# The Effect of Symbiotropin on Muscle Strength and Body Composition in Older Women

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## Abstract

The effect of Symbiotropin on muscle strength and body composition in older women. Aims: This investigation assessed the effects of a 12-week programme of Symbiotropin supplementation on muscle strength and body composition in older women. Studies into the effect of human growth hormone (hGH) on physical and physiological effects of the ageing process, has led to a proliferation of dietary supplements claiming to reverse these effects. Methods: Twenty-eight female participants aged 45-67 were randomly assigned in a blind, randomised placebo-controlled design, to a supplement (S, N=14), or placebo group (P, N=14). The S group took one Symbiotropin tablet dissolved in water every night for 12 weeks, the P group took one identical-looking glucose tablet, also dissolved in water, every night. Measurements of muscle strength using a Cybex II isokinetic dynamometer, and body composition using waist circumference and skinfolds to calculate percentage body fat were made pre-study, at six weeks and on completion of the study. Participants were asked not to make any major dietary or physical activity alterations. Results: Paired samples t-tests indicated significant increases in muscle strength and decreases in waist circumference and percentage body fat occurred in the S group ($p<0.05$), and also a significant decrease in percentage body fat in the P group ($p<0.05$). A t-test for equality of means produced significant differences in only percentage body fat between the two groups. Conclusions: These findings indicate that Symbiotropin supplementation can increase muscle strength and decrease percentage body fat, without any dietary or physical activity modification. Long-term studies are needed to test effectiveness and safety over longer periods, and other variables such as aerobic capacity. Key words: HUMAN GROWTH HORMONE SECRETAGOGUE, AGEING, SUPPLEMENTATION, PERCENTAGE BODY FAT, MUSCLE PERFORMANCE.

The United Kingdom, along with other Western nations, has an ageing population. The 2001 national census showed that for the first time there are now more people over 60 than there are children under 16 (10). This ageing of the population reflects longer life expectancy, the fact that there have not been any events with a corresponding effect on life expectancy like that of the first and second world wars, and the fact that the 'baby boomers', those born between 1946 and 1964 are now reaching 'middle age'. This situation also presents major socio-economic implications because living longer does not necessarily mean living well, and the State faces the possibility of having to care for a large population of older adults who may be unable to care for themselves. This has led to increased scientific interest in the ageing process of the human body, and ageing is now seen by many as a disease rather than an inevitable consequence of getting older, primarily because it is progressive and degenerative, it affects every cell, tissue, and organ of the body, and ultimately ends in death. Although there are well documented methods of slowing the ageing process by physical activity (54), nutrition (55), under-nutrition (9, 27), and vitamin and mineral supplementation (59), it has until recently been thought of as irreversible. However modern science is now developing methods of actually halting and reversing the ageing process. Some of these methods, such as stem cell research and gene therapy, are very recent discoveries and inaccessible to most of the population. However hormone therapy involving human growth hormone somatotropin (hGH) and growth hormone (GH) secretagogues like Symbiotropin, are now well-established products that claim to reverse the ageing process, are available in tablet form, classed as food supplements not drugs, and are readily available.

Changes in body composition in older adults, particularly the increase of percentage body fat (%BF) and sarcopenia are well documented (8, 22, 44, 45, 57), and a definitive consequence of skeletal muscle atrophy with ageing is the reduction in muscle strength. Muscle strength appears to be relatively well maintained until 50 yeas of age, thereafter a 15% loss in muscle strength per decade occurs between 50 and 70 years (43), with a 30% loss in muscle strength in the years between 70 and 80 (16). This change in body composition and decrease in skeletal muscle strength appears to be a factor in the onset of age-related diseases that lead to disability and infirmity including coronary heart disease, atherosclerosis, cerebrovascular disease, diabetes, obesity, osteoporosis, and osteoarthritis. Rudman (1985) found that between the ages of thirty and seventy-five, adipose tissue on average expands by 100% and bone mass declines by an average of 20%. Therefore, because of their implications in the age-related diseases outlined, obesity management and the preservation of quality lean tissue are integral to maintaining function and quality of life in older adults, and these factors form the basis of anti-ageing research involving hGH.

It was around fifty years ago that it was first proposed that ageing and the diseases of ageing have their origin in, and are controlled by the hypothalamus/pituitary complex located at the base of the brain. This hypothesis was termed "The Neuroendocrine Theory of Ageing and Degenerative Disease," and two conclusions from this theory were that it is impossible to retard the development of the main degenerative diseases without retarding the rate of normal ageing, and the main mechanisms of ageing and degenerative disease are reversible phenomena. hGH is actually a small protein molecule that contains 191 amino acids in a single polypeptide chain, and is fundamentally implicated in the ageing process of the human body. It is the most common hormone secreted by the anterior pituitary gland, and its rate of production peaks during adolescence when accelerated growth occurs. The hypothalamus is the central control centre that regulates the secretion of somatotropin from the pituitary. The usual release of hGH in the brain depends on the interplay between a hormone that promotes hGH release, growth hormone-releasing hormone (GHRH) and one that inhibits it called somatostatin. GHRH stimulates the production and release of hGH from the anterior pituitary somatotrophs, assisted by the GH secretagogue (GHS) ghrelin (50, 62, 83). Somatostatin inhibits the secretion, but not the synthesis of hGH, and it is more effective in inhibiting hGH stimulated by GHRH than hGH stimulated by the GHS ghrelin (60). GH is released in pulses that take place during the day and night, with its release being especially prominent during the early phases of sleep. These pulses of hGH secretion are converted in the liver within just 20 minutes to Insulin-like Growth Factor Type I (IGF-1). Although IGF-1 is not insulin, it acts like insulin as it promotes glucose transfer through cell membranes into the cell, and it elicits most of the effects associated with hGH. It is measured in the blood and is the surrogate marker of growth hormone in the body.

Due to mechanisms not fully understood, the amount of growth hormone secreted into the body starts to decline after peaking during late adolescence (79, 80). At the age of twenty-one the measurable level of hGH in

the body is 10 mg per decilitre of blood, and at sixty-one the level is 2 mg per decilitre of blood – a decrease of 80 per cent. This reduced level of secretion, referred to as somatopause, coincides with the process of ageing that the body undergoes over a period of time which results in reduced muscle mass, increased body fat, thinning and wrinkling of skin, thinning hair, greying of hair, reduced energy, reduced muscle strength, decreased libido, less restful sleep, and other physiological changes. More specifically, between ages thirty and seventy-five years, there is a 20-50% reduction in the size of muscle, liver, kidney and spleen. The reduction in lean body mass has been shown to reflect atrophic processes in skeletal muscle, liver, kidney, spleen, skin and bone (63).

The landmark studies that established the link between hGH and ageing were conducted in the 1990s and showed that age reversal was possible with the use of hGH (63) Further studies have shown the effect of hGH therapy on body composition (1, 2, 3, 4, 12, 13, 14, 17, 18, 23, 38, 39, 53, 77), and skeletal muscle strength (33, 37, 38, 39, 64, 65). GH replacement therapy has also shown beneficial normalising effects on parameters such as cardiac and renal function, thyroid hormone metabolism, bone metabolism, sweat secretion, total and regional fuel metabolism and psychological well being (2, 3, 35, 47, 52). Rudman et al (1990) studied adult men aged between 61 and 73 years who had measured deficiencies in hGH. They were injected with GH produced from recombinant DNA synthesis initially for a period of six months, and results showed an increase in lean body mass of 8.8%, and decrease in fat mass of 14.4%, an increase in bone density of 1.6%, and an increase in skin thickness of 7.1%. The participants did not exercise. These effects of human growth hormone on lean body mass and adipose-tissue mass were equivalent to 10 to 20 years of reversed ageing. The decrease in fat-mass is particularly significant in ageing because the increase in fatty tissue is related to a variety of cardiovascular problems, while the loss of lean body mass is linked to older adults losing energy, strength, and mobility. Any factor that can slow or reverse the trend towards more fatty tissue will in effect slow or reverse the ageing process itself. As well as the physiological benefits of hGH therapy observed in studies and already outlined, growth hormone deficiency is also synonymous with various physical and physiological complaints that collectively influence quality of life (QoL), including mood fluctuations, disturbed sleeping patterns, low libido, and low energy levels (47).

One key characteristic of hGH is that it is an anabolic hormone as opposed to a catabolic hormone such as the stress hormones. Thus, the age-reversing results of Rudman's and other studies were achieved because of hGH's regenerative properties on tissues throughout the body. hGH plays a key role in the ageing process partly because it improves utilisation of fat as a source of energy by stimulating lipolysis and fat oxidation. All fat cells have hGH receptors, and when it binds to these receptors, it triggers a series of enzymatic reactions in the cells to break down fat, making it available as fuel and reducing the size of fat cells. Studies have also shown that cortisol and insulin facilitate lipid accumulation by expressing lipoprotein lipase (LPL). hGH and testosterone inhibit the expression of LPL, which markedly stimulates lipolysis (33). hGH increases lean body mass through stimulation of protein synthesis, and reduction of protein oxidation, without inhibiting protein catabolism (39). Another characteristic of the ageing process is weight-gain, and this can partly be attributed to long term IGF-1 deficiency, as seen in older adults, slowing carbohydrate metabolism, leading to insulin resistance and often weight gain. These effects can be reversed with hGH, which increases glucose turnover (39). All of these factors can be attributable to the results of Rudman's studies.

When Rudman extended his study into a seventh month, several participants developed debilitating carpal tunnel syndrome, and others developed severe arthritis, high blood pressure, congestive heart disease, and diabetic-like conditions. Although the side effects diminished when the drug was discontinued, so did the benefits. This study led to further research into hGH in an attempt to gain the benefits and avoid the harmful side effects. These further studies investigated the body's mechanisms for producing hGH. It had been thought that the production of hGH in the body naturally decreased as an individual got older, however the production of the hormone does not decline with age, but the body continues to produce hGH well into old age. What actually declines is the body's efficiency in releasing the hGH that it is still producing. Due to reasons not yet discovered, hGH remains sequestered in pituitary somatotrophs, rather than being secreted into the body. It has already been established that specific hGH releasing peptides called GHS's were identified to be instrumental in enhancing the body's production, release and utilisation of IGF-1 (56). GHS's are a natural polyamino acid chain that are postulated to initiate the pituitary gland to release growth hormone. While hGH causes the body to act as if the pituitary has released growth hormone, GHS's actually cause the release of it. Hence a secretagogue causes the bodies own natural processes to produce growth hormone. The GHS Ghrelin was only recently discovered in 1999 by Kojima et al (41), and the true physiological importance of GHS's is now just being discovered by further research (15, 67). The secretagogue Symbiotropin being tested in this study is based on the discovery in 1981 of peptides that are similar in structure to naturally occurring pain substances such as enkaphalin in the human brain. Enkaphalin acts like a natural form of morphine in ameliorating pain perception, and for some unknown reason, also stimulates GH release.

As already mentioned, GHS's act independently of the inhibitory hGH substance somatostatin, making them of extreme interest to researchers because they appear to increase the active anabolic derivative of hGH, IGF-1, and therefore they have a potential benefit in treating many catabolic diseases. The advantage of these peptides is that they are available orally, unlike hGH or IGF-1, which must be administered only by injection. Synthetic GHS's have been developed, which include GH-releasing peptide (GHRP), a synthetic hexapeptide, which has been demonstrated to be a potent, relatively selective GHS in humans (7, 29). Other compounds have been developed that mimic the stimulatory actions of GHRP on GH release in animals and man (26, 71). Further research studied the effects of oral treatment with the GHS MK-677 on GH secretion and body composition in otherwise healthy obese males (75). This study was randomised, double blind, parallel, and placebo controlled. Twenty-four obese males, aged 18–50 years, with body mass indexes greater than 30 kg/m2 and waist/hip ratios greater than 0.95, were treated with MK-677 25 mg (n = 12) or placebo (n = 12) daily for 8 weeks. Results reported IGF1 increased by approximately 40% with MK-677 treatment, and serum IGF-binding protein-3 was also significantly increased. GH was significantly increased after the initial dose of MK-677, and these increases persisted at 2 and 8 weeks of treatment. Fat-free mass increased significantly in the MK-677 treatment group when determined with dual energy x-ray absorptiometry, however total and visceral fat were not significantly changed with active therapy. The researchers concluded that 8 weeks treatment with MK-677 in healthy obese males caused a sustained increase in serum levels of GH, IGF-I, and IGF-binding protein-3, and changes in body composition and energy expenditure were of an anabolic nature, with a sustained increase in fat-free mass and a transient increase in basal metabolic rate. They did not measure changes in body fat.

Similar to Svensson et al, Chapman et al (11) investigated the effect of the hGH releasing peptide MK-677, on the GH/IGF1 axis in selected growth hormone deficient adults. Nine severely hGH-deficient men, who had been treated for their deficiency with growth hormone injections during child-

hood were studied. In a double-blind rising-dose design, subjects received once daily oral doses of 10 or 50 mg MK-677 or placebo for 4 days over two treatment periods separated by at least 28 days. Results showed that serum IGF-1 and GH concentrations increased in all subjects after treatment with both 10 and 50 mg/day MK-677. These key studies support the hypothesis that the synthetic secretagogue MK-677 increases serum levels of GH, IGF1, and IGF-binding protein-3, and produces a sustained increase in fat-free mass and a transient increase in basal metabolic rate. GHS's were seen as preferred alternatives to hGH injections because they not only eliminated the need for injections, but they produced similar benefits, but without the harmful side effects.

It was based on the findings of studies with drug versions of oral GHS's, that a natural supplement form; Symbiotropin was developed. The primary ingredient in the supplement is pituitary peptides, similar in structure to the drug versions, together with what the developers call 'chaperone molecules', that enhance both the effectiveness and delivery of the supplement in the body. Symbiotropin also contains several known GH-releasing amino acids, such as arginine, glutamine, GABA, glycine, lysine and tyrosine, that are delivered into tissues and not broken down beforehand by the chaperone molecules. The supplement also contains a legume found in the tropical rain forest called Lacuna bean that is naturally high in L-dopa, which is a known GH releaser.

Symbiotropin (Pro hGH) has been investigated in a study evaluating 36 individuals with low levels of IGF-1 for changes in serum IGF1 levels and other noticeable changes, over a period of 12 weeks (31). Participants experienced a 30% average increase in IGF-1. The researchers also noted positive participant self-assessments in areas of endurance and body composition, hair and skin condition, sexual function, wound healing, immune function, and mental function, and noted significant improvements in all areas ranging from 21-71%. However, although these results were telling, participant self-assessment is not as reliable as clinical observation of these physical and mental changes. The clinical observations that the researchers made in this study showed significant improvements in blood sugar management in diabetic participants, lowered prostate specific antigen, improved cardiac and pulmonary function, improved blood pressure management, and improvement in menopausal symptoms, though they give no indication of how these observations were measured.

The aim of this study was to investigate the effect of GHS Pro hGH percentage body fat, and muscle strength in the study group of women aged 45-70. It used validated methods of body composition assessment and muscle strength evaluation, to test the effectiveness of the supplement which is widely sold as an 'anti-ageing' supplement. Ageing is associated with reduced GH, IGF-1, increased body fat particularly abdominal fat, and decreased lean body mass and muscle strength, as well as other physical changes that will not be measured in this study, though participant self-assessments will be noted. It is hypothesised that the GHS Pro hGH will cause an increase in muscle strength, and a decrease in percentage body fat in women aged 45-70 years.

## Materials and Methods

This study was approved by the St Mary's College Ethics Committee, (see Appendix 1). All participants gave written informed consent (see Appendix 2). A randomised, controlled, masked placebo design was used to study the effects of 12 weeks of oral administration of the GHS Pro hGH. Twenty-eight females between 45-67 years were randomly recruited using advertisements in local newspapers and a university noticeboard. Twenty-five of the participants were white, and three were of African origin. Respondees were sent an information pack about the study (see Appendix 3), and the final 28 subjects were randomly placed, depending on the order they arrived at the testing centre, into the study group to receive Pro hGH, or the control group to receive a matching dose of placebo daily for 12 weeks (n = 14 per group). The Pro hGH dose was administered by the participants themselves, and consisted of one tablet dissolved in a 250ml glass of water, and taken every night before retiring. The placebo used was an effervescent glucose tablet produced by the manufacturers of Pro hGH. Participants were asked to inform their general practitioner that they were taking part in this study if they were under medical supervision for any condition. The placebo group was offered the supplement after completion of the study, and the participants were not instructed with any new information about changing their nutritional habits or physical activity (PA) routines, but asked not to change their ordinary daily calorific intake or physical activity during the course of the study.

Before the start of the study, participants' weight in kilogrammes, waist circumference in centimetres, percentage body fat, and muscle strength were measured. Waist circumference was measured in the standing position with a flexible plastic tape placed around the navel. Waist circumference was used rather than waist to hip ratio, as waist size gives a better indicator of visceral fat proportions (19, 81). Measures for percentage body fat were calculated using skinfold (SKF) measurements taken by Harpenden Callipers. In order that measures were consistently taken from the same sites on the body, guidelines for their anatomical location were adhered to (28). Measures were taken from the middle of the triceps muscle using a vertical fold; the biceps, again using a vertical fold and in the middle of the muscle; the subscapular, using a diagonal fold and just below the angle of scapular; and suprailiac, just above the suprailiac crest. Three readings in rotation were taken for each measurement. Percentage body fat from SKF was calculated using the Durnin & Wormersley equation (21).

All subjects were tested for both knee extension and flexion strength in the right leg with the Cybex II isokinetic dynamometer. Isokinetic tests were measured at 60°.s. Average torque values were collected throughout the range of motion in Newton-metres relative to body weight. The test involved the subject sitting in an upright position with the hips flexed to 90 degrees. Pelvic and thigh straps were used to stabilise the hips and thighs. The axis of rotation of the knee joint was identified, and the input shaft of the dynamometer was aligned with the axis of rotation of the knee joint. The length of the lever arm was adjusted so that the participant's shin contacted the shin pad above the ankle, and the ankle strap was secured when the knee was at full flexion. The participant held the side handles of the machine, or they could fold their arms across the chest (the position was kept constant throughout every test).

The leg movements were explained and demonstrated, and the subject first warmed up by making 5 sub-maximal repetitions. After a rest of about 5 minutes, the participant performed the test. The speed was set at 60 degrees, the lowest speed. Maximal strength was measured by performing three repetitions, resting for a period of 3-5 minutes between each one. Muscle strength was measured by peak isokinetic torque. The participants were asked to indicate if they felt undue discomfort or pain, and the test was halted. The highest scores for flexion and extension of each leg was noted, and finally the participants were taken through a series of stretches of the quadriceps and hamstrings after the testing session. All measurements were taken before commencing the study, at six weeks, and on completion of the study at 12 weeks.

Results were statistically analysed using SPSS. Descriptive statistics for the dependent variables were computed to determine mean and standard deviation values. T-tests for independent samples were used to assess the

between group differences, and within-group differences were analysed using a series of T-tests for related samples.

In addition to the measured data, because growth hormone deficiency in older adults is also associated with physical and psychological changes that affect QoL, participants were also asked to make a note of and report any other changes that they experienced during the course of the study. They were not instructed on any changes to look out for, and despite the existence of a QoL Assessment of Growth Hormone Deficiency in Adults Questionnaire that has been shown to have good reliability and construct validity (20, 48), they were not given this because these QoL variables were not being tested. They were simply asked to report any changes that they felt.

## Results

Twenty-eight participants were initially recruited to take part in this study, however due to compliance failure with the testing schedule, only 10 participants completed the study from the placebo (P) group, and 12 participants completed from the study (S) group. The average age of the participants was 54.6 years (±6.9) years (see table 1), and there were no significant differences ($p>0.05$) between the two groups with regard to body weight at the beginning of the study. Participants weight, percentage body fat (%BF), waist circumference, and isokinetic muscle strength were recorded at the beginning of the study, then all of the variables except for body mass (which was not a tested variable), were measured half-way through the trial at six weeks, then on completion at twelve weeks. The descriptive statistics are presented as the mean and standard deviation of all of the variables: waist circumference, sum of skin-folds, percentage body fat, and muscle strength.

Paired samples t-tests indicated significant decreases in percentage body fat (%BF) and waist circumference in the study (S) group ($p<0.05$), and significant increases in muscle strength for both flexors and extensors in the study group ($p<0.05$) at 12 weeks. Also in the S group, the six-weeks data indicated a significant decrease in percentage body fat (%BF) ($p<0.05$), and significant increases in muscle strength for both flexors and extensors ($p<0.05$), but no significant decrease in waist circumference ($p>0.05$). In the placebo (P) group, a paired samples t-test indicated that the only variable that produced a significant result was for %BF at 12-weeks ($p<0.05$). All other data at both 6 and 12 weeks produced no significant changes ($p>0.05$). For waist circumference, the average decrease was 1.8%, and the largest decrease 6.7% in the S group (see table 2). A t-test for equality of means produced significant differences in only percentage body fat data collected at 12 weeks between the two groups, due to them both producing significant results for this variable. However the average decrease in %BF in the P group was 4%, and in the S group over double that figure at 8.9% (see table 3).

**Table 1. Age and weight of study participants**

| Participant P group | Age (yrs) | Weight (kg) | Participant S group | Age (yrs) | Weight (kg) |
|---|---|---|---|---|---|
| 1 | 58 | 73 | 1 | 50 | 68 |
| 2 | 56 | 64 | 2 | 54 | 77 |
| 3 | 57 | 62 | 3 | 64 | 62 |
| 4 | 63 | 50 | 4 | 45 | 64 |
| 5 | 45 | 74 | 5 | 50 | 64 |
| 6 | 64 | 81 | 6 | 64 | 70 |
| 7 | 64 | 66 | 7 | 49 | 61 |
| 8 | 48 | 99 | 8 | 50 | 70 |
| 9 | 46 | 65 | 9 | 58 | 66 |
| 10 | 61 | 72 | 10 | 46 | 68 |
| 11 | 56 | 75 | 11 | 53 | 87 |
| 12 | 47 | 62 | 12 | 63 | 65 |
| 13 | 50 | 94 | 13 | 67 | 65 |
| 14 | 50 | 60 | 14 | 51 | 88 |
| Mean | 54.6 | 71.2 | Mean | 54.5 | 69.6 |
| Standard deviation | 6.9 | 13.2 | Standard deviation | 7.2 | 8.5 |

For isokinetic muscle strength, paired samples t-tests indicated significant increases in the S group only ($p<0.05$). For the flexors, the largest increase was 600%, and for the extensors, and the largest increase was 244%, (from the same participant). These results were due to the participant, who suffers from arthritis of the spine, registering very little muscle strength at the commencement of the study and showing gains in strength during the course of the trial, however because of these large increases, her results were excluded from the final data analysis.

The overall increase in peak torque at 12 weeks was 8.7% in the P group, and 25.85% in the S group. Figure 1 shows the mean percentage difference between the pre and post intervention measures for all four variables at 6 weeks, and Figure 2 shows the mean percentage differences at 12 weeks.

Table 2 shows the results for waist circumference after 12 weeks. Data indicates a mean percentage increase of 0.08 for the placebo group, and a significant decrease of –1.8% for the study group ($p<0.05$).

Table 3 shows the results for %BF after 12 weeks, indicating significant mean percentage decreases of –4.9% in placebo group and –9.6 in study group.

Tables 3 and 4 show results of changes in isokinetic muscle strength after 12 weeks of intervention. The mean percentage increases of 17.1% for flexors and 15.5% for extensors in the placebo group were not significant, and the mean percentage increases of 79.7% and 35.70% for flexors and extensors in the study group were significant changes.

Figures 1 and 2 show the mean percentage differences between pre and post measures for all variables at 6 and 12 weeks. Blue indicates the placebo group, and red the study group.

Figure 1. Mean percentage differences between pre and post measures for all variables at 12 weeks

There was also evidence of other positive subjective responses from the participants in the study group, the most common response being increased energy levels felt during the first four weeks by many of the participants (see Appendix 4). Other responses included feeling that arms had become leaner, more restful sleep, and increased libido. All of the participants in the study group felt one or more positive change except for one who suffered a bereavement during the course of the study, and another who was on anti-depressants. They both expressed that their minds were on things other than the study. No side effects were observed during the trial in any of the participants.

**Table 2. Waist circumference results at 12 weeks**

| P group participant | Waist pre (cm) | Waist post (cm) | % difference | S group participant | Waist pre (cm) | Waist post (cm) | % difference |
|---|---|---|---|---|---|---|---|
| 1 | 89 | 88 | -1.12 | 1 | 89 | 94 | 5.6 |
| 2 | 79 | -- | -- | 2 | 104 | 101 | -2.9 |
| 3 | 79 | 75 | -5 | 3 | 80 | -- | -- |
| 4 | 68.5 | 68 | -0.7 | 4 | 79 | 75 | -5 |
| 5 | 76 | 80 | -5.2 | 5 | 81.5 | 81 | -0.6 |
| 6 | 105 | -- | -- | 6 | 104 | 100 | 3.8 |
| 7 | 89 | 89 | 0 | 7 | 79 | 79 | 0 |
| 8 | 118 | 118 | 0 | 8 | 84 | 78 | -7.1 |
| 9 | 80 | 80 | 0 | 9 | 83 | -- | -- |
| 10 | 82 | 84 | 2.4 | 10 | 86 | 83 | -3.5 |
| 11 | 101 | -- | -- | 11 | 103 | 96 | -6.7 |
| 12 | 87 | 87 | 0 | 12 | 92 | 89 | -3.2 |
| 13 | 94 | 94 | 0 | 13 | 82 | 82 | 0 |
| 14 | 71 | -- | -- | 14 | 104 | 102 | -2 |
| Mean | 86.25 | 86.3 | 0.08 | | 90.62 | 88.33 | -1.8 |
| SD | 13.39 | 13.42 | | | 10.39 | 9.85 | |

**Table 3. Percentage body fat results at 12 weeks**

| P group participant | %BF pre | %BF post | % difference | S group participant | %BF pre | %BF post | % difference |
|---|---|---|---|---|---|---|---|
| 1 | 38.8 | 34.3 | -11.5 | 1 | 38 | 38.4 | 1 |
| 2 | 31.2 | -- | -- | 2 | 47 | 39.8 | -15.3 |
| 3 | 35.5 | 32 | -9.8 | 3 | 33.5 | -- | -- |
| 4 | 30 | 29 | -3.3 | 4 | 40.8 | 36.2 | -11.2 |
| 5 | 38.4 | 35.5 | -7.5 | 5 | 39 | 33 | -15.3 |
| 6 | 40.8 | -- | -- | 6 | 45.6 | 40.3 | -11.6 |
| 7 | 37.2 | 36.7 | -1.3 | 7 | 34.7 | 32.5 | -6.3 |
| 8 | 48 | 47.9 | -.2 | 8 | 37 | 35.1 | -5.1 |
| 9 | 33.7 | 31.3 | -7.1 | 9 | 35.2 | -- | -- |
| 10 | 35.6 | 35.6 | 0.0 | 10 | 32 | 29.1 | -9 |
| 11 | 43.1 | -- | -- | 11 | 41.8 | 39.5 | -5.5 |
| 12 | 35.2 | 32.5 | -7.6 | 12 | 35 | 29 | -17.1 |
| 13 | 38.4 | 37.9 | -1.3 | 13 | 41.1 | 37.6 | -8.5 |
| 14 | 32.6 | -- | -- | 14 | 45 | 39.8 | -11.5 |
| Mean | 37.08 | 35.27 | -4.9 | | 39.75 | 35.85 | -9.6 |
| SD | 4.66 | 5.19 | | | 4.67 | 4.11 | |

## Discussion

The purpose of this study was to test whether the GHS Symbiotropin Pro hGH can decrease percentage body fat, and increase muscle strength in the study group of women aged 45-67. This specific group was chosen because the declining functional capacity of older adults is a major concern, and the loss of muscle mass and strength is a prime cause. The data collected indicates that Symbiotropin Pro hGH can significantly increase isokinetic muscle strength in both flexors and extensors, and decrease waist circumference and percentage body fat over a period of twelve weeks.

These findings are consistent with numerous other studies involving hGH administration and body composition (1, 2, 3, 4, 12, 13, 14, 17, 18, 23, 38, 39, 53, 63, 77), and studies involving hGH and muscle strength (33, 37, 38, 39, 64, 65). This is the first study testing the effect of Symbiotropin on body composition and muscle strength. The mechanisms by which Symbiotropin exerts its effects on muscle and fat tissue to produce the results of this study may be ascribed to the anabolic and lipolytic effects of GH. Symbiotropin as a GHS, resists the effects of the GH inhibitor somatostatin, helping to increase the body's release of hGH. This in turn may have improved the utilisation of fat as a source of energy and inhibits the expression of LPL stimulating lipolysis (33), which may account for the decrease in %BF. Increased levels of hGH in the body also increases lean mass by stimulating protein catabolism (39), which may account for the increase in isokinetic muscle strength.

The significant decrease in %BF in the P group may be accounted for by a combination of the 'placebo effect', whereby a psychological belief in the treatment and a subjective feeling of improvement leads to a change in dietary and PA behaviour eliciting a positive response. The timing of the study may also be a factor, as the study commenced soon after the New Year, participants may have lost weight due to resuming normal nutritional habits after a season usually associated with an increase in calorific consumption. This is supported by the fact that in the P group there was no significant increase in muscle strength, which can only be produced by hGH or GHS therapy as this and other mentioned studies show, and resistance training (RT).

The results of this study are noteworthy because the consequences of sarcopenia can be extensive. Individuals are more susceptible to falls and fractures, impaired in ability to regulate body temperature, slower in metabolism, and may suffer an overall loss in the ability to perform everyday tasks (32). Muscle atrophy appears to result from a gradual loss of both muscle fibre size and number. A gradual loss in muscle cross-sectional area is consistently found with advancing age; by age 50, about ten per cent of muscle area is gone. After 50 years of age, the rate accelerates significantly. Muscle strength declines by approximately 15 per cent per decade in the sixties and seventies and by about 30 percent thereafter. Although intrinsic muscle function is reduced with advancing age, age-related decrease in muscle mass is responsible for almost all loss of strength in the older adult. The number of functional motor units also declines with advancing age, which requires surviving motor units to innervate a greater number of muscle fibres. Inactivity has been shown to play a role in preventing loss of muscle mass and strength, and RT is the key intervention to counter this and maintain or increase lean body mass, particularly the type II fast muscle fibres associated with strength and power that atrophy quicker. Among women over 50, 83% do not participate in enough PA to benefit their health (70). Because adherence to an PA routine is generally low in most population groups and especially older adults (70), the alternative of taking a dietary supplement that can produce an increase

**Table 4. Isokinetic muscular performance - Flexors at 12 weeks**

| P group participant | Peak torque pre | Peak torque post | % difference | S group participant | Peak torque pre | Peak torque post | % difference |
|---|---|---|---|---|---|---|---|
| 1 | 33 | 38 | 15 | 1 | 43 | 35 | -18.6 |
| 2 | 43 | -- | -- | 2 | 5 | 35 | 600 |
| 3 | 41 | 42 | 2.4 | 3 | 11 | -- | -- |
| 4 | 26 | 46 | 77 | 4 | 20 | 47 | 135 |
| 5 | 73 | 62 | 15 | 5 | 27 | 45 | 66 |
| 6 | 31 | -- | -- | 6 | 27 | 22 | -18 |
| 7 | 53 | 46 | -13.2 | 7 | 56 | 61 | 9 |
| 8 | 69 | 39 | -43.5 | 8 | 41 | 52 | 26.8 |
| 9 | 50 | 66 | 32 | 9 | 47 | -- | -- |
| 10 | 33 | 52 | 57.5 | 10 | 69 | 83 | 20.2 |
| 11 | 60 | -- | -- | 11 | 37 | 49 | 32.4 |
| 12 | 60 | 62 | 3.3 | 12 | 39 | 50 | 28.2 |
| 13 | 42 | 53 | 26 | 13 | 39 | 53 | 36 |
| 14 | 49 | -- | -- | 14 | 43 | 60 | 39.5 |
| Mean | 48 | 50.6 | 17.1 | | 36.3 | 50.63 | 32.4 |
| SD | 15.83 | 10.07 | | | 16.49 | 15.33 | |

**Table 5. Isokinetic muscular performance - Extensors at 12 weeks**

| P group participant | Peak torque pre | Peak torque post | % difference | S group participant | Peak torque pre | Peak torque post | % difference |
|---|---|---|---|---|---|---|---|
| 1 | 52 | 58 | 11.5 | 1 | 80 | 61 | -23 |
| 2 | 56 | -- | -- | 2 | 9 | 31 | 244 |
| 3 | 60 | 64 | 6.7 | 3 | 14 | -- | -- |
| 4 | 37 | 54 | 46 | 4 | 54 | 53 | -1.8 |
| 5 | 102 | 106 | 4 | 5 | 47 | 58 | 23.4 |
| 6 | 48 | -- | -- | 6 | 43 | 37 | -14 |
| 7 | 79 | 83 | 5 | 7 | 94 | 103 | 9.5 |
| 8 | 79 | 50 | -36.7 | 8 | 73 | 88 | 20.5 |
| 9 | 50 | 94 | 88 | 9 | 47 | -- | -- |
| 10 | 56 | 69 | 23.2 | 10 | 89 | 121 | 36 |
| 11 | 83 | -- | -- | 11 | 46 | 77 | 67.3 |
| 12 | 94 | 91 | 3.2 | 12 | 49 | 65 | 32.6 |
| 13 | 47 | 45 | 4.2 | 13 | 58 | 69 | 19 |
| 14 | 65 | -- | -- | 14 | 89 | 103 | 15.7 |
| Mean | 65.6 | 71.4 | 15.5 | | 60.91 | 72.16 | 19.3 |
| SD | 21.61 | 20.88 | | | 24.88 | 27.37 | |

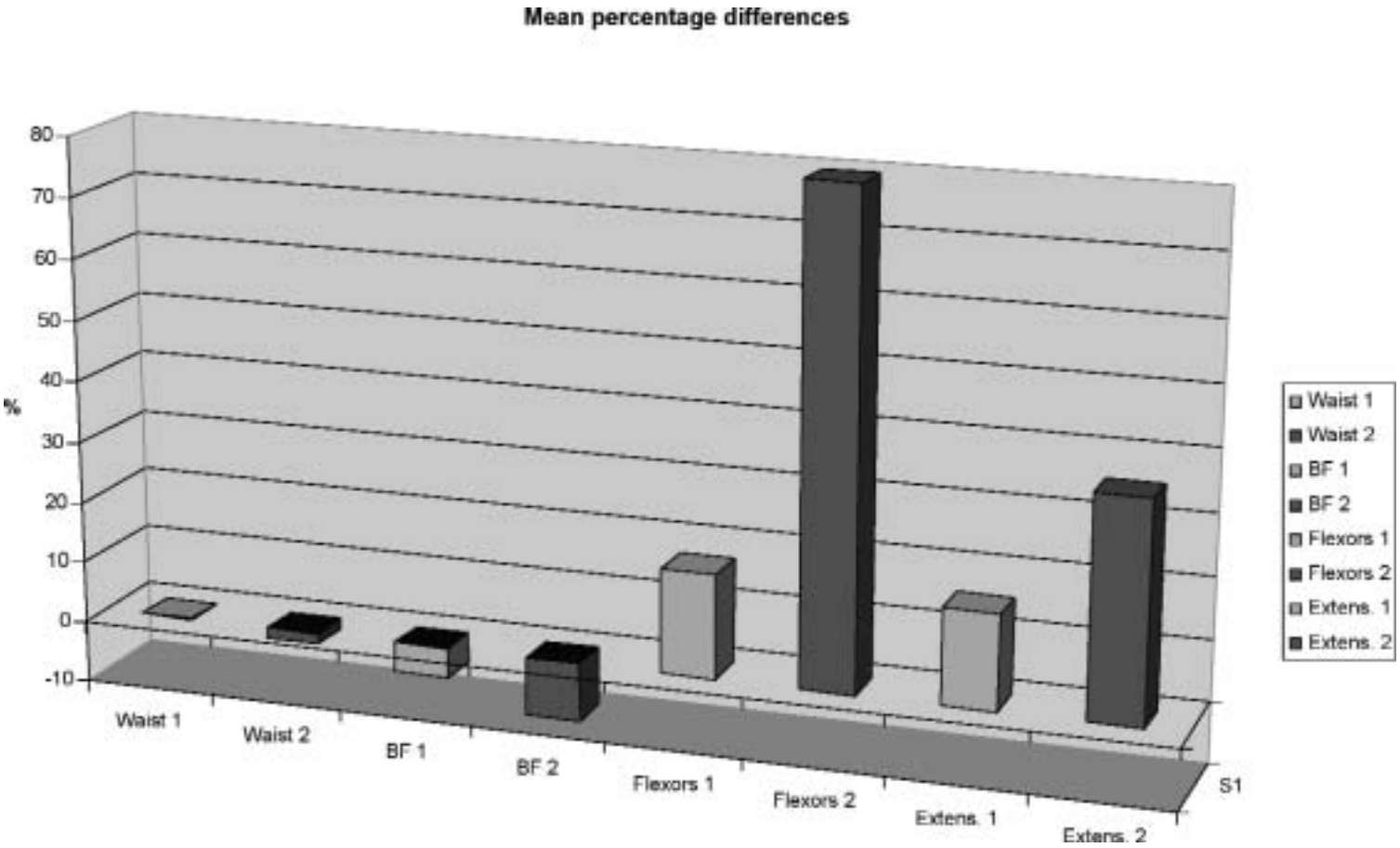
in muscle strength, and reduce %BF without having to exercise would be fundamentally attractive to many individuals.

Ageing and functional decline is now being taken so seriously that the United States National Institutes of Health have funded a seven year longitudinal study, targeted towards understanding the functional decline of healthier older adults, by focusing on older adults in transition from good health to frailty. The Health, Aging, and Body Composition Study (HEALTH ABC) cohort consists of 3,075 black and white men and women aged 70-79, and results so far have found that lower strength with older age was predominantly due to a lower muscle mass. Age and body fat also had significant inverse associations with strength and muscle quality. The researchers concluded that both preservation of lean mass and prevention of gain in fat may be important in maintaining strength and muscle quality in old age (51). The HEALTH ABC study also founds that among older adults, higher levels of visceral fat are associated with greater aortic stiffness (73), and higher levels of fat tissue increases risk of developing type 2 diabetes (25). These studies demonstrate the links between increased body fat, and decreased muscle strength with serious illness, functional capacity and quality of life in older adults.

Improved muscle strength can make the difference between an older adult being on their feet, or confined to the use of a stick or wheelchair, between being reliant on others and living in a home or living independently. Increased muscle strength has been shown to maintain independence and wellbeing (84), improve balance and coordination (72), and reduce risk of falls (68). A fall can have a devastating effect on an individuals independence, confidence and quality of life, often leading to a spiral of inactivity and further decline (76). The loss of muscle power in older adults at the rate of 30% per decade (69), is most pronounced in women (30), therefore improving muscle strength is a particular concern for women. In women over 50, 28% do not have the strength and power in their leg muscles to be able to climb the stairs easily, compared with 7% of men, and in women aged 70-74 this figure rises to 47% (70). The decrease is strength in women over 50 is greater than decreases in aerobic capacity and flexibility (70). Studies show that these figures can be drastically reduced by an increase in skeletal muscle strength, which results show can be achieved by treating growth hormone deficiency (GHD) with GH therapy.

GHD in adults is associated with reduced muscle mass and muscle strength, and previous studies involving hGH have also shown a significant increase in muscle strength. A study involving two years of hGH treatment in GH-deficient adults (33), increased and normalised isokinetic and isometric muscle strength. The GH-deficient subjects had lower isometric knee extensor, knee flexor, and hand-grip strength than the reference population. hGH treatment produced significant results in isometric knee extensor and flexor strengths. The increase in muscle strength was more marked in younger patients and in patients with lower initial muscle strength than predicted. Another study showed that participants who had been on GH therapy for a year, showed significantly increased isometric strength in the quadriceps muscle when compared with those who had been taking the therapy for four months or had taken a placebo (37), and other studies show similar results of GH treatment increasing muscle strength and mass (38, 39, 64, 65). These studies differ fundamentally in that the participants were GH deficient adults. This study chose participants randomly who were not known, or tested to show profound GHD, yet the results were as in earlier studies, still significant.

Before hGH research, resistance training was the established and




effective method of combating sarcopenia, increasing muscle mass and strength, and studies involving older adults have produced significant increases in both strength and muscle mass. One study involved 39 women with a mean age of 59, who were placed in a control group or strength training group that trained twice weekly for twelve months (49). In the study group, the one repetition max was increased by 74% (lattissimus dorsi pull-down), 35% (knee extensor), and 75% (leg press). The control group showed increases of 13%, 3.7%, and 18% respectively. Most strength gains in the study group occurred within the first twelve weeks of the study. Other studies have shown that older individuals can increase and maintain muscle mass with resistance training. One study showed that 70 year old men who had resistance trained since 50 years, had muscle cross-sectional area and strength comparable to a group of 28-year-old sedentary subjects (40). In another study, a group of 90-year-old individuals had a mean area enlargement of 12% in trained muscles after eight weeks of resistance training (24). These studies demonstrate that similar gains in muscle strength that were achieved in this study can be obtained from a programme of progressive resistance training, although, once again the potential problem of adherence to a physical activity programme has to be overcome.

Although there is a strong body of research supporting the role of GH as a means of increasing muscle strength or mass, research does exist that does not support a role for GH, either alone or combined with RT, as a means of increasing muscle strength in healthy male older adults (42). This study involved 31 men (age, 74 ± 1 yr), who were assigned to either RT group and placebo (n = 8), RT + GH (n = 8), GH (n = 8), or placebo (n = 7). Measurements of isokinetic quadriceps muscle strength; quadriceps muscle power; quadriceps muscle fibre type, size, and myosin heavy chain (MHC) composition; quadriceps cross-sectional area (CSA); body composition (dual-energy x-ray absorptiometry scanning); and GH-related serum markers were performed at baseline and after 12 weeks. Results found that GH alone had no effect on isokinetic quadriceps muscle strength, power, CSA, or fibre size. However, a substantial increase in MHC 2X isoform was observed with GH administration alone, and this may be regarded as a change into a more youthful MHC composition, possibly induced by the rejuvenating of systemic IGF-I levels. RT plus placebo caused substantial increases in quadriceps isokinetic strength, power, and CSA; but these RT induced improvements were not further augmented by additional GH administration. In the RT + GH group, there was a significant decrease in MHC 1 and 2X isoforms, whereas MHC 2A increased. RT, therefore, seemed to overrule the changes in MHC composition induced by GH administration alone. Changes in body composition confirmed previous reports of decreased fat mass, increased fat-free mass, and unchanged bone mineral content with GH administration, and worryingly, a high incidence of side effects were reported. It is difficult to account for these results, though it is possible that the GH used was inhibited by the actions of somatostatin, or the dosage may have been incorrect, especially as the participants experienced side-effects.

In conclusion, this data suggests that the GHS secretagogue Symbiotropin is a viable alternative to hGH injections, and cardiovascular and RT in normalising body composition and increasing muscle strength. Strength is a crucial component of quality of life. As life expectancy increases, the age-related decline in muscle strength becomes a matter of increasing importance. Maintenance of muscular strength significantly impacts an older person's ability to perform activities of daily living. In addition, maintaining and increasing strength to meet and exceed performance goals is important to a growing number of older adults who wish to live a fit, active lifestyle. In comparison to other studies involving hGH therapy and muscle

strength, this study is notable in that it produced significant results after only twelve weeks, whereas some studies lasted two years (33). Also participants in this study took one tablet per dose, whilst two tablets per dose have been used in previous studies involving Symbiotropin and is the recommended dose. Only one tablet was taken because that is the dosage that was approved by the Ethics Committee. The implications of hGH therapy are potentially enormous. According to research, all older adults are deficient in hGH (79), and other studies have shown that by age 70 to 80, 38% of the American adult population is as deficient in growth hormone as children who fail to grow normally because of a hormonal lack (63). If ageing is, as this and other studies suggest, a pituitary deficiency disease, then GHS treatment, which is more readily available as a food supplement than hGH which requires costly injections, may bring back the higher GH levels of youth which are associated with peak bodily functioning. GH treatment is not just for those who are grossly deficient. In middle and late adulthood, all adults experience a series of progressive alterations in body composition, including a loss of lean body mass, an increase in fat tissues, and atrophy of skeletal muscle, liver, kidney, spleen, skin and bone. It is possible that GH replacement will in the future become as routine as steroid, thyroid hormone, and sex hormone replacement therapy in management of the hypopituitary adult. The major restriction to the widespread use of GH is cost, which makes the GHS's a more attractive option. The prospect of GH replacement becoming routine, however, does raise a number of issues. The most fundamental of these relates to the selection criteria of patients who may benefit from GH therapy, as these results have shown that it is not only the severely GHD adult that can benefit. Whether the next generation of older adults, the 'baby boom' generation should be advised and recommended to take a supplement that may intervene in the ageing process, improve their quality of life, and may also extend their life-spans, or whether nature should be allowed to 'take it's course', is a topic that needs to be debated.

The results from this study, and the subjective changes also noted warrant further investigation and study into the therapeutic and anti-ageing potential of Symbiotropin. Further research could include a long-term study involving the safety and effectiveness of Symbiotropin treatment to show that it is as safe as GH therapy. A review of long-term (two and three year) studies involving lower doses of hGH found no evidence to suggest that this therapy caused any unfavourable long-term side-effects (61). GHD in adults is associated with abnormal average body composition, characterised by an increase in adipose tissue mass and a decrease in muscle mass and isokinetic skeletal strength. These changes are the logical results of the metabolic abnormalities that characterise the GHD syndrome. Long-term GH replacement therapy normalises body composition and increases muscle strength, and as the results of this study suggest, so does a 12 week course of the GHS Symbiotropin. Other research could also include men, though the majority of the studies conducted into hGH and ageing include male participants. And other variables could be tested, for example aerobic capacity. There were certain limitations involved in this study. A participant in the S group suffers from arthritis of the spine, and had very little strength at the initial testing stage, however made large improvements in strength during the course of the study. Her percentage differences of 600% for flexors and 244% for extensors may have had an effect on the results, though without her data, the mean increase in isokinetic muscle strength in the study group was still significant at 32.4% for flexors, and 16.8% for extensors. Improvements to the study design would include increasing the dosage of the supplement in the S group to two tablets per night, which is the recommended dosage by the manufacturers. This may have produced more profound results, or similar results but over a faster period of time. There was a high drop-out rate in this study (6 of the 28), and this may have been avoided if more participants had been chosen who lived close to the testing site, as a failure to attend the tests was a factor for the fall-out rate. There were also limitations regarding the reliability of the testing methods, in particular the percentage body fat measurements, because some of the participants were obese.

Caring for older adults is a major issue today with declining numbers of care homes, and insufficient pensions, this research adds to the increasing volume of studies that serve to enlighten the next generation of older adults the 40-60 year olds, increasing their awareness of the effects of ageing, and highlighting the effectiveness of certain anti-ageing methods to decrease the likelihood of their living dependent lifestyles when they reach older adulthood.

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## Appendix 4

Participants reported changes in study and control group (blank spaces indicate no noticed changes)

| Participant | Increased energy | Improved sleep | Felt leaner | Other changes noted |
|---|---|---|---|---|
| P1 | | | | |
| P2 | Did not complete study | | | |
| P3 | | | | |
| P4 | | | | |
| P5 | | | | |
| P6 | Did not complete study | | | |
| P7 | | | | |
| P8 | | | | |
| P9 | | | | |
| P10 | | | | |
| P11 | Did not complete study | | | |
| P12 | | | | Improved skin condition |
| P13 | | | | |
| P14 | Did not complete study | | | |
| S1 | Yes | Yes | | Improved mood |
| S2 | Yes | Yes | Yes | Hospital test revealed 0 fat reading in liver, improved mood |
| S3 | Did not complete study | | | |
| S4 | | | | |
| S5 | | | | Felt fitter, lower cholesterol reading |
| S6 | Yes | Yes | Yes | Less aches and pains, increased energy almost immediately, increased stamina, improved mood |
| S7 | Yes | | Yes | Improved muscle tone on face and legs, after a week on the supplement menstrual cycle restarted, hair condition improved |
| S8 | Yes | | | Improved muscle tone |
| S9 | Did not complete study | | | |
| S10 | | | | |
| S11 | Yes | Yes | | Hot flashes stopped, felt more aches and pains |
| S12 | | | Yes | Improved muscle tone in arms |
| S13 | Yes | Yes | Yes | Increased stamina, improved muscle tone, elevated mood |
| S14 | Yes | Yes | Yes | Increased libido, improved muscle tone |