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Equations for estimating the oxygen cost of walking in stroke patients: systematic review

**Running Head:** Estimating the oxygen cost of walking in stroke

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# **Equations for estimating the oxygen cost of walking in stroke patients: a systematic review**

## **Abstract**

**Objective.** To report all equations that can potentially be used to estimate the oxygen cost of walking ( $C_w$ ) without using a respiratory gas exchange analyzer and to provide the level of reliability of each equation.

**Data sources.** Weblines, Medline, Scopus, ScienceDirect, Bielefeld Academic Search Engine (BASE), and Wiley Online Library databases from 1950 to August 2019 with search terms related to stroke and oxygen cost of walking.

**Methods.** This systematic review was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and the methodological quality of included studies was determined with the Critical Appraisal Skills Programme (CASP).

**Results.** We screened 2065 articles, and 33 were included for full-text analysis. Four articles were included in the data synthesis (stroke individuals=184). Analysis reported 4 equations estimating  $C_w$  that were developed from logistic regression equations between  $C_w$  and self-selected walking speed. The equations differed in several methodological aspects (characteristics of individuals, type of equation,  $C_w$  reference measurement methods). The Compagnat et al. study had the highest quality (CASP score=9/9).

**Conclusions.** This literature review highlighted 4 equations for estimating  $C_w$  from self-selected walking speed. Compagnat et al. presented the best quality parameters, but this work involved a population restricted to individuals with hemispheric stroke sequelae.

**Keywords.** oxygen cost, energy expenditure, stroke, prediction method, walking

## Introduction

The limitation of an individual's physical mobility is a common effect of stroke and frequently leads to lower participation in physical activity (PA)[1]. Increased PA has been demonstrated as a relevant treatment, with positive effects on impairment recovery, activity limitation, social participation and quality of life [2–4]. Furthermore, PA is now recommended in the entire stroke recovery pathway [2].

PA is defined as “any bodily movement produced by skeletal muscles that requires energy expenditure (EE)” [5,6]. In clinical practice, medical practitioners seldom measure EE because of the difficulty in setting up a viable recording system [7]. The gold-standard procedures (i.e., direct or indirect calorimetry) have the downside of being expensive and restrictive [8]. Questionnaire-based reporting methods have the advantage of being inexpensive and easily achievable; however, for stroke individuals, this method can be affected by cognitive impairments that can alter the reporting of PA [7,9]. In addition, the EE estimates in these questionnaires refer to EE charts based on studies of healthy individuals [10]. This transposition may not be appropriate because the oxygen demand during PA has been reported as significantly different between stroke individuals and healthy individuals [11,12]. For instance, the energy cost of walking ( $C_w$ ) costs twice as much oxygen on average for stroke individuals than for healthy individuals for an equivalent walking speed [12].

The  $C_w$  is presented as an excellent outcome measure for quantifying the EE [13]. Indeed, because  $C_w$  represents the volume of oxygen per unit of distance, one can convert the individual's walking activity into EE by multiplying the distance travelled by the caloric value of oxygen [13]. This method is similar to that of Ainsworth et al., with the difference that a walked distance is used rather than activity duration [14].

$C_w$  is not commonly measured because it requires the use of portable respiratory gas exchange analyzers that are expensive, complex and restrictive [15]. Experience has shown

that wearing a breathing mask while walking may be poorly tolerated by patients. Additionally, the technical modalities of use (calibration process of the device, operation, calculation of the  $Cw$ ), are neither short nor simple. Therefore, this method is not feasible in regular clinical practice [16]. Several authors have shown that  $Cw$  can be estimated from walking speed [13,17]. This method uses a  $Cw$  prediction equation constructed from a regression model between walking speed and  $Cw$ . Several equations that differ significantly in terms of methodological aspects have been reported [13,17]. These differences concern the sample size and characteristics, such as the type of stroke impairment, walking aid, and walking speed. Additionally, different devices have been used to measure  $Cw$  and walking speed, which can affect the reliability of the prediction equation. Also, the statistical analysis used to assess the reliability of the equations varies (coefficient correlation; Bland-Altman analysis). No systematic literature review has synthesized all these points, which are all fundamental for the use of these estimation equations in daily practice.

The purpose of this literature review was to report all equations that can be used to estimate  $Cw$  without using a respiratory gas exchange analyzer in a stroke population and to describe the parameters of the construction method and reliability.

## **Materials and methods**

### ***Research questions***

What are the equations that can be used to estimate  $Cw$  without using a respiratory gas exchange analyzer in a stroke population?

What is the reliability (accuracy, agreement, precision, test–retest reliability) of these equations?

### ***Search strategy***

The electronic literature was searched from 1950 to the present in Weblin, Medline, Scopus, ScienceDirect, Bielefeld Academic Search Engine (BASE) and the Wiley Online

Library. The search words were “oxygen cost” OR “oxygen rate” OR “energy expenditure” OR “energy rate” OR “energy cost” OR “oxygen” AND “stroke” OR “cerebrovascular disease” OR “hemiplegia” OR “brain injury”. The search was limited to titles and abstracts. Articles were included if they 1) studied populations with walking impairment caused by a stroke and 2) reported a Cw estimation equation. We excluded articles clearly unrelated to the theme (e.g., did not include individuals with stroke or assessed activities other than walking) or were written in languages other than English or French.

This systematic review was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The PRISMA guidelines consist of a 27-item checklist and a four-phase flow diagram to ensure the transparent and complete reporting of systematic reviews and meta-analyses [18].

### ***Study selection***

After removing duplicates, the search results were screened for eligibility by 2 reviewers (MC and SM) who independently evaluated titles and abstracts of retrieved articles. Abstracts that did not provide enough information regarding the inclusion and exclusion criteria were retrieved for full-text evaluation. Reviewers independently evaluated full-text articles and determined study eligibility. In case of disagreement, a third reviewer (JCD) served as a referee.

### ***Data extraction and quality assessment***

A data collection form was developed and used to extract data from studies selected for inclusion following a full-text review. This process utilized the Population, Intervention, Comparator, Outcome and Study Design (PICOS) framework [19].

The methodological quality of included studies was determined with the Critical Appraisal Skills Programme (CASP). We used the CASP checklist for diagnostic test studies (see Supplementary files) [20,21]. We chose this scale because we considered that the

equation was a test to evaluate the Cw. Thus, we assimilated the Cw prediction equation to a diagnostic test with a similar construction methodology. To detail these elements: we had to have information on the initial population for construction of the model, the reference method used, the evaluation of a new population and the reliability parameters used to evaluate the reliability of the equation. This approach refers to the World Health Organization's recommendations for the selection of diagnostic tests [22]. In this checklist, 9 of the 12 questions required a Yes, No or Can't tell response. Clearly reported information was marked as Yes and scored 1. No or Can't tell answers were both scored 0. By using this method, we could calculate a score related to the specific aspects of methodological quality assessed by the checklist. Question 7 concerned the results of the statistical analysis of the diagnostic test evaluation, in particular the reliability parameters. Therefore, we summarized the reliability parameters reported by the authors in a specific table (Table 3). To simplify the interpretation of these parameters, we ordered them by category (accuracy, precision, agreement) according to the recommendations of Hinkle et al. [23]. Question 8 referred to evaluating the cost benefit of an alternative to the test. We responded that this issue had not been addressed in the work included for the analysis. The CASP checklist's final question focused on the implications for practice. Thoughtful consideration was given to this particular question during the process of data extraction and synthesis.

### ***Data synthesis***

The results, precision and implications for practice for each study were assimilated by using information from the data extraction forms and CASP checklists. The percentage of agreement between both reviewers for methodological quality assessment was calculated based on items within the score-based items of the CASP checklist (number of items in common agreement/total number of items).



The compiled data synthesized the sample sizes, patient characteristics (time since stroke, severity of impairment, gait characteristics and walking ability), Cw measurement description and the prediction equation description. The extracted data were discussed and agreed upon by the reviewers to ensure accurate representation for each study.

This systematic review was presented to the International Prospective Register of Systematic Reviews (PROSPERO), but the progress of the work, including the analysis of the quality of the articles, was initiated at the time of submission to PROSPERO, which did not allow for registration in PROSPERO.

## **Results**

### ***Study selection***

The literature search identified 2065 articles. After removal of duplicates, 752 articles progressed to the first-stage review of titles and abstracts. The evidence selection process is summarized in Figure 1. Thirty-three articles were included for the full-text analysis. Finally, 4 articles met the inclusion criteria and were included in the data synthesis (Fig. 1).

### ***Study characteristics***

The 4 selected studies had variable designs and population characteristics [13,17,24,25]. The studies of Tesio et al., Zamparo et al. and Polese et al. were not designed to evaluate the reliability of the Cw prediction equation because they focused on the association between self-selected walking speed (Sfree) and Cw in stroke patients. The only study designed to test the reliability of the Cw prediction equation was by Compagnat et al.

A total of 184 stroke patients were included in the analysis. For each study, the population characteristics were heterogeneous. The sample sizes ranged from 20 to 54 individuals. The clinical characteristics of the participants were not reported in the work of Tesio et al. because the authors performed a synthesis of 5 studies [26–30] before the definition of the Cw prediction equation. Unfortunately, because of the age of the included works, we could not

collect the characteristics of the included populations. Polese et al. and Compagnat et al. clearly described the type of stroke and the functional independence for activities of daily living (assessed by the Barthel Index) for included individuals. Compagnat et al. mainly included hemispheric stroke patients. The location of stroke was not specified in the other studies; Zamparo et al. reported that individuals were affected by hemiplegia. This finding indicates 2 possible locations of these patients' stroke: a hemispherical lesion or a brain stem lesion. The level of walking ability and Cw values varied among studies. The complete population characteristics are summarized in Table 1.

### ***Quality assessment***

The quality of the selected works was also variable, with a mean (SD) quality score of 6.25 (2.5). The percentage of agreement between the two reviewers was 100%. The work of Compagnat et al. was ranked 9/9 on the CASP classification and that of Tesio et al. 3/9 because of poor description of the population and primary outcomes (Table 2).

### ***Oxygen cost prediction equations***

Four equations to estimate the Cw were reported across all studies. All these equations were constructed by logistic regression between walking speed and oxygen cost yet differed according to their type and constant values. Thus, Zamparo et al. and Compagnat et al. reported an equation as a power ( $Cw = a \times S_{free}^b$ ). The Zamparo et al. equation was converted to a logarithmic format as follows:  $\ln(Cw) = 1.27 - 0.718 \times \ln(S_{free})$ . Compagnat et al. reported the following equation:  $Cw = 0.2109 \times S_{free}^{-0.877}$ . Polese et al. and Tesio et al. found a polynomial relationship ( $Cw = a \times S_{free} + b \times S_{free}^2 + c$ ). The equation by Polese et al. was  $Cw = 0.95 - 1.28 \times S_{free} + 0.47 \times S_{free}^2$ . The Tesio et al. equation was  $Cw = 0.434 - 0.007 \times S_{free} + 4.567e - 5 \times S_{free}^2$ .

## ***Reliability assessment of the Cw prediction equations***

### **Measurements of Cw and gait speed**

In the studies by Polese et al., Compagnat et al., and Zamparo et al., the Cw was measured by indirect calorimetry to construct the relationship between Cw and Sfree. Different calorimetry devices were used: Zamparo et al. used the Oxynos I-C analyzer (Leybold Heraeus, Switzerland), whereas Compagnat et al. and Polese et al. used the Metamax3b (Cortex Medical, Leipzig, Germany). Tesio et al. reported that Cw was measured by using a portable Douglas bag.

Sfree was measured during a 6-min walk test in the studies by Compagnat et al. and Zamparo et al. In the Polese et al. study, it was measured during a 10-m walk test. The Tesio et al. study did not report a description of the Sfree measurement method.

For the same walking speed, each method calculated a different value for the Cw. The Sfree/Cw relationships are illustrated in Figure 2.

### **Reliability parameters of the Cw prediction equations**

The methodology used to assess the reliability of the Cw prediction equations was also heterogeneous. Only Compagnat et al. designed their study to test the reliability of the Cw prediction equation. The authors included an analysis of the coefficient of determination and a Bland-Altman plot analysis between the estimated and measured values of Cw. Furthermore, the authors tested their prediction equation in a second population of stroke individuals with similar characteristics. The reliability parameters were excellent ( $R^2=0.98$ ,  $MB=-0.02 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$ ; 95% limits of agreement =  $-0.31$  to  $0.26 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$ ). The studies by Zamparo et al., Polese et al. and Tesio et al. reported only the association between walking speed and Cw. Zamparo et al. reported a correlation coefficient of 0.92 between Cw and Sfree. Polese et al. reported a coefficient of determination of 0.81 between Cw and Sfree. Tesio et al. reported a

correlation coefficient of 0.66. These studies did not explore the reliability of their equations on a second population.

## **Discussion**

This work is the first to review equations used to estimate the oxygen cost of walking in individuals with stroke sequelae. We report on 4 equations that are all derived from a logistic regression equation between the self-selected walking speed and  $C_w$ . These prediction equations were nevertheless constructed from diverse populations and different  $C_w$  measurements. Thus, we found significant differences between the  $C_w$  prediction equations.

The differences between these equations can be explained first by the characteristics of the included participants. Indeed, the  $C_w$  in individuals with stroke sequelae is extremely variable, and can vary by a factor of 10 between 2 individuals [12,13]. A selection of individuals with similar  $C_w$  may disregard those with an unfavorable  $C_w$ , who will therefore not contribute to the construction of the prediction equation. In the study of Tesio et al., the participant sample had a low  $C_w$  ( $C_{w\text{Tesio}}=0.15 \text{ mL.kg}^{-1}\text{m}^{-1}$ ), considering that the average oxygen cost for the healthy able-bodied person is about  $0.14 \text{ mL.kg}^{-1}\text{m}^{-1}$ , with a high level of walking ability ( $S_{\text{free}}=1.25 \text{ ms}^{-1}$ )[25]. Therefore, the most disabled individuals were not included in this study. This  $C_w$  prediction equation might not be suitable for a more severely affected population.

The type of stroke can also affect the logistic regression equation. Indeed, the type of impairment was recently reported to alter the  $C_w/S_{\text{free}}$  relation [31,32]. For an equivalent walking speed, patients with post-stroke ataxic walking showed a 30% increase in  $C_w$  as compared with individuals with spastic hemiparesis caused by a hemispheric stroke [31,32]. Among the 4 studies examined, only Compagnat et al. considered the type of impairment in constructing the prediction model. Tesio et al., Polese et al. and Zamparo et al. did not describe the clinical presentation of individuals and location of the stroke.

Moreover, we report the greatest difference and variability of  $Cw$  estimates for very slow walking speeds ( $<0.3 \text{ ms}^{-1}$ ). The prediction models may not be adapted below these walking speeds, which appear more like “trampling”, which is strongly influenced by balance control strategies [33]. It would certainly be necessary to reflect on a walking speed range for which this type of equation is considered suitable.

The number of included individuals is also fundamental to the development of the prediction model. Indeed, the initial sample must be representative of the targeted population for the results to be generalized to the entire patient population. However, the populations of the studies selected in this literature review ranged from 20 to 50 participants. Therefore, these equations should be confirmed with larger cohorts.

The choice of the type of equation is also a factor of variation. During the logistic regression analysis, the author must choose between several types of equations (power, logarithmic, exponential, polynomial, etc.) [34], which will affect the resulting equation significantly [35]. Our work found 2 types of equations: power and polynomial. However, the polynomial type seems ill-adapted because it does not consider the exponential increase in  $Cw$  in patients with low walking speeds (Fig. 2). Therefore, this technical modality must be considered when designing the model.

Finally, the device chosen to measure  $Cw$  can also be a factor of variation when constructing the  $Cw$  prediction equation. In this work, we report on 2 devices: the Metamax3B and Oxynos 1-C analyzer. The Metamax3B has shown its reliability for low- to moderate-intensity activities [36,37]. However, it has not yet been validated in stroke individuals. The Oxynos 1-C is an older device that has not been validated in healthy individuals or stroke patients, to our knowledge. The reliability of the measurement device should be carefully considered because there may be measurement variations of up to 15% on  $VO_2$  between portable respiratory gas exchange measuring devices [38]. Hence, this

parameter is essential to judge the accuracy of the reference  $C_w$  value and therefore the reliability of the prediction equation of the  $C_w$ .

### ***Practical implications***

The goal of this systematic review was to inform and advise medical practitioners on the most reliable and suitable equations to predict the  $C_w$  of their patients in daily practice. In terms of elaboration and validation methodology, the equation formulated by Compagnat et al. presented the best quality parameters. However, this work was restricted to individuals with hemispheric stroke sequelae, and this equation cannot be adapted for individuals with other types of stroke (e.g., cerebellar stroke). Therefore, a different equation must be determined for individuals with ataxic post-cerebellar stroke because the  $C_w/S_{free}$  relation seems to be different for these individuals.

Regarding practical implications, these  $C_w$  prediction equations can be used to quantify the EE of stroke patients when walking [13]. The practitioner can estimate the  $C_w$  by measuring the walking speed at a self-selected speed in a 10-m test, a fast and reliable procedure [17]. Then, the prediction equation can be used to calculate the  $C_w$  and thus define the distance needed to achieve the recommended EE objectives to obtain a positive impact on health [13]. In addition to this method, the practitioner may also use an actimeter to measure the distance walked [39], to judge whether the patient is achieving the recommended level of EE (1000 kcal per week) [40,41].

Recent work has also shown that the integration of the  $C_w$  into the algorithm designed to calculate the EE estimated by an actimeter significantly improves the reliability of the estimations [42]. In future devices, manufacturers could ideally integrate into the proprietary algorithms one of the  $C_w$  prediction equations with the characteristics of stroke patients to enhance the accuracy of these tools.

## ***Limitations***

This work has several limitations, such as the difficulty in comparing the selected works in the literature review. Indeed, we compared a study designed to evaluate the reliability of a prediction model with other work designed to evaluate the association between walking speed and Cw. As a result, these studies do not present the same methodologies, which can complicate comparison, particularly when assessing the quality of studies using the CASP tool. The study by Tesio et al. was possibly underrated because of this. In addition, the level of description of the populations (type of stroke, level of impairment and functional capacity) was also missing for several studies, which may limit the explanations for the variations found in the Cw estimates. More studies predicting Cw are required to test the strength of the reliability of the models used. Another limitation of this work concerns the sources of the literature review in that we did not have access to the EMBASE database. Therefore, we may have missed some articles in this database. However, access to other databases (Medline, Scopus) certainly significantly reduced this risk.

## ***Conclusions***

This systematic review highlighted 4 equations to estimate Cw that were developed according to the close relation between Cw and walking speed. These equations use logistic regression equations. They differed in several methodological aspects (characteristics of individuals, type of equations, reference methods of Cw measurement). The Compagnat et al. equation had the highest quality scores, but this work was restricted to a specific population of stroke patients with hemispheric stroke sequelae. Further work on larger cohorts is needed to confirm the reliability of these equations.

## **Figure legends**

Figure 1. Flow diagram of study screening process.

Figure 2. Modeling of the oxygen cost prediction equations.

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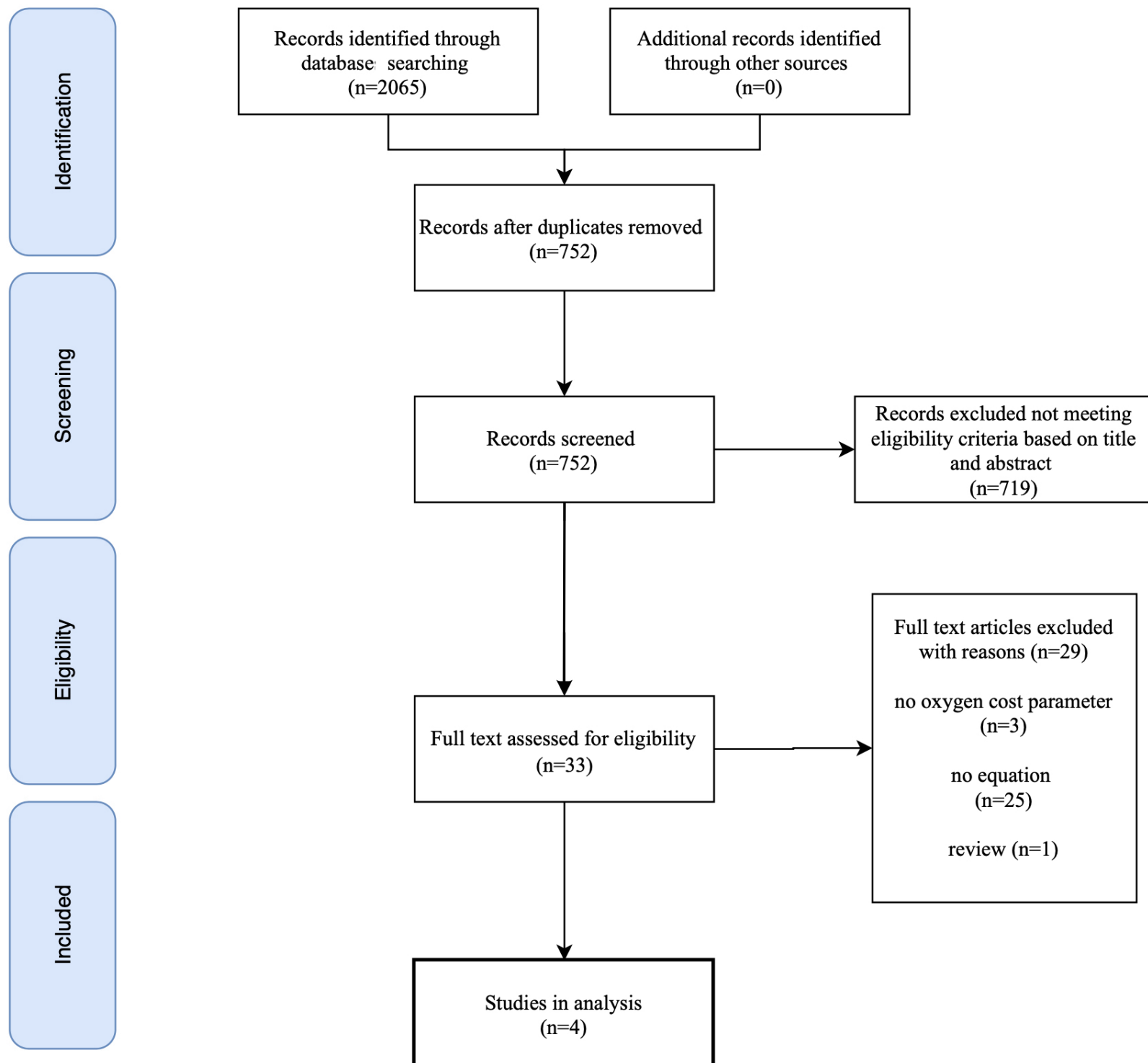
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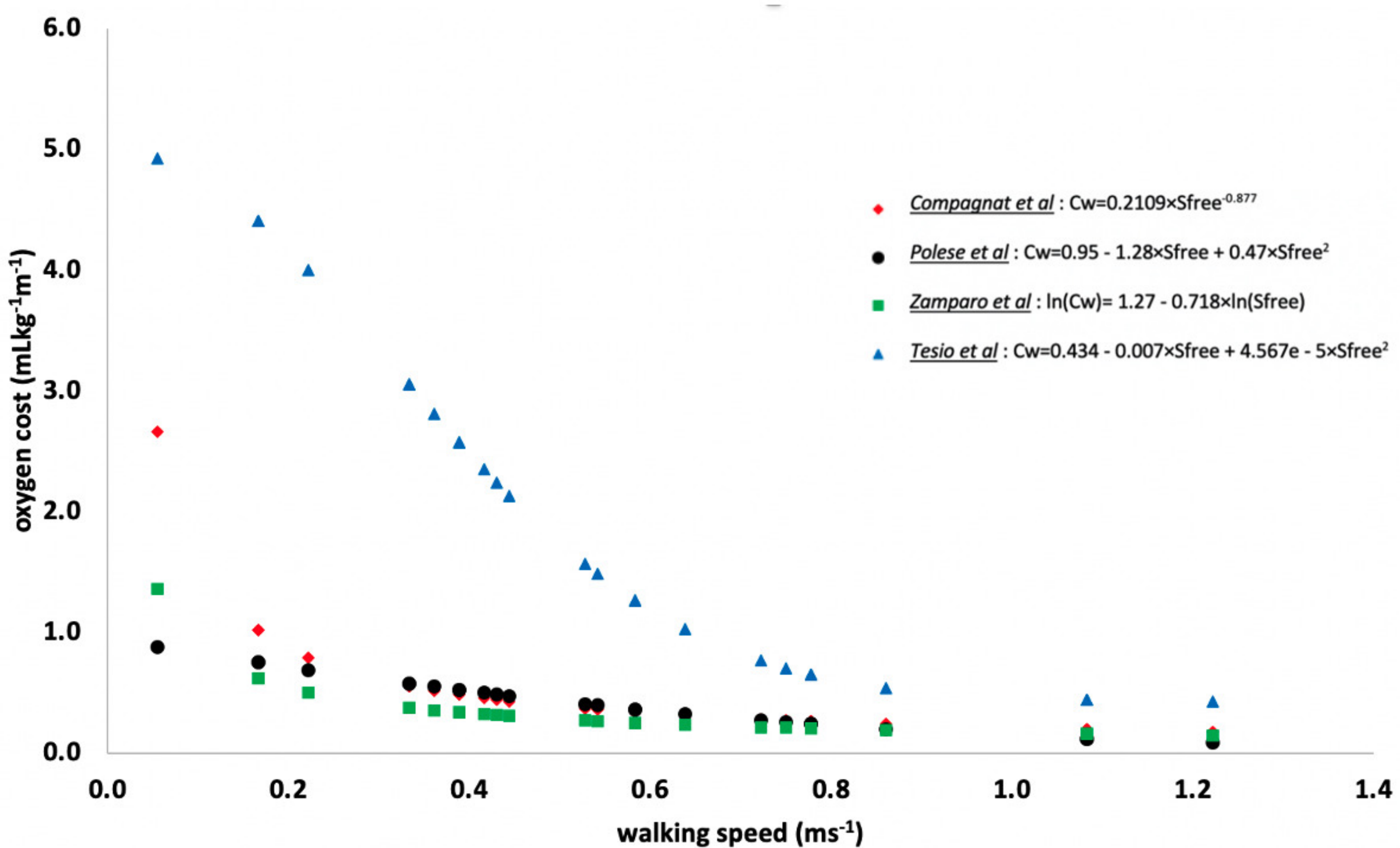
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**Table 1.** Description of the studies retained.

Study identification	Sample count	Age (years)	Time since stroke (days)	Localization of stroke	Walking aid	Cw (mLkg <sup>-1</sup> m <sup>-1</sup> )	Walking speed (ms <sup>-1</sup> )
Compagnat et al.	55	65.1 (15.7)	52.5 (9-5110)	Hemispheric	Cane=25, Walker=8, No aid=22	0.54 (0.51)	0.54 (0.30)
Polese et al.	55	59 (14)	1500 (90)	NA	NA	0.24 (0.11)	1.21 (0.44)
Tesio et al.	54	NA	NA	NA	NA	0.15 (NA)	1.25 (NA)
Zamparo et al.	20	58 (11)	1515 (90-15840)	NA	NA	NA	0.48 (0.22)

Data are mean (SD or range).

Cw, oxygen cost of walking; NA, not available

**Table 2.** Study quality assessment with the Critical Appraisal Skills Programme (CASP) tool.

<b>Study identification</b>	<b>Q1</b>	<b>Q2</b>	<b>Q3</b>	<b>Q4</b>	<b>Q5</b>	<b>Q6</b>	<b>Q7</b>	<b>Q8</b>	<b>Q9</b>	<b>Q10</b>	<b>Q11</b>	<b>Q12</b>	<b>Sum</b>
Compagnat et al.	Yes	Yes	Yes	Yes	Yes	Yes	Cf table 3	NA	Yes	Yes	Yes	Implications for research and clinical practice	<b>9</b>
Polese et al.	Yes	Yes	Yes	Yes	No	Yes	Cf table 3	NA	Can't tell	Can't tell	Yes	Implications for research and clinical practice	<b>6</b>
Tesio et al.	Yes	Yes	Yes	Can't tell	Can't tell	No	Cf table 3	NA	No	No	No	Contribution to the body of knowledge, but the authors did not discuss practical and research implications	<b>3</b>
Zamparo et al.	Yes	Yes	Yes	Yes	No	Yes	Cf table 3	NA	Can't tell	Can't tell	Yes	Discussion about clinical but not research implications	<b>6</b>

NA, not available



**Table 3.** Reliability parameters of oxygen cost prediction equations of selected studies.

Study identification	Sample count	Cw reference measurement method	Cw (mLkg <sup>-1</sup> m <sup>-1</sup> )	Accuracy	Agreement	Precision	Test–retest reliability
Compagnat et al.	55	Metamax3b	0.81 (1.10)	MD = 4% (p>0.05)	Mean bias = -0.02 mL.kg LoA (-0.31; 0.26) r=0.99 (0.97-0.99)	Mean value = 0.83 (1.12)	NA
Polese et al.	55	Metamax3b	0.24 (0.11)	NA	R <sup>2</sup> =0.81	NA	NA
Tesio et al.	54	Portable Douglas bag	0.15 (NA)	NA	r=0.66	NA	NA
Zamparo et al.	20	Oxynos I-C analyzer	NA	NA	r=0.92	NA	NA

Data are mean (SD or range).

Cw, oxygen cost of walking; NA, not available; MD, mean difference with the reference method; Mean bias, in reference to Bland-Altman analysis; LoA, limits of agreement of Bland-Altman analysis; r, correlation coefficient; R<sup>2</sup>, determination coefficient; Mean, mean value of the estimate according to the prediction equation with its standard deviation.