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A capstone project submitted to the Graduate Faculty in Physical Therapy in partial fulfillment of the requirements for the degree of Doctor of Physical Therapy, The City University of New York

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This manuscript has been read and accepted for the Graduate Faculty in Physical Therapy in satisfaction of the capstone project requirement for the degree of DPT

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ABSTRACT
THE EFFECTS OF COOLING DURING GAIT ON GAIT ENDURANCE IN PERSONS WITH MULTIPLE SCLEROSIS USING THE SIX MINUTE WALK TEST

By

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Background: Persons with MS (pwMS) are limited in their mobility due to thermosensitivity. Exercising at a sufficient volume and intensity to increase mobility can result in increased core temperatures and resultant worsening of symptoms. The use of cooling garments to lower core temperature has been found to be a successful means of allowing pwMS to exercise for longer periods. Previous studies have relied on precooling for an extended period of time prior to activity, to achieve improved exercise performance. Cooling during the performance itself, or pericooling, may allow for similar performance gains to be realized without spending the time needed for precooling.

Objectives: The purpose of this study is to examine the effects of pericooling on the Six Minute Walk Test (6MWT) performance in pwMS. It was hypothesized that pwMS would have better 6MWT performance while wearing a cooling vest then compared to a noncooled condition. If our hypothesis were correct, it would suggest that pwMS could achieve improved exercise performance without engaging in precooling activities.

Methods: A randomized crossover design was used. Patients were randomized into cooled or uncooled conditions. Cooled subjects would perform a 6MWT, donning a commercially available cooling vest immediately prior to the walk. Walks would be performed once a week for three weeks. Total 6MWT distance and minute-by-minute distance was recorded. Fatigue during
the walk was measured using the Visual Analog Scale of Fatigue. Uncooled subjects would perform the identical protocol without a cooling device. Following the three walks in one condition, subjects would undergo a two-week washout period and then repeat the same protocol in whatever condition they did not experience initially.

**Results:** Six females with mild MS (EDSS 2.67) completed the study. Pericooling resulted in walking significantly, \( (F(1,17) = 4.63, p = .046, \text{ partial } \eta^2 = .214) \) farther in the cooled condition (1257’) than in the uncooled condition (1154’). There was no significant difference in VAFS scores between the 2 conditions.

**Conclusions:** Pericooling, delivered via a commercially available cooling vest resulted in better 6MWT scores than an uncooled condition in pwMS. As most studies of cooling in MS utilize cooling prior to an activity, these results indicate an alternative and less time consuming means of achieving the beneficial effects of cooling.
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INTRODUCTION

Multiple Sclerosis (MS) is a chronic neurological disease, which involves inflammation, axonal demyelination, and oxidative stress (Romme Christensen et al., 2013) in the central nervous system that can be relapsing and remitting or progressive (Frohman, Davis, & Frohman, 2011). While the etiology of the demyelinating lesions is unclear, these lesions have been shown to be in both gray and white matter and are the primary cause of neurological and physical symptoms (Lucchinetti et al., 2011).

Research suggests that demyelinating lesions result in scar tissue, which leads to changes in axonal physiology, loss of saltatory properties of electrical conduction, reduction in conduction velocity, and a predisposition to conduction block (Frohman et al., 2011). This can be especially disruptive to the propagation of action potentials, which need to travel across myelin sheath gaps known as nodes of Ranvier. Nodes of Ranvier in healthy myelinated axons are typically about one micrometer in length. The physiology of the myelinated axons allows for a current that is between three and seven times greater than necessary to produce an action potential. This excess is known as the safety factor (Smith & McDonald, 1999). However, demyelinated axons have a much lower safety factor, which can be less than the current itself. This decrease in the safety factor occurs because the current is no longer insulated by the myelin sheath, which propels the current from one node to the next. The current is therefore improperly directed along the axolemma and is dispersed, resulting in decreased conduction of current to the next node. In addition, the widening of the nodes results in an increase in electrical capacitance, further reducing the safety factor. As long as the safety factor is greater than one, conduction will continue to occur, albeit at a slower rate than typical. Cases in which the safety
factor is below one result in the failure of the conduction of the action potential from one node to the next and can ultimately lead to a conduction block. In the event of a conduction block, the individual will exhibit more severe symptoms, which are determined by the location of demyelination. This demyelination can occur anywhere in the CNS for example, if the motor neurons are affected, individuals will present with paralysis, and if the optic nerves are affected, individuals will present with blindness (Smith, 1994).

While pwMS exhibit a variety of physical, cognitive, and neurological symptoms, the most commonly experienced symptom is fatigue (Karpatkin, 2005). Fatigue can be primary or secondary in nature. Primary fatigue is directly caused by the disease and can be the result of axonal demyelination, inflammation, and degeneration of axons. Secondary fatigue is indirectly caused by the disease and can be a result of sleep deprivation, pharmacological treatments, and muscle disuse (Braley & Chervin 2010). Psychological factors also play a role in an individual’s perception of fatigue (Kos, Kerckhofs, Nagels, D'Hooghe, & Ilsroukx, 2008).

Researchers have found that the clinical signs that accompany demyelination are worsened by an increase in body temperature (Davis, Wilson, White, & Frohman, 2010). Davis et al. suggests that an increase in body temperature affects the propagation of action potential and the refractory period, and further contributes to conduction blocks. Primarily, an increase in temperature shortens the action potential duration, thereby decreasing the amount of time for depolarization of the demyelinated axolemma to its firing threshold. A temperature increase, in conjunction with a decreased safety factor, increases the likelihood of a conduction block (Smith, 1994).

Heat exposure can have rapid effects on both physical and cognitive functions. It can cause increased fatigue, decreased muscle strength, gait difficulties and an inability to think
clearly (Geisler et al., 1996). Heat-induced exacerbations are found in approximately 60-80% of MS patients and are usually reversible when the source of heat is removed (Davis et al., 2010). Many individuals with MS are extremely sensitive to even small changes in temperature such that exposure to the sun can cause an individual with a limping gait to be unable to walk, and a hair dryer can exhaust an individual of energy entirely (Baker, 2002). Heat can have such severe implications that one may need to be supported in a warm bath in order to prevent drowning (Smith, 1994).

The effects of heat exposure in individuals with MS are exacerbated by deficits in neural control of homeostatic body temperature, which impacts both autonomic and endocrine thermoregulation by diminishing hypothalamic thermal response and sweat gland function (Davis et al., 2010). Sweating, one of the primary heat dissipation mechanisms in the body is paramount in maintaining internal temperature. Several studies have reported diminished sweating responses in individuals with MS. Some studies tested subjects using quinizarin powder, a gray substance that changes its shade to blue when exposed to sweat. Others delivered a cholinergic agonist transdermally that stimulated eccrine sweat glands without the involvement of the CNS. In addition, to ensure that thermoregulatory effector responses were being sufficiently engaged, another study utilized a whole body heating tube-lined suit as opposed to a locally induced agonist. Decreased sweat gland output was observed in all of the experiments, suggesting that CNS lesions or impairments in neural control of sudomotor pathway could contribute to reduced sweat function in individuals with MS (Davis et al., 2010).

Because exercise increases core body temperature, it can also result in heat exacerbations for pwMS, and those with thermosensitivity can be less inclined to exercise. Fjelstad, Brittain, Fjelstad, and Pardo (2010) studied the relationship between thermosensitivity and physical
activity in 77 pwMS. Subjects indicated their level of physical activity through questionnaires, and self-reported the presence or absence of temperature-induced symptoms. Those with self-reported thermosensitivity relayed considerably lower levels of physical activity than those without (p<0.05). This demonstrates that thermosensitivity can be responsible for reduced physical activity in pwMS.

Exercise, however, is extremely beneficial for pwMS, and various studies have demonstrated the value of aerobic training for pwMS. In a study done by Petejan et al. (1996), after a 15-week aerobic training program subjects demonstrated gains in maximum oxygen consumption (VO$_2$ max) and upper and lower extremity strength and decreases in skinfolds, triglycerides, LDL’s, depression, and fatigue, suggesting that individuals with MS generate the same responses to exercise as those without MS. In a longer study conducted by Rodgers and Mulcare (1999) that coursed the span of six months, improvements were seen in VO2max, whereas in a shorter study conducted by Mostert and Kesselring (2002) that coursed the span of four weeks, improvements were not seen with VO2max. This suggests that the length of training might be a factor in improving this parameter.

Resistance training has also been shown to be efficacious. An eight-week lower extremity resistance training study conducted by Harvey, Smith, and Jones (1999) revealed improvement in chair transfer time. In addition, a three-month progressive resistive exercise program study conducted by Kraft et al. (1996) showed improvement in functional tasks, such as stair climbing and ambulation and increased muscle strength of the trained limbs (as cited in Dalgas, Stenager, & Ingermann-Hansen, 2008).

Romberg et al. (2004) studied 95 pwMS to evaluate the effect of a six month combined resistance and aerobic exercise program on walking speed (median EDSS: 6 for experimental
Patients in the experimental group were given an inpatient exercise routine during the first three weeks and then proceeded to complete a progressive home exercise program consisting of three strength training, and one aerobic routine each week from weeks 4-20. One strength training routine was added for weeks 21-26. Patients kept a diary to record adherence to these routines. Patients in the control group were asked to refrain from making any major changes in their level of physical activity during these six months. Walking speed was assessed by measuring the time it took for subjects to perform the 25 Foot Walk Test (25FWT) and 500 meter walk test (500MWT) at maximum speed. Walk time was significantly decreased in both tests in the experimental group after the six months of exercise. Though 25FWT time also decreased in the control group, the change was much greater in the experimental group. No change was observed in 500MWT time in the control group. This study illustrates that exercise can significantly improve the walking speed in pwMS.

Exercise has various other benefits in addition to its physical implications. It can provide significant psychological benefits for pwMS by giving them a feeling of control over their lives (Johnson, 1996). Studies have shown that exercise can reduce the depression and anxiety experienced by pwMS (Turner 2009). Exercise can also reduce secondary fatigue caused by disuse (Karpatkin, 2005). However, pwMS may be prevented from reaping the benefits of exercise due to their sensitivity to temperature elevation.

Cooling prior to exercise, also known as precooling, has been suggested as a means of reducing this temperature elevation and allowing pwMS to exercise with fewer heat induced symptoms. Cooling methods include drinking cold beverages, immersing one’s limbs in cold water and wearing cooling garments (White, Wilson, Davis, & Petajan, 2000). Ku, Montgomery, Lee, Luna, and Webbon (1999) differentiate between cooling garments that use
active and passive cooling. In an active cooling garment, such a liquid cooling garment, a liquid coolant is circulated through the garment and then to a portable chiller or heat exchange unit where it is cooled down again. In a passive cooling garment the temperature depression is accomplished through ice packs in the pockets of the garment or the use of evaporative cooling. Active cooling garments provide better temperature control and have been shown to be a more effective means of cooling. However, passive cooling garments tend to be lighter, more portable, easier to use, and less expensive than active cooling garments (Meyer-Heim et al. 2007).

In fact, cooling has been found to increase exercise endurance even in the general population. Tyler and Sunderland (2011) performed a crossover study to explore the effect of cooling via a cooling collar on the perceived level of thermal strain. They found that wearing the cooling collar increased the time taken to reach volitional exhaustion and that the subjects in the cooled condition could exercise longer before reaching identical levels of perceived exertion despite having higher rectal temperatures and heart rates at this point. This study suggests that the experience of feeling cool allows individuals to exercise longer despite higher body temperature.

Subjective measures have been used to explore the effects of precooling on performance in pwMS. Flensner and Lindencrona (1999) studied the effects of a cooling suit on the self-care ability of MS patients. The quasi-experimental before-and-after single case study included ten persons in variable stages of MS, who were instructed to wear a cooling cap and waist coat daily for a period of at least four weeks. Data were collected using the MS Self-Care Activities of Daily Living (ADL) Scale, open-ended interviews before and after the intervention, and daily diaries. Six out of ten subjects reported marked improvements in their ability to walk indoors
and outdoors and five out of ten reported significantly increased ability to move and transfer. Additionally, five out of ten reported increased strength and energy in the performance of activity. Flessner and Lindencrona (2002) studied 8 people in various stages of MS to determine if the use of a cooling suit influenced their experience with fatigue in daily life. They used a single case-control design approach in which the subjects were instructed to wear a cooling head cap and waist coat for several sessions daily for at least four weeks. The outcomes were measured through self-assessment using the Fatigue Impact Scale, open-ended interviews before and after the intervention, and daily diaries. Seven out of eight subjects reported decreased levels of muscular fatigue, and six out of eight reported that it was easier to participate in social activities. Although subjective measures are valuable in reflecting a patient’s perception of fatigue, more objective measures are necessary to quantify the actual benefits of cooling.

Several studies have used objective measures to determine the efficacy of using precooling to diminish various MS symptoms. Feys et al. (2005) studied the effect of cooling on intention tremors in 18 pwMS (Mean Expanded Disability Status Scale (EDSS of 5.8) who exhibited an intention tremor in at least one upper limb. The subjects’ forearms were cooled down using a cryomanchet with cold liquid circulating inside to keep skin temperature constant. In one group, the skin was cooled down to 18 degrees Centigrade (the deep cooling group), and in another, it was cooled to 25 degrees Centigrade (the moderate cooling group). Intention tremor was measured using a wrist step-tracking device, which measured wrist flexion and extension as the subjects performed a directed task-the step tracking task and the finger-to-nose test. Assessments were made prior to cooling, immediately post-cooling, and after 10, 20, and 30 minutes had elapsed. The subjects in the deep cooling group did worse on the finger tapping task right after cooling, but their performance returned to normal after ten minutes
(p<.001). Their speed also decreased in the step tracking task, though it improved over the next 30 minutes of evaluation (p<.0001). The accuracy of this task increased initially but returned to normal after ten minutes (p<.001). Both the path length and the number of changes in direction (both of which were indicators of tremor) were significantly decreased in this group (p<.0001 for both). The moderate cooling condition did not exhibit any significant changes in the finger tapping test or in the performance of the step tracking task. However, subjects demonstrated significantly reduced tremor amplitude immediately after cooling (p<.05) as well as reduced tremor frequency. These changes lasted throughout the three minutes of evaluation after cooling. This study indicates that cooling can significantly decrease intention tremor in pwMS.

Schwid et al. (2003) performed a randomized crossover study to determine the acute and chronic effects of a cooling suit on pwMS. Seventy-five pwMS (mean EDSS of 3.3) and heat sensitivity participated in this experiment. To test the acute effects of cooling, patients were randomly assigned to either low dose (75 degrees Fahrenheit) or high dose (55 degrees Fahrenheit) cooling. After ten minutes of rest, patients wore the appropriate cooling garment for 60 minutes and then rested again for 30 minutes without the garment. Neurological assessments were performed before cooling and after the 30-minute rest using the MS Functional Composite (MSFC). To assess the chronic effects of cooling, half of the subjects were instructed to wear the cooling garments, which were set at a high dose temperature, at home one hour a day for four weeks. The remaining subjects wore no cooling garment and were simply observed. Neurological assessments were performed before the cooling and then again at the end of four weeks after a high dosed cooling period identical to the one performed in the acute phase of the experiment. Subjects also filled out daily self-evaluation measures of fatigue and neurological function using the Modified Fatigue Impact Scale (MFIS) and the Rochester
Fatigue Diary (RFD) and by rating energy level, muscle strength and cognitive function on a nine-point Likert Scale. The groups were reversed after a one-week washout period, and the tests were repeated. In the acute phase of the experiment, a small improvement in the MSFC was shown in the high dose cooling group (p=.0073) while the low dose group only exhibited a trend toward improving (p=.087). In the chronic phase, subjects whom had been cooled for one hour each day for a month improved on the MSFC after the acute cooling session (p=.041) while those patients in the observational group showed no significant changes (p=.21). Patients reported less fatigue on both the MFIS and the RFD (p<.001 for both) during the month of cooling. Additionally, 75.3% of patients reported having more energy during the cooling month as compared to 39.4% of the observational group (p<.0001), 57.8% of the cooled group reported increased strength during this month as compared to 30.9% in the observational group, and 55.0% of the cooled patients reported cognitive improvements compared to 30.7% in the observational month (p<.0001 for all three measures). This experiment shows that cooling can be a useful way to decrease various symptoms of MS.

Syndulko, Woldanski, Baumhefner, and Tourtellotte (1995) performed two pilot experiments, which studied the immediate and cumulative effects of cooling on functional impairments due to MS. Nine heat-sensitive individuals with MS participated in the first experiment, which studied the immediate effects of cooling utilizing a single group repeated measure design. The experiment consisted of a screening session comprised of a neurological exam and testing sessions. The testing sessions involved an examination period both before and after a resting period, which included a variety of tests for lower extremity speed, standing balance, and tandem gait within parallel bars. On two of the three sessions, the subjects were cooled for 90 minutes during the resting period using a different cooling garment on each day.
No statistically significant changes of any measures were produced by either of the cooling garments, which is in contrast to the results produced by other studies. These results can possibly be attributed to the small temperature changes that these garments produced of \(-0.6\pm0.4\) degrees Celsius and \(0.5\pm0.25\) degrees Celsius as well as the fact that a resting period alone in an air-conditioned environment can produce a tympanic temperature drop of up to \(0.4\) degrees Celsius. This finding may suggest that the non-cooled session was an unfit control for this experiment since the air-conditioned environment alone can serve as a beneficial cooling device.

The second experiment performed by Syndulko et al. (1995) studied the cumulative effects of cooling on functional impairments due to MS. Seventeen thermosensitive individuals with MS participated in the experiment, which used an unblinded, parallel group design. The participants were initially divided into two groups: a low-high cooling group and a high-high cooling group. The low cooling protocol produced larger temperature drops than expected of up to \(-0.4\) C and was therefore an invalid control, and a non-cooled group was later added. The experiment involved a nine-week program. The first three weeks were baseline testing weeks in which the subjects practiced at home walking, maintaining balance, etc. During the following six weeks the subjects utilized one of two cooling protocols in addition to the home practice, and subjects in the non-cooled group did the home practice without any cooling protocols. During this six-week period, the subjects in the cooling group were cooled during their weekly evaluations while those in the control group were not. There were statistically significant improvements in both standing balance \((p=0.0091)\) and tandem gait \((p=0.0191)\) due to the immediate effects of cooling. Eight out of 12 subjects reported that the cooling therapy produced immediate improvement in function, ambulation, and increased energy lasting up to two to three
hours after cooling. The tandem gait test showed improvement over time (p=.0062) as did lower extremity coordination (p=.0302). This experiment illustrates the positive immediate and cumulative effects of cooling, however, it fails to address its effects on more functional gait activities.

Numerous studies have been conducted to specifically assess the effect of precooling on ambulation in pwMS. White et al. (2000) performed a randomized control trial testing the effect of precooling on walking performance in six ambulatory individuals with chronic MS (mean EDSS score of 3.1±0.9) who had self-reported thermosensitivity and fatigue. The research consisted of two 30-minute sub-maximal exercise sessions (combined arm leg ergometry), one of which was preceded by precooling using an emersion bath. The number of steps and time required to walk 25 feet were recorded before, immediately after, and 30 minutes following the exercise sessions. Results showed that the frequency of steps immediately after exercise was significantly better for the precooled sample (P<.05). Though walk time also improved in the cooled subjects, these results were of borderline significance (p=.057). In addition, subjects in the precooled group reported fewer heat induced symptoms such as ataxia, blurred vision, foot drop and had lower rates of perceived exertion (RPE) during exercise (12 precooled: 14 non cooled, P < .05). Although the small sample size poses a limitation, this study suggests that precooling may be a viable method of reducing exercise-induced fatigue in individuals with MS.

Nilsegard, Denison, and Gunnarsson (2006) studied 43 heat-sensitive pwMS (median EDSS score of 4.0) to determine the effect of wearing a commercially produced cooling vest on various measures of gait. This study utilized a randomized crossover design, in which subjects were tested before and after a 45-minute session of wearing this vest. The vest was cooled in a
freezer at -20 degrees Celsius for one group and was left at 22 degrees Celsius for the other. The primary measures were the ten and 30-meter timed walk, which evaluated the time and mean stride length of the subjects walking ten and 30 meters respectively. Both speed and stride length significantly improved in both the ten and 30-meter timed walk tests. This study illustrates that a cooling vest can successfully improve speed of ambulation in pwMS but fails to address the effect of precooling on walking endurance.

Meyer-Heim et al. (2007) examined the short-term effects of pericooling, cooling during an exercise activity, using a lightweight cooling-garment technology on the functional abilities of 20 thermosensitive individuals with MS (EDSS ≤ 6.5) in a single blinded, balanced cross over study. During the assessments, the subjects wore a properly working cooling device on one day and inoperable one for sham control on the other. The study measured walking capacities (25FWT), body sway, muscle strength, and spasticity. The cooling garment was found to significantly improve the 25FWT (p=.035), lower limb strength (p=.004 and p=.037), and MS functional composite (MSFC) (p=.017). While, this study examined the effects of pericooling on the walking abilities of thermosensitive individuals, it failed to address its effects on longer more functional distances.

Coyle, Krupp, Doscher, Deng and Milazzo (1996) researched the effects of cooling on the timed walk, muscle strength, and coordination. The study utilized a randomized cross over trial to examine 11 ambulatory relapsing and remitting thermosensitive MS patients (mean EDSS 2.7 ± 0.6). The subjects participated in two 45-minute sessions using a cooling garment. The cooling session lowered their core body temperatures by at least 1 degree Celsius, and the sham cooling session lowered their core body temperatures by less than 0.5 degrees Celsius. The subjects were evaluated before and after the cooling and sham cooling sessions. The variables of
interest were 25FWT lower extremity strength, and coordination. After cooling the core body temperature of the subjects by at least 1 degree Celsius, significant improvements were noted in all evaluated areas. With the times walk test, 73% of cooled subjects improved by one to ten seconds (p=.0010) while the sham cooling subjects exhibited no improvements. Additionally, in the cooled group, muscle strength improved in both upper and lower extremity muscles (p=.0010). The study illustrates the effects of cooling on the ability of thermosensitive individuals to walk short distances.

Grahn, Murray, and Heller (2008) studied the effects of cooling on walking longer distances in pwMS. This study examined the effects of cooling one hand on the physical capacity of ten independently ambulating individuals with chronic MS and a history of thermosensitivity (midrange EDSS) using randomized paired trials. A baseline assessment examined the subjects’ physical performance on a treadmill and ability to walk long distances. During the subsequent sessions, the treadmill was adjusted to 65% of the maximum workload. The cooling session involved placing one hand in the cooling device (18-21°C) prior to the onset of treadmill activity and throughout the exercise. Mean exercise durations were analyzed, and the cooling treatment extended the exercise duration by an average of 35% (p<.0003). This study illustrates that hand cooling can improve the ability of pwMS to walk long distances.

Although the study by Grahn et al. showed positive results, testing ambulation using a treadmill is not necessarily generalizable to functional walking since treadmill walking differs from over ground walking in many ways. Because the surface is in motion, some muscles are more active than they would be on ground, while others are less active. Furthermore, on a treadmill the surface is constant in contrast to over ground walking in which surfaces
vary. Lastly, on a treadmill, one will maintain a constant speed while with over-ground walking, one’s speed will vary with time. Therefore, the use of a treadmill to measure the effects of cooling on gait endurance will not be identical to the effects of cooling on gait endurance in functional environments.

Reynolds, Short, Westwood, and Cheung (2011) looked at the effect of head and neck cooling on both short term and long term ambulation in pwMS. The researchers utilized a double blinded crossover design and tested six female MS patients (EDSS range: 2.5-6.5, no mean recorded) with heat sensitivity. Participants were each subjected to the pre-cooling, sham cooling, and no cooling conditions on three separate visits. In the cooled condition, participants wore a head and neck cooling device for 60 minutes prior to ambulation testing and then performed through the 6MWT, the 25FWT, and the Timed Up and Go Test (TUG). In the sham cooling phase, they wore a similar device before testing that allowed the participants to experience the cooling sensation without any significant decrease in body temperature, and in the non-cooled condition, they simply rested for 60 minutes prior to testing. There was a significant improvement in the 6MWT seen in the cooled group (p=.036) as compared to the other two groups. TUG scores were better in both the sham and cooled group than the non-cooled group (p=.004), and there was no significant difference in the 25FWT (p=.135). The authors concluded that pre-cooling can improve ambulation in pwMS, though the small sample size limits the reliability of this study.

Previous studies have examined the effects of both precooling and pericooling on short distance ambulation, however, the effects of cooling on long distance ambulation has not been well studied. While Grahn et al. (2008) studied the effects of pericooling on long distance walking, the ambulation measure using a treadmill doesn’t reflect a functional
environment. Reynolds et al. (2011) studied the effects of precooling on long distance ambulation using the more functional 6MWT, but further studies are necessary due to the small sample size. Additionally, pericooling may be a more practical form of cooling in the daily life of an MS patient because it does not require extensive preparation before each activity. Pericooling may also be a more effective form of cooling due to the constant presence of a cooling source throughout activity.

**PURPOSE**

Persons with Multiple Sclerosis are known to have difficulty with ambulation endurance. Because thermosensitivity is a prominent feature of MS, elevation of body temperature generated by walking can contribute to these limitations. Cooling has been shown to improve short distance walking in pwMS, but its effects on long distances are not well studied. The purpose of our study is to examine the effects of peri-cooling on gait endurance in pwMS. We hypothesize that the use of a cooling garment will significantly improve gait endurance. If our hypothesis is proven correct, cooling during gait can be used to enhance both therapeutic and functional environments, maximizing patient performance in activities that involve walking.
METHODOLOGY

RESEARCH DESIGN
This study utilized a randomized crossover design, in which subjects served as their own controls.

SUBJECTS
A sample convenience consisting of 6 subjects were recruited from Herb Karpatkin Physical Therapy in New York, NY using flyers detailing the nature of this study (see appendix A). Subjects signed informed consent forms (see appendices B and C), approved by the Institutional Review Board at Hunter College. The inclusion criteria comprised of a definitive diagnosis of MS, the ability to ambulate continuously for six minutes with or without a device, and the ability to understand and sign an informed consent. Participants were excluded if they had any type of orthopedic or cardiopulmonary condition preventing their ability to walk six minutes, were using steroids or had an exacerbation of their MS-specific symptoms immediately prior to or during the study.

PROCEDURES
During the initial session, participants filled out an intake form (see appendix D), detailing subject demographics such as MS type, years since diagnosis, age, gender, EDSS level, medications, and assistive devices. They also filled out a Fatigue Severity Scale (FSS) (see appendix E) and the Multiple Sclerosis Impact Scale (MSIS-29) (see appendix F). Subjects were randomly assigned into a cooled or uncooled group for the first phase using a lottery system. Subjects were tested twice weekly for 3 weeks. Sessions began with a 15 minute seated rest
period, after which subjects were asked to rate their baseline fatigue using the Visual Analogue Fatigue Scale (VAFS) (see appendix H). The testing then comprised of the 6MWT, in which the subjects were asked to walk as far as they could at their best comfortable pace in six minutes. All subjects were accompanied by an examiner, who guarded them throughout the entirety of the 6MWT. The distance was measured minute by minute by another examiner who followed the subject’s walking path with a measuring wheel. Fatigue was then assessed after the 6MWT using the VAFS, and the difference between the fatigue reported before and after the six minute walk was recorded. The members of the cooled group donned a cooling vest immediately preceding the 6MWT, which they wore for the duration of the test. The cooling vest was constructed of canvas and held nine ice packs, weighing a total of 4 pounds. The members of the uncooled group performed an identical procedure without the cooling vest. After the three measurements were completed, there was a two-week washout period to limit the training effects of the testing. There was then a crossover in which the subjects switched groups, and testing was repeated in the opposite condition for another three sessions.
Figure 1: Methodology Flow Chart
EDSS, Expanded Disability Status Scale; FSS, Fatigue Severity Scale; VAFS, Visual Analogue Fatigue Scale; MSIS, Multiple Sclerosis Impact Scale; 6MWT, 6 Minute Walk Test;
RESULTS

The purpose of this study was to examine differences between exercise conditions (i.e., cooled versus uncooled) with regard to fatigue, length of walking time (in minutes), and the percentage difference in walking time (in minutes) with a sample of six adult females diagnosed with MS. The mean age of the six participants was 51.33 years ($SD = 2.87$), and ages ranged from 32 to 69 years. The mean length of years since diagnosis was 20.50 years ($SD = 2.53$) with length of years since diagnosis ranging from four to 35 years.

To determine if significant differences emerged across conditions with regard to the three variables of fatigue, walking time, and percentage difference in walking time, a repeated-measures multivariate analysis of variance (MANOVA) was conducted. Due to the small sample size, bootstrapping (using a replication sample of 1000) was employed. Bootstrapping is a relatively common statistical procedure in MS studies, including clinical trials, with small samples (see Humphreys, Drummond, Phillips, & Lincoln, 2013; Palacios, Alonso, Bronnum-Hansen, & Ascherio, 2011; Saxton et al., 2013).

Because the repeated-measures MANOVA involved just two levels of repeated measures, the assumption of sphericity was not relevant to this analysis. Results from the repeated-measures MANOVA showed a trend toward significance: Wilks $\lambda (3,15) = 0.65$, $F(3,15) = 2.65$, $p = .087$, partial $\eta^2 = .346$. An examination of the individual variables showed one significant result with regard to walking time, $F (1,17) = 4.63$, $p = .046$, partial $\eta^2 = .214$. In the cooled exercise condition, participants walked an average of 1257.13 feet ($SD = 375.50$) whereas in the uncooled exercise condition, participants walked an average of 1164.56 feet ($SD = 302.81$). While fatigue scores decreased in the cooled exercise condition ($M = -6.28$, $SD = 17.40$) from the
uncooled exercise condition ($M = -1.39$, $SD = 14.84$), this decrease in fatigue was not significant $F (1,17) = 1.14$, $p = .300$, partial $\eta^2 = .063$. The lack of significance was likely due to the large variance in fatigue scores in both conditions, but especially in the cooled exercise condition. There were no significant differences in exercise conditions with regard to percentage difference in walking time across the cooled exercise condition ($M = .58$, $SD = .01$) and uncooled exercise condition ($M = .55$, $SD = .10$), $F (1,17) = 1.85$, $p = .192$, partial $\eta^2 = .098$.

**DEMOGRAPHICS AND SUBJECT CHARACTERISTICS**

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<th>Age, mean (SD)</th>
<th>x 51.33, range 32-69 years (+2.87)</th>
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<tr>
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<td>RR 2</td>
</tr>
<tr>
<td></td>
<td>SP 3</td>
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<tr>
<td>FSS</td>
<td>x 3.76, range 1.78-5.22</td>
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<td>MSIS</td>
<td>x 61.67, range 34-83</td>
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<tr>
<td>Taking Anti-spasticity Meds</td>
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<tr>
<td>Assistive device</td>
<td>3</td>
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<td>Years since dx, mean (SD)</td>
<td>x 20.5, range 4-35 years (+2.53)</td>
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Table 1: Demographics and Clinical Characteristics of Participants (n=6)

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<th>EDSS</th>
<th>FSS</th>
<th>MSIS-29</th>
<th>Anti-Fatigue Meds</th>
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Table 2: Subject Demographics & Characteristics

MS, Multiple Sclerosis; EDSS, Expanded Disability Status Scale; FSS, Fatigue Severity Scale; RR, relapsing-remitting; SP, secondary progressive; PP, primary progressive
### Table 3: 6MWT minute by minute walking distance and VAFS in cooled condition

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<th>MINUTE 3 (ft.)</th>
<th>MINUTE 4 (ft.)</th>
<th>MINUTE 5 (ft.)</th>
<th>MINUTE 6 (ft.)</th>
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<td>minute 6 (ft.)</td>
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Table 4: 6MWT minute by minute walking distance and VAFS in uncooled condition
Figure 2: Mean 6MWT Distance Cooled Vs. Uncooled

Figure 3: Mean Difference in VAFS Cooled Vs. Uncooled
Figure 4: Mean 6MWT Distance Cooled Vs. Uncooled Subjects 1-6
DISCUSSION

In this study, we examined the effect of pericooling on gait endurance in persons with MS via the 6MWT. We hypothesized that the use of a cooling garment would significantly improve gait endurance in our subjects. Though various previous studies examined the effect of pre-cooling on gait (White et al., 2000, Nilsegard, Dension and Gunnarsson, 2006, Grahn, Murray and Heller, 2008 etc.), we specifically studied the use of pericooling, which may be more functional in therapy and daily living since it does not require extensive preparation before the activity is executed. Our results indicated that our hypothesis was correct and that the application of a cooling vest during walking improved 6MWT scores compared to an uncooled condition. Subjects walked significantly greater distances while wearing the vest and walked an average of 1257.12 feet compared to 1164.56 feet in the uncooled condition ($p = .046$). The mean VAFS score decreased in both conditions as subjects reported less fatigue after performing the 6MWT. The decrease in fatigue was greater in the cooled condition, though this difference was not statistically significant ($p=.300$). Additionally, when comparing the percentage of distance covered each minute of the 6MWT, there was also no significant difference between the two conditions ($p = .192$).

MECHANISMS

MS is a chronic disease of the central nervous system, which involves axonal demyelination, inflammation, and oxidative stress (Romme Christensen et al., 2013). Demyelinating lesions in the central nervous system lead to the formation of scar tissue and cause changes in axonal physiology, decreased conduction velocity, and a predisposition for conduction blocks (Frohman et al., 2011). While pwMS can exhibit a wide range of physical,
cognitive, and neurological symptoms, the most commonly experienced symptom is fatigue (Krupp et al. 1988).

For many pwMS, an increase in body temperature leads to worsening of symptoms. This phenomenon, known as thermosensitivity, affects 60-80% of pwMS (Davis et al., 2010). Heat can contribute to various impairments in pwMS, including increasing fatigue, decreasing strength, and increasing gait deviations (Geisler et al., 1996). On a neuronal level, it has been suggested that heat contributes to conduction blocks by altering the propagation and the refractory period of the action potential (Smith, 1994). Furthermore, pwMS often have deficits in thermoregulation, which can exacerbate this effect.

It is possible that the use of a cooling vest increased ambulation endurance in our subjects by decreasing the effects of thermosensitivity. Physical activity, such as walking, increases core temperatures. The increase in temperature can lead to increased fatigue, decreased strength, and increased gait deviations limiting ambulation endurance. A cooling vest decreases body temperature, thereby ameliorating these effects.

It is also possible that the cooled condition had a psychological impact on patients that contributed to their improved ambulation. As Tyler and Sunderland (2011) concluded, the use of a cooling collar can decrease perceived exertion during exercise in healthy individuals. This suggests that cooling decreases perception of fatigue even in the general population. Additionally, in the MS population specifically, most pwMS are aware that heat makes their symptoms worse, and our subjects were aware that the vest was cold. Their increased distance may have been in part due to the perception that they would perform better with the vest. Similarly, simply wearing the vest, which was clearly the experimental condition, may have geared them to ambulate greater distances.
It is possible that the cooling vest also provided proprioceptive input which increased balance or motor control in the cooled subjects. A study performed by DaCosta and McDonough demonstrated that a weighted vest decreased lateral sway during gait in children with sensory integration disorder (2005). It is possible that the cooling vest used in our study, which weighed four pounds, also provided proprioceptive input that contributed to increased balance and gait improvements. However, DaCosta and McDonough’s study involved children between the ages of five and 12 whose deficits were specifically related to processing sensory information, and therefore increased sensory input targeted these deficits. It is unclear if a weighted vest would be helpful in a population such as ours in which the gait deficits are not due to a sensory integration disorder.

The effect of using a weighted vest on gait in pwMS was examined in a 2014 study performed by Gorgas et al. In this study, subjects were given selectively weighted vests, in which the weight was distributed based on the balance deficits of each subject. The distribution of weight was determined based on an assessment of lateral sway with perturbations in each direction and was customized for each participant. Gorgas et al. found that wearing the weighted vest increased velocity, cadence, and time spent in single leg support in both pwMS and controls. However, it is unclear if the vest that we used in our study, which was standardized and not individualized to the needs of each participant, would have a similar effect. In fact, it is equally feasible that the vest used could have a negative impact on balance if the distribution of weight was not optimal for a specific subject.

Though heat is known to increase fatigue in pwMS (Davis, Wilsons, White & Frohman, 2010), the decrease in fatigue in the cooled condition was not statistically significant in this study ($p=.300$). Fatigue is a subjective measure that cannot easily be quantified, and its origin is not
always definable. In pwMS, fatigue can be due to demyelination and axonal loss characterized by the disease itself, or it can be induced by a variety of secondary factors. These include difficulty sleeping, decreased activity levels, medication usage, depression, pain, and various other psychological factors (Kos, Kerckhofs, Nagels, D’Hooghe & Ilsroukx, 2008). This study could not control for the variety of factors that may have influenced fatigue.

Additionally, it is important to note that on average the patients in both conditions reported decreased fatigue after the 6MWT. This suggests that the perception of fatigue was not the limiting factor that led to decreased ambulation endurance in the uncooled condition. However, it is important to note that the small sample size may have played a role in the reported decrease in fatigue across both conditions. Despite bootstrapping, the small n limits generalizability especially since fatigue is so subjective. A larger sample size would provide more reliable data about the changes in fatigue during the 6MWT.

The finding that there was no significant difference in the percentage of distance covered in each minute of the 6MWT across the two conditions may support the notion that fatigue was not the prime limiting factor in ambulation endurance. If fatigue were the cause of decreased ambulation, we would have expected a consistent decline in distance covered in each progressive minute in the uncooled condition and more stable numbers in the cooled condition. However, even in the uncooled condition, the percentages remained relatively stable throughout the duration of the walk for many of the subjects.

Perhaps the decrease VAFS ratings with the 6MWT can be attributed to the psychological influences on fatigue. As Noakes 2012 states “sensations of fatigue…. [are] largely independent of the real biological state of the athlete at the time they develop… Subconscious and conscious mental decisions made by winners and losers, in both training and
competition, are the ultimate determinants of both fatigue and athletic performance.” Motivation is an essential factor in fatigue perception. It is therefore possible that the excitement of accomplishing the six minute walk led to a decreased perception of fatigue with walking in both conditions as reflected by the VAFS.

This discussion highlights the multifactorial nature of fatigue and therefore, the inherent difficulty in measuring fatigue in pwMS. It is interesting to note that the EDSS scores of our subjects did not directly correlate with their FSIS scores, further emphasizing that the perception of fatigue is not a representation of true disability. It is possible the 6MWT was not aggressive enough to induce a perceptible degree of fatigue in these subjects. Some of the participants in the study walk for longer periods of time regularly and perhaps would require a greater duration of ambulation before the onset of fatigue. Interestingly, the only subject with a consistent increase in fatigue throughout trials also had a significantly higher EDSS score than the other subjects, reflecting that the increase in perceived fatigue with the 6MWT correlates with decreased baseline walking ability.

Though fatigue was not perceived to increase, the decrease in mean walking distance in the uncooled condition suggests that on some level fatigue did interfere with their walking ability. However the subjective, multifactorial nature of fatigue limits our ability to quantify its effect on walking performance. It is also possible that the other symptoms associated with thermosensitivity, such as spasticity and gait deviations, were the main cause for the decrease in ambulation distance rather than fatigue perception. Cooling, which prevents the onset of thermosensitive symptoms, ameliorates all of these effects allowing for increased walking distance.
LIMITATIONS

There were a number of limitations observed during this study. MS is widely variable in its presentation, including symptom severity and frequency, age of onset, and affected areas of the body. Additionally, there is variability in the patients’ ability to cope psychologically with their disease. Though our study represented a wide range of MS presentations, a larger sample size is needed to get a true sense of how cooling impacts pwMS as a whole, and therefore the small sample size (six) limits the generalizability of this study. It is possible, for instance that the decrease in fatigue with the 6MWT was due to specific characteristics of the individuals studied, and that in a larger sample, the results would be different. Though the diversity of our subjects adds to the generalizability of our results, a larger sample size is needed to obtain a more accurate understanding of the effect of a cooling vest on pwMS.

Another limitation of this study was the possibility of a phenomenon called Hawthorne Effect, whereby subjects of an experiment alter their behavior when they know they are being examined, often in an effort to please the examiner or provide what they feel are the correct results. Participants were patients of the faculty advisor for this research project and may have discussed with him the effects of cooling on pwMS during their therapy sessions in the past. Since he is a significant facilitator and advocate in their health and well-being, these discussions could have influenced their performance based on an awareness of his hypothesis.

Reporting and assessment of fatigue on a VAFS is subjective and susceptible to varied interpretation by the participants. Thresholds differ between subjects. What some subjects consider exhaustion, others view as mildly low energy, suggesting that personality and sensitivity may impact reporting of fatigue levels. There is also the possibility that these interpretations can change from day to day depending on the variable presentation of
psychological and physical symptoms with MS. A study performed by Flachenecker et al. in 2002 examined multiple scales used to measure fatigue in MS and found a poor correlation between the scales due to the multifactorial nature of fatigue. The study found that depression scores were highly correlated with fatigue since MS patients with depression showed significantly higher FSS scores than those without. Additionally, the feeling of accomplishment from having completed a task of importance (in this case, a research trial) may have diverted attention from or even mitigated awareness of fatigue. This variability in the perception and reporting of fatigue makes it a very difficult measure to collect with baseline consistency from one trial to the next. Perhaps a quantifiable measure, such as change in body temperature, would be beneficial to compare with the acquired measurement of distance walked since it eliminates the process of participant interpretation.

Scheduling also posed a possible limitation to this study. Due to work and family obligations, time of day that testing occurred differed among subjects, some of whom could only come early in the morning, while others could only come later in the day or early evening. Therefore, while some subjects were tested after a full night’s sleep, others may have experienced a day of substantial activity prior to testing. However, testing times were consistent with each individual, and therefore level of fatigue due to previous activity was relatively consistent. Additionally, due to scheduling conflicts intervals between testing ranged from one-two weeks.

Outdoor and testing environment temperature also contributed to the limitations of this study. Even though all subjects underwent a 15 minute rest period before each walking trial, there was variability in both weather and building temperature from week to week, often, but not always, with an inverse relationship whereby colder outdoor temperatures yielded warmer indoor
temperatures and vice versa. These direct environmental influences might have had an effect on body temperature, varying the baseline from which cooling with the vest began.

The vest had multiple characteristics other than temperature, which makes it difficult to isolate the effect of cooling on gait. The cooling vest used in this study, constructed out of canvas, had nine pockets into which ice packs were placed during cooling trials. The weight of the vest, though reported by all subjects to cause no discomfort or adverse response, presents a limitation to the study as the trial that incorporated pericooling required an additional, though nominal, load to the subjects. Conversely, the vest may have provided proprioceptive and psychological benefits to its wearers, resulting in improved walking performance during pericooling trials. Though this limits our ability to isolate the effect of cooling on gait, it provides more information on the practical uses of the vest in the therapeutic context.

During the course of the study, there were two reported injuries due to falls outside of the testing trials, which may have impacted walking performance. When questioned by the researchers, however, the two subjects who had sustained the falls contended that they were able to carry out the trial with no difficulty as a consequence of their injuries.

Recording the feet walked at each minute of the 6MWT was subject to human error. Measurement was performed by following the walking path of the subject with a hand-held wheel and recording how many feet the subject walked each minute. While the path was linear and pre-planned with few direction changes, the trajectory of the wheel was prone to slight lateral curving during its course. Possible measurement errors may have contributed to a small amount of variation in the collected results.

Another possible limitation of the study was that some subjects engaged in conversation with their walk test administrators during trials, while other subjects kept discussion to a
minimum for the duration of the walk test. Since certain individuals are more naturally social, it is unclear whether or not this difference in behavior had an affect on their walking performance. While it may have distracted or placed unnecessary demands on the subject, thus impeding performance, it may just as likely have put the subject at ease and improved performance. To further eliminate external influence on performance, future testing might encourage minimal or no conversation during the walk trial to encourage focus on the physical task at hand. Conversely, the purpose of this study was to observe the effects of pericooling on walking, and conversation with walking is customary and often necessary.

FUTURE STUDIES

In addition to increasing the sample size and regulating more factors during testing trials such as time of day and weather, there are several considerations that might be addressed with future studies. This same study could be conducted in which a cooled condition is compared to a sham cooling. Sham cooling is a process in which subjects in the uncooled group wear vests that provide a significantly lower level of cooling to evoke the perception of being cooled without the associated physiological effects. This would distinguish between the physiological and psychological effects of cooling. Likewise, to eliminate the extra weight of the cooling garment, the walk test might be conducted in a corridor cooled to a specific and regulated temperature. Additionally, all subjects may be required to wear the same outfits so that they have an equivalent layer of insulation between their skin and the external temperature imposed on them. To further quantify the subjects’ baseline and thermosensitivity, testers may consider taking measurements of body or skin temperature to determine how affected each subject is by the cooling process. Future studies can also compare precooling to pericooling to see if there is any benefit to precooling over the more functional pericooling.
Another consideration for testing the effects of cooling during gait might be to calculate the number of steps taken during the 6MWT in addition to distance travelled. This measurement takes into account individual stride lengths based on height and functional ability, and therefore, provides a quantifiable and more individual report of walking response in both cooled and uncooled trials. Additionally, future studies could explore the changes in gait kinematics with a cooling vest to determine more precisely the mechanism by which cooling increases the ambulation distance. Future studies could also explore the effect of cooling on other functional measures, such as balance and coordination, and could examine the effect of cooling on longer distance ambulation, which may be more likely to induce perceptible fatigue in ambulatory individuals with MS.

**CLINICAL SIGNIFICANCE**

Pericooling is a time conserving approach in comparison to precooling. Pericooling does not require individuals to arrange their schedules in order to set aside time to precool before performing physical activity. Rather, pericooling allows the individual to don the vest just as they are beginning the activity. As it is, many individuals with MS report that performing basic ADLs is extremely time consuming and that they do not have the extra time to pre-cool as it would make a simple task, such as going to a supermarket, a full day excursion. Pericooling can be a very practical means by which pwMS can increase their productivity and maintain a more active and functional lifestyle without requiring them to set aside time to precool. Additionally, the individual can spontaneously decide to participate in an activity without extensive preparation.

The use of a cooling vest for pericooling can also have practical implications during physical therapy sessions as it can effectively manage heat related symptoms and allow the
individual to ambulate more functional distances. This will allow physical therapy sessions to be more productive since it doesn’t require the individual to don the vest prior to the session, a task that can be very time consuming and require the individual to arrive earlier.

Cooling vests are a very practical means of decreasing core temperature and lessening the effects of thermosensitivity. The vests contain multiple insulated pockets that hold the ice packs. They are lightweight (four pounds) and can be worn over clothing to provide cooling relief that can last up to a few hours. Individuals can order multiple sets of ice packs, which can be stored in the freezer for use at any time. Furthermore, the vests are extremely affordable, and many programs, such as the MSAA Cooling program, offer the vests free of charge for pwMS.

**CONCLUSION**

Many individuals with MS are heat sensitive and experience fatigue when their core temperature rises with exercise. This affects their ability to ambulate functional distances. Our results show that the use of a cooling vest during ambulation has positive effects on ambulation distance. This can have important implications for ameliorating the effects of thermosensitivity and improving exercise tolerance. The use of a cooling vest is a convenient and affordable intervention that does not require extensive preparation and can therefore be a practical intervention. Future studies are necessary to ascertain if there is any advantage to precooling over pericooling.
Do you want to contribute to MS research?

Volunteers needed for a study to determine the effect of using a cooling vest on gait endurance in persons with Multiple Sclerosis.

Participant requirements:
- Must be able to walk for 6 minutes unassisted with or without an assistive device
- Must have had no exacerbations within the last 3 months.
- Must not be currently taking steroidal medication.
- Must be available January-April 2014.

Study to be conducted at:
Hunter College Brookdale Health Science Campus
425 East 25th Street New York, NY 10010
*Travel expenses will be reimbursed.

If interested, contact:
Herb Karpatkin, PT, Dsc
Telephone: 212 396 7115
Email: Hkarpatk@hunter.cuny.edu
APPENDIX B: CONSENT TO PARTICIPATE IN A SCREENING PROCESS

Hunter College
Program in Physical Therapy
City University of New York

Consent to Participate in a Screening Process

Investigators:
Herbert I. Karpatkin, PT, DSc.
Esther Sosowsky, SPT
Meghan Higgins, SPT
Elisheva Zinberg, SPT
Hunter College, Program in Physical Therapy
City University of New York
212-481-5051

Purpose and Background
Dr. Herbert Karpatkin, PT DSc is a professor at Hunter College in the Physical Therapy Department. Esther Sosowsky, Meghan Higgins, and Elisheva Zinberg are doctoral students in the Physical Therapy Program at Hunter College. They are conducting a study examining the effects of cooling on gait endurance in persons with multiple sclerosis (MS). You are being asked to participate in the screening process to determine eligibility for this study that will help determine if wearing a cooling garment while walking allows persons with MS to walk longer distances. You were selected for participation because you are a person with MS over 18 years of age who walks as a regular means of transportation. There will be an anticipated 15 subjects that will participate in this screening process. Your participation in the screening process is voluntary. You may choose to not participate from the start and you may choose to stop at any time during the process.

Procedures
On the first day, you will fill out a demographics questionnaire in Hunter College, after which you will be interviewed by researchers to address any necessary follow up questions in order to determine if you are eligible for the study. All subsequent sessions will also take place at the Physical Therapy Department of Hunter College, at 425 east 25th street, basement level.

- The screening process will involve answering questions about your medical history including length of time with MS, medications, use of assistive devices for walking such as canes, walkers, or splints, and whether you have a history of non-MS complications such as a cardiac condition or orthopedic problems. The researchers will also look at information from your medical records such as your Expanded Disability Scale Score (EDSS) and MS Quality of Life score (MS QOL-54).
- If your responses indicate that you are eligible, you will be asked to participate in this study.
If you are not eligible to participate, the information obtained from you during the screening process will be omitted from this study and shredded to protect your privacy.

None of the procedures or questionnaires in this study is experimental. The only experimental aspect of this study is the gathering of information for the purpose of analysis.

**Risks**
There are minimal risks to you for participating in the screening process of this study. The screening process will require a maximum of 15 minutes of your time. Confidentiality of the information will be safeguarded by de-identifying subjects and filing any identifying information in a locked cabinet located at Dr. Karpatkin’s private practice. All identifying information will be destroyed at the conclusion of the study. If deemed ineligible, or if at any time you choose not to participate, data will be destroyed. You have the choice to refuse to answer any item in any of the questionnaires or forms.

**Benefits**
There are no direct benefits to you resulting from the screening process.

**Alternatives**
The alternative to this study is nonparticipation without repercussions or penalties.

**Financial Considerations**
Other than the cost of travel to and from the Hunter College Brookdale Campus, there are no costs incurred by you for participation in the screening process.

**Confidentiality**
Strict confidentiality will be maintained. Knowledge of your identity and participation in the screening process will be limited to Dr. Karpatkin, the collaborating physical therapy students, and IRB members and staff. Information about your participation will only be disclosed in the event of an emergency requiring hospitalization, and in such a case will be disclosed to the treating hospital physician and your primary care physician. Under expected non-emergency circumstances, no individual identifying information about you will be disclosed. Where possible, all identifying references about you will be removed and replaced by a numeric code. Participation in this research is voluntary and involves minimal loss of your privacy. All questionnaires and data about you that will be used in computer analysis will have number codes rather than your name. Your name will not be recorded on the information or reported in any scientific paper or professional meeting to protect your identity. All data will be reported in aggregate (group) fashion at a professional meeting or in a scientific journal so that no one can identify any information about you. If data is used for a publication in the medical literature or for teaching purposes, no names will be used. A master list of code numbers as well as all other data pertaining to you and other subjects will be kept confidential by the researchers and will be stored in a locked file cabinet in the faculty research advisor’s office. Data that will be used for computer analysis will be kept on a flash drive and only researchers involved in this study and IRB members and staff will have access to the records and information about this study. All original hardcopy data will be shredded seven years after completion of the study. The code key
connecting names to numbers will be kept in the research office of Dr. Karpatkin. Confidentiality will be maintained to the extent allowed by law.

**Withdrawal**
You may terminate your participation from the screening process prior to the start or at any time during the process without penalty or repercussion.

**Contact Information**
If you have questions about the screening process, you can contact Dr. Karpatkin, at (212) 481-5051. You should contact the Hunter College Human Research Protection Program (HRPP) Office at hrpp@hunter.cuny.edu or 212-650-3053, if you have questions regarding your rights as a subject or if you feel you have been harmed as a result of your participation in this research.

**Signatures**
I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I give my consent to participate in the screening process to determine if I am eligible to participate in the research study. I have received (or will receive) a copy of this form for my records and future references.

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<th>Participant’s Name</th>
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<th>Researcher’s Name</th>
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APPENDIX C: CONSENT TO PARTICIPATE AS A RESEARCH SUBJECT

Hunter College
Program in Physical Therapy
City University of New York

Consent to Participate as a Research Subject

Investigators:
Herbert I. Karpatkin, PT, DSc.
Esther Sosowsky, SPT
Meghan Higgins, SPT
Elisheva Zinberg, SPT
Hunter College, Program in Physical Therapy
City University of New York
425 E 25th St
New York, NY 10010
212-481-5051

Purpose and Background
Dr. Herbert Karpatkin, PT DSc is a professor at Hunter College in the Physical Therapy Department. Esther Sosowsky, Meghan Higgins and Elisheva Zinberg are doctoral students in the Physical Therapy Program at Hunter College. They are conducting a research study examining the effects of wearing a cooling vest on gait endurance in persons with Multiple Sclerosis (MS). You are being asked to participate in a research study that will help determine if wearing a cooling garment during ambulation allows persons with MS to walk longer distances. You were selected for participation because you are a person with MS over 18 years of age who walks as a regular means of getting around/commuting. There will be an anticipated 15 subjects that will participate in this research study. Your participation in this study is voluntary. You may choose to not participate from the start and you may choose to stop at any time during the study.

Procedures
All sessions will take place at the Physical Therapy Department of Hunter College, at 425 east 25th street, basement level. On the first day, you will fill out a demographics questionnaire as well as a simple fatigue survey and a quality of life scale. You will then be randomly assigned into a cooled or uncooled group, and will receive the corresponding vest (with or without cooling capabilities, depending on the group). Wearing the vest, you will perform a timed walking trial, and then fill out a quick fatigue survey. Each session will last approximately 45 minutes on two occasions per week for 3 weeks followed by 2 weeks without intervention. You will then repeat this protocol wearing the other kind of vest, for 3 more weeks.

The study procedures in detail are as follows:
If you agree to participate in the study, you will complete a questionnaire in Hunter College with the researchers to determine if you are eligible for the study. The screening will ask questions about your medical history including length of time with MS,
medications, use of assistive devices for walking such as canes, walkers, or splints, and whether you have a history of non-MS complications such as a cardiac condition or orthopedic problems. The researchers will also look at information from your medical records such as your Expanded Disability Status Scale Score (EDSS) and MS Quality of Life score (MS QOL-54).

If your responses indicate that you are eligible, you will be asked to participate in this study.

If you are not eligible to participate, the information obtained from you during screening will be removed from this study and destroyed/shredded to protect your privacy.

If you are chosen to continue, you will complete one form that will inquire about your level of fatigue, and another that will inquire about the physical and psychological impact of MS on your life.

You will then be randomly assigned to one of two groups: cooled or uncooled.

You will receive one of two vests, depending on your assigned group, with or without cooling capabilities.

After a fifteen minutes seated rest period, you will be asked to perform a single 6-minute continuous walk. The walk should be performed at your best comfortable pace. You will be guarded by Dr. Karpatkin for the entire walk. You will also be followed with a wheelchair by one of the collaborating physical therapy students for the entire walk.

Immediately after completing the walk, you will fill out a fatigue form that asks about your level of fatigue at that moment. The distance that you walk will be recorded every minute. You will be asked to perform this timed walk twice a week for the initial 3-week period.

Following the initial 3-week period, there will be a 2-week detraining period, during which no walking intervention will take place.

After the 2-week detraining period, you will return and perform the 6-minute walk wearing the vest that you did not wear during the first 3-week session. If you wore a cooled vest during the first 3 weeks, you will be asked to perform the walk wearing an uncooled vest during the second 3-week training period. If you wore an uncooled vest during the first 3 weeks, you will wear a cooled vest during the second 4-week training period. As with the first 3-week period, immediately before and after the timed walk, you will complete the form related to your current level of fatigue. Distances will be measured in the same manner as previously. You will be free not to answer any item in any of the questionnaires or forms.

At each visit, please bring with you any walking devices such as canes, walkers, splints etc. that you would normally use for walking. Please bring the same comfortable walking shoes to all sessions.

The total time expected for each session is 45 minutes.

None of the procedures or questionnaires in this study is experimental. The only experimental aspect of this study is the gathering of information for the purpose of analysis.

**Risks and/or Discomfort**

There are minimal risks to you from participation in this study. You may experience some fatigue-related discomfort as a result the walking protocol. Because fatigue is the most common
symptom in persons with MS, it is important to note that any fatigue experienced may be characteristic of the disease itself, as opposed to a result of the testing conditions. The walking protocol of this study is not expected to worsen your fatigue, or any other aspect of your MS in any way. Dr. Karpatkin will walk beside you for the entire walk. You will also be followed by one of the physical therapy students with a wheelchair. Despite these safeguards, there is a chance that you could incur an orthopedic injury from the walking or that you may fall and get injured. If this should occur we will immediately contact your primary care physician and if necessary take you to the emergency room.

If you feel bothered or upset as a result of participation, or for any reason wish to not continue you may simply ask to stop and we will immediately end the procedure. You will be free not to answer any item in any of the questionnaires or forms.

**Benefits**
There may be no direct benefits to you as an individual. You may experience an increase awareness of your fatigue levels, and how they may vary based on the use of a cooling garment.

**Alternatives**
The alternative to this study is not to participate, without repercussions or penalties.

**Voluntary Participation:** Your participation in this study is voluntary, and you may decide not to participate without prejudice, penalty, or loss of benefits to which you are otherwise entitled. If you decide to leave the study, please contact the principal investigator Esther Sosowsky, SPT at (718)-483-0621 or via email es125@hunter.cuny.edu to inform her of your decision.

**Financial Considerations**
Other than the cost of travel to and from the Hunter College Brookdale Campus, there will be no costs incurred by you for participation in the study. You will receive an $80.00 MetroCard to cover your travel-related expenses. This money does not obligate you to continue the study if at any point you wish to stop. You may terminate your participation at any time and you will still receive this compensation.

**Confidentiality**
The data will be collected using the two fatigue surveys that you fill out and by measuring the distance walked within each timed walk. Strict confidentiality will be maintained. Knowledge of your identity and participation in this study will be limited to Dr. Karpatkin, the collaborating physical therapy students, and the IRB members and staff. Information about your participation will only be disclosed in the event of an emergency requiring hospitalization, and in such a case will be disclosed to the treating hospital physician and your primary care physician. Under expected non-emergency circumstances, no individual identifying information about you will be disclosed. Where possible, all identifying references about you will be removed and replaced by a numeric code. Participation in this research is voluntary and involves minimal loss of your privacy. All questionnaires and data about you that will be used in computer analysis will have number codes rather than your name. Your name will not be recorded on the information or reported in any scientific paper or professional meeting to protect your identity. All data will be reported in aggregate (group) fashion at a professional meeting or in a scientific journal so that
no one can identify any information about you. If data are used for a publication in the medical literature or for teaching purposes, no names will be used. A master list of code numbers as well as all other data pertaining to you and other subjects will be kept confidential by the researchers and will be stored in a locked file cabinet in the faculty research advisor’s office. Data that will be used for computer analysis will be kept on a flash drive and only researchers involved in this study and IRB members and staff will have access to the records and information about this study. All original hardcopy data will be shredded seven years after completion of the study. The code key connecting names to numbers will be kept in the research office of Dr. Karpatkin. Confidentiality will be maintained to the extent allowed by law.

Withdrawal
You may terminate your participation from this study prior to the start or at any time during the study without penalty, repercussion, or loss of compensation.

Contact Information
If you have questions about the study, you can contact Dr. Karpatkin, at (212) 481-5051. You should contact the Hunter College Human Research Protection Program (HRPP) Office at hrpp@hunter.cuny.edu or 212-650-3053, if you have questions regarding your rights as a subject or if you feel you have been harmed as a result of your participation in this research.

Signatures
I have read (or have had read to me) the contents of this consent forms and have been encouraged to ask questions. I have received answers to my questions. I have received answers to my questions. I give my consent to participate in this study. I have received (or will receive) a copy of this form for my records and future references.

Participant’s Name __________________________ Signature __________________________ Date __________

Researcher’s Name __________________________ Signature __________________________ Date __________
APPENDIX D: SCREENING QUESTIONS AND SUBJECT DEMOGRAPHIC INFORMATION

**Screening Questions**

Do you have a definitive diagnosis of MS?
Yes  No

Are you able to understand and sign informed consent?
Yes  No

Can you ambulate continuously for six minutes with or without an assistive device?
Yes  No

Do you have any type of orthopedic or cardiopulmonary condition preventing your ability to walk six minutes?
Yes  No

Have you had a recent exacerbation of your symptoms?
Yes  No

Have you taken steroidal medication within the past 4 weeks?
Yes  No

**Subject Demographic Information**

Age: __________  Gender: M / F  Date of Birth: _________________

Type of Multiple Sclerosis: __________________________________________

Year since diagnosis of Multiple Sclerosis: __________________________

Expanded disability status scale (EDSS) Score: _______________________

Fatigue Severity Scale (FSS) Score: _________________________________

MSIS Score: ____________________

Use of assistive device: _____________________________________________

Use of anti-spasticity medications: _________________________________

Use of fatigue medication: _________________________________________

Use of any other medication: _______________________________________

Any other medical Diagnoses: _______________________________________


APPENDIX E: FATIGUE SEVERITY SCALE (FSS)

Fatigue Severity Scale (FSS)

Your Name

Date: ________________________________  Date of birth: ____________________

This questionnaire contains nine statements that rate the severity of your fatigue symptoms. Read each statement and circle a number from 1 to 7, based on how accurately it reflects your condition during the past week and the extent to which you agree or disagree that the statement applies to you.

***A low value (e.g. 1) indicates strong disagreement with the statement, whereas a high value (e.g. 7) indicates strong agreement.

**During the past week, I have found that:**

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<tr>
<th>Statement</th>
<th>Disagree</th>
<th>Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. My motivation is lower when I am fatigued</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>2. Exercise brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>3. I am easily fatigued.</td>
<td>1 2 3 4 5 6 7</td>
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</tr>
<tr>
<td>4. Fatigue interferes with my physical functioning.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>5. Fatigue causes frequent problems for me.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>6. My fatigue prevents sustained physical functioning.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>7. Fatigue interferes with carrying out certain duties and responsibilities.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>8. Fatigue is among my three most disabling symptoms.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>9. Fatigue interferes with my work, family or social life.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
</tbody>
</table>

**Total Score: _______**
APPENDIX F: MULTIPLE SCLEROSIS IMPACT SCALE (MSIS-29)

- The following questions ask for your views about the impact of MS on your day-to-day life during the past two weeks
- For each statement, please circle the one number that best describes your situation
- Please answer all questions

<table>
<thead>
<tr>
<th>In the past two weeks, how much has your MS limited your ability to...</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do physically demanding tasks?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Grip things tightly (e.g. turning on taps)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Carry things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In the past two weeks, how much have you been bothered by...</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Problems with your balance?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Difficulties moving about indoors?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Being clumsy?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Stiffness?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>8. Heavy arms and/or legs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. Tremor of your arms or legs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. Spasms in your limbs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11. Your body not doing what you want it to do?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>12. Having to depend on others to do things for you?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Please check that you have answered all the questions before going on to the next page

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<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limitations in your social and leisure activities at home?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Being stuck at home more than you would like to be?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Difficulties using your hands in everyday tasks?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Having to cut down the amount of time you spent on work or other daily activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Problems using transport (e.g. car, bus, train, taxi, etc.)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Taking longer to do things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Difficulty doing things spontaneously (e.g. going out on the spur of the moment)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Needing to go to the toilet urgently?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Feeling unwell?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Problems sleeping?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Feeling mentally fatigued?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Worries related to your MS?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Feeling anxious or tense?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Feeling irritable, impatient, or short tempered?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Problems concentrating?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Lack of confidence?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Feeling depressed?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Please check that you have circled ONE number for EACH question

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APPENDIX G: DATA ENTRY TABLE

<table>
<thead>
<tr>
<th>Subject #</th>
<th>VAFS (mm)</th>
<th>Min 1 (ft.)</th>
<th>Min 2 (ft.)</th>
<th>Min 3 (ft.)</th>
<th>Min 4 (ft.)</th>
<th>Min 5 (ft.)</th>
<th>Min 6 (ft.)</th>
<th>TOTAL (ft.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooled</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>TRIAL 1</td>
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<td></td>
</tr>
<tr>
<td>TRIAL 2</td>
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<tr>
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<tr>
<td>Uncooled</td>
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<tr>
<td>TRIAL 3</td>
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<td></td>
</tr>
</tbody>
</table>

APPENDIX H: VISUAL ANALOG FATIGUE SCALE

Visual Analog Fatigue Scale

Please indicate your current level of fatigue by drawing a vertical line on the scale below

No fatigue | Extremely severe fatigue
REFERENCES


