

# Retrospective Assessment of Changes in Perceived Health Status during Continuous Use of a Dietary Supplement

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## Abstract

Dietary factors play an important role in human health. Specifically, nutritional interventions may have an impact on the hypothalamic-pituitary axis resulting in positive health outcomes. A retrospective health status survey of 386 respondents was conducted to investigate the potential of a dietary supplement, Nutrifii™ Renew, for improving various health outcomes in comparison to a multivitamin/mineral control group. Among those who ingested Renew, 95% reported experiencing at least some improvement in one or more health categories. Compared to the multivitamin/mineral group, the Renew group reported earlier and/or greater improvements in several health status categories including sleep, reproductive health, memory, energy/stamina, skin and hair quality, flexibility, exercise recovery and feeling rested in the morning. A clear majority (84.9%) of Renew consumers reported experiencing noticeable improvement in some aspect of their health within one month. Among those who felt an improvement in sleep, most reported experiencing a change within one week. These improvements were likely due to the synergistic effects of L-arginine, L-citrulline, L-lysine, and botanical extracts on nitric oxide production, growth hormone (GH) release, and sleep quality. The observed improvements in skin elasticity and hair growth may be related to increased GH levels and IGF-1 production. Overall, these findings suggest that Renew may have potential as a dietary intervention for improving various health outcomes beyond those provided by multivitamin/mineral supplementation alone. Further studies are needed to confirm these findings and elucidate the underlying mechanisms of action.

## Keywords

Dietary Supplement, Health Status, Retrospective Survey

## 1. Introduction

The hypothalamic-pituitary axis (HPA) is an integral part of homeostatic control. Upon receiving feedback from the nervous system and different tissues of the body, the hypothalamus regulates the function of the pituitary gland through various releasing and inhibiting hormones. In response to these hypothalamic hormones, the pituitary will produce hormones that will, in turn, elicit responses from other glands and target organs. Among the hormones produced by the anterior portion of the pituitary is growth hormone [1]. Growth hormone (GH), as its name implies, stimulates growth and development, especially during childhood and adolescence. In adults, GH plays an important role in maintaining muscle and bone mass, promoting lipolysis, carbohydrate metabolism, cardiovascular function, aerobic exercise capacity and cognitive function. However, adults begin to experience a progressive decline in GH secretion which decreases by approximately 15% for every decade of life [2]. GH secretion rates may decline to less than one-quarter of the maximum achieved in mid-to late puberty [3]. This decline can, of course, have profound effects on overall health and is associated with changes in body composition, diminished physical and cognitive function, thinning of the skin, and reduced quality of life [4].

Nutritional interventions have been found to have a positive impact on GH secretion. A study involving young healthy males demonstrated that co-ingestion of 1200 mg L-lysine and 1200 mg L-arginine provoked a significant increase in blood GH levels [5]. Another clinical trial revealed that 3 weeks of consuming L-arginine and ornithine, a precursor of L-citrulline, increases serum GH levels in strength-trained athletes [6] [7]. Arginine supplementation also increased GH levels in elderly volunteers [8]. Several other studies have likewise demonstrated the pro-GH influence of L-arginine supplementation [9].

GH deficiency is associated with several impaired health states [10]. Conversely, improved blood levels of GH and insulin-like growth factor 1 (IGF-1), a major mediator of GH's biological activity, are associated with improved health status [11]. Against this background, a dietary supplement, Nutrifii™ Renew (Partner. Co, Midvale, Utah, USA), was formulated with a blend of amino acids (L-arginine, L-Lysine, citrulline and beta-alanine), botanical ingredients, gamma-aminobutyric acid (GABA) and several nutrients to address declines in GH production in adulthood. The botanical ingredients in this dietary supplement synergistically inhibit DPP-4, an enzyme that reduces GH secretion. Further, case reports of individuals consuming this supplement suggest that the combination of ingredients is effective in restoring some level of GH production, or at the very least, produces perceived improvements in symptoms that may be associated with improved GH status [12].

The current study was conducted to further evaluate the perceived health benefits of this dietary supplement blend (Nutrifii™ Renew, hereafter referred to as Renew) among a larger number of consumers. Multivitamin and mineral supplement consumers were included as a control or reference, group. While not

a true placebo group, as vitamins and essential minerals are biologically active, this group provides a comparison by which any unique perceived health benefits, beyond those expected from common nutrients, may be detected.

## 2. Methods

### 2.1. Participants and Retrospective Survey

Possible participants were identified through sales records for the Renew and multivitamin/mineral supplements. Those who had purchased these supplements were contacted via email. If the purchaser indicated a willingness to participate in this study, they were sent a link to an online survey designed to gather relevant information. Informed consent was obtained from each participant. The survey was presented to an ethics committee for review and approval and was conducted in accordance with recommendations of the National Research Council of the National Academies and as outlined by the American Association for Public Opinion Research [13].

Using the online survey, demographic information (age, gender, country/region of residence) was collected from all participants. Information regarding the length of time of supplement use was also gathered. Participants were then asked to select one of several agreement options—strongly agree, agree, somewhat agree, somewhat disagree, disagree, strongly disagree, not applicable—after being presented with the request, “Please consider how you felt before you started taking the dietary supplement for the following statements.” The health statements they were asked to consider are summarized in **Table 1**.

**Table 1.** Health statements to which survey participants were asked to respond by selecting one of several agreement options.

Health statements
Trouble falling and/or staying asleep
Decreased libido and/or sexual function
Brain fog and/or a lack of memory function
A lack of energy and/or stamina
Hard to lose, stubborn body fat
Dull, sagging and/or wrinkled skin
Dull, slow-growing and/or thinning hair
Graying hair
Trouble feeling rested after waking up in the morning
Joint discomfort
Trouble with flexibility
Aches and pains in my bones and/or joints
Trouble recovering after exercise

Participants were then asked to select a level of improvement experienced—no improvement, very little improvement, some improvement, good improvement, great improvement—relative to the same health statements in **Table 1**, when presented with the request, “Now, please consider your experience after you started taking the dietary supplement. Rate the level of improvement you may be experiencing with the following health statement.” This was followed up with the question, “Approximately, how long did it take for you to notice this improvement?” In response, participants were then able to select among the various lengths of time—less than 1 week, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, more than 8 weeks. An open section for additional feedback was also offered to capture any comments that participants wanted to offer regarding their experience with the dietary supplements.

## 2.2. Data Analysis

Categorical response rates were calculated as percentages. Intergroup differences in demographics, baseline perceived health status, improvements in perceived health and duration of supplement ingestion until the appearance of noticeable improvements were investigated. Chi-square tests were used to evaluate these differences among the responses of the Renew and multivitamin/multimineral groups.

## 3. Results

There were 386 respondents in this study (ages 25 to  $\geq 70$  years; males,  $n = 77$  among both groups), with the majority ( $n = 287$ ) being Renew consumers. There were no significant differences in age or gender distribution between the two groups. Relative to perceived health prior to supplementation, there were no significant differences except in two areas. A greater percentage of those in the Renew group felt that they had more sleep difficulties and poorer skin quality than those in the multivitamin/multimineral group. Just over 71% of those in the Renew group agreed, to some extent, that they had trouble falling or staying asleep whereas just over 57% of those in the multivitamin/multimineral supplement agreed that sleep was an issue for them. A clear majority of those who consumed Renew was not sleeping well enough, while only a slight majority felt that way in the other group. Responses regarding the prevalence of dull, sagging and/or wrinkled skin were similar to those regarding sleep. About 73% of the Renew group agreed, at least somewhat, that they had poor skin quality prior to ingesting Renew. Among the multivitamin/multimineral group, just over half (53%) felt that they had some degree of dull, sagging, or wrinkled skin. But both groups were similar in the fact that sleep and skin quality were perceived to be a problem for most people. There were no other statistically significant differences in levels of agreement with the other 11 health statements. As such, the two groups appeared to be very similar in age, gender and perceived health status prior to their ingestion of the supplements.

Most participants (65.4%) had taken Renew for more than 8 weeks. Only 8.0% had been taking it for less than 4 weeks before participating in the survey. The remainder had taken Renew between 4 and 8 weeks (3.1% for 4 weeks, 4.9% for 5 weeks, 7.3% for 6 weeks, 3.5% for 7 weeks, 7.7% for 8 weeks). Among the group taking Renew, there were 2.5 times more total agreement responses (somewhat agree, agree or strongly agree) than disagreement responses to the 13 health statements. In fact, only 7 respondents did not agree with any of the health statements. This indicates a very high percentage of people in this group experiencing some health challenges.

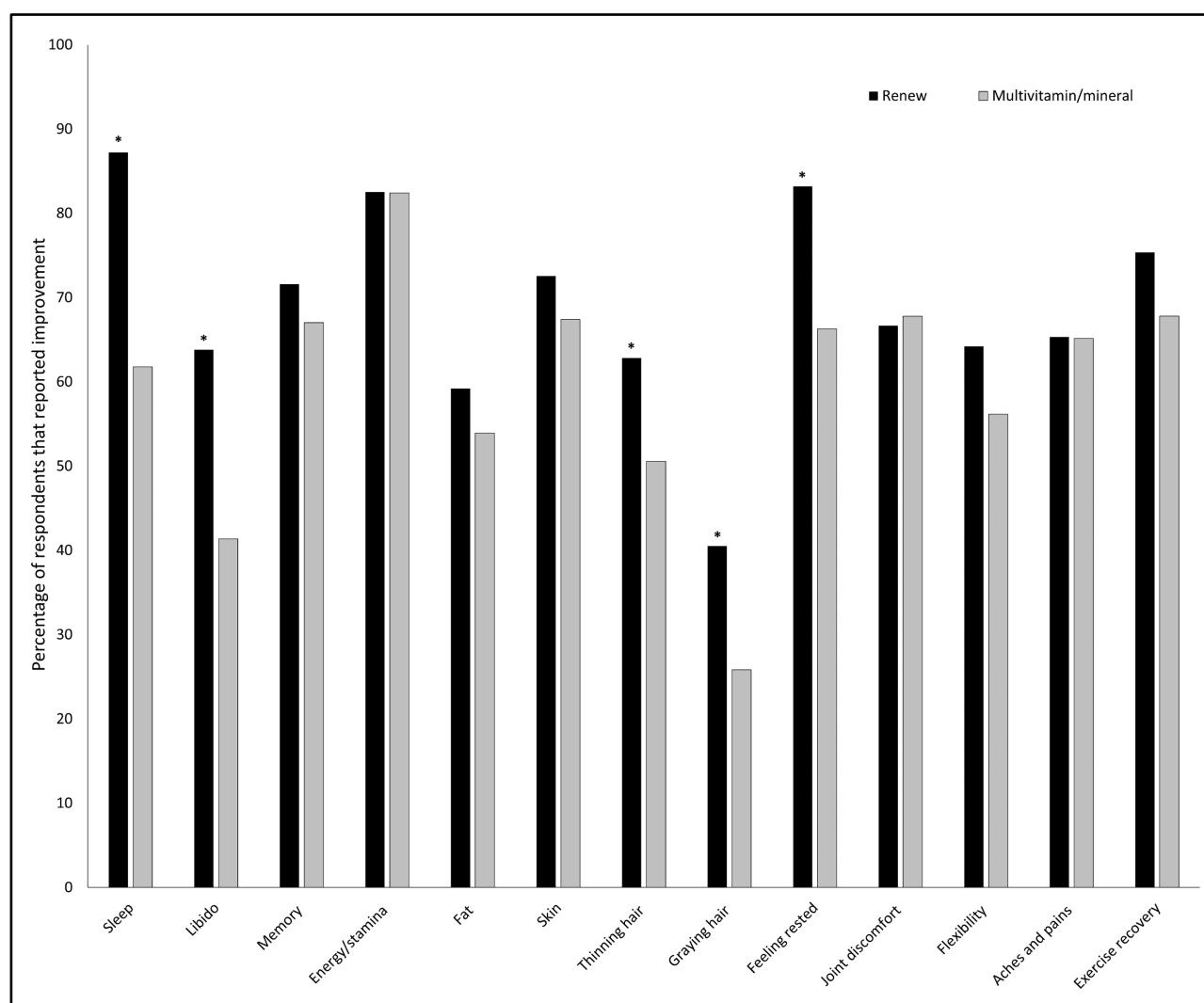
Percentages of the varying levels of perceived improvements among those who were taking Renew are summarized in **Table 2**. Among this group, 95% reported that they experienced at least some improvement in one or more health categories. Only 11 of the 281 respondents did not report at least some improvement in at least one area. Within each health statement category, a clear majority of participants (>58%) taking Renew reported experiencing at least some level of improvement. The only exception was graying hair, in which only around 41% observed some improvement or better. Further, more than

**Table 2.** Percentage of participants reporting various levels of improvement after taking renew.

Health Statement	Percentage of Participants Reporting Various Levels of Improvement				
	Great improvement	Good improvement	Some improvement	Very little improvement	No improvement
Trouble falling and/or staying asleep	32.25	31.88	22.83	6.52	6.52
Decreased libido and/or sexual function	10.80	21.20	31.70	14.70	21.60
Brain fog and/or a lack of memory function	12.50	26.70	32.20	15.80	12.80
A lack of energy and/or stamina	23.10	35.40	24.20	9.00	8.30
Hard to lose, stubborn body fat	9.90	18.20	30.70	20.40	20.80
Dull, sagging and/or wrinkled skin	14.00	24.00	34.40	12.90	14.70
Dull, slow-growing and/or thinning hair	14.44	18.15	30.37	15.93	21.11
Graying hair	5.30	13.20	22.20	24.10	35.30
Trouble feeling rested after waking up in the morning	32.60	26.40	24.30	8.70	8.00
Joint discomfort	11.00	24.30	31.30	13.20	20.20
Trouble with flexibility	11.00	21.20	31.90	15.40	20.50
Aches and pains in my bones and/or joints	11.72	21.25	32.23	17.22	17.58
Trouble recovering after exercising	15.60	29.30	30.40	9.60	15.20

58% reported good or great improvements in sleep, energy/stamina, and feeling rested after waking in the morning. Over 32% reported good or great improvements in cognition/memory, skin quality, hair quality, joint discomfort, flexibility, aches and pains and recovery after exercise.

A larger percentage of Renew consumers than multivitamin/mineral consumers reported some improvement or better in 12 of the 13 health status categories, **Figure 1**. In five health-status categories, the difference was significant: “trouble falling and/or staying asleep” ( $P < 0.0001$ ), “decreased libido and/or sexual function” ( $P < 0.01$ ), “dull, slow-growing and/or thinning hair” ( $P < 0.05$ ), “graying hair” ( $P < 0.05$ ) and “trouble feeling rested after waking up in the morning” ( $P < 0.0001$ ). The positive response rate (some improvement or better) in the Renew group was approximately 41.1% larger for falling/staying asleep, 54.2% higher for libido/sexual function, 25.5% more for feeling rested and 56.8% greater for group were even more dramatic. The fraction of the Renew group reporting



**Figure 1.** Comparison of perceived improvements in different health status categories in Renew and multivitamin/mineral groups. \* $P < 0.05$ .

good or great improvement in graying hair was 175.3% greater than in the multivitamin/mineral group ( $P < 0.05$ ). The proportion of those reporting good or great improvements in staying/falling asleep, libido sexual function and feeling rested after waking were 105.3%, 73.5% and 64.4%, respectively, more than in the multivitamin/mineral group ( $P < 0.05$ ).

The percentages of Renew consumers who reported noticing some degree of improvement in the various health status categories, at different time points, are presented in **Table 3**. Most people (84.9%) reported experiencing noticeable improvement in some aspect of their health within one month of consuming Renew daily. Further, 62.1% reported some level of improvement within one week. With falling and/or staying asleep, 63.5% reported improvement by 1 week. In fact, 41.2% reported feeling improvement in less than one week. By 4 weeks, the percentage increased to 89.7%. Regarding those who noticed feeling more rested in the morning, 87.5% of those taking Renew felt an effect in 4 weeks or less, with 49.5% experiencing improvement within 1 week. 85.0%

**Table 3.** Percentage of renew consumers reporting when improvement in health was first noticed while consuming the supplement daily.

Health Statement	Percentage of Respondents First Noticing Improvement at Specified Time									
	<1 week	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	>8 weeks
Trouble falling and/or staying asleep	41.20	22.30	14.60	6.90	4.70	0.90	1.70	0.00	3.90	3.90
Decreased libido and/or sexual function	14.90	13.50	22.30	6.10	16.20	2.00	4.10	1.40	5.40	14.20
Brain fog and/or a lack of memory function	12.00	21.30	20.80	9.30	14.80	2.20	2.20	0.50	7.70	9.30
A lack of energy and/or stamina	20.30	20.30	21.70	10.40	12.30	1.90	3.30	0.00	3.30	6.60
Hard to lose, stubborn body fat	6.70	14.80	9.40	11.40	18.10	2.70	7.40	2.70	10.70	16.10
Dull, sagging and/or wrinkled skin	7.10	8.70	13.10	11.50	24.60	2.70	7.10	1.60	9.80	13.70
Dull, slow-growing and/or thinning hair	6.50	7.10	9.10	13.00	26.60	5.80	7.10	1.30	9.10	14.30
Trouble feeling rested after waking up in the morning	29.60	19.90	15.30	8.30	14.40	1.40	0.90	0.00	4.20	6.00
Joint discomfort	13.80	11.40	19.80	10.80	19.80	3.00	3.60	0.60	6.00	11.40
Trouble with flexibility	10.60	13.70	11.80	15.50	20.50	2.50	5.60	0.00	8.10	11.80
Aches and pains in my bones and/or joints	13.50	12.90	16.00	9.20	22.70	4.90	1.20	1.80	7.40	10.40
Trouble recovering after exercising	12.40	14.60	20.50	13.00	23.20	2.20	3.20	0.50	2.70	7.60

noticed an improvement in energy and/or stamina by 4 weeks, while 40.6% noticed this in 1 week or less. Sleep quality, and the subsequent improvement in energy levels, appear to be major targets of this dietary supplement.

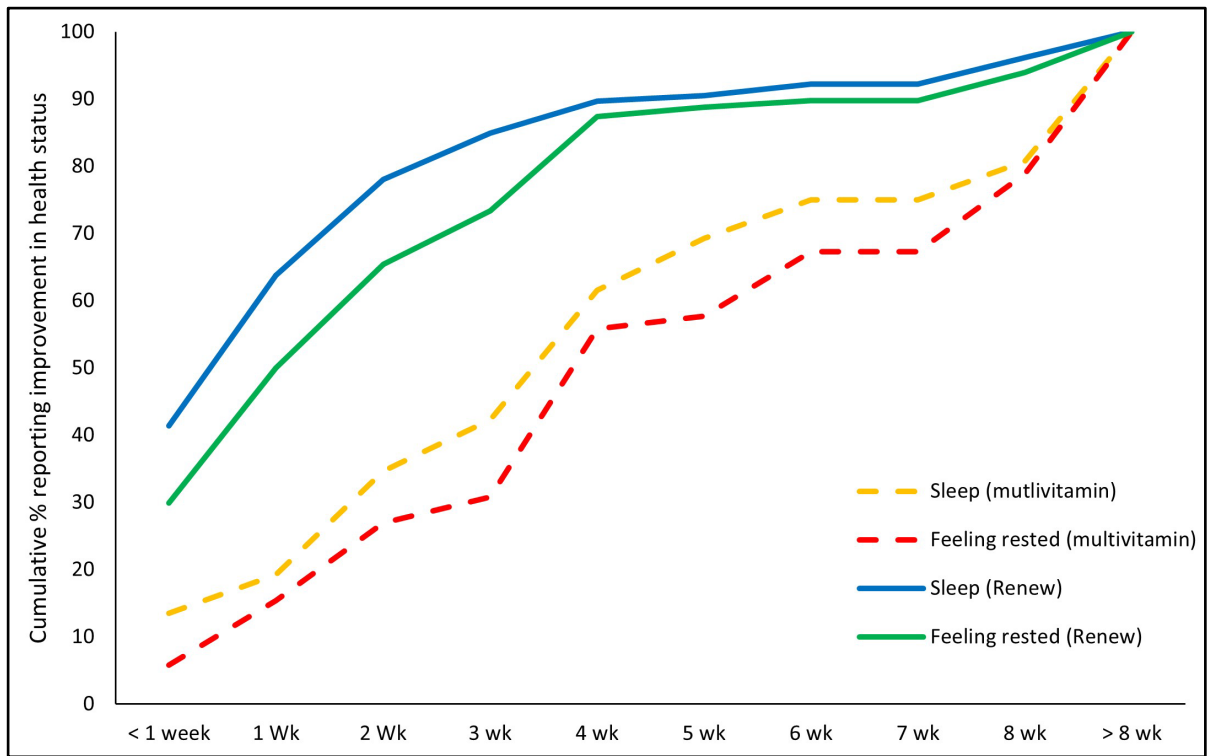
The percentages of respondents who reported noticeable benefits in the other health status categories within 1 week and then by 4 weeks were, respectively, as follows: decreased libido and/or sexual function, 28.4% and 73.0%; brain fog and/or a lack of memory function, 33.3% and 78.2%; hard to lose, stubborn body fat, 21.5% and 60.4%; dull, sagging and/or wrinkled skin, 15.8% and 65.0%; dull, slow-growing and/or thinning hair, 13.6% and 62.3%; joint discomfort, 25.2% and 75.6%; trouble with flexibility, 24.3% and 72.1%; aches and pains in my bones and/or joints, 26.4% and 74.3%; trouble recovering after exercising, 27.0% and 83.7%.

In general, those taking Renew reported experiencing the appearance of several perceived health benefits sooner than those taking multivitamin/mineral supplements. At every time point up to 8 weeks, the cumulative percentages of those noticing an improvement in health status are greater in the Renew group than in the multivitamin/mineral group. This difference was significant for several health status categories including the following: trouble falling and/or staying asleep ( $P < 0.0001$ ); brain fog and/or a lack of memory function ( $P = 0.001$ ); lack of energy and/or stamina ( $P = 0.006$ ); dull, sagging and/or wrinkled skin ( $P = 0.003$ ); dull, slow-growing and/or thinning hair ( $P = 0.007$ ); trouble feeling rested after waking up in the morning ( $P < 0.0001$ ); trouble with flexibility ( $P = 0.016$ ); and trouble recovering after exercising ( $P = 0.010$ ). Two of the most notable examples of the differences in the timing of noticeable changes in health status are related to sleep and feeling rested in the morning, **Figure 2**. Within a few days, a significant number of those ingesting Renew experienced an improvement in sleep and in feeling rested in the morning after waking.

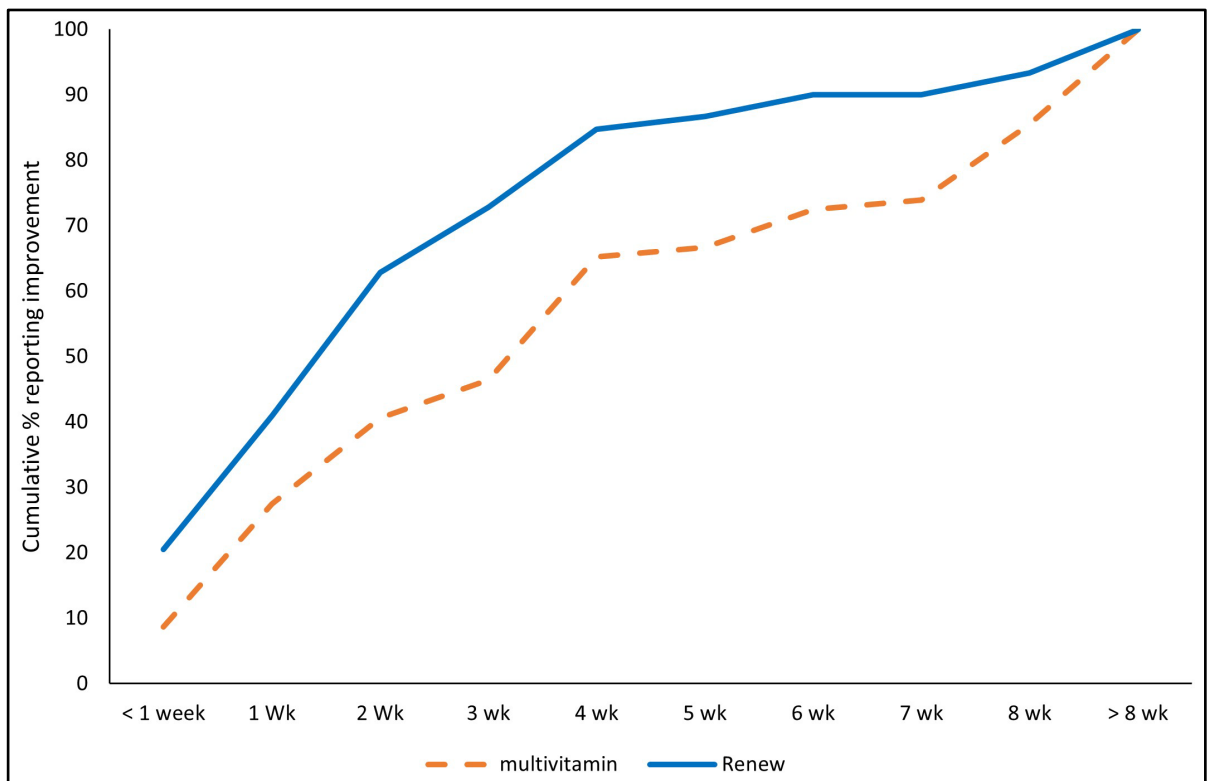
The percentage of those reporting an improvement in sleep in less than one week was approximately three times greater in the Renew group than in the multivitamin/mineral group. The percentage in the Renew group that experienced improvements in feeling rested within the same time frame was over five times greater than that of the multivitamin/mineral group. The intergroup differences seen in the time of onset of perceived improvements in sleep and restfulness are dramatic and appear very early. These differences are maintained until after 8 weeks. It is important to note that all cumulative percentages will eventually reach 100% since this is a comparison of when positive changes were first noticed among all those in each supplement group that reported experiencing improvements in the various health status categories.

For improvements in energy and/or stamina, the first-week emergence rate in the Renew group was more than double that of the multivitamin/mineral group, **Figure 3**. As with sleep and feeling rested after waking, consistently larger percentages of the Renew group reported earlier appearances of improvements in energy and/or stamina than those of the multivitamin/mineral group.





**Figure 2.** Time by which various percentages of respondents in the Renew and multivitamin/mineral groups reported feeling improvements in falling and/or staying asleep and feeling rested after waking up in the morning.

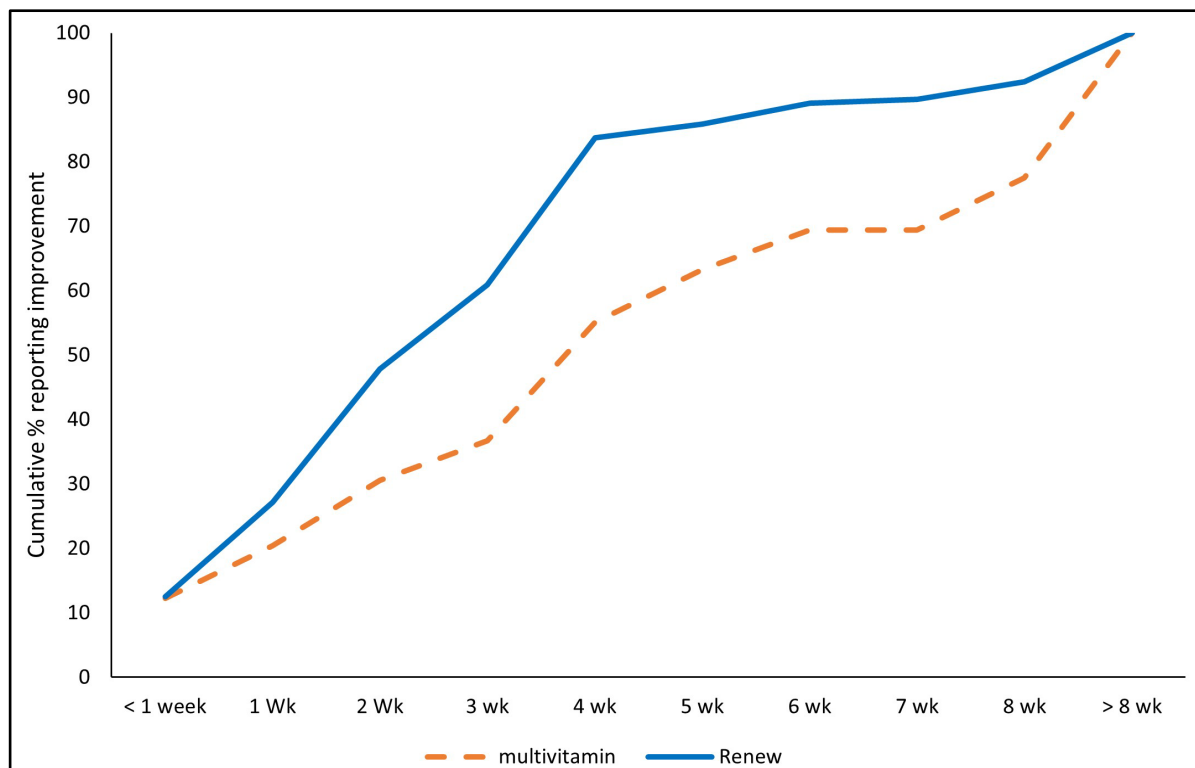


**Figure 3.** Time by which various percentages of respondents in the Renew and multivitamin/mineral groups reported feeling improvements in energy and/or stamina.

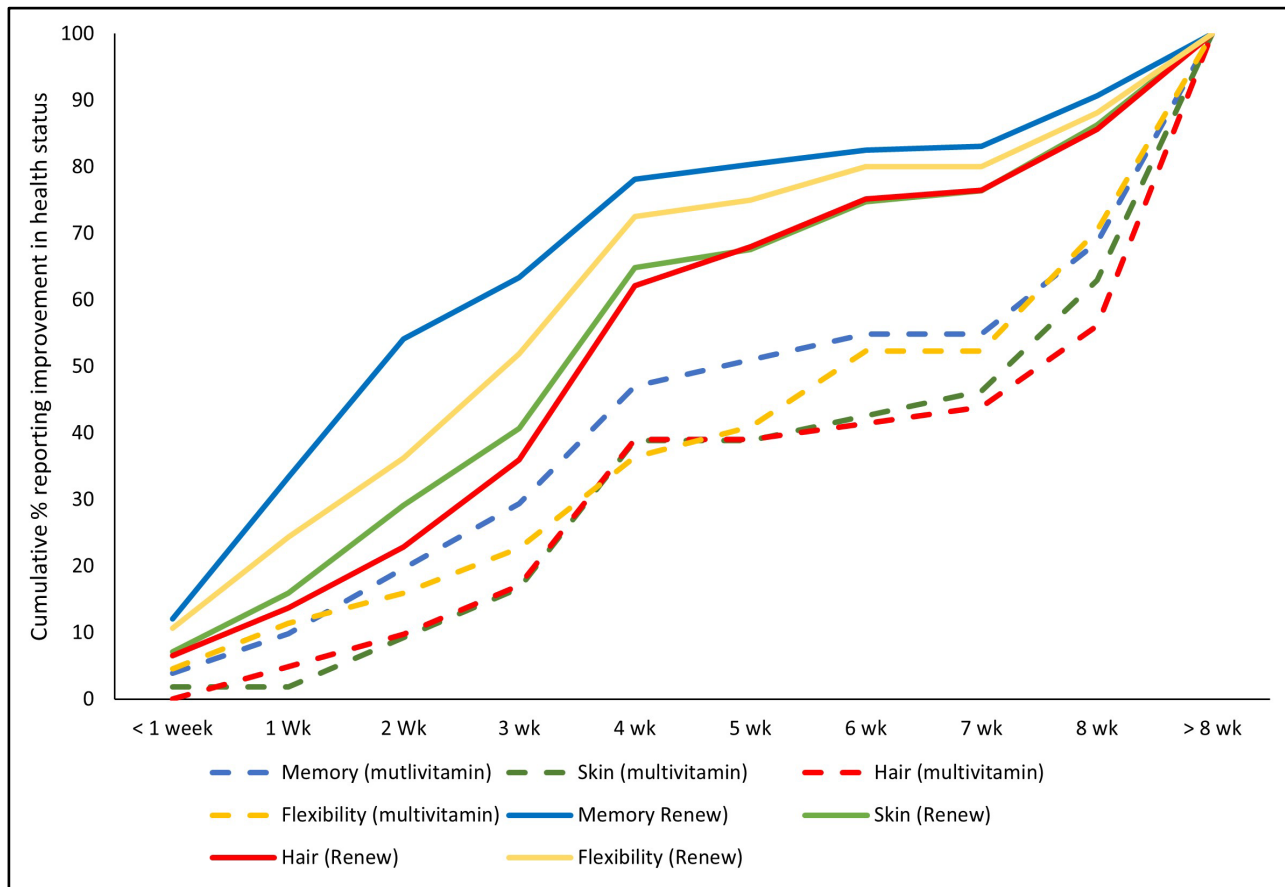
More than 80% had felt an improvement by week 4, as was the situation with sleep and restfulness. The similar patterns of appearance in these three health status categories are likely interrelated. Improved sleep can obviously lead to feeling well-rested in the morning. Sleep deprivation may reduce physical endurance [14]. Conversely, improved sleep status improves overall energy levels as well as physical stamina [15].

With trouble recovering after exercising, there is little to no difference in the percentage of people who first experience improvement during the first few days of taking either Renew or the multivitamin/mineral supplements. However, the cumulative percentages increasingly diverge until 4 weeks, **Figure 4**. Afterward, the difference remains significant until after 8 weeks. With more than 80% of the Renew group reporting the emergence of a noticeable improvement in exercise recovery by week 4, there was not as much week-to-week increase in the remaining four weeks. Indeed, only 10% reported experiencing the appearance of an improvement between weeks 4 and 8. But in the multivitamin/mineral group, about 55% had experienced an improvement in exercise recovery during the first four weeks. Approximately 22% in this group did not report experiencing any such improvement until they had ingested a multivitamin/mineral supplement for more than one month and up to 8 weeks.

The other health status categories in which there was a significant difference between the timing of the first appearance of improvements followed similar



**Figure 4.** Time by which various percentages of respondents in the Renew and multivitamin/mineral groups reported feeling improvements in recovery after exercise.



**Figure 5.** Time by which various percentages of respondent in the Renew and multivitamin/mineral groups reported feeling improvements in specific health status categories.

patterns. Notable differences between the Renew and multivitamin/mineral groups occurred in less than one week, accompanied by the majority of those taking Renew feeling an improvement within the first four weeks (**Figure 5**). Finally, no significant adverse events were associated with the use of Renew.

#### 4. Discussion

We learn from this survey that most people felt some improvement in their health when taking either supplement. This is not surprising given the voluntary purchase of the supplements in expectation of health benefits. Thus, the comparison between the experiences of the two supplement groups is important in our effort to estimate the potential efficacy of Renew as well as explore health outcomes that may be useful for further evaluation in human clinical trials. The use of a multivitamin/mineral control, or reference, group provides some advantages. The importance of vitamins and essential minerals in maintaining health, and even life, is well established, and supplementation of these nutrients may have several potential benefits to health [16]. This is even truer in conditions of nutrient deficit [17]. Therefore, the multivitamin/mineral group provides a comparison against an effective intervention against which the potential

efficacy of Renew may be assessed.

Four weeks of multivitamin/mineral supplementation was reported to reduce physical and cognitive fatigue in healthy young adults following exercise [18]. A meta-analysis indicated that multivitamins may be a useful strategy for increasing immediate free recall memory [19]. Further, a 16-week trial found that participants who had taken a daily multivitamin supplement reported greater improvements in energy levels, mood, and sleep than those in a placebo group [20]. Multivitamin supplementation also led to significant decreases in fatigue and sleep disorders in women with chronic fatigue syndrome [21]. In our survey, Renew consumers reported slightly higher rates of improvement in memory function and energy/stamina. But these improvements were reported to appear significantly earlier in those taking Renew versus those only ingesting multivitamin/mineral supplements. With falling or staying asleep, improvement was significantly greater in those taking Renew, both in percentage and in time of appearance of improvement, suggesting that the blend of ingredients may provide benefits that go beyond those provided by vitamins and essential minerals alone.

Additional comparisons are likewise useful. A one-year intervention study found a significant increase in testosterone levels in men who had ingested more than 5 times the daily value of vitamin D [22]. Vitamin D deficiency is associated with reproductive dysfunction in men between the ages of 18 and 40 years [23]. In women ages 27 to 38 years, there is a positive correlation between serum vitamin D levels and hormone status, indicating that this vitamin may increase fertility through the modulation of androgen activity [24]. Thus, it appears that vitamin supplementation may provide some benefit to libido and/or sexual function. In fact, approximately 40% of those in the multivitamin/mineral group reported improvements in this area. But the Renew group reported significantly greater rates, with just over 63% experiencing at least some improvement in reproductive health and half of these claiming good or great levels of improvement. L-arginine is certainly a contributing factor to these improvements. A review of several clinical trials reveals that libido is increased in females by L-arginine supplementation regardless of age [25]. Another study of 120 men with erectile dysfunction (ED) of varying etiologies found that they had low L-arginine and L-citrulline levels [26]. A systemic review and meta-analysis provide evidence for the efficacy of arginine-related supplements for mild to moderate ED [27]. L-citrulline supplementation also improved ED in a one-month, single-blinded study involving patients with mild ED [28].

The mechanism of action behind these improvements likely involves increased circulating nitric oxide (NO) production from L-arginine by endothelial nitric oxide synthase (eNOS) activity. As mentioned previously, L-citrulline is a precursor of L-arginine and may help increase plasma levels and subsequent circulating NO [29]. L-lysine is an arginase inhibitor, which further shunts L-arginine metabolism towards nitric oxide production by eNOS [30]. The increased NO leads to dilation of the blood vessels which, consequently, causes

vasocongestion of the reproductive organs. This is one of the major mechanisms by which the combination of these three amino acids (L-arginine, L-citrulline and L-lysine) impacts reproductive function.

The earlier appearances of improvements in energy and/or stamina and exercise recovery may also be due to the combination of the amino acids. L-arginine increases NO and mitochondrial biogenesis in athletes within 4 weeks of daily supplementation [31]. L-arginine also improved aerobic and anaerobic athletic performance [32]. These results are presumably mediated via increased NO production and NO cell signaling [33]. For exercise recovery, NO may also promote muscle repair [34]. But NO may also aid recovery by accelerating lactate excretion from the body [35].

Another important feature of these amino acids is their well-known ability to impact GH production. L-arginine, especially in combination with L-lysine, limits the production and release of somatostatin by the hypothalamus [36]. As this effect is dose-dependent, improved absorption and transport of these amino acids across the blood-brain barrier will influence the degree of GH production. L-arginine and L-lysine are actively transported across the blood-brain barrier by System  $\gamma^+$  (gamma-plus) transporters [37]. L-arginine and L-citrulline co-ingestion increases blood levels of L-arginine more than just L-arginine alone because L-citrulline avoids first-pass metabolism by the liver and is converted into L-arginine [38] [39]. The increased availability of L-arginine to the hypothalamus, following active transport across the blood-brain barrier, results in greater suppression of somatostatin release by the hypothalamus and allows greater GH release from the pituitary. An increase in GH biosynthesis and the subsequent increase in IGF-1 will promote muscle repair and growth, which may explain an additional mechanism responsible for the perceived improvements in exercise recovery and stamina.

As stated earlier, the botanical ingredients in this dietary supplement synergistically inhibit DPP-4. As DPP-4 is a proteolytic enzyme that degrades growth hormone-releasing hormone, the blend of botanical ingredients may offset GH decline in adults [40] [41]. DPP-4 also degrades glucagon-like peptide-1 (GLP-1), a peptide that contributes to blood glucose control by stimulating insulin secretion from pancreatic  $\beta$  cells [42]. Lower glucose levels, in turn, stimulate GH release from the pituitary [43]. Therefore, these ingredients influence circulating GH levels through at least two biological pathways.

Sleep also influences GH production [44]. Gamma-aminobutyric acid (GABA) supplementation can augment sleep and maybe a major contributor to the improvements reported with trouble falling and/or staying asleep and trouble feeling rested after waking up in the morning. GABA reduced sleep latency (time required to fall asleep) by several minutes in human volunteers and improved the early stages of sleep, while increasing the total non-rapid eye movement (non-REM) sleep time [45] [46]. It also improved sleep quality within 4 weeks for those with insomnia [47]. Improved sleep quality and time may also improve other health status categories evaluated in this survey, such as energy and/or

stamina and brain fog and/or a lack of memory.

The potential for GABA to increase GH production is not just limited to indirect improved-sleep evidence. Co-ingestion of GABA and whey protein for 12 weeks significantly increased growth hormone levels and increased lean mass in young men, especially when compared to ingesting whey protein alone [48]. In an 8-week clinical trial, GABA supplementation significantly improved triglycerides, fat/lean mass, growth hormone levels, insulin-like growth factor levels, muscle strength and joint flexibility of middle-aged Japanese women [49]. For women with dry skin, fatigue and sleep disorder, taking a GABA supplement for 8 weeks increased skin elasticity of the cheek [50]. Such skin improvements are associated with increased GH levels. Evidently, GABA may contribute to significant and rapid improvements in several healthy status categories.

In a cross-sectional study involving 617 middle-aged volunteers, increased serum IGF-1 was associated with a lower perceived age due to reduced facial wrinkling [51]. IGF-1 helps regulate cellular proliferation and migration during hair follicle development [52]. This property of IGF-1 may be responsible for the increased rates of improvement in thinning hair reported by the Renew group. The observation that dermal papillary cells from balding scalp follicles secrete significantly less IGF-1 than non-balding scalp follicles lends support to this possible mechanism of action [53]. Vitamin intake, especially higher vitamin D intake, has been associated with some increase in circulating IGF-1 levels [54]. The significantly greater rate of improvements reported by the Renew group in regard to dull, sagging and/or wrinkled skin and dull, slow-growing and/or thinning hair suggests that one or more of these ingredients has a more significant impact on GH and IGF-1 production than vitamins and minerals alone.

## 5. Conclusion

In conclusion, the results of this survey suggest that the dietary supplement, Renew, may provide potential health benefits beyond those provided by multivitamin/mineral supplements alone. The improvements reported by Renew users in categories such as energy/stamina, exercise recovery, and sleep may be attributed, in part, to the combination of amino acids (L-arginine, L-citrulline, and L-lysine) included in the supplement. The mechanisms behind these improvements likely involve increased nitric oxide (NO) production, which leads to vasodilation and vasocongestion of the reproductive organs and muscle repair and growth. Additionally, the botanical ingredients in Renew may offset growth hormone (GH) decline in adults by inhibiting DPP-4 degradation of growth hormone-releasing hormone. The inclusion of GABA in Renew may also contribute to GH production, as well as improve sleep quality, skin elasticity, and muscle strength. Furthermore, the greater rates of improvement in categories such as dull, sagging, and/or wrinkled skin and dull, slow-growing, and/or thinning hair reported by Renew users suggest that one or more of the ingredients in Renew may have a more significant impact on GH and insulin-like growth fac-

tor-1 (IGF-1) production than vitamins and minerals alone. Overall, these findings suggest that Renew may have the potential to provide a range of health benefits to users beyond those typically associated with multivitamin/mineral supplements. However, it is important to note that this study was limited by its reliance on self-reported data and the lack of a placebo control group, making it difficult to determine the true efficacy of the supplement. Additionally, the survey was only administered to users of Renew and multivitamin/mineral supplements, making it difficult to generalize the results to the broader population. Therefore, further research, including randomized controlled trials, is needed to confirm the potential health benefits of Renew and its individual ingredients. Nonetheless, these findings suggest that it may hold promise as a dietary supplement for individuals looking to improve their overall health and wellness.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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