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ORIGINAL REPORT

PREDICTION OF OXYGEN UPTAKE DURING LEVEL TREADMILL WALKING IN PEOPLE WITH MULTIPLE SCLEROSIS

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Objective: **To determine whether the oxygen uptake (VO_2) during walking at different speeds in people with multiple sclerosis is underestimated by available prediction equations and whether such underestimation relates to the validity of their assumptions.**
Design: **Cross-sectional comparison.**
Subjects: **Eighteen adults with multiple sclerosis and 18 adults without multiple sclerosis.**
Methods: **VO_2 was measured at rest and during treadmill walking at 2.0, 3.0 and 4.0 mph with open-circuit spirometry. The actual VO_2 was compared with that estimated by both the American College of Sports Medicine and the van der Walt and Wyndham equations.**
Results: **The differences between the actual VO_2 and that estimated by both equations were significantly higher than zero across speeds for both groups ($p<0.001$). The underestimation increased with increasing speed ($p<0.001$) for both groups and was greater for participants with multiple sclerosis than those without multiple sclerosis ($p<0.011$). The inaccurate prediction by the American College of Sports Medicine formula was associated with an underestimation of the net VO_2 per meter ($p<0.001$), and this was higher for participants with multiple sclerosis ($p<0.007$).**
Conclusion: **Rehabilitation and exercise professionals should recognize that the American College of Sports Medicine and the van der Walt and Wyndham equations underestimate VO_2 during treadmill walking in individuals with and without multiple sclerosis.**

Key words: multiple sclerosis; energy expenditure; prediction equations; physical activity; disability.

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INTRODUCTION

Physical activity levels are lower in individuals with multiple sclerosis (MS) than in the general population (1), thereby increasing the risks of inactivity-related morbidity (2). Physical activity and exercise training programs can alleviate symptoms (3) and improve mobility (4), fitness (5, 6) and quality of life (7) in people with MS. One of the most common forms of physical activity in persons with MS, which is often used by rehabilitation and exercise professionals to promote mobility and health in this population, is walking (5, 6). Effective walking programs are designed with a careful selection of the appropriate intensity, which is based on an estimation of the oxygen uptake (VO_2) during walking at a given speed (8). However, current equations for VO_2 estimation have been developed for healthy adults and may thus be inappropriate for persons with MS. This is important for rehabilitation and exercise professionals who must design physical activity programs for individuals with MS in a way that maximizes mobility and fitness benefits while avoiding possible complications of increasing core-temperature (6).

Available VO_2 prediction equations for level walking include one published by the American College of Sports Medicine (ACSM) (9) and one developed by van der Walt and Wyndham (10). The ACSM formula assumes a linear relationship between VO_2 and speed and is considered most accurate for speeds between 1.9 and 3.7 mph; however, its accuracy both within and above this range has not received adequate experimental evaluation. Conversely, the van der Walt and Wyndham formula assumes a curvilinear relationship between VO_2 and speed and has been developed for speeds between 2.0 and 5.0 mph. Both of these equations have been generated based on empirical evidence from small samples of young men and may underestimate the actual VO_2 in persons with MS. This is because persons with MS show higher VO_2 than persons without MS when walking at a given speed (11–13); however, whether these equations significantly underestimate the VO_2 in individuals with MS must be evaluated with direct empirical information. The ACSM formula, in particular, assumes that the resting VO_2 is 3.5 ml/kg/min and that the net oxygen uptake required to walk a meter (net VO_2/m) is 0.1 ml/kg/m across speeds (9). Past research in people with MS has reported net VO_2/m values higher than those assumed by the ACSM formula; however, whether this finding affects the accuracy of the ACSM equation for individuals with MS has not been examined directly.

The present study therefore examined whether the van der Walt and Wyndham and the ACSM equations accurately predict the actual VO_2 during level walking in people with and without MS. It was hypothesized that both formulas would underestimate the VO_2 of individuals with MS across different

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speeds. This study also examined whether the assumptions of the ACSM equation (i.e. resting $VO_2 = 3.5$ ml/kg/min and net $VO_2/m = 0.1$ ml/kg/m) are valid for individuals with MS. It was hypothesized that inaccurate VO_2 prediction by the ACSM equation would be associated with an underestimation of the net VO_2/m rather than the resting VO_2 of people with MS.

METHODS

Participants

The study participants were 18 individuals (14 women, 4 men) with a definite diagnosis of MS and 18 healthy individuals without MS. We targeted this sample size based on the size of samples of previous research documenting differences in energy expenditure in persons with MS compared with controls during treadmill walking (12). The 2 groups of participants did not differ in sex, age, height, body mass and body mass index (Table I). All participants were ambulatory and were not using assistive devices such as a cane, crutch or walker. Participants with MS were in early disease stages (time from MS diagnosis was 8.4 ± 7.2 years) and had limited mobility problems (Patient Determined Disease Steps (PDDS) scale (14) score 1.3 ± 1.2). The clinical course of MS was relapsing-remitting in 17 of the participants, whereas in 1 participant it was of the progressive type. The protocol was approved by the Institutional Review Board and all participants provided written informed consent.

Procedures

Participants attended a single testing session in a noise-free and thermo-neutral (21ºC) laboratory and were instructed to avoid food, caffeine and exercise for 3 h prior to the session. The session commenced with the completion of demographic and health history questionnaires. Participants with MS also completed the PDDS scale. Body mass and height were measured with participants wearing shoes and light clothing. Thereafter, participants sat in a chair quietly for 10 min to bring their physiologic functioning to resting levels. Following this period, expired gases were measured during 6 min of quiet, stable sitting on a chair and during 3 level walking trials, each lasting 6 min, using an open-circuit spirometry system (TrueMax 2400, Parvo Medics, Salt Lake City, UT, USA). The pneumotachometer and the gas analyzers were calibrated prior to the session, using a 3-l calibration syringe and gases of known concentration, respectively. The 3 walking trials were conducted on a treadmill (Trackmaster, TMX425C, Full Vision, Inc., Newton, KS, USA) without hand-rail support and were separated by 6 min of sitting. The 6-min periods of quiet seated rest were long enough for energy expenditure to return to baseline levels; this was verified by sampling expired gases before beginning the next period of walking. We selected treadmill walking as a means of precisely controlling speed from which available equations predict VO_2. The walking speeds were 2.0, 3.0 and 4.0 mph and were presented in a randomized order. The accuracy of treadmill speed and grade (0%) was confirmed with a tachometer and a digital inclinometer, respectively, before and after the study.

Table I. *Sex, age, anthropometric characteristics and resting oxygen uptake ($V0_2$) of individuals with multiple sclerosis (MS) and individuals without multiple sclerosis (non-MS)*

	Group	
	MS (*n* = 18)	Non-MS (*n* = 18)
Sex (women to men ratio)	14:4	14:4
Age, years, *n* (%)	41.9 (12.6)	39.1 (11.9)
Body mass, kg, *n* (%)	72.1 (16.4)	72.8 (15.0)
Height, cm, *n* (%)	167.7 (13.1)	171.8 (7.6)
Body mass index, kg/m^2, *n* (%)	26.1 (7.4)	24.7 (5.1)
Resting $V0_2$, ml/kg/min, *n* (%)	3.7 (0.5)	3.8 (0.4)

Between-group differences in continuous variables were not statistically significant ($p > 0.05$) in independent *t*-tests; resting VO_2 was not significantly higher than 3.5 ml/kg/min ($p > 0.05$) for either group.

Data analyses

The VO_2 (in both ml/kg/min and l/min) was determined as the average over the last 3 min of the resting and walking periods. Thus, participants had 3 min to achieve steady-state VO_2, a time that is considered adequate (15). Indeed, all participants showed minimal change in VO_2 (< 100 ml/min) during the last 3 min at each walking intensity. In addition, the net VO_2/m (ml/kg/m) was calculated by subtracting the resting VO_2 from the VO_2 during walking and then dividing by the treadmill speed in m/min. The VO_2 at each speed was further estimated with the ACSM formula for level walking (VO_2 (ml/kg/min) = 0.1S + 3.5, where S is walking speed (m/min)) and with the van der Walt and Wyndham prediction equation (VO_2 (l/min) = 0.00599M + 0.000366MV2, where M is body mass (kg) and V is walking speed (km/h)). The differences in each participant's actual VO_2 from the VO_2 estimated by the above equations were computed for each speed and were used as dependent variables in statistical analyses.

The differences of the actual from the estimated VO_2 for each speed were analyzed with 1-sample *t*-tests with a comparison value of 0 (i.e. no error in estimation). The agreement between the estimated and the actual VO_2 for each speed was further evaluated with Bland-Altman plots (16). One-sample t-tests were also used to examine whether the resting VO_2 and the net VO_2/m for each group differed from the values assumed by the ACSM formula (3.5 ml/kg/min and 0.1 ml/kg/m, respectively). The degree to which the resting VO_2 and the net VO_2/m were associated with the difference between the actual VO_2 and that estimated by the ACSM equation were evaluated with Pearson's correlation coefficient. The effects of MS and walking speed on the differences between actual and estimated VO_2 as well as on the net VO_2/m were analyzed with 2 × 3 (group × speed) mixed-model analyses of variance (ANOVA) with group as a between-subjects factor and speed as a within-subjects factor. The Greenhouse-Geisser adjustment was applied when appropriate (i.e. violation of compound symmetry based on Machley's test). Between-group independent-samples *t*-test at each speed with Bonferroni-adjusted alpha (0.017) was performed when warranted by significant interaction effects. Significant speed effects were examined using paired *t*-tests between speeds with Bonferroni-adjusted alpha (0.017). When the group-by-speed interaction was significant, these tests were performed separately for each group, contingent upon significant within-group repeated-measures ANOVA. The alpha level was 0.05. Statistical analyses were performed with SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The van der Walt and Wyndham and the ACSM equations underestimated the actual VO_2 during walking in participants both with and without MS. The differences of the actual from the estimated VO_2 were significantly higher than zero at all speeds ($p < 0.001$) for both groups. The VO_2 underestimation by the van der Walt and Wyndham and the ACSM equations was confirmed by the Bland-Altman plots, as indicated by negative mean error of agreement at each speed (Fig. 1). The plots further indicated that the underestimation of VO_2 demonstrated large between-individual variability. Importantly, this variability appeared greater in participants with MS than in those without, and more individuals with MS were closer to the lower limits of agreement.

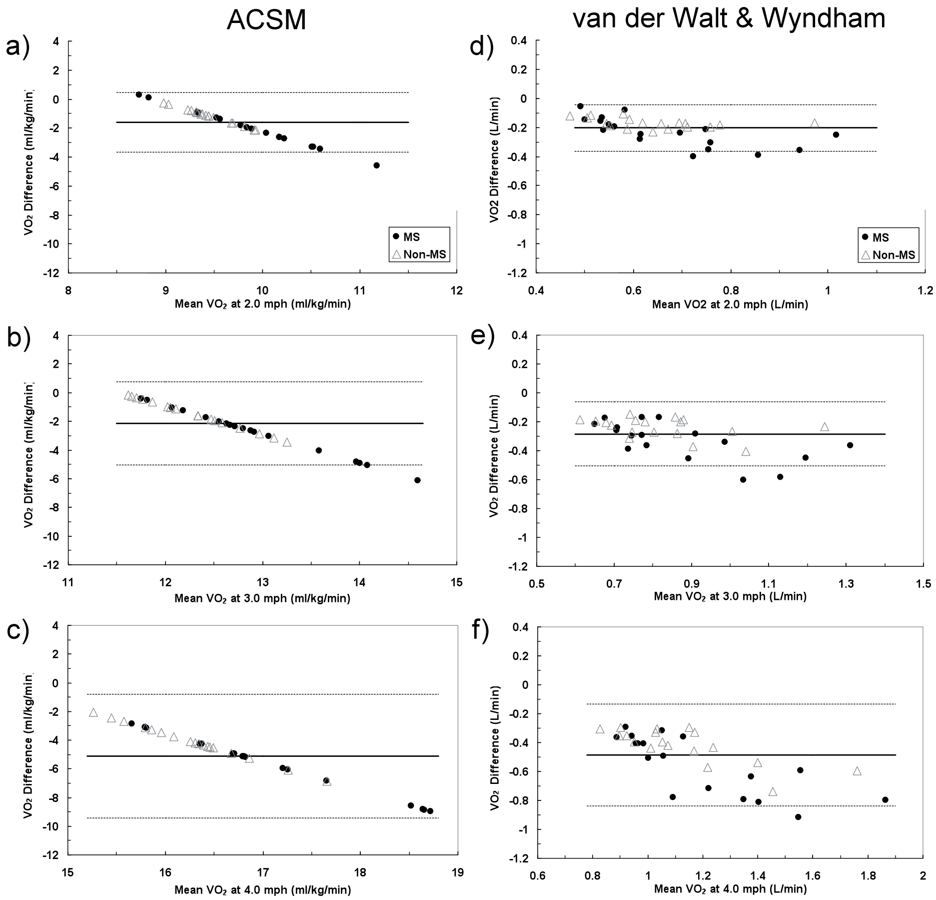

Fig. 1. Bland-Altman plots of the differences between actual oxygen uptake (VO_2) and estimated VO_2 as a function of mean $V0_2$ during walking in individuals with multiple sclerosis (MS) and without multiple sclerosis (non-MS). (a, b, c) Differences from VO_2 estimated with the American College of Sport Medicine (ACSM) equation at 2.0, 3.0 and 4.0 mph, respectively. (d, e, f) Differences from VO_2 estimated with the van der Walt and Wyndham equation at 2.0, 3.0 and 4.0 mph, respectively. Mean VO_2 is the average of actual and estimated VO_2. Solid and dotted lines are mean and 1.96 standard deviation (SD) of the differences for pooled data of both groups.

Consequently, the degree of underestimation by the van der Walt and Wyndham equation was greater for participants with MS than those without MS, and increased as a function of speed for both groups (Fig. 2). For participants with MS, underestimation at 2.0, 3.0 and 4.0 mph was 0.2, 0.3 and 0.6 l/min, respectively. For participants without MS, underestimation at the respective speeds was 0.2, 0.2 and 0.4 l/min. The difference between the actual and the predicted VO_2 showed significant group and speed main effects ($p < 0.001$) without a group-by-speed interaction. Follow-up analyses showed that the difference between the actual and the predicted VO_2 was greater at faster than at slower speeds ($p < 0.001$).

Similarly, the VO_2 underestimation by the ACSM formula was greater for participants with MS than participants without

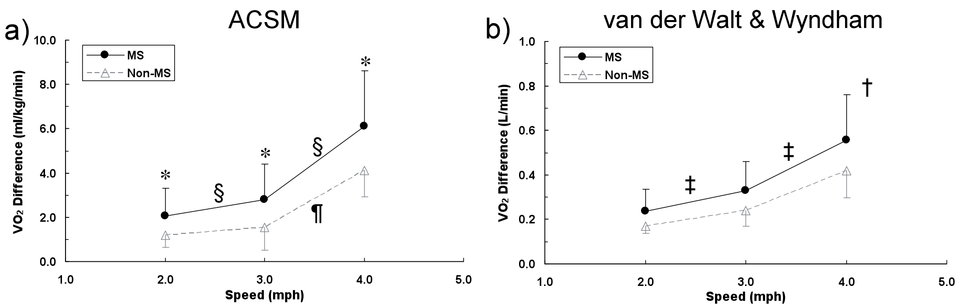

Fig. 2. Mean and standard deviation (SD) differences of actual oxygen uptake ($V0_2$) from estimated $V0_2$ as a function of walking speed in individuals with multiple sclerosis (MS) and without multiple sclerosis (non-MS). (a) Difference from VO_2 estimated with the American College of Sport Medicine (ACSM) equation. (b) Difference from $V0_2$ estimated with the van der Walt and Wyndham equation. For convenience, the opposite of the differences is shown. *$p < 0.017$ between groups; †$p < 0.001$ for main effect of group (MS vs non-MS) across speeds; §$p < 0.017$ between speeds for MS group; ¶$p < 0.017$ between speeds for non-MS group; ‡$p < 0.017$ between speeds for pooled data of both groups. Only the significant differences between adjacent speeds are shown.

MS and increased as a function of speed for both groups (Fig. 2). For participants with MS, underestimation at 2.0, 3.0 and 4.0 mph was 2.0, 2.8 and 6.1 ml/kg/min, respectively. For participants without MS, underestimation at the respective speeds was 1.2, 1.5 and 4.1 ml/kg/min. The difference between the actual and the predicted VO_2 exhibited a significant group-by-speed interaction ($p = 0.046$). Follow-up analyses showed that the difference was greater for those with MS than those without at all speeds ($p < 0.011$). For the MS group, all between-speed comparisons of the difference between the actual and the predicted VO_2 were significant, with faster speeds showing greater VO_2 differences than slower ones ($p < 0.001$). Similar results were obtained for the group without MS, except that the comparison between the VO_2 difference at 2.0 and 3.0 mph was not statistically significant.

The inaccurate prediction by the ACSM formula appeared to be caused by an underestimation of the net VO_2/m, which was higher for participants with MS than those without. Although the resting VO_2 did not differ from the assumed 3.5 ml/kg/min ($p > 0.05$; Table I), the net VO_2/m was significantly higher than 0.1 ml/kg/m at all speeds ($p < 0.001$) for participants with and without MS. Furthermore, the net VO_2/m showed significant main effects for group and speed ($p < 0.007$) without an interaction (Fig. 3). For participants with and without MS, the net VO_2/m at 4.0 mph was significantly higher than that at 2.0 or 3.0 mph. The difference between the actual VO_2 and that estimated by the ACSM equation was strongly associated with the net VO_2/m ($r = -0.89$; $p < 0.001$), but not with the resting VO_2 ($r = 0.11$; $p > 0.05$).

DISCUSSION

Both the van der Walt and Wyndham and the ACSM equations underestimated the actual VO_2, and the degree of underestimation was greater in participants with MS than those without MS. This finding is consistent with previous research that has reported greater rates of oxygen uptake during walking than those expected based on the above equations for people with and without MS (12, 17–19), although neither study compared the actual VO_2 with the estimated one as was done in the present study. One possible explanation for this general underestimation might relate to the fact that both equations have been derived from small samples of young people. Notably, the van der Walt and Wyndham equation was derived from only 6 young men. By comparison, the present investigation included both men and women of a wider age-range. Therefore, the above equations may not reliably predict the energetic cost of walking in adults of various ages, particularly in those with MS. The end result is that practitioners should use caution in the application of these equations for prescribing the intensity of walking in persons with MS, because use of these equations is likely to produce an over-prescription leading to unwanted fatigue in this population. Thus, a more accurate equation needs to be developed for people with MS.

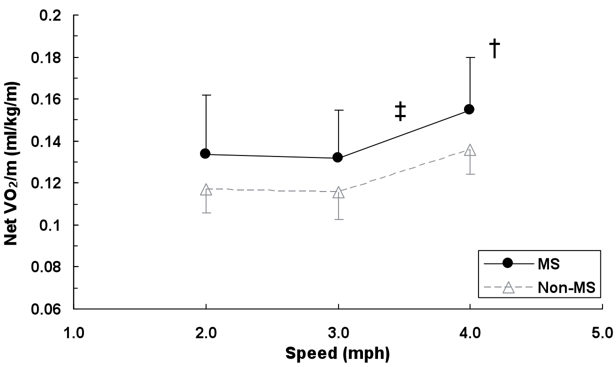

Fig. 3. Mean and standard deviation (SD) net oxygen uptake per meter (net VO_2/m) as a function of walking speed in individuals with multiple sclerosis (MS) and without multiple sclerosis (non-MS). †$p < 0.05$ for main effect of group (MS vs. non-MS) across speeds; ‡$p < 0.017$ between speeds for pooled data of both groups. Only the significant differences between adjacent speeds are shown.

The underestimation by the ACSM formula appears to be related to the validity of its underlying assumptions. The formula assumes that the net VO_2/m is 0.1 ml/kg/m for all people. However, this value has been derived primarily from young, healthy, fit individuals (20) who might have had greater walking economy and it may not apply to larger populations. Consistent with early research in healthy adults (21), the actual net VO_2/m in participants without MS in the present study was higher than the assumed 0.1 ml/kg/m both within and above the range for which the ACSM formula is most accurate and it was even higher in participants with MS. Not surprisingly, the net VO_2/m was strongly associated with the underestimation of VO_2. In contrast, the resting VO_2 of individuals with and without MS was not higher than the 3.5 ml/kg/min assumed by the ACSM equation and was not related to the underestimation of the VO_2. These results, therefore, suggest that the inaccuracy of the ACSM equation is caused primarily by an underestimation of the net VO_2/m, particularly for people with MS.

Notably, the amount of underestimation by both prediction equations increased as a function of speed for both groups of participants. This effect can be also seen in the Bland-Altman plots, which demonstrate that the 95% limits of agreement between the actual and the estimated VO_2 increase with faster speeds. For the ACSM formula, the effect of speed appears to be due to the fact that the net VO_2/m was not constant across speeds, but increased between 3.0 and 4.0 mph. This was expected and it potentially explains why the ACSM formula is not considered as accurate for speeds above 3.7 mph. However, the nature of the relationship between net VO_2/m and walking speed seems to suggest that even at speeds close to 3.7 mph the net VO_2/m may be higher than that at 3.0 mph. This is supported by past research showing that the response of the net VO_2/m to walking speed is curvilinear and, for the range of speeds in the present study, it appears to increase (20, 22, 23). Furthermore, even though the net VO_2/m was constant between 2.0 and 3.0 mph, the ACSM formula still underestimated the VO_2 in participants with and without MS at those speeds. As stated above, both the ACSM and the van der Walt and Wyndham equations have been derived from samples of young people for whom the effect of speed on energy expenditure may have been milder than that of the general population.

The degree of underestimation by both formulas was greater for participants with MS than participants without MS. This is a natural consequence of the fact that people with MS have higher VO_2 when walking at a given speed (12, 13). Notably, the basic shape of the responses of the VO_2 differences and the net VO_2/m to walking speed appeared to be similar in both groups. This is suggestive of a systematic cause of the differences between groups that produced an amplification of the effects of a change in speed in people with MS. This may be caused by leg spasticity (11), which could potentially increase the VO_2 and the net VO_2/m by a relatively constant factor across speeds. The actual causes of the higher VO_2 during walking in people with MS cannot be determined from the present results. The practical significance, however, is that the validity of using these equations to predict the energetic cost in adults, particularly those with MS, appears questionable. This proposition is strengthened by the Bland-Altman plots, which demonstrated that the amount of underestimation at a given speed varied greatly between people and was greater among those with higher walking VO_2, who tended to be participants with MS. Furthermore, there was great variability in the mean of the actual and predicted VO_2 when walking at a given speed, particularly among participants with MS. Such effect in persons with MS may be a consequence of between-people variability in disease severity. Hence, the prediction equations appear to have limited individual predictability in adults, especially in those with MS.

Healthcare professionals who design physical activity programs for individuals with MS should be aware that both the van der Walt and Wyndham and the ACSM equations may underestimate actual exercise intensity. For example, the ACSM formula predicts that level walking at 3.0 mph requires a VO_2 of 11.5 ml/kg/min. For a person with MS with a maximal aerobic capacity of 35 ml/kg/min, this value represents only 33% of her/his maximal VO_2. However, if this person's actual VO_2 at 3.0 mph were 16 ml/kg/min as in several participants with MS in the present investigation, walking at 3 mph would reflect an intensity of 46% of her/his maximal VO_2 or 13% higher than the predicted level. Furthermore, the underestimation of actual exercise intensity will be even greater for faster walking speeds. If clinicians use available equations, they may inappropriately prescribe exercise intensities that are too high, thus increasing the risk of undue fatigue. Such failure to prescribe the appropriate intensity may decrease the adherence of persons with MS to walking programs. Until an accurate prediction equation becomes available, healthcare professionals may be cautiously selecting walking intensities by trial-and-error that elicit a heart rate and a sense of effort within the target training zones of heart rate and ratings of perceived exertion, respectively.

Several limitations of the present study should be acknowledged. First, the study did not include a session of familiarization with treadmill walking and the VO_2 underestimation may partially reflect unfamiliarity with treadmill walking, although all participants reported being comfortable while walking on the treadmill. Second, persons with MS may have become fatigued across the 3 different walking speeds, and, if this occurred, the residual fatigue might have been a factor in the greater error in estimation among those with MS. Third, this study did not evaluate the accuracy of the ACSM equation during walking on an incline. However, even if the vertical component of this equation were error-free, the amount of underestimation due to the horizontal component would not be attenuated. Finally, the present study included mostly women and its findings may not be generalizable to men. However, one should note that MS affects more women than men and that our sample characteristics were roughly consistent with the demographics of MS (24).

Future research should attempt to develop an equation to predict with acceptable accuracy the energetic cost during level and incline walking in people with MS. However, given the variability in disease progression between people, such a formula may need to consider disease stage as a possible predictor. Importantly, the causes of the higher energy expenditure during walking in persons with MS should be identified. Such knowledge may lead to interventions that can alleviate these causes, thus promoting mobility and health in individuals with MS.

In conclusion, the ACSM and the van der Walt and Wyndham equations underestimate the energetic cost of level treadmill walking. The amount of underestimation is greater in individuals with MS, for whom walking elicits a higher energetic cost. Rehabilitation and exercise professionals should be aware of the potential to underestimate exercise intensity when designing walking programs for health promotion in people with MS.

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