

Timed loaded standing in female chronic fatigue syndrome compared with other populations

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Abstract—Patients with chronic fatigue syndrome (CFS), like patients with osteoporosis, have similar difficulties in standing and sitting. The aim of the study was to compare combined trunk and arm endurance among women with CFS ($n = 72$), women with osteoporosis ($n = 30$), nondisabled women ($n = 55$), and women from non-industrialized countries ($n = 58$) using the timed loaded standing (TLS) test. TLS measures how long a person can hold a 1 kg dumbbell in each hand in front of him or her with straight arms. TLS was higher in the industrialized nondisabled population than in the non-industrialized study population ($p < 0.001$) and in patients with osteoporosis ($p = 0.002$). TLS was lower in patients with CFS than in nondisabled controls ($p < 0.001$). After adjusting for age, body height, and weight, combined trunk and arm endurance was lower in CFS patients than in osteoporotic patients, even though the patients with osteoporosis were more than 25 yr older ($p < 0.001$). In CFS, TLS was lower than in the non-industrialized group ($p = 0.02$). Since only women were studied, external validity of the results is limited to adult female patients with CFS. TLS revealed a specific biomechanical weakness in CFS patients that can be taken into account from the onset of a rehabilitation program. We propose that influencing the quality, rather than the quantity, of movement could be used in the rehabilitation.

Key words: chronic fatigue syndrome, deformation, endurance, graded exercise/exposure therapy, movement, non-industrialized population, osteoporosis, physical performance, timed loaded standing, trunk.

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INTRODUCTION

Ongoing fatigue forms a major health problem in industrialized countries. Chronic fatigue syndrome (CFS) is defined by the U.S. Centers for Disease Control and Prevention as a condition characterized by self-reported unexplained persistent or relapsing fatigue of at least 6 mo duration and the concurrent occurrence of multiple nonspecific symptoms, including sore throat, muscle and joint pain, headache, tender cervical or axillary lymph nodes, unrefreshing sleep, and postexertional malaise [1].

Physical complaints as a result of military actions—especially combat situations—are known from World War I on. Different terms—such as Da Costa syndrome, irritable heart, shell shock, neurocirculatory asthenia, and battle fatigue—have been used to coin the difficult to understand soldier's medical conditions following war situations [2]. More recently, the terms posttraumatic

Abbreviations: BMI = body mass index, CFS = chronic fatigue syndrome, TLS = timed loaded standing.

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stress syndrome, and survivor's guilt syndrome have been used [3–4].

Chronic pain and fatigue form the core elements of the medical complaints, often described as idiopathic [5]. Solutions for these complaints have been searched for in the last decades. One of the most investigated postwar complaints is CFS. A sample of 23 participants showed that 43 percent met the CFS criteria [6–7].

Physical and psychological causes have been proposed to understand these complaints [8]. Most people with chronic pain and fatigue understand their condition to be physical in nature and are resistant to psychological theories [9–10]. In order to diminish the occurrence of these unexplained symptoms among veterans, more research is needed [5,11–12].

The amount of physical activity performed during daily life in CFS is lower than in nondisabled controls and seems to correlate with symptom severity and variability [13–16]. A systematic literature review revealed no definite conclusion in relation to physiological exercise capacity in patients with CFS [13]. Lower daily physical activity implies that patients with CFS might experience difficulties with certain activities like standing upright for a prolonged time. For humans, being upright (either standing or sitting) for a long, uninterrupted period of time is not how our bodies are built [17]. When a working task has to be executed, the active, muscular part of the spine has to function in a way that is not congruent with the nonrotatory recruitment of motor units [18].

Patients with CFS report difficulties being upright for a prolonged time, sometimes even after just a few minutes. Yet, studies examining the ability of patients with CFS to stay upright are essentially lacking. This is surprising because many daily activities require muscle endurance of the trunk to allow an upright position, often combined with upper-arm movements.

Shipp et al. used timed loaded standing (TLS), a measure of combined trunk and arm endurance in a population of women with osteoporosis complaining of similar physical inabilities [19]. Women with osteoporosis also show pronounced balance problems compared with women without osteoporosis [20]. They found moderately strong and statistically significant correlations between TLS and 16 of 18 measures of physical impairment and function in women with osteoporosis with known fractures. Functional reach distance, gait velocity, Medical Outcomes Study Short Form 36 Physical Function Subscale, shoulder

flexion strength, and 6 min walk distance were most strongly associated with TLS time [19].

We used TLS in CFS ($n = 72$) and compared the results with nondisabled controls ($n = 55$) and patients with osteoporosis ($n = 30$) without known fractures. Living in an industrialized country could require different abilities and skills than living in a context without modern devices—almost all dependent on electricity—used to ease living, especially work. So we tested people in an environment that has not changed much over decades or generations, non-industrialized societies ($n = 58$; 40 African and 18 Indian). These populations live in rural, agricultural societies in which nutrition and way of life (slower pace, no electricity, walking for transport, etc.) are different from in industrialized societies. In total, 215 participants were measured. The study aimed at examining whether TLS of women with CFS differs from nondisabled controls, non-industrialized populations, and patients with osteoporosis.

METHODS

Timed Loaded Standing Test

TLS measures the time (in seconds) a person can stand while holding a 1 kg dumbbell in each hand with the arms at 90° of shoulder flexion, elbows extended, and wrists in neutral pronation/supination. This is shown in Figure 1.

The TLS test is a physical performance measure of combined trunk and arm endurance simulating functional performance of the trunk in daily activities, most of which require the trunk to remain erect and stable while the upper limbs are used [19]. TLS has been shown to generate reliable data, with good intraclass correlation coefficients for same-day intertrial and 6 to 10 d test-retest reliability in 127 women with osteoporosis with vertebral fractures [19]. TLS has been used for assessing combined trunk and arm endurance in people with vertebral osteoporosis.

Participants and Populations

In total, 215 individuals were measured, divided into four populations. The CFS population consisted of 72 female patients and was compared with 55 female nondisabled controls and 30 female patients with osteoporosis without known fractures. The study group from non-industrialized countries, in total 58, consisted of 40 African and 18 Indian women.

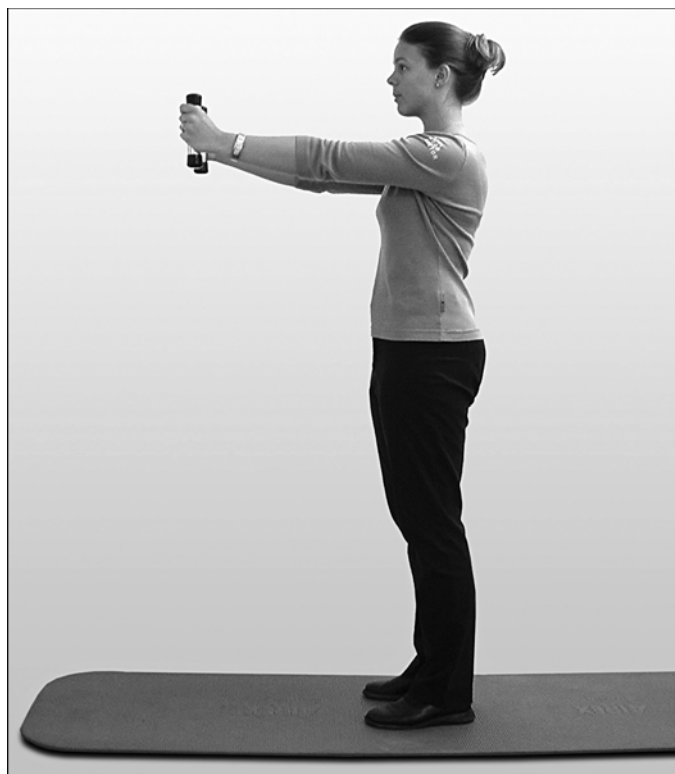


Figure 1.

Timed loaded standing test. For equipment and specific procedure, refer to Shipp et al. [19].

Chronic Fatigue Syndrome Population

One physician (G. Moorkens) from the Outpatient Clinic of General Internal Medicine at the Antwerp University Hospital, Belgium, recruited CFS patients fulfilling the 1994 Centers for Disease Control criteria [1]. The tested population included 72 adult Belgian women who were not pregnant (mean age 41 yr, range 20–56 yr) and had no major psychological comorbidity.

Nondisabled Controls

The nondisabled female controls ($n = 55$) consisted of nurses and physicians recruited from the participating hospitals (mean age 41 yr, range 31–48 yr). Study participants had not reported sick leave during the last 24 mo and were pain-free and without any (chronic) disease.

Patients with Osteoporosis Without Known Fractures

The population studied and measured consisted of women ($n = 30$) attending the nuclear medicine department, referred by other specialists for confirming the diag-

nosis of osteoporosis (mean age 69 yr, range 60–78 yr). The diagnostic criteria for osteoporosis from the Belgian Health Institute, following the International Society of Densitometry, were used [21].

Non-Industrialized Population

An African and an Indian population were studied to have an idea of TLS in subjects unrelated to the culture and demands of industrialized countries. Those persons studied were not required to be upright for 16 uninterrupted hours in daily life, but could allow themselves very easily to lie down or to rest for a short or even longer period of time during the day. They were doing their regular daily activities in order to provide for their basic needs. All Indian and African participants were active in their communities.

Africa ($n = 40$). All adult females (mean age 37 yr, range 17–72 yr) living in one compound were included. All lived in an agricultural community without any electricity available. The compound was linked to the rest of the environment (the village of Busura, Kombo Central, Western Division in the Gambia) with a single road. All TLS measurements in Africa were performed by the same researcher. When date of birth was unknown and age was reported, 0.5 yr was added in order not to bias the averages too low.

India ($n = 18$). Eighteen Indian women (mean age 39 yr, range 21–66 yr) were measured by the same researcher in the region of Bangalore, India, and in rural outposts (Mandya, Kolar Gold Fields). The region is very poor, most inhabitants are vegetarian, and the diet consist mainly of “staple food” (rice) [22]. All persons measured in this population reported never having worn shoes, or only in extremely rare cases (e.g., flip-flops, and then only worn as an adult when visiting the hospital). Subjects were asymptomatic adults. Also, prior to the recordings, personal data were collected: participants were weighed and their height was measured. The same correction was applied as in the African population when only age was reported.

Study Design

The study was designed as a case-controlled comparison, and the data collection took place at several locations. CFS and nondisabled controls were measured at the Outpatient Clinic of General Internal Medicine at the Antwerp University Hospital, Belgium. Patients with osteoporosis were measured at the Department of Nuclear Medicine, Jan Palfijn Hospital, Ghent, Belgium. The non-industrialized populations were measured in the Gambia and India.

The study protocol was approved by the Ethics Committee of the University Hospital Antwerp. All potential study participants were informed about the study by a member of the research group, then asked to read an information leaflet. Next, written informed consent was obtained from all participants. After collecting information on personal characteristics and measuring participants' weight and height, the TLS test was completed. In order to prevent bias from pooling of sex data, only females were allowed to participate [13].

Statistical Analysis

Normality of data was checked for all parameters through quantile-quantile plots and Shapiro-Wilk test. Body height and surface area were distributed normally, but this was not the case for age, weight, body mass index (BMI), and TLS, even after log-transformation. Therefore, nonparametric tests were used.

Normally, distributed continuous variables are represented as mean with their standard deviation; for non-normally distributed continuous variables, medians are given together with their lower and upper quartiles.

For comparing two groups, we used an unpaired *t*-test for normally distributed continuous variables and the

Mann-Whitney U test for non-normally distributed random variables or ordinal scores.

The difference in TLS between groups, controlling for differences in age, height, and weight, was determined by a general linear model. The square root of TLS has been used to obtain normality of the residuals. In the post hoc comparisons, the stepdown Bonferroni-Holm correction was used to adjust for multiple testing.

RESULTS

Overview of Results

An overview of the results can be found in the boxplot in **Figure 2**. No significant differences in TLS scores were measured between the African and Indian populations (82.65 ± 37.23 vs 85.56 ± 44.47 , respectively; $W = 337$, $p = 0.71$). Therefore, both data sets were pooled.

The TLS in the four populations (nondisabled controls, non-industrialized, osteoporosis, and CFS populations) are plotted in **Figure 2**. **Table 1** adds the statistical figures needed to underpin the boxplot.

More details are given in the next section comparing populations one by one.

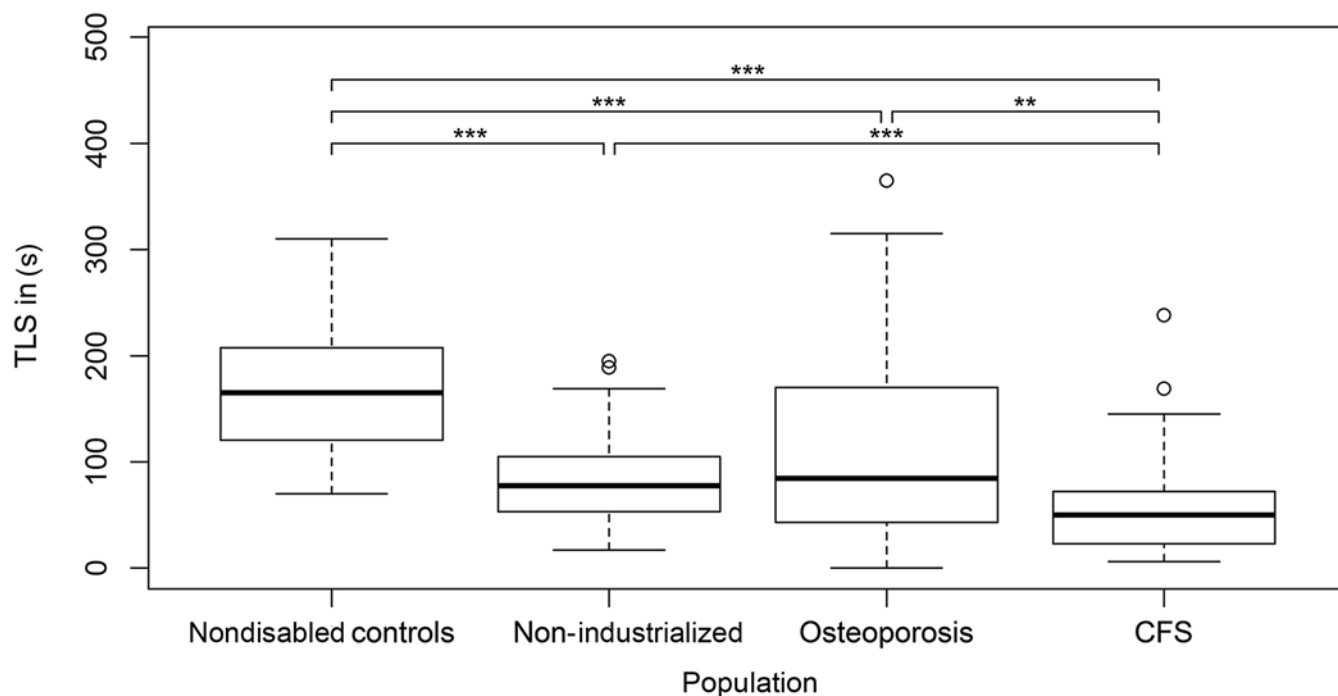


Figure 2. Boxplot for timed loaded standing (TLS) for four populations. ** $p < 0.01$. *** $p < 0.001$. CFS = chronic fatigue syndrome.

Comparing the Four Populations One by One

Nondisabled Industrialized Country Controls Versus People from Non-Industrialized Countries

TLS, as well as body weight, height, and body surface area, were significantly lower in the non-industrialized populations studied than in the nondisabled controls. A linear regression model was used to compare TLS in an industrialized nondisabled population and a non-industrialized population, adjusted for age, body height, and weight (**Table 2**). TLS in the industrialized nondisabled population was higher than in the non-industrialized study population (**Figure 2, Table 3**, $p < 0.001$).

Nondisabled Controls Versus Osteoporosis Patients

TLS was significantly shorter in patients with osteoporosis than in the nondisabled controls ($p < 0.001$).

After adjusting for the differences in age (significantly higher in osteoporotic patients), length, and weight (**Table 2**), we see a significantly longer TLS in nondisabled controls than in the patients with osteoporosis (**Table 3**, $p = 0.002$).

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Patients with Osteoporosis Without Vertebral Fractures Versus Persons from Non-Industrialized Countries

Comparing our industrialized osteoporotic population without fractures to a non-industrialized population showed no significant difference in TLS results (**Table 3**).

Chronic Fatigue Syndrome Patients Versus Nondisabled Controls in an Industrialized Population

TLS was significantly lower in patients with CFS than in nondisabled controls (**Figure 2**, $p < 0.001$). Patients with CFS were significantly smaller with a higher BMI than in the nondisabled controls (respectively $p = 0.01$ and $p = 0.03$). After adjusting for age, height, and weight (**Table 2**), a significant difference remained in TLS between nondisabled controls and CFS patients ($p < 0.001$, linear regression model).

Table 1.

Data comparing different populations measured. Numbers are given as mean (range) unless otherwise stated.

	Nondisabled Controls	Non-Industrialized	Osteoporosis	CFS
N	55	58	30	72
Age (yr)	41 (31–48)	32 (23–50)*	69 (60–78)***†††	43 (32–48)††††
Height (cm), mean \pm SD	167.6 \pm 6.5	157.6 \pm 6.7***	159.1 \pm 6.9***	164.6 \pm 6.4***†††††
Weight (kg)	63 (57–70)	56 (52–65)*	60 (54–68)	65 (57–76)††
Body Mass Index	21.6 (20.8–23.5)	22.7 (20.4–26.6)	23.7 (21.7–25.3)	23.8 (21.1–27.2)*
Body Surface (m ²), mean \pm SD	1.66 \pm 0.15	1.50 \pm 0.18***	1.54 \pm 0.17**	1.66 \pm 0.20†††††
TLS (s)	165 (120.5–207.5)	77.5 (53–104)***	84.5 (43.3–161.5)***	50 (23–70.5)***†††††

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ compared with nondisabled controls.

† $p < 0.05$, †† $p < 0.01$, ††† $p < 0.001$ compared with people from non-industrialized countries.

‡ $p < 0.05$, ‡‡ $p < 0.01$, ‡‡‡ $p < 0.001$ compared with patients with osteoporosis.

CFS = chronic fatigue syndrome, SD = standard deviation, TLS = timed loaded standing.

Table 2.

Multiple linear regression model for timed loaded standing.

	Estimate	Standard Error	95% Confidence interval		Pr(> t)
			Lower	Upper	
Group (ref = nondisabled controls)	—	—	—	—	<0.001
Non-Industrialized		0.61	−5.43	−3.01	<0.001
Osteoporosis		0.78	−4.46	−1.36	<0.001
CFS		0.51	−6.81	−4.79	<0.001
Age (yr)	−0.02	0.02	−0.05	0.01	0.27
Length (cm)	−0.03	0.03	−0.09	0.04	0.40
Weight (kg)	0.01	0.02	−0.03	0.04	0.73

CFS = chronic fatigue syndrome.

Table 3.Post hoc comparisons between different populations based on model in **Table 2**.

	Estimate	Standard Error	<i>p</i> -Value*
Non-Industrialized vs Nondisabled Controls	-4.22	0.61	<0.001
Osteoporosis vs Nondisabled Controls	-2.91	0.79	0.002
Osteoporosis vs Non-Industrialized	1.31	0.82	0.38
Osteoporosis vs CFS	2.89	0.75	<0.001
Non-Industrialized vs CFS	1.58	0.54	0.02
CFS vs Nondisabled controls	-5.80	0.51	<0.001

*With Bonferroni-Holm correction.

CFS = chronic fatigue syndrome.

Patients with Chronic Fatigue Syndrome Versus Patients with Osteoporosis

TLS was significantly lower in patients with CFS than in patients with osteoporosis (**Figure 2**, $p = 0.003$). Also, patients with CFS were significantly larger, having a larger body surface area than patients with osteoporosis (respectively $p < 0.001$ and $p = 0.002$). After adjusting for age, body height, and weight (**Table 2**), the difference in TLS between patients with osteoporosis and patients with CFS was even more pronounced (**Table 3**, $p < 0.001$).

Patients with Chronic Fatigue Syndrome Versus Non-Industrialized Population

Data on fatigue as a symptom in Africa and India are scarce and often related to infectious diseases and nutritional status. TLS was significantly lower in patients with CFS than in a non-industrialized population (**Figure 2**, $p < 0.001$). CFS patients were significantly larger and had a higher weight and greater body surface area than the volunteers from non-industrialized countries (respectively $p < 0.001$, $p = 0.003$ and $p < 0.001$).

After adjusting for age, body height, weight, and surface, we found a significantly lower TLS in CFS patients than in the non-industrialized group (**Table 3**, $p = 0.02$).

DISCUSSION

With respect to standing upright and physical activity, CFS patients have a similar problem as patients with osteoporosis: it is difficult for both populations to keep their spines vertical. Women with osteoporosis with vertebral fractures who endorsed having back tiredness when standing and working with the arms in front of the body, sitting to rest because of back tiredness or pain, and

planning rest periods because of back tiredness or pain had significantly lower TLS times, supporting the validity of the TLS data.

This is the first study of combined trunk and arm endurance testing in various study populations, including CFS. The TLS test revealed a specific biomechanical weakness in CFS patients. This weakness became apparent when comparing TLS in CFS with the other populations measured. TLS in CFS was much shorter than in patients with osteoporosis who were more than 25 yr older.

TLS results in both non-industrialized societies were much lower than in nondisabled industrialized controls, and although being more than 30 yr younger, people from the non-industrialized groups performed the test for a shorter period of time than osteoporotic patients from industrialized nations.

The complaints of patients affected by CFS may be understood in relation to the short TLS and their apparent weakness in holding their spines upright, especially for a prolonged time, be it in a sitting position, a standing position, or when walking.

CFS patients' complaints of reduced exercise capacity and/or of perceived greater effort during exercise can be linked to the fact that less muscle strength has been found in CFS. Both deconditioning and central factors have been used to explain this muscular weakness in CFS [23–24].

Patients with CFS not only are weaker from a muscular point of view but also show an inability to sustain target activity levels [25]. Gait in patients with CFS shows abnormalities when compared with sedentary controls [26]. Physiological cost of walking in CFS is greater than in nondisabled subjects [27–28]. During treadmill walking, a subtle abnormality in vagal activity was noticed that could explain, in part, postexertion symptom exacerbation [29]. Female patients with CFS's aerobic power indicates a low normal fitness level without cardiopulmonary

abnormality [30]. Patients with CFS are weaker than sedentary and depressed controls but also as unfit as sedentary controls [23]. Female CFS patients' aerobic power indicates a low normal fitness level without cardiopulmonary abnormality [30].

Regarding working status, the majority of participants at a trial remained functionally impaired over time and stayed unemployed at follow-up [31].

In a review on this topic, Nijs et al. wrote the following: "Patients with CFS perform less physical activity during daily life, and have less peak isometric muscle strength compared to healthy sedentary control subjects." This review concluded that the available data point toward a reduced physiological exercise capacity in CFS [13].

Comparing our data with previous findings is impossible because previous studies in the field of physical performance measurements in CFS have used other measures with less ecological validity, like muscle strength and exercise performance testing [13,32–34]. Further research could help us to understand the fundamentals of these findings. It can therefore be considered, from the very onset of rehabilitation, to take into account the low endurance of patients with CFS to resist gravity when upright.

Finally, a few methodological issues regarding the present study have to be mentioned. Since only women were studied, external validity of the results is limited to adult female patients with CFS. A few parameters of the included participants were not taken into account, such as menopausal state, level of education, and intelligence. And as usual, longitudinal data are required to examine the stability of these findings in a condition such as CFS, which is characterized by high health status fluctuations over time.

The sample size of this study was of sufficient power and used a measurement that has proven validity for measuring trunk and arm endurance. The TLS test has been shown to generate reliable data, but its true validity remains to be examined, including comparison with a gold standard.

CONCLUSIONS

Women with CFS have lower combined trunk and arm muscle endurance than nondisabled controls, non-industrialized populations, and osteoporotic patients. The TLS might be useful for assessing low combined trunk arm endurance in women with CFS. Further studying of the nature and etiology of the decreased combined trunk

and arm muscle endurance in CFS patients is warranted. In addition, studies examining whether specific exercise interventions are able to restore the specific weakness found here are necessary.

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Study concept and design: J. b Eyskens, J. Nijs.

Acquisition of data: J. b Eyskens, A. Sand, K. D'Août.

Analysis and interpretation of data: J. b Eyskens.

Drafting of manuscript: J. b Eyskens, J. Nijs.

Critical revision of manuscript for important intellectual content:

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Statistical analysis: K. Wouters.

Study supervision: G. Moorkens.

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Participant Follow-Up: The authors plan to inform participants, for whom contact information is available, of the publication of this study.

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