] | 20 | 17/3 | n/r | >6 | ≥3 | n/a | n/a | Assistive devices and/or lower limb orthoses | Light handrail hold for balance + AFO (N = 15) | | TM | 0.48 (0.28) | OG CWS | 5 |
| Danks (2016) [26] | 55 | 33/22 | 54 (11) | 47 (n/r) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | | TM | 0.27 (0.09) | TM CWS | 5 |
| Dawes (2006) [27] | 7 | 2/5 | 46 (12) | 3 (2) | 2.1 (0.7) | n/a | n/a | Assistive devices and/or lower limb orthoses | Handrail support allowed + supervision | | TM | 0.27 (0.09) | OG CWS | 5 |
| Dawes (2005) [28] | 14 | 8/6 | 46 (8) | >6 | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | | TM | 0.15 (0.03) | End-effector CWS | 5 |
| Delussu (2014) [63] | 6 | 4/2 | 66 (15) | 2 (1) | 3 (1) | n/a | n/a | Assistive devices and/or lower limb orthoses | Gait Trainer + harness with 0% BWS | | TM | 0.43 (0.05) | End-effector CWS | 5 |
| Dobrovolny (2003) [29] | 53 | 44/9 | 65 (8) | 37 (46) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | | | TM | 0.45 (0.36) | OG CWS | 5–10 |
| Engl (2004) [30] | 12 | 11/1 | 63 (7) | 42 (24) | ≥4 | n/a | n/a | Assistive devices and/or lower limb orthoses | Walker (N = 1), cane (N = 3), AFO (N = 3) | | TM | 1.00 (0.30) | OG CWS | 6 |

(continued)
| Authors                  | Male/Female | Age (years) | Time since stroke (months) | FAC (0–5) | BBS (0–150) | FMA-LE (0–14) | Modality of assistance                                                                 | Description of assistance                                                                 | Walking surface | Speed (m/s) | Type of speed | Duration (min) |
|------------------------|-------------|-------------|---------------------------|-----------|-------------|--------------|-------------------------------------------------------------|--------------------------------------------------------------------------------------------|----------------|-------------|--------------|----------------|
| Famani (2016) [31]     | n/r         | n/r         | >6                        | ≥4        | n/a         | n/a          | Assistive devices and/or lower limb orthoses                 | Barefoot + prefabricated solid AFO                                                         | TM             | 0.62 (0.12) | TM CWS       | 5              |
| Finley (2017) [32]     | 11/4        | 58 (12)     | 78 (146)                  | n/a       | n/a         | 23 (6)       | Assistive devices and/or lower limb orthoses                 | Handrail without force instructions                                                        | TM             | 0.43 (0.30) | TM CWS       | 5              |
| Fredricksson (2019) [33]| 17/2        | 59 (13)     | 44 (n/r)                  | ≥4        | n/a         | n/a          | Assistive devices and/or lower limb orthoses                 | Light handrail support, 15% BWS (W = 1)                                                   | TM             | 0.47 (0.13) | TM CWS       | 7–10           |
| Ganley (2008) [34]     | 7/25        | 50 (5)      | >6                        | ≥4        | n/a         | n/a          | Assistive devices and/or lower limb orthoses                 | Light handrail support, 15% BWS (W = 1)                                                   | /              |             |              |                |
| Gjellesvik (2017) [73] | 31/19/12    | 55 (13)     | 21 (14)                   | ≥4        | 52.9 (4.4)  | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | OG             | 1.00 (0.29) | OG Fast      | 6              |
| Ijslens (2013) [35]    | 12/8/4      | 47 (17)     | 3 (2)                     | 4.6 (0.5) | 49.9 (5.5)  | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | /              |             |              |                |
| Kafri (2015) [36]      | 15/12/3     | 58 (10)     | 2 (1)                     | 4.7 (0.6) | 50.0 (5.9)  | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | TM             | 0.91 (0.30) | TM CWS       | 5              |
| Jung (2014) [64]       | 8/6/12      | 59 (11)     | 67 (54)                   | ≥4        | n/a         | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | OG             | 1.05 (0.22) | OG CWS       | 5              |
| Jung (2017) [37]       | 12/7/5      | 62 (9)      | 2 (0.4)                   | ≥4        | n/a         | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | /              |             |              |                |
| Kafri (2014) [38]      | 11/7/4      | 50 (12)     | >6                        | ≥4        | 23.6 (6.5)  | n/a          | Assistive devices and/or lower limb orthoses                 | Standard height adjustable cane                                                            | /              |             |              |                |
| Kremer (2006) [65]     | 10/2/8      | 54 (14)     | 53 (34)                   | 2.5 (1.7) | n/a         | n/a          | Rigid exoskeleton                                           | Lokomat 100% guidance force + 100% BWS                                                   | TM             | 0.28        | Imposed      | 3              |
| Leder (2016) [66]      | 12/9/3      | 55 (12)     | 4 (2)                     | 2–4       | n/a         | n/a          | Unassisted                                                  | Lokomat 100% guidance force + 30% BWS                                                     | OG             | 0.35 (0.18) | OG CWS       | 6              |
| Lee (2017) [39]        | 10/6/4      | 65 (19)     | 1 (0.3)                   | 2.5 (0.5) | 20.1 (3.3)  | n/a          | Rigid exoskeleton                                           | Lokomat 100% guidance force + 50% BWS                                                    | TM             | 0.39        | Imposed      | 3              |
| Lewis (2011) [40]      | 36/30       | 71 (10)     | 2 (n/r)                   | ≥4        | n/a         | n/a          | Unassisted                                                  | Lokomat 60% guidance force + 30% BWS                                                     | OG             | n/r         | OG CWS       | 3              |
| Macko (1997) [41]      | n/r         | 67 (3)      | 36 (10)                   | ≥4        | n/a         | n/a          | Unassisted                                                  | Lokomat 60% guidance force + 50% BWS                                                     | TM             | 0.78 (0.25) | TM CWS       | n/r            |
| Macko (2001) [42]      | 23/19/4     | 67 (8)      | 28 (26)                   | ≥4        | n/a         | n/a          | Unassisted                                                  | Lokomat 100% guidance force + 50% BWS                                                    | TM             | 0.39        | Imposed      | 3              |
| Massaad (2010) [43]    | 6/2/4       | 47 (13)     | 159 (98)                  | ≥4        | n/a         | n/a          | Unassisted                                                  | Lokomat 60% guidance force + 50% BWS                                                     | TM             | 0.50        | Imposed      | 3              |
| Michael (2005) [44]    | 50/28/22    | 65 (n/r)    | 10 (n/r)                  | ≥3        | n/a         | n/a          | Unassisted                                                  | Lokomat 60% guidance force + 50% BWS                                                     | TM             | 0.69 (0.30) | OG CWS       | 6              |

(continued)
| Authors                          | Stroke population | Walking intervention | Modality of assistance | Description of assistance | Walking surface | Speed (m/s) | Type of speed | Duration (min) |
|---------------------------------|-------------------|----------------------|-----------------------|--------------------------|------------------|-------------|--------------|----------------|
| (year)                          | n     | Age (years) | Time since stroke (months) | FAC (0–5) | BBS (56) | FMA-LE (34) |                           |                        |                     |               |               |
| **Modai (2015) [45]**           | 13 n/r | 41 (10)       | n/r                   | ≥4                          | n/a      | n/a     | Assistive devices and/or lower limb orthoses | Cane (N = 9)       | OG         | 0.39 (0.20) | OG CWS       | 5                   |
| **Platts (2006) [2]**           | 8 5/3 | 61 (8)       | 26 (13)               | ≥4                          | n/a      | 16 (4)  | Assistive devices allowed (American Thoracic Society recommendations 6MWT) | OG         | 0.54 (0.21) | OG CWS       | 6                   |
| **Polese (2017) [46]**          | 10 6/4 | 63 (9)       | 24 (15)               | ≥4                          | n/a      | 25 (3)  | Assistive devices allowed (American Thoracic Society recommendations 6MWT) | OG         | 1.15 (0.27) | OG CWS       | 6                   |
| **Polese (2018) [74]**          | 55 33/22 | 59 (14)     | 25 (14)               | ≥4                          | n/a      | n/a     | Assistive devices and/or lower limb orthoses | Unassisted       | /          | 0.70 (0.25) | OG CWS       | 5                   |
| **Resiman (2009) [5]**          | 16 n/r | 57 (9)       | 38 (31)               | ≥4                          | n/a      | 20.0 (6.7) | Assistive devices and/or lower limb orthoses | Permitted to hold onto a front harness + with 0% BWS | TM         | 0.62 (0.21) | TM CWS       | 5                   |
| **Salbach (2014) [47]**         | 16 14/2 | 71 (8)       | 24 (13)               | ≥4                          | 40.7 (12.3) | n/a | Assistive devices and/or lower limb orthoses | Assistive devices allowed (American Thoracic Society recommendations 6MWT) | OG         | 0.71 (0.50) | OG CWS       | 6                   |
| **Schiemanck (2015) [48]**      | 8 4/4 | 50 (14)       | 65 (32)               | ≥4                          | n/a      | n/a     | Assistive devices and/or lower limb orthoses | AFO (N = 8)       | OG         | 0.86 (0.27) | OG CWS       | 6                   |
| **Stoller (2014) [49]**         | 18 7/11 | 61 (11)     | 2 (1)                 | 1.1 (0.8)                   | n/a      | n/a     | Rigid exoskeleton | Lokomat passive mechanical work rate + individual % BWS | TM         | 0.57 (0.05) | n/r         | 5                   |
| **Stookey (2013) [4]**          | 23 11/12 | 61 (8)       | 70 (43)               | n/a                         | n/a      | n/a     | Assistive devices and/or lower limb orthoses | Lokomat active mechanical work rate (40% maximal work rate) + individual % BWS | TM         | 0.57 (0.05) | n/r         | 10                  |
| **Stoquart (2008) [50]**        | 19 n/r | 53 (15)       | 52 (56)               | ≥4                          | n/a      | n/a     | Unassisted | /                | TM         | 0.54 (0.14) | TM CWS       | ≥ 2 (after SS) |
| **Thijssen (2007) [52]**        | 20 n/r | 50 (12)       | n/r                   | ≥4                          | n/a      | n/a     | Unassisted | /                | TM         | 0.41 (0.23) | TM CWS       | 90%                  |
| **van Nunen (2012) [53]**       | 27 15/12 | 60 (13)     | 59 (58)               | 4.3 (0.7)                   | n/a      | n/a     | Unassisted | Without orthosis | TM         | 0.46 (0.24) | n/r         | 5                    |

Continues values are reported as mean (SD). Abbreviations: 6MWT: 6-minute walking test; BBS: Berg Balance Scale; BWS: bodyweight support; CWS: comfortable self-selected walking speed; FAC: functional ambulation category; FMA-LE: Fugl-Meyer Assessment – Lower Extremity; (HK)AFO: (hip knee) ankle-foot orthosis; MWS: maximal walking speed; N: number; n/a: not assessed; n/r: not reported; OG: overground; SS: steady-state; TM: treadmill.

*Retrospectively assessed based on eligibility criteria.

*Authors reported that walking with the unpowered soft exosuit did not significantly modify the energy cost of walking [20].
Table 2. Risk of bias assessment.

| Author (year)          | Sampling bias | Performance bias | Detection bias | Attrition bias | Reporting bias |
|------------------------|---------------|------------------|---------------|---------------|---------------|
| Awad (2016) [19]       | +             | ?                | –             | –             | ?             |
| Awad (2017) [20]       | +             | ?                | –             | +             | ?             |
| Boyne (2016) [22]      | ?             | ?                | –             | +             | ?             |
| Bregman (2010) [23]    | +             | ?                | –             | ?             | ?             |
| Brouwer (2009) [58]    | +             | –                | –             | –             | ?             |
| Carver (2011) [59]     | ?             | ?                | –             | –             | +             |
| Chantraine (2005) [25] | +             | ?                | –             | ?             | ?             |
| Danielsson (2000) [60] | +             | ?                | –             | ?             | ?             |
| Danielsson (2004) [61] | +             | ?                | –             | ?             | ?             |
| Danielsson (2007) [62] | +             | ?                | –             | –             | ?             |
| Danks (2016) [26]      | +             | –                | –             | –             | –             |
| David (2006) [27]      | +             | –                | –             | –             | –             |
| Dawes (2005) [28]      | ?             | –                | –             | ?             | ?             |
| Delussu (2014) [63]    | +             | ?                | –             | –             | ?             |
| Dobrovolsky (2003) [29]| ?             | –                | –             | –             | –             |
| Eng (2004) [30]        | +             | ?                | –             | –             | ?             |
| Farmani (2016) [31]    | +             | –                | –             | –             | ?             |
| Finley (2017) [32]     | ?             | ?                | –             | ?             | –             |
| Fredrickson (2016) [33]| +             | –                | –             | –             | –             |
| Ganley (2015) [34]     | ?             | ?                | –             | –             | –             |
| Gjellesvik (2017) [73] | +             | ?                | –             | –             | ?             |
| Ijmker (2013) [35]     | +             | ?                | –             | –             | ?             |
| Ijmker (2015) [36]     | +             | ?                | –             | –             | ?             |
| Jung (2014) [64]       | ?             | –                | –             | –             | ?             |
| Jung (2017) [37]       | +             | ?                | –             | –             | –             |
| Kafri (2014) [38]      | +             | +                | –             | –             | ?             |
| Krew (2006) [65]       | +             | ?                | –             | –             | ?             |
| Leddy (2016) [66]      | ?             | ?                | –             | –             | ?             |
| Lee (2017) [39]        | +             | +                | –             | –             | ?             |
| Lewis (2011) [40]      | +             | ?                | –             | –             | ?             |
| Macko (1997) [41]      | +             | ?                | –             | +             | –             |
| Macko (2001) [42]      | +             | ?                | –             | –             | –             |
| Massaad (2010) [43]    | ?             | ?                | –             | –             | ?             |
| Michael (2005) [44]    | +             | ?                | –             | –             | –             |
| Modai (2015) [45]      | +             | +                | –             | –             | ?             |
| Platts (2006) [2]      | +             | –                | –             | –             | –             |
| Polese (2017) [46]     | ?             | –                | –             | –             | –             |
| Polese (2018) [74]     | +             | –                | –             | –             | –             |
| Reisman (2009) [5]     | ?             | ?                | –             | –             | ?             |
| Salbach (2014) [47]    | ?             | ?                | –             | –             | ?             |
| Schiemack (2015) [48]  | +             | ?                | –             | –             | ?             |
| Stoller (2014) [49]    | +             | –                | –             | –             | ?             |
| Stookey (2013) [4]     | ?             | ?                | –             | –             | –             |
| Stoquart (2008) [50]   | ?             | ?                | –             | –             | ?             |
| Stoquart (2012) [51]   | ?             | +                | –             | ?             | ?             |
| Thijssen (2007) [52]   | +             | ?                | –             | –             | –             |
| van Nunen (2012) [53]  | ?             | ?                | –             | –             | ?             |

*: high bias; ?: unclear bias; –: low bias.

Sampling bias: high (recruitment of volunteers, patients in only one centre, specific target population within eligibility criteria of this systematic review, or patients with health problems other than stroke that could affect the rate of energy consumption or cost during walking), unclear (not addressed or insufficient reporting to permit judgement); Performance bias: high (crossover studies: no randomization of walking sessions or insufficient rest between sessions to rule out order effects), unclear (no restrictions of food, caffeine, nicotine or alcohol intake or activities prior to walking tests reported), low (RCTs, before-after trials, reliability studies: only pre- or first assessment is of interest for this systematic review); Detection bias: low (respiratory gas measurements considered not influenced by lack of blinding of outcome assessor); Attrition bias: high (missing data likely to have relevant impact on observed effect or related to true outcome), unclear (no missing data or not likely to have relevant impact on observed effect); Reporting bias: high (specified outcomes of interest for this systematic review were listed in methods, but not listed in results), unclear (no pre-specified registered protocol was available).

A single study reported gross energy cost rates during footplate walking with end-effector assistance (n = 6, crossover design) [63]. Means of 0.42 ml/kg/m (95% CI 0.34–0.50), 0.34 ml/kg/min (95% CI 0.26–0.42) and 0.31 ml/kg/m (95% CI 0.23–0.39) were reported for walking with 0, 30, and 50% BWS.

Net energy cost in ml/kg/m
Pooled results identified a net energy consumption rate of 0.25 ml/kg/m (95% CI 0.09–0.42) with important significant heterogeneity during unassisted overground walking (I²=87%, p = 0.005; Figure 4). Subgroup analysis based on time after stroke and type of speed was not applicable because the subgroups contained only a single study or a single subgroup contained all studies (Table 3). Another single study (n = 7, cross over design) reported net...
Figure 2. Pooled gross energy consumption (ml/kg/min) during (A) unassisted overground walking, (B) unassisted treadmill walking, (C) overground walking with assistive devices and/or lower limb orthoses, (D) treadmill walking with assistive devices and/or lower limb orthoses, (E) treadmill walking with rigid exoskeleton assistance, and (F) footplate walking with end-effector assistance. Legend: a: Study for which a summary mean and standard error of the rate of oxygen consumption during multiple walking interventions was calculated, CI: confidence interval, IV: inverse variance, n: number, random: DerSimonian and Laird random effects model, SE: standard error, VO2: volume oxygen, WS: walking speed.
### Table 3. Subgroup analyses based on time after stroke and type of speed for outcomes that demonstrated high heterogeneity.

| Outcome | Assistance modality | Subgroup | Number of independent groups | Pooled mean (95% CI) | Heterogeneity | \( \chi^2 \) | p-value | \( \chi^2 \) test |
|---------|---------------------|----------|-----------------------------|----------------------|---------------|---------|---------|-------------|
| | | Overall | | | | | | | |
| Gross energy consumption (ml/kg/min) | Unassisted over-ground walking | Time after stroke | Subacute | 9 | 11.67 [10.04–13.29] | 93% | <0.00001 | |
| | | | Chronic | 6 | 11.95 [9.69–14.21] | 95% | <0.00001 | |
| | | | Mixed | 3 | 11.08 [10.03–12.13] | 0% | 0.97 | |
| | | | Type of speed | Comfortable | 6 | 10.55 [9.93–11.16] | 0% | 0.57 | |
| | | | | Maximum | 1 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 2 | 10.76 [9.02–12.50] | 79% | 0.03 | |
| | Unassisted treadmill walking | Overall | 6 | 9.76 [8.98–10.54] | 87% | <0.00001 | |
| | | Time after stroke | Subacute | 0 | n/a | n/a | n/a | |
| | | | Chronic | 6 | 9.76 [8.98–10.54] | 87% | <0.00001 | |
| | | | Mixed | 0 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 1 | n/a | n/a | n/a | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 3 | 9.18 [8.60–9.77] | 72% | 0.03 | |
| | | | | Mixed | 2 | 11.60 [10.24–12.95] | 59% | 0.12 | |
| | Gross energy cost (ml/kg/m) | Unassisted over-ground walking | Time after stroke | Subacute | 1 | n/a | n/a | n/a | |
| | | | Chronic | 5 | 11.12 [9.85–12.40] | 73% | 0.005 | |
| | | | Mixed | 2 | 9.19 [6.68–11.70] | 93% | <0.00001 | |
| | | | Type of speed | Comfortable | 3 | 10.48 [9.14–11.82] | 88% | <0.00001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Overground walking with assistive devices and/or lower limb orthoses | Overall | 9 | 10.48 [9.14–11.82] | 88% | <0.00001 | |
| | | Time after stroke | Subacute | 0 | n/a | n/a | n/a | |
| | | | Chronic | 6 | 11.12 [9.85–12.40] | 73% | 0.005 | |
| | | | Mixed | 3 | 9.85 [8.98–10.54] | 95% | <0.00001 | |
| | | | Type of speed | Comfortable | 3 | 10.48 [9.14–11.82] | 88% | <0.00001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Treadmill walking with assistive devices and/or lower limb orthoses | Overall | 8 | 9.69 [8.97–10.41] | 70% | 0.002 | |
| | | Time after stroke | Subacute | 0 | n/a | n/a | n/a | |
| | | | Chronic | 8 | 9.69 [8.97–10.41] | 70% | 0.002 | |
| | | | Mixed | 0 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 7 | 9.70 [8.82–10.57] | 71% | 0.002 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Footplate walking with end-effector assistance | Overall | 2 | 7.14 [3.17–11.10] | 90% | 0.001 | |
| | | Time after stroke | Subacute | 1 | n/a | n/a | n/a | |
| | | | Chronic | 0 | n/a | n/a | n/a | |
| | | | Mixed | 1 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 2 | 7.14 [3.17–11.10] | 90% | 0.001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Gross energy cost (ml/kg/m) | Unassisted over-ground walking | Time after stroke | Subacute | 0 | n/a | n/a | n/a | |
| | | | Chronic | 2 | 0.24 [0.22–0.26] | 0% | 1.00 | |
| | | | Mixed | 3 | 0.67 [0.53–0.80] | 0% | 0.83 | |
| | | | Type of speed | Comfortable | 4 | 0.56 [0.48–0.67] | 92% | <0.00001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Unassisted treadmill walking | Overall | 4 | 0.45 [0.44–0.46] | 58% | 0.07 | |
| | | Time after stroke | Subacute | 2 | 0.45 [0.45–0.45] | 0% | 1.00 | |
| | | | Chronic | 2 | 0.38 [0.37–0.39] | 0% | 0.01 | |
| | | | Mixed | 0 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 4 | 0.45 [0.44–0.46] | 58% | 0.07 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Overground walking with assistive devices and/or lower limb orthoses | Overall | 4 | 0.43 [0.17–0.70] | 91% | <0.00001 | |
| | | Time after stroke | Subacute | 1 | n/a | n/a | n/a | |
| | | | Chronic | 2 | 0.23 [0.05–0.42] | 77% | 0.04 | |
| | | | Mixed | 1 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 4 | 0.43 [0.17–0.70] | 91% | <0.00001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 0 | n/a | n/a | n/a | |
| | | | | Mixed | 0 | n/a | n/a | n/a | |
| | Treadmill walking with assistive devices and/or lower limb orthoses | Overall | 12 | 0.37 [0.31–0.43] | 90% | <0.00001 | |
| | | Time after stroke | Subacute | 0 | n/a | n/a | n/a | |
| | | | Chronic | 12 | 0.37 [0.31–0.43] | 90% | <0.00001 | |
| | | | Mixed | 0 | n/a | n/a | n/a | |
| | | | Type of speed | Comfortable | 8 | 0.39 [0.30–0.48] | 93% | <0.00001 | |
| | | | | Maximum | 0 | n/a | n/a | n/a | |
| | | | | Imposed | 4 | 0.33 [0.27–0.38] | 67% | 0.03 | |

(continued)
Table 3. Continued.

| Outcome                          | Assistance modality          | Subgroup       | Number of independent groups | Pooled mean (95% CI) | Heterogeneity |
|---------------------------------|------------------------------|----------------|------------------------------|----------------------|---------------|
| Net energy cost (ml/kg/m)       | Unassisted over-ground walking | Overall        | 6                            | 4.87 [3.80–5.94]     | 85% <0.00001 |
|                                 |                              | Time after stroke | 0                            | n/a                  | n/a           |
|                                 |                              | Subacute        | 3                            | 3.75 [2.17–5.33]     | 85% 0.001     |
|                                 |                              | Chronic         | 3                            | 5.04 [4.14–5.93]     | 54% 0.11      |
|                                 |                              | Mixed           | 6                            | 4.86 [2.86–6.85]     | 89% <0.00001 |
|                                 |                              | Comfortable     | 6                            | 4.87 [3.80–5.94]     | 85% <0.00001 |
|                                 |                              | Maximum         | 0                            | n/a                  | n/a           |
|                                 |                              | Imposed         | 0                            | n/a                  | n/a           |
|                                 |                              | Mixed           | 0                            | n/a                  | n/a           |
| Net energy cost (ml/kg/m)       | Overground walking with assistive devices and/or lower limb orthoses | Overall | 4                            | 3.69 [2.91–4.47]     | 81% 0.001     |
|                                 |                              | Time after stroke | 0                            | n/a                  | n/a           |
|                                 |                              | Subacute        | 4                            | 3.69 [2.91–4.47]     | 81% 0.001     |
|                                 |                              | Chronic         | 2                            | 4.12 [3.55–4.69]     | 0% 0.78       |
|                                 |                              | Mixed           | 2                            | 3.40 [2.38–4.42]     | 82% 0.02      |
|                                 |                              | Comfortable     | 4                            | 3.69 [2.91–4.47]     | 81% 0.001     |
|                                 |                              | Maximum         | 0                            | n/a                  | n/a           |
|                                 |                              | Imposed         | 0                            | n/a                  | n/a           |
|                                 |                              | Mixed           | 0                            | n/a                  | n/a           |
| Net energy cost (ml/kg/m)       | Treadmill walking with assistive devices and/or lower limb orthoses  | Overall | 4                            | 4.46 [2.90–6.01]     | 92% <0.00001 |
|                                 |                              | Time after stroke | 0                            | n/a                  | n/a           |
|                                 |                              | Subacute        | 4                            | 4.46 [2.90–6.01]     | 92% <0.00001 |
|                                 |                              | Chronic         | 1                            | n/a                  | n/a           |
|                                 |                              | Mixed           | 3                            | 3.99 [2.39–5.58]     | 93% <0.00001 |
|                                 |                              | Comfortable     | 3                            | 3.99 [2.39–5.58]     | 93% <0.00001 |
|                                 |                              | Maximum         | 0                            | n/a                  | n/a           |
|                                 |                              | Imposed         | 0                            | n/a                  | n/a           |
|                                 |                              | Mixed           | 1                            | n/a                  | n/a           |

CI: confidence interval; gross: amount of energy consumption including resting level; net: amount of energy consumption above resting level; n/a: not applicable because no or only one independent group was included.

Energy cost rates during unassisted treadmill walking (0.22 ml/kg/m, 95% CI 0.20–0.24) and treadmill walking with soft exoskeleton assistance (0.20 ml/kg/m, 95% CI 0.18–0.21) [20].

Gross energy cost in J/kg/m
A single study reported gross energy cost rates during treadmill walking with assistive devices and/or lower limb orthoses (n = 15, crossover design) [32]. Reported net energy costs were: 12.2 J/kg/m (95% CI 5.52–18.88), 13.8 J/kg/m (95% CI 6.59–21.01), 10.7 J/kg/m (95% CI 5.27–16.13) and 8.5 J/kg/m (95% CI 4.13–12.87) for walking at CWS, 80% CWS, 120% CWS, and MWS.

Net energy cost in J/kg/m
Pooled results were reported in Figure 5. Important significant heterogeneity was found in all walking modalities. Subgroup analysis based on time after stroke substantially decreased heterogeneity in two modalities: unassisted treadmill walking in the chronic stage after stroke (5.04 J/kg/m 95% CI 4.14–5.93, I² = 54%, p = 0.11), and overground walking with assistive devices and/or lower limb orthoses in the chronic stage after stroke (4.12 J/kg/m, 95% CI 3.55–4.69, I² = 9%, p = 0.78). Subgroup analysis based on the type of speed was not applicable in any of the walking modalities because the subgroups contained only a single study or a single subgroup contained all studies.

Discussion
To our knowledge this is the first systematic review that summarizes post-stroke gross and net energy consumption (ml/kg/min) and cost (ml/kg/m and J/kg/m) during steady-state level surface walking with different assistance modalities – i.e., assistive devices and lower limb orthoses, BWS, end-effectors, and exoskeletons. In that way, this meta-analysis elaborates on the meta-analysis of Kramer et al. [3], who examined the energy requirements of unassisted walking (only a habitual AFO was allowed).

According to the guidelines of the American College of Sports Medicine (ACSM) [14], the identified exercise intensities were light (<10.5 ml/kg/min) to moderate (10.5–21.5 ml/kg/min) during unassisted walking (8.6–19.9 ml/kg/min) and walking with assistive devices and/or lower limb orthoses (6.7–12.8 ml/kg/min), and light during walking with BWS (9.42–9.88 ml/kg/min), rigid exoskeleton assistance (6.5–7.8 ml/kg/min), and end-effector assistance (5.2–9.2 ml/kg/min). These results suggest that comfortable walking, unassisted and with the use of assistive devices and/or lower
limb orthoses, can be used to incorporate low- to moderate-intensity exercise in ambulatory patients after chronic stroke (FAC ≥4). If patients cannot walk, or balance and safety issues are a concern (FAC <3), clinicians may consider the use of BWS systems, rigid exoskeletons or end-effector devices in the subacute to early chronic stage after stroke (median time since stroke: 4.5 months). The results suggest that these modalities can be used to incorporate low-, but not moderate-, intensity exercise in the subacute to early chronic stage after stroke (median time since stroke: 4.5 months). However, it is crucial to keep in mind that patients with stroke have very low levels of cardiorespiratory fitness (with peak oxygen consumption levels ranging from 8 to 22 ml/kg/min in literature) [67]—meaning that some patients must work near exhaustion to reach moderate-intensity exercise.

Current pooled results suggest that overground walking is more energy efficient when patients with stroke are unassisted

Figure 3. Pooled gross energy cost (ml/kg/m) during (A) unassisted overground walking, (B) unassisted treadmill walking, (C) overground walking with assistive devices and/or lower limb orthoses, and (D) treadmill walking with assistive devices and/or lower limb orthoses. Legend: a: Study for which a summary mean and standard error of the rate of oxygen cost during multiple walking interventions was calculated, CI: confidence interval, IV: inverse variance, n: number, random: DerSimonian and Laird random effects model, SE: standard error, VO2: volume oxygen, WS: walking speed.
A \textbf{Unassisted overground walking}

| Study or Subgroup | Mean (ml/kg/m) | SE | Weight | Mean IV, Random, 95% CI |
|-------------------|----------------|----|--------|------------------------|
| Dawes 2005 (28)   | 0.35           | 0.06 | 43.9% | 0.35 [0.23, 0.47]     |
| Canley 2015 (34)  | 0.18           | 0.01 | 56.1% | 0.18 [0.16, 0.20]     |
| Total (95% CI)    | 0.25 [0.09, 0.42] |    |        |                        |

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 7.81$, df = 1 ($P = 0.005$); $I^2 = 87$
Test for overall effect: $Z = 3.02$ ($P = 0.003$)

Figure 4. Pooled net energy consumption (ml/kg/m) during unassisted overground walking. Legend: a: Study for which a summary mean and standard error of the rate of oxygen consumption during multiple walking interventions was calculated, CI: confidence interval, IV: inverse variance, n: number, random: DerSimonian and Laird random effects model, SE: standard error, VO$_2$: volume oxygen, WS: walking speed.

(A) \textbf{Unassisted overground walking}

| Study or Subgroup | Mean (J/kg/m) | SE | Weight | Mean IV, Random, 95% CI |
|-------------------|---------------|----|--------|------------------------|
| Bregman 2010 (23) | 4.52          | 0.91 | 26.8% | 4.52 [2.74, 6.30]     |
| Ijmkere 2013 (35) | 4.54          | 0.61 | 33.0% | 4.54 [3.34, 5.74]     |
| Ijmkere 2013 (35) | 2.58          | 0.36 | 40.1% | 2.58 [2.27, 2.89]     |
| Total (95% CI)    | 3.75 [2.17, 5.33] |    |        |                        |

Heterogeneity: $\tau^2 = 1.59$; $\chi^2 = 13.52$, df = 2 ($P = 0.001$); $I^2 = 85$
Test for overall effect: $Z = 4.65$ ($P < 0.00001$)

(B) \textbf{Unassisted treadmill walking}

| Study or Subgroup | Mean (J/kg/m) | SE | Weight | Mean IV, Random, 95% CI |
|-------------------|---------------|----|--------|------------------------|
| Chantraine 2005 (25) | 5.5           | 0.61 | 16.4% | 5.30 [4.30, 6.70]     |
| Ijmkere 2013 (35) | 6.45          | 0.84 | 13.8% | 6.45 [4.80, 8.10]     |
| Ijmkere 2013 (35) | 3.19          | 0.32 | 19.2% | 3.19 [2.56, 3.82]     |
| Ijmkere 2013 (35) | 5.25          | 0.63 | 16.1% | 5.25 [4.02, 6.48]     |
| Massaad 2010 (43) | 3.86          | 0.69 | 15.5% | 3.86 [2.51, 5.21]     |
| Stoquart 2008 (50) | 5.4           | 0.35 | 19.0% | 5.40 [4.71, 6.09]     |
| Total (95% CI)    | 4.87 [3.80, 5.94] |    |        |                        |

Heterogeneity: $\tau^2 = 1.45$; $\chi^2 = 33.71$, df = 5 ($P < 0.00001$); $I^2 = 85$
Test for overall effect: $Z = 8.93$ ($P < 0.00001$)

(C) \textbf{Overground walking with assistive devices and/or lower limb orthoses}

| Study or Subgroup | Mean (J/kg/m) | SE | Weight | Mean IV, Random, 95% CI |
|-------------------|---------------|----|--------|------------------------|
| Bregman 2010 (23) | 3.91          | 0.81 | 14.2% | 3.91 [2.32, 5.50]     |
| Ijmkere 2013 (35) | 2.95          | 0.16 | 32.5% | 2.95 [2.64, 3.26]     |
| Schiemann 2015 (48) | 4.15        | 0.31 | 28.4% | 4.15 [3.54, 4.76]     |
| Total (95% CI)    | 3.69 [2.91, 4.47] |    |        |                        |

Heterogeneity: $\tau^2 = 0.46$; $\chi^2 = 15.65$, df = 3 ($P = 0.001$); $I^2 = 81$
Test for overall effect: $Z = 9.24$ ($P < 0.00001$)

(D) \textbf{Treadmill walking with assistive devices and/or lower limb orthoses}

| Study or Subgroup | Mean (J/kg/m) | SE | Weight | Mean IV, Random, 95% CI |
|-------------------|---------------|----|--------|------------------------|
| Finley 2017 (32)   | 6.48          | 1.1  | 18.7% | 6.48 [4.32, 8.64]     |
| Ijmkere 2013 (35) | 4.59          | 0.49 | 26.2% | 4.59 [3.63, 5.55]     |
| Ijmkere 2013 (35) | 2.66          | 0.2  | 28.6% | 2.66 [2.27, 3.05]     |
| Ijmkere 2013 (35) | 4.84          | 0.45 | 26.6% | 4.84 [3.96, 5.72]     |
| Total (95% CI)    | 4.46 [2.90, 6.01] |    |        |                        |

Heterogeneity: $\tau^2 = 2.16$; $\chi^2 = 37.24$, df = 3 ($P < 0.00001$); $I^2 = 92$
Test for overall effect: $Z = 5.62$ ($P < 0.00001$)

Figure 5. Pooled net energy cost (J/kg/m) during (A) unassisted overground walking, (B) unassisted treadmill walking, (C) overground walking with assistive devices and/or lower limb orthoses, and (D) treadmill walking with assistive devices and/or lower limb orthoses. Legend: a: Study for which a summary mean and standard error of the rate of oxygen cost during multiple walking interventions was calculated, CI: confidence interval, IV: inverse variance, n: number, random: DerSimonian and Laird random effects model, SE: standard error, VO$_2$: volume oxygen, WS: walking speed.
rather than when they use assistive device and/or lower limb orthoses (Figure 3). During treadmill walking, these results were reversed, suggesting that on a treadmill, patients benefit from using assistive devices and/or lower limb orthoses (i.e., handrail and lower limb orthoses). However, we should be cautious interpreting these results, because pooled means demonstrated substantial heterogeneity.

Our meta-analysis demonstrated wide variation in reported gross and net energy consumption (ml/kg/min) and cost (ml/kg/min and J/kg/min). Significant important heterogeneity was observed in all outcomes and walking modalities, except for gross energy consumption during treadmill walking with rigid exoskeleton assistance ($I^2 = 49\%$). We tried to explain the heterogeneity by subgrouping our results based on time after stroke (between 2 weeks and 3 months post-stroke and over 3 months post-stroke) and type of speed (CWS, MWS, or imposed walking speed). Unfortunately, we were restricted in our ability to explain heterogeneity because often subgroup analysis was irrelevant (i.e., a single subgroup contained all studies). Most studies included patients with chronic stroke and examined the energy requirements of comfortable walking.

When subgroup analyses based on time after stroke were relevant, subgrouping data decreased heterogeneity (14–93\% decrease), exposing a potential relationship with the time post-stroke. However, we could not investigate this relationship thoroughly, because only four studies investigated patients in the subacute stage after stroke. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation. Recruiting patients in this stage may be very challenging because it can be hard to convince patients, who already face many problems and discomforts, to engage in rehabilitation.

Subgrouping the results according to the type of speed (as pre-specified) only once decreased heterogeneity below 50\%. In most meta-analyses, studies were included in a single subgroup, i.e., the CWS subgroup. The considerable variation in CWS across studies, conceivably explains the persisting heterogeneity. In this meta-analysis, we focused on time after stroke and type of speed as factors that may explain heterogeneity, but other potential sources of heterogeneity could have been also: differences in walking ability [35,46], cardiorespiratory fitness [67], hemiparesis and spasticity [50], cognitive ability, accuracy and precision of respiratory gas analyses systems [69,70], or the degree of familiarization with the assistance modality (first-time use vs. habituated) [52,71]. However, these aspects were not consistently reported in the included studies.

Up to now, it is unclear whether bodyweight-supported and robot-assisted walking can reach moderate intensity. Studies examining the exercise intensity of these modalities are low in number (seven studies [27,39,49,53,60,63,65]), have small sample sizes (8–19 participants) and show inconsistencies. Krewer et al. [65] found no effect of increasing walking speed (1–2 kmph at 30\% BWS and 100\% GF) or decreasing robotic guidance (100–60\% GF at 30\% BWS and 2 kmph) on the energy requirements of Lokomat walking, while Lee et al. [39] reported that at 1.8 kmph, lowering the robotic guidance (100–60\%) significantly decreased the energy requirements. Slightly more evidence is available that decreasing the level of BWS could increase the energy requirements of walking (3 out of 4 studies) [27,60,63,65]. Interaction effects between BWS, walking speed and robotic guidance should be further studied in large sample size studies.

**Study limitations**

Because most studies allowed the use of both assistive devices and lower limb orthoses, we combined these types of assistance modalities. This may have generated heterogeneity because it is likely that the energy requirements of walking with assistive devices differ from walking with lower limb orthoses. However, we did not identify studies that investigated this hypothesis. Also, we may have included participants that did not use an assistive device or orthosis in this category. Several studies allowed participants to use their habitual aid if necessary [2,4,39,47,53,63], but did not report the number of participants actually using an aid [19,46,53,63]. In the studies that did report aid use, 31–44\% of the participants did not use an aid [2,4,39,47].

Variety in reporting outcome measures (gross vs. net and millilitres vs. Joules) resulted in restricted data comparison across studies – especially net values in ml/kg/min (one study [33]) and ml/kg/m (three studies [28,32,34]) were hardly ever reported. In future studies, it may be recommended to report net values over gross values, because net values take into account testing conditions (e.g., variation in environmental factors or personal routines) and show less systematic error and day-to-day variation [72].

**Conclusion**

Understanding the energy requirements of walking with various assistance modalities is important for clinicians to estimate the degree to which patients with stroke will be challenged in therapy. This systematic review and meta-analysis supports that walking, unassisted, or with the use of assistive devices and/or lower limb orthoses, induces low- to moderate-intensity exercise after chronic stroke, as recommended by exercise guidelines for stroke survivors. In patients who cannot walk independently, the use of BWS, rigid exoskeletons or end-effector assistance induces low-intensity exercise. Future large sample size studies should explore how dependent walkers can exercise at moderate intensity using bodyweight-support systems and robotic devices.

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POST-STROKE ENERGY CONSUMPTION AND COST

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