
# Assessing the Quality of Life and Health Outcomes of Androgenic Alopecia Patients using Propecia

By

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# Abstract

Most dermatologists prescribe the drugs Minoxidil and Propecia (Finastride) to improve the symptoms of Androgenic Alopecia in male patients, and subsequently their Quality of Life. However, it has been noticed that patients who were using Propecia have developed some serious side effects such as erectile dysfunction, lack of libido, depression and in some cases suicidal thoughts, which cause a decrease in the Quality of Life of the patient instead of improving it.

In our study we assessed the Quality of Life of 90 Androgenic Alopecia patients who are using Propecia only and compared them to 157 Androgenic Alopecia who are using Minoxidil only. We used the self-reporting SF-36 Quality of Life Scale and added the variables Age, Duration of Using Propecia and Patients' Compliance.

We found a statistical significance decrease in the Quality of Life of patients using Propecia in comparison to patients using Minoxidil. The Role Limitation Due to an Emotional Problem was the most effected health component of the SF-36 Quality of Life scale.

Also we found a correlation between the duration of using Propecia and the worsening of the Quality of Life score. Ages of the patients and their compliance were not found to be related to the score.

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# CHAPTER I

## 1.1 Introduction

Male Pattern Hair Loss, Androgenic Alopecia, have always been noted in the human race since the early civilizations. The effort and the energy spent to get find a cure to the condition has been constant. From the aromatic oils, special potions, all the way to using laser and high-tech devices in order to stop the progress of hair shedding and initiating the hair regrowth.

Androgenic Alopecia, the medical term, has been proven to alter the psychosocial status of the individuals who are suffering from that condition. As it progresses, its impact on the Quality of Life of the patient becomes more apparent.

Improving patient's Quality of Life is the ultimate purpose of the medical intervention. Achieving that goal means that the intervention was successful.

In our study, patients who are suffering from Androgenic Alopecia (male pattern hair-loss), seek medical intervention since because of Quality of Life has been lowered as a result of their condition. Low self-esteem, lack of confidence in body image that causes hardship in finding a spouse and a career and being a target of unflattering comments are all reasons making the patient more eager to get medical advise.

Most dermatologists prescribe the drugs Minoxidil and Propecia (Finastride), which both have been proven to stop the process and hair loss and initiate hair re-growth in Androgenic Alopecia.

Actually, Propecia has showed dramatic improvements in a 5-year study done by Merck, the drug makers.

However, it has been noticed that patients who were using Propecia have developed some serious side effects such as erectile dysfunction, lack of libido, depression and in some cases suicidal thoughts. The problem is that many patients are not aware of those symptoms and do not relate the drug to the result in a lowered Quality of Life.

Looking panoramically at the whole experience, from the lowered Quality of Life of the patient as a result of Androgenic Alopecia, then going through seeking medical intervention and the course of treatment and all the way to the ultimate result of it, whether the side effects occurred or not, makes assessing the Quality of Life of the patients who are using the drug is a necessity. In this study, we compare the Quality of Life of Androgenic Alopecia patients who are using Propecia (Finasteride) to those who are on Minoxidil and find out who had a better health out come from the intervention.

## 1.2 Background and Statement of the Problem

Propecia has become a very popular drug among dermatologists. However, even though the efficacy of the drug is evident, Propecia has shown some serious side effects that impacted some of the patients' lives dramatically. Depression, sexual impotence, loss of libido and even suicidal thoughts are all some of the side effects the drug has shown. Actually, Propecia's side effects were prevalent that some class lawsuits have been filed Androgenic Alopecia the company that makes the drug, Merck.

Not only that, there are some websites out there are dedicated for helping patients who used the drug and guide them through their "new life" after using the drug and experiencing the side effects. (PropeciaHelp.com)

With that on the surface, makes the question of "is it really worth it?". If patients are taking the medication to get their hair back along with the confidence to improve their Quality of Life, then later on developing some serious side effects that might literally take away their lives, then what is the point of the treatment?

## 1.3 Objectives and Significance of the Research

This research was directed towards evaluating the health outcome and assessing the Quality of Life of the patients who are using the medication to treat the symptoms of Androgenic Alopecia. The study focused on the overall outcome of using the drug.

We added the following elements (age, duration of use and compliance) to get a clearer picture of the result and find if there is an association between those variables and the Quality of Life of the patient using the drug Propecia.

The research answered the following questions:-

1- Is the Quality of Life in general of the patients using Propecia has been altered in comparison to the patients who are using Minoxidil to treat the condition?
2- Which health component among the quality of life scale we are using got affected the most by Propecia?
3- Is there a link between the patient's age and the level of Quality of Life of the patient using Propecia?

4- Which health component got affected the most in each age group?

5- Which age group got affected the most by Propecia?

6- Is there a correlation between the duration of using Propecia and the level of Quality of Life?

7- Is the patient's compliance to the medication play a role in worsening the case of the Quality of Life or not?

8- Do the duration of using Propecia together with the patient's compliance of taking medication effect the result of the Quality of Life?

9- Do the duration of using Propecia together with patient's age effect the result of the Quality of Life?

10- Do the compliance of the patient together with the patient's age effect the result of the Quality of Life of the patient?

11- Do the 3 factors combined, the age, the duration of used and the compliance, played a role in effect the Quality of Life score?

## 1.4 Research Hypotheses

1. Patients using Propecia have lower Quality of Life in comparison to other patients using diff.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

2. Age of Androgenic Alopecia patient using Propecia affects his Quality of Life score.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

3.Duration of using the Propecia affects the Quality of Life score of Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

4.Compliance of Androgenic Alopecia patient to the drug Propecia affects the Quality of Life score.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

5. Combining the 2 variables of age and duration affects the level of Quality of Life score in Androgenic Alopecia patients using Propecia.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

6-Combiing the 2 variables of age and compliance affects the level of Quality of Life score in Androgenic Alopecia patients using Propecia.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

7.Combining the 2 variables of compliance and duration of using Propecia affects the Quality of Life score of the Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

8- Combining the 3 variables of age, duration and compliance affects the Quality of Life score of the Androgenic Alopecia patient.

## 1.5 Study Limitations

In our study we have found several study limitations that played a role in preventing us from getting the clearest picture about Propecia's effect on the Quality of Life of the Androgenic Alopecia patients.

First we were not able to find enough scientific publications in the literature covering the incidence and prevalence of Androgenic Alopecia in Saudi Arabia in general and the northern region in specific, where the study took place.

Also we did not find publications regarding the Quality of Life of Androgenic Alopecia patients in Saudi Arabia, where the scores are expected to be different than most of studies that was conducted in different countries. The reason is the traditional Saudi Arabian dress for men includes a head garment that covers the hair, and the symptoms of Androgenic Alopecia. That head garment is very essential in the lifestyle of Saudis because it is a mandatory, by the Saudi Arabian government, to be worn at any governmental institution. On top of the fact, this head garment is preferred by most Saudi men to wear at all social and formal events.

We found out that some Androgenic Alopecia patients use a cheaper alternative for the drug. Proscar is a 5 mg Finasteride medication. Some patients tend to buy it instead of the 1 mg form of Finasteride and split the pill into 4 quarters and then take a piece every day to get the desired result from Propecia which is instructed to be taken in the same way. That action unable us from getting more participants in the study and subsequently played a role in biasing the results.

# CHAPTER II

## Literature Review

### 2.1 What is Androgenic Alopecia?

Androgenic Alopecia is the male pattern baldness. It is caused by the susceptibility of hair follicles to Androgenic miniaturization, which leads to hair loss.

In this case the scalp hair is thinning progressively based on hereditary and androgen factors; which occurs mainly in males and sometimes in females. This case affects the social and psychological status of the beings negatively. Fifty percent of the males affected are fifty years old; starting to sense it by age of twenty (1)

Males with Androgenic Alopecia have mainly clinical presentation as Hamilton-Norwood, a pattern distribution, which is not frequently observed in females. As for the triangular pattern it starts with the recession of hair front line followed by a vertex thinning.

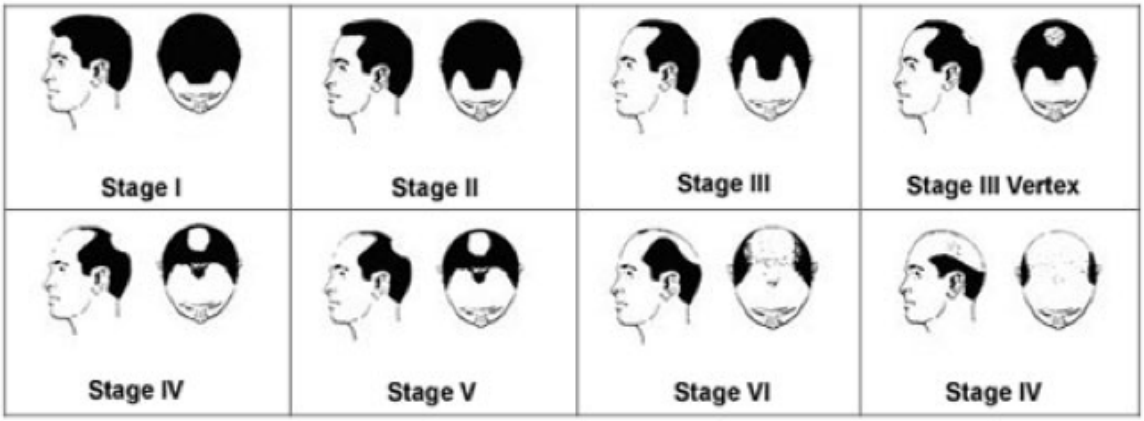


Figure 1: Hamilton-Norwood Hair Distribution

The etiopathogensis is primarily androgen-dependent, modulated by the testosterone metabolite Dihydrotestosterone (DHT) and the expression of hair follicle-related androgen receptor. Also the genetic factors have been implicated in the pathogenesis of Androgenic Alopecia (2)

Males have greater incidence of Androgenic Alopecia than females, however some evidence suggests that the clear differences in incidence might be a reflection of various expression in males and females (3)

In men, Androgenic Alopecia occurs as hair thinning at the temples and crown of the head having a gradual conversion of terminal hairs into indeterminate then into vellus hairs (4). The usual ratio of reduction of hair from terminal to vellus is about 4:1 and after miniaturization of follicles, fibrous tract fills that part (5)

Anterior, mid, temporal and vertex parts of the scalp are the typical areas of involvement. The occurrence of hair loss happens over the course of years. The hair follicle is a skin

organ that produces hair, which has complicated biological structure, and specific growth cycles take place in regulating its growth.

A consecutive transformation of mature follicle starts from Anagen; active hair shaft production, to Catagen; apoptosis-driven regression, to Telogen; resting phase with the involution of hair follicle (6).

The long life transformation of hair follicle is affected by various growth factors, as the follicle functioning differs in different phases, controlling the active phase and promoting apoptosis to stimulate Catagen and Telogen (7). The primary growth factors which affect the hair follicle are: vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin 1-like growth factor, and fibroblast growth factor (FGF).

Platelets transform growth factor beta (TGFβ1 and β2), EGF, and VEGF through releasing large amounts of platelet- derived growth factor PDGFaa, PDGFbb, and PDGFab) (8)

## 2.2 Biochemistry of the disorder

A research was conducted on subjects suffering from Androgen-Insensitivity-Syndromes or 5α- reductase deficiency. The results showed that the Dihydrotestosterone DHT stimulate the occurrence of Androgenic Alopecia through the activation of androgen receptors in hair follicles; as the DHT is five times the tenacity of testosterone causing higher potency of activation (9). The two main forms of 5-α-reductase, known as type1 and type 2 have differences in tissue distribution; as type 2 acts more active in hair follicles, however the two types contribute to Androgenic Alopecia. Testosterone in men is the main source of DHT, however Dehydroepiandrosterone DHEA, a weaker

androgen, acts as precursors for DHT in women. After the androgen receptor binding occurred, the intra-cellular cascade has not yet been clearly defined . However, the results of that binding of raising the cytokines production, has been documented, such as the Telogen-phase-enhancing-cytokine TGF-beta l and 2(10)(11). Different locations have different intensity of androgen receptors in hair follicles; as the occipital hair follicles with low number of androgen receptors have weak or no response to DHT inconstant to the scalp vertex and fronto-temporal area mainly observe hair loss (12).

## 2.3 Genetics and Diagnostic Tests

The views of the fact that Androgenic Alopecia is determined by genetics more than the environmental influence are stronger. The androgen responsiveness is mainly determined by the androgen receptor polymorphisms, yet 5α-reductase, aromatase and sex hormone binding globulin (SHBG) genes may have influence together with other hormone metabolism associated genes (13).It has been claimed that the (Hair DX$^{TM}$), a test used to predict the future occurrence of Androgenic Alopecia, finds a polymorphism in a certain gene. However that claim has not been cleared yet (14)(15)

Two major genetic risk loci for Androgenic Alopecia have been identified in numerous studies: X- chromosomal AR/EDA2R locus and PAX1/FOXA2 locus on chromosome twenty. A comparative recent German genome-wide-association study compared more than 1100 sever cases of Androgenic Alopecia and indicated that HDAC9 is a third susceptibility gene of Androgenic Alopecia. Fine- mapping was used to analyze the results of this study, then was replicated in an Australian sample (16)

## 2.4 Quality of life with Androgenic Alopecia

Even though Androgenic Alopecia is dermatologically considered a mild condition, its psychological and behavioral impact has been documented (17).

Patients with Androgenic Alopecia have dissatisfaction in self-image and potential adverse psychosocial factors, which have negative effects of their Quality of Life (18). Alopecia has various psychosocial complications including: depression, low self-esteem, altered self-image, and less frequent social engagement (19). It is necessary to provide patients with correct information that is medically approved (20) as the Androgenic Alopecia patients may ask for inappropriate and unproven therapies available in nonmedical settings with great expense to the consumer (21).

In a study conducted by Alfonso et al., 2005 (22) the personal attractiveness and social life of the male subjects with Androgenic Alopecia were affected by hair loss. Another study by Williamson et al., 2001 (23) showed that low self-esteem and loss of self-confidence were also affected by hair loss. It is well known that hair loss causes significant distress in men as shown in a study done by Cash et al., 1993 (24). The study showed Androgenic Alopecia is a stressful condition affecting the psychological functioning of an individual. Another study by Cash, 1992 (25) found that there is larger psychological impact of hair loss on younger men and those with earlier onset hair loss; as such groups in adolescence years face the challenge of fitting in with their peers, as the stress of hair loss could be a burden to their coping abilities.

According to Quality of Life of patients with Androgenic Alopecia some characteristics have been determined such as: experience in previous non-hair care, hospital visits for

Androgenic Alopecia treatment, young age, longer duration of Androgenic Alopecia and severe Androgenic Alopecia. The worse hair loss cases those who have previous experiences in non-medical hair care and hospital visits for Androgenic Alopecia treatment. In addition, such findings prove that patients' Quality of Life are strongly and reliably related to the patients' perception of Androgenic Alopecia (20) such findings cope with the results of Cash in 1999 (18) that persons who seek Androgenic Alopecia treatment experience more psychosocial impairment and substantial distress than the male controls. Those issues negatively affect self-esteem leading to difficulties in finding life partners, and the decrease in confidence makes it harder for the patient to find employment (26).

However, Sawant et al (27), reported that patients of younger age group have healthier lifestyle than that of the older age group according to five assessed parameters: eating habits, physical activity, occupation, leisure and recreation, emotional health and addictions. The scores of younger patients indicate their more positive outlook towards life, better ability to cope with peers and better sleeping habits ($t=2.60$, $P=0.013$). That can be explained by the fact that the time period the patient has been experiencing the condition is less in younger patients than older ones. Meaning older patients have gone through more social and emotional experience after the occurrence of the condition.

Also as mentioned, because these days fashion and media has been portraying shaved heads as a trend, younger patient feel less stigmatized. The prevailing culture of metro-sexual helped the younger patients however, they fared worse in the subscale entitled "emotions' (27). There is an increased social acceptance towards baldness, also in social life and interaction especially with the opposite sex (28).

Another study by Alfonso in 2005 (22) illustrated that becoming bald, getting older are the most concerns of patients as part of their personal attractiveness. The two groups of patients in this study felt ' stigmatization', which includes feeling like an outsider and being laughed at by others. Such feelings may occur because of the exaggerated pressure to gain social acceptance.

Another important issue is the relationship between the degree of hair loss and psychosocial variables associated with Androgenic Alopecia, a study by Wells et al., 1995 (29) illustrated that some results of hair loss are: loss of self-esteem, depression, introversion, neuroticism and feeling unattractive (30). In their two studies,Van der Donk et al. in 1994 and Van Passchier et al. in 1991 (31)(32), proved that there is psychological impairment accompanying Androgenic Alopecia despite the psychosocial problems caused by lower Quality of Life. In the same line, the study of Sawant et al. in 2010 (27) showed that when SCL- 90 (the symptom check list) outpatient psychiatric rating scale was administered to both groups, there was not any significant impairment in psychological functioning in both the age groups. The symptoms of depression and obsessive- compulsive disorder were more in the older group than in the younger group. Also, in the study of Franzoi et al. 1990 (33) it was found that men with Androgenic Alopecia had more public self-consciousness and see themselves less attractive.. The degree of visibility of hair loss in male pattern baldness might affect their Quality of Life. Patients were classified into two groups based on their current Norwood- Hamilton stage of Androgenic Alopecia, group with less visible hair loss (stage IIa to III) and group with more visible hair loss (stage IIIa to IV). Patients with more visible hair loss scored higher, meaning worse level, on the emotions, self-assurance, functioning and

stigmatization subscales, such results correlated with the perception of visible balding by the peer group (27).

The impact of Androgenic Alopecia on patients was found to be more related to the emotional and psychological states derived from their Alopecia than to the clinical objective assessment. Patients' feeling of low self-esteem was The coping strategies of avoidance were chosen more frequently by Androgenic Alopecia subjects who scored positive in the 12-item General Health Questionnaire (GHQ-12) and who had Alexithymia- (personality construct characterized by the subclinical inability to identify self emotions). In female subjects with Androgenic Alopecia, alexithymia modified all coping strategies but not in male subjects with Androgenic Alopecia. Physicians should take into consideration that the influence of Androgenic Alopecia is not limited to symptoms, and help people to treat their emotional responses to Alopecia such as: anger, worry, and their beliefs about the consequences of their condition and how it will affect their daily life (34).

## 2.5 Different Ways to Assess Quality of Life in Androgenic Alopecia Patients

The following scales were used in the previously mentioned studies to evaluate the Quality of Life in Androgenic Alopecia patients regarding the impact of the condition on the patient's life.

### 2.5.1 Dermatology Life Quality Index

The Dermatology Life Quality Index or DLQI, developed in 1994, was the first dermatology-specific Quality of Life instrument. It is a simple 10-question validated questionnaire that has been used in over 40 different skin conditions in over 80 countries and is available in over 90 languages. Its use has been described in over 1000 publications including many multinational studies. The DLQI is the most frequently used instrument in studies of randomized controlled trials in dermatology. Certain items in the index were modified to ensure that they are appropriate for Alopecia patient, as shown in the question list below. One of the endpoints of the studies is the mean DLQI score for the first-visit patients. The other major endpoint was the mean improvement in the DLQI score from the baseline to few months later. Each question has four alternative responses with corresponding scores of 0, 1, 2 and 3, respectively. The DLQI is calculated by summing the scores of all questions, using the total scores ranging from 0–30, the lower score indicates a lower Quality of Life.

1 Over the last week, how have you been affected by Alopecia? Have you felt burning, pain, itching, irritation or oils on your scalp?

2 Over the last week, how embarrassed, frustrated or self- conscious have you felt because of your Alopecia?

3 Over the last week, how much has your Alopecia interfered with your shopping or

other outdoor activities?

4 Over the last week, how much has your Alopecia influenced your hair style? Do you need to wear a hat, wig or special hair type to cover the thinning area?

5 Over the last week, how much has your Alopecia affected any social or leisure activities?

6 Over the last week, how much has your Alopecia made it difficult for you to do any sport or hobbies?

7 Over the last week, has your Alopecia prevented you from working or studying?

8 Over the last week, how much has your Alopecia created problems with your partner or any of your close friends or relatives?

9 Over the last week, how much has your Alopecia caused any sexual difficulties?

10 Over the last week, how much of a problem has the treatment for your Alopecia been, for example by making your home messy or taking up time?

11 Assess your Alopecia condition yourself from score 0–100 (VAS).

Items 1 and 2 indicate symptoms and feelings; 3 and 4 indicate daily activities; 5 and 6 leisure; 7 work and school; 8 and 9 personal relationships; 10 treatment; DLOI dermatology and life quality index. (35)

### 2.5.2 Visual Analogue Scale (VAS)

An assessment scale method, that uses the patient's own perception of his dermatological condition. The scale is based on his pre-treatment assessment then post-treatment assessment. The VAS is a simple tool for measuring the satisfaction of the patients concerning the state of their hair loss and the effect of the treatment. The satisfactory level is scaled from 0 to 100

DLQI and VAS were found to be reliable tools to assess the Quality of Life of patients who used Propecia to treat Androgenic Alopecia.(36)

### 2.5.3 Hair-Specific Skindex-29 (Hairdex)

The Skindex-29 scale, which was originally developed by Chren et al. in 1997 (37), was modified to assess the Quality of Life of patients with Androgenic Alopecia. The words 'skin' and 'skin condition' on the Skindex-29, were replaced by 'scalp' or 'Androgenic Alopecia', respectively, and the Skindex-29 itself was renamed as the Hair Specific Skindex-29 (Hairdex). This questionnaire consisted of three kinds of scales: a symptom scale (7 items), a function scale (12 items), and an emotion scale (10 items). Patients responded to each question with a number ranging from 0 (never bothered) to 5 (always bothered). Responses to each item were transformed to a linear scale, ranging from 0 (never bothered) to 100 (always bothered). A high score indicates severely impaired Quality of Life, and a low score reflects mild damage in the Quality of Life (20).

Although the Hairdex index was designed by Fischer et al. in 2001 (28), its usage is limited and hard to utilize when comparing Quality of Life of Alopecia patients with patients that have other skin diseases. Consequently, some terminology of the Skindex-29 to 'Alopecia' or 'scalp' has been modified, and then had the name: Hair Specific Skindex-

29 (Hairdex). Concerning topic dermatitis, psoriasis and acne, the Skindex scale is a validated, reliable, sensitive, and specific measure of how much patients are bothered by their dermatologic conditions (38).However, a Skindex score has not been validated for use in Androgenic Alopecia

### 2.5.4 Symptom Check List-90-R (SCL-90-R)

Is an out-patient psychiatric rating scale which consists of 90 questions to evaluate psychopathology. The respondents reported how much discomfort they experienced over the past week and past day with selected symptoms/psychological states. Responses were scored on a 0 to 4 continuum (0=not at all, 4=extremely).The SCL-90-R covers nine symptom dimensions, which are: [1] somatization (perceptions of bodily dysfunction); [2] obsessive–compulsive; [3] interpersonal sensitivity (feelings of personal inadequacy or inferiority); [4] depression; [5] anxiety; [6] hostility; [7] phobic anxiety; [8] paranoid ideation and [9] psychoticism. The Symptom Checklist-90-R (SCL-90-R) instrument helps evaluate a broad range of psychological problems and symptoms of psychopathology. It is also useful in measuring patient progress or treatment outcome, and also can be useful in clinical trials to help measure the changes in symptoms such as: depression and anxiety. (39)

### 2.5.5 Short Form (SF-36)

The SF-36 health survey is a widely used generic, including 36-item, self-reported health status questionnaire assessing eight domains of health status [1] physical functioning; [2] role limitation due to physical problem; [3] bodily pain; [4] mental health; [5] role limitation due to emotional [6] social functioning; [7] vitality; [8] health change; [9] general health. A score from 0 to 100 is calculated for each subscale, with higher scores indicating better Quality of Life. It has been validated and translated into different languages including Arabic (40). Physical functioning domain addresses physical activities associated with daily life such as: bathing, walking, or carrying groceries. Physical –role domain; assesses how physical health affects work. Bodily pain domain: measures pain severity and how it interferes with daily activities. Mental health domain; assesses the subject's mood, specifically focusing on feelings of sadness, depression and anxiety. Emotional role domain; addresses how the subject's emotional state's influence on work and other daily activities. Social functioning domain; measures how much emotional or physical problems have impacted the patient's usual social activities. Vitality domain; assesses how energetic or tired the subject feels. Finally, General health domain; describes how the patient perceives his health status.

## 2.6 Treatments of Androgenic Alopecia

There are two treatments for Androgenic Alopecia: medical and surgical. Oral Finasteride and topical Minoxidil are the two proven medications for Androgenic Alopecia (6).

### 2.6.1 Minoxidil

Although the method of action is unknown, Minoxidil lengthens the duration of Anagen phase and may increase the blood supply to follicle (41). The Regrowth is pronounced at the vertex more than in the frontal areas, and not noted for at least 4 months. It is essential to keep the topical treatment with drug as the discontinuation of treatment results in rapid reversion to the pretreatment balding pattern.

### 2.6.1.1 Mechanism of Action

Minoxidil needs to be transformed to its active metabolite to test its effect, Minoxidil-sulphate, which is transformed by enzyme sulphotranspherase that exists in the outer root sheath of Anagen follicles. Its active metabolite, Minoxidil sulphate opens ATP- sensitive potassium channels in cell membrances, which has a vasodilating effect. However, vasodilatation does not seem to be the cause for Minoxidil to promote hair growth. Studies on skin blood flow after topical Minoxidil application produced inconsistent results (4).

Possible effects of Minoxidil on the hair follicles are: a) high expression of vascular endothelial growth factor (VEGF) mRNA in the dermal papilla. This means that angiogenesis in the dermal papilla was induced by the drug. b) An active Cytoprotective prostaglandin synthase-1; a Cytoprotective enzyme which stimulates hair growth. c) High expression of hepatocyte growth factor (HGF) m-RNA; it is a promoter of hair growth (42).

### 2.6.1.2 Efficacy- males

The same criteria have been found out by about 34 studies of treating Androgenic Alopecia by Minoxidil. Generally, the efficacy of Minoxidil solution 2% and 3% applied twice daily in most of the trials of assessment. The mean change from baseline total hair count ranged between 5.4 hairs/cm2 and 29.9 hairs/cm2 (11.0 – 54.8%) at 4 to 6 months and between 15.5 hairs/cm2 and 83.3 hairs/cm2 (14.8-248.5%) at 12 months .

The total mean of hair count changes in the majority of the studies with in 4 to 6 months, and was statistically significant compared to placebo (P between 0.074 and <0.0001). The older trials switched the placebo group at 12 months to Minoxidil treatment.

There was significant difference between the mean changes in non-vellus hair count and placebo (p between <0.05 and 0.01) and a mean change in non-vellus hair counts was between 4.7 hairs/$cm^2$ (17.2-59.4%) at 6 months, between 9.4 hairs/$cm^2$ (8.8-443.8%) at 12 months. There was a significant difference between the total and nonvellus hair counts at 6 and 12 months, and baseline hair counts (p between 0.01 > p< 0.0001) (43)(44)(45)(46)(47)(48)(49)(50).

### 2.6.1.3 Dosage

The mean changes from non-vellus hair counts were not significantly different for Minoxidil 0.1%, 1%, 2% at 6 months. Minoxidil 3% solution, applied twice daily was not significantly different from Minoxidil 2%, twice daily (mean change from total hair count/nonvellus hair count at 4 respectively 12 months) (51).

In two studies showing a comparison between Minoxidil 2% solution; twice daily, and Minoxidil 5% solution; twice daily, were included in the evidence-based analysis (Price et al., (7) (51). Both studies showed that the result of Minoxidil 5% group was superior to Minoxidil 2% (mean change from baseline non-vellus hair count 18.6 hairs/cm2 (12.3%) vs. 12.7 hairs/cm2 (8.8%) at 12 months, $p = 0.025$, mean % change from baseline total hair count 30% vs. 25% at 24 months, $p = 0.455$).

Olsen et al. showed that applying Minoxidil twice daily showed better results than applying it once. The mean change from baseline total hair count after applying the medication twice shows 64.4 hairs/cm2, whereas increase has reached only 44.1 hairs/cm2 when applying just once at 33 months period. (51).

#### 2.6.1.4 Instructions for use/ practicability

Treatment with Minoxidil partially transfer miniaturized (intermediate) to terminal hair, and produces at least a partial normalization of the hair follicle morphology. Minoxidil should be applied as 1 ml of solution with a pipette or half a cup of foam to dry hair and scalp; once in the morning and Androgenic Alopecia in the evening, then left in place for at least four hours. When using spray applicator it has to be spread evenly over the affected areas. After application the hands should be washed with warm water.

The effectiveness of the treatment should be assessed at least 6 months after initiation of therapy. The treatment should be maintained as long as the effect is to be desired by the patient in order to prevent hair loss. During the first months of therapy the patients may experience increased hair shedding. This is transitory and only indicates that the drug is stimulating Telogen follicles to re-enter Anagen. It is important to inform the patient

about a possible Telogen shedding, before the treatment is started. If shedding occurs, therapy should be maintained.

### 2.6.1.5 Minoxidil Side Effects

Most of the seriosus side effects of Minoxidil such as dizziness, sudden weight gain and hypotension are a result from the tablet form of the medication. However the foam and liquid forms of Minoxidil, which are the forms used to treat Androgenic Alopecia topically, are generally safe with very minor of side effects being reported. (52) The main 2 well documented side effects are dermatitis (skin irritation conditions) and hypertrichosis. (growth of unwanted hair) more frequently in female patients.(53)

## 2.6.1.5.1 Dermatitis

A mail survey was performed on professional clinicians who are members of the American Academy of Dermatology. The survey was about the side effect of Minoxidil the clinicians have encountered. Only 2% of the results reported mild skin irritation at the site of the application and change in hair texture becoming dry (54)

## 2.6.1.5.2 Hypertrichosis

1333 female patients took part in a study to evaluate Minoxidil-induced hypertrichosis, 4% of the patients has reported dose-related level of facial hair. (53) and Campese in 1981 (55) had stated that reversible-hypotrichosis is found in almost all patients who used Minoxidil systemically, not topical.

### 2.6.1.6 Combination Therapies

A study by Berger et al. 2003 (56) couldn't prove that combination of Minoxidil 5% solution and Pyrithione zinc shampoo is superior to Minoxidil monotherapy. Minoxidil 5% solution; twice daily combined with Pyrithione zinc shampoo 1x/d vs. Minoxidil 5% solution twice daily and placebo shampoo showed mean change from baseline of total hair count of 6.2 hairs/cm2 and 12.3 hairs/cm2 respectively.

In the comparative study of Bazzano et al. (57) compared male and female patients taking Minoxidil 0.5% solution, 2x/d, Tretinoin 0.025% solution, 2x/d, placebo and the combination of Minoxidil 0.5% with tretinoin 0.025%. About 58% of the patients of the Tretinoin group, and 66% of the patients with the combined treatment had at least 20% or more increase from baseline total hair count.

Shin et al. 2007 (58) failed to prove significant difference between Minoxidil 5% solution, twice daily, and a combination of Minoxidil 5% and tretinoin 0.01%, once daily. The mean change from baseline total hair count at 18 weeks was 15.9 hairs/cm2 (12.8%) vs. 18.2 hairs/cm2 (14.7%) (p not significant).

Topical Minoxidil 2% solution, 2x/d in combination with an oral hormonal contraceptive led to a mean change from baseline total hair count of 16.1 hairs/cm2 (8.6%) at 6 months, 16.9 hairs/cm2 (9.1%) at 12 months, whereas cyproterone acetate 50 mg in combination with oral hormonal contraceptive led to decreased values (-2.8 hairs/cm2 (-1.4%) at 6 months, -7.8 hairs/cm2 (-3.9%) at 12 months ($p < 0.001$) (59).

## 2.7 Propecia

Finasteride is taken orally and is an 5-alpha reductase type 2 inhibitor, it is not an anti-androgen (60). Men only can use the drug because it can produce ambiguous genitalia in a developing male fetus. Finasteride decreases the progression of Androgenic Alopecia in males who are treated, and, in many patients, it has stimulated new re-growth.

### 2.7.1 Mechanism of Action

A single oral administration of Finasteride 1 mg decreases serum dihydrotestosterone (DHT) in addition, scalp DHT up to 70% compared to baseline. Long-term administration is not observed with Tachyphylaxis (sudden decrease in the response to a drug after its administration) . Finasteride is fastly absorbed after oral intake with maximum plasma level occurring 1 to 2 hours after drug intake. The serum half-life of the drug is about 6 hours. 90% of the drug is connected to the plasma proteins. Finasteride is metabolised in the liver by hydroxylation and oxidation using P 450 3A4 pathway, however without interaction with other drugs known for metaboliztion by this cytochrome also, such as warfarin, theophylline, digoxine, propanolol and others (61).

### 2.7.2 Efficacy – males

18 studies on the efficacy of Finasteride in male patients suffering from Androgenic Alopecia assessed the efficacy of Finasteride monotherapy in male patients with Androgenic Alopecia. 12 studies showed grade A2 evidence, 5 grade B and 1 grade C. 12 studies were placebo controlled (62)(63)(64)(65)(66)(67)(68)(69)(70)(50)(71)(72)(73)

### 2.7.3 Treatment Results

All trials illustrated that the intake of Finasteride 1 mg daily led to a significant increase in total hair counts compared to placebo. The mean change from baseline total hair count was 7.0 hairs/cm2 (3.3%) in the frontal/centro-parietal region ($p < 0.0001$ vs. placebo) (74) and 13.5 hairs/cm2 (7.3%) in the vertex ($p < 0.0001$ vs. placebo) at 6 months.

The mean increase from baseline total hair counts at 12 months was between 7.2 hairs/cm2 (3.6%) and 36.1 hairs/cm2 (29.1%) for the vertex (p between < 0.05 and 0.001 vs. placebo) (74) (63) (65) (69) and 9.3 hairs/cm2 (4.9%) and 9.6 hairs/cm2 (4.6%) in the frontal/centro-parietal region (p between < 0.01 and 0.001 vs. placebo) (75)(69). Meanwhile, the placebo group showed mean changes from baseline total hair count between 2.4 hairs/cm2 (1.4%) and -10.1 hairs/cm2 (-5.2%).

The global expert panel assessment rated between 37 % and 54 % of the patients as improved at 12 months ($p < 0.001$ vs. placebo). Moreover, subjective assessments by investigator and patients showed significant improvements in the Finasteride group.

There were long-term results for 24, 36 and 48 months. The mean changes were 13.0 hairs/cm2 (6.2%) at 24 months from baseline total hair counts (68), 8.5% at 36 months (69), 7.2% at 48 months (76)

There was statistically significant different comparing to placebo. Price et al. (69)(76) reported that the increase in hair weight at 12 to 48 months was (20.4% at 12 months, 21.5% at 24 months, 19.5% at 36 months and 21.6% at 48 months versus -5.2%, -14.2%, -14.8% or -24.5% in the placebo group, $p< 0.001$).

### 2.7.4 Dosage

Concerning concentration, two studies examined different Finasteride dosages that could be included in the evidence-based evaluation (77)(61). Roberts et al. examined Finasteride 0.01 mg, 0.2 mg, 1 mg and 5 mg versus placebo. The mean change from baseline total hair counts under Finasteride therapy (0.2 mg, 1 mg and 5 mg) was significantly different with placebo at 6 and 12 months ($p < 0.001$), while the dosage of 0.01 mg showed progressing hair loss (difference to placebo not statistically significant).

The differences in mean change from baseline total hair count between the Finasteride groups (0.2 – 5mg) did not reach significance. Kawashima et al. illustrated that 58% respectively 54% improvement in global expert panel assessment for Finasteride 1 mg respectively 0.2 mg. The effectiveness in both groups were comparable and significant different to placebo ($p< 0.001$).

### 2.7.5 Propecia vs. Minoxidil

Only few data is available concerning comparing the Propecia 1 mg daily and Minoxidil solution. Two studies investigated Finasteride 1 mg Androgenic Alopeciainst twice daily topical application of Minoxidil 2% solution Khandpur et al in 2002 (68) and Saraswat in 2003 (50), both showed superiority for Finasteride. The mean change from baseline total hair count was 36.1 hairs/cm2 (29.1%) for Finasteride at 12 months 1 mg and 19.6 hairs/cm2 (14.8%) for Minoxidil 2%, twice daily application ($p = 0.003$) (Saraswat and Kumar, 2003). 87% of the patients taking Finasteride versus 42% of the Minoxidil 2% patients were rated as improved ($p < 0.001$) (68).

In -placebo-controlled clinical trial of 1553 men, the efficacy of Finasteride (1 mg) has been shown in male Androgenic Alopecia patients aged 18 to 41 with Norwood/Hamilton stage II-V. Sixty-six percent showed regrowth, and 83% showed stabilization after a 2-year follow up in a double-blind(6). Finasteride is normally prescribed as a once daily oral dose of 1 mg. Although , the medication affects vertex balding more than frontal hair loss, it increases re-growth in the frontal area as well. Finasteride must be continued because discontinuation results in disorder gradual progression (78).

A 10-year follow-up study of men using Finasteride 1 mg daily for Androgenic Alopecia showed that better improvements were noted in patients older than 30 years or men who had higher Androgenic Alopecia grades. Amazingly, the efficacy of the medication was not reduced with time, and in some cases improved later on (78).

A Japanese study was conducted on 3177 men to observe the efficacy and safety of Finasteride in the treatment of Androgenic Alopecia. Photographs were assessed in 2561 men who completed the 42-month study, 11.1% of those men showed great re-growth, 36.5% moderate growth, and 39.5% had a slight increase in hair growth. Adverse effects occurred in 0.7% of the men, and there were no safety problems observed with long-term use. The study concluded that in Japanese men with Androgenic Alopecia, who use long-term oral Finasteride, maintained progressive hair re-growth without recognized adverse effects (79).

### 2.7.6 Instructions for Use / Practicability

The bioavailability of Finasteride 1 mg following oral intake ranges from 26-170% with a mean of 65% (80). It was found that the average peak plasma is 9.2 ng/ml measured 1-2

hours after administration. The bioavailability of Finasteride was not related to food intake, as Finasteride is extensively metabolized in liver by Cytochrome P450 3A4 enzyme subfamily and excreted both in urine and feces. The terminal half-life is approximately 5-6 hours in men between 18-60 years of age and 8 hours in men more than 70 years of age (80).

Finasteride is not prescribed for women as it is contraindicated in pregnant women, because of the risk of feminisation of a male foetus. Finasteride treated men must therefore avoid donating their blood. The level of Finasteride in the semen of treated man is very low even with regular intake of Finasteride 5 mg/day, and there is no risk in case of sexual relation with pregnant women, so the use of a condom is not necessary for this reason.

Normally, the recommended dosage is 1 mg a day, however a dose study recommended lower dosage of 0.2 mg/day led also to significant improvement compared to placebo. Consequently, if a patient forgets a pill, it is not recommend to take two the next day. Moreover, in case of adverse event a dosage of 0.2 mg/ day or a dosage of 0.5 to 1 mg every other day can be discussed, though no clinical studies are available on this question.

Before assessing the efficacy, there is a minimal period of use of 6 months for reducing hair loss and 12 months for re-growth of hair. If a patient intends to switch from Minoxidil to Finasteride combination therapy for at least 3, better 6 months should be taken before stopping Minoxidil to avoid significant hair loss while Finasteride action can take over.

Finasteride reduces PSA level in case of starting the treatment after 45 years and monitoring the PSA level should be considered. The PSA levels should be double to compensate the reduction resulted from Finasteride, which lead to an interpretation of the test.

Mysore in 2012 also illustrated that in patients who fear the side effects, administration of lower daily doses or staggered pulse doses of the drug should be considered to promote patient compliance, as it is sounds rationale for such regimens(81). Plasma half-life of Finasteride is 6-8 hours and tissue binding is 4-5 days (9). Doses of 0.2 mg are adequate to suppress both scalp skin and serum DHT levels, however 0.2 mg caused 55% DHT suppression, 5 mg per day achieved 69% DHT suppression (81).

The efficacy has been demonstrated for all end points for Finasteride at doses of 0.2 mg/day or higher, also 1 and 5 mg demonstrating similar efficacy that was superior to lower doses (82). Therefore the drug may be initially administered at 0.5 mg daily or one tablet alternate days, to gain confidence of the patient and the 1 mg/day dosage may be restored once patient is comfortable about the drug. The value of such a regimen was shown in a preliminary study by (83). However, further large, long term studies are needed to establish the value of such regimens (81).

### 2.7.7 Post-Finasteride Syndrome

A large number of men have reported intolerable adverse effects after starting Finasteride therapy and continue to experience these effects after stopping the medication (84). These

peripheral or secondary effects have undesirable consequences that are collectively becoming known as Post-Finasteride Syndrome (85). Symptoms range from minor to severe. Physical effects can include chronic fatigue, gynecomastia (the development of breasts), muscle atrophy, thinning skin, and penile and scrotal shrinkage. Sexual changes include: decreased libido, intermittent erectile dysfunction, and impotence. Cognitive effects include: a difficulty in maintaining attention and an overarching "brain fog." Psychological effects also include emotional sensitivity, depressed affect, and excessive anxiety leading to functional decline (86).

Few researches have been conducted on the long-term effects of particular sexual dysfunction (86) Researches, in systematic review, evaluated 12 randomized clinical control trials that focused on the efficacy and safety of Finasteride terapy (87). Results of the review reported that moderate evidence exists that the daily use of Finasteride slows Androgenic Alopecia by improving hair count; however, there may be an associated increase in the risk for sexual dysfunction.

In a recent study, researchers sought to characterize the type and duration of persistent sexual adverse effects associated with the use of Finasteride for Androgenic Alopecia , and conducted standardized interviews ($N = 71$) in a group of otherwise healthy men (age 21-46 years), who reported new symptoms that endured for at least 3 months after stopping the medication (88). The mean duration of Finasteride use in this sample was 28 months; 94% reported low libido; 92%, erectile dysfunction, 92%, decreased arousal; and 69%, difficulty achieving orgasm. The researchers concluded that physicians who treat Androgenic Alopecia with Finasteride should have warned their patients of the potential risks of persistent sexual adverse effects the results from using Propecia

Prospectively, investigators followed healthy men younger than 40 years ($N$ = 54) who reported persistent sexual adverse effects associated with Propecia; they sought to determine whether the adverse effects resolved or endured over time .The men were assessed at 3 months after stopping the medication and after 9 to 16 months. The primary outcome measured was sexual function—libido, arousal, erectile function, ability to reach orgasm, and orgasm satisfaction—via the Arizona Sexual Experience Scale. The scale has reported a sensitivity and a specificity of 82% and 90%, respectively, to identify sexual dysfunction (89). During the reassessment, 96% of subjects reported continued sexual adverse effects and 89% met the Arizona Sexual Experience Scale criteria for sexual dysfunction. The study concluded that most men who had developed persistent sexual side effects continued to have symptoms for many months and even years, despite discontinuation of the drug (88).

Several studies have investigated the effects of Finasteride on male fertility (90)(91)(92). It was concluded that in some men even low-dose Finasteride can reduce sperm counts (91).

Irwig in 2012 reported significant higher rates of depressed affect and suicidal thoughts among former users of Finasteride for Androgenic Alopecia (75%) than those in controls (10%; $p$< .0001). Moreover, there were moderate to severe depressive symptoms in 64% of the Finasteride group and in 0% of the controls; 44% of the former Finasteride users who experienced suicidal thoughts, as did only 3% of the controls ($p$< .0001). It is thought that neurosteroids and neuroactive steroids play a significant role in neuroprotection, augment memory, and have anxiolytic and antidepressant properties (93).

Production of neurosteroids occurs in the central nervous system from adrenal and gonadal steroids (94). The synthesis of these endogenous regulators requires the presence of 5-α reductase, and Finasteride has been shown to inhibit its biosynthesis (95). Depression has also been associated with the dysregulation of neurosteroids and androgen deficiency (96)(97).

### 2.7.8 Combination Therapies

Leavitt studied 79 male patients undergoing hair transplantation, and showed that the combination with Finasteride 1 mg daily led to increase of hair counts after 12 months, however hair transplantation alone resulted in decreased hair count in the frontal area.The mean change from total baseline hair count 18.5 hairs/cm2 (12.6%) vs. -13.5 hairs/cm2 (-8.9%, p = 0.019) (72).

The combination of Finasteride 1 mg daily with Minoxidil 2% solution twice daily respectively ketoconazole 2% shampoo, 3x weekly to Finasteride 1mg daily and Minoxidil 2% solution twice daily were compared by Khandpur as monotherapies. In 12 months, 100% of the patients of each combined therapy, 87% for Finasteride and 42% for Minoxidil 2% solution were rated as improved by investigator. The combination of Minoxidil 2% and Finasteride 1 mg was statistically significant more than Finasteride or Minoxidil monotherapies (68). Furthermore, Diani in 1992 illustrated an additive effect of Finasteride and Minoxidil in stump-tail macaque. Working mechanism of Minoxidil and Finasteride treatments are different, consequently, the association of both drugs is possible and can be considered in motivated patients.(98)

## 2.8 Other Drugs

There are some drugs potentially found to support the existing medications for treating Androgenic Alopecia, however the drugs are not FDA approved. (99).

However, there is a drug called Dustasteride is currently being studied to treat Androgenic Alopecia. It is found to be 3 times stronger as Propecia in inhibiting type II 5-alpha-resuctase isoenzym and 100 times stronger in inhibiting type I. The drug full clinical trails has not been done yet and only reached phase II when it was studied in the U.S.

Another form of treatment is the HairMax Laser-Comb. It is a low-level laser light therapy. It comes in form of a brush that has red laser-light-outlets.

It was advertised as 501K -FDA approved. However that approval means the device is safe to use rather than beneficial with a good efficacy.(100).

But we should mention that a 26-week double blind study was conducted where the study group given the HairMax device and the control group was given a fake device, there was a significant improvement in hair regrowth among the study group. (101).

Latanoprost 0.1% is a prostaglandin analogue that is used to treat Glaucoma. One of its noted effect on the eye was increase in thickness, length and number of eyelashes. A 24-week study was conducted by applying Latanoprost 0.1% topical treatment on 2 mini-

zones of Androgenic Alopecia on 16 male patients. The study has showed improvement in the zones treated by the medication compared to the baseline, where the medication was not applied (42).

Androgenic Alopecia is very common; therefore, not surprisingly, it may accompany other forms of hair loss. Cases of Telogen effluvium often occur in patients with underlying Androgenic Alopecia. Consequently, a search for treatable causes of Telogen effluvium (eg, anemia, hypothyroidism), especially in patients with an abrupt onset or a rapid progression of their disease, is presented (100).

A phase 1, double-blind clinical trial designed to evaluate the safety of a bioengineered, non-recombinant, human cell–derived formulation containing Follistatin, Keratinocyte Growth Factor (KGF), and vascular endothelial growth factor (VEGF) was performed to assess the efficacy in stimulating hair growth. Twenty-six subjects were entered into the study and none showed an adverse reaction to the single intradermal injection. After 1 year, a statistically significant increase in total hair count continued to be seen (102)

Promoting the use of a newer modality of platelet-rich plasma (PRP) resulted from the oncerns about the efficacy and safety during the requisite long-term treatment of Androgenic Alopecia with the FDA-approved oral Finasteride and topical Minoxidil therapy, and showed beneficial effect. PRP has been used in the past to prevent infection and speed up the wound healing process by reducing bleeding/swelling after surgery by the plastic-, dental-, general-, neuro-, and orthopedic surgeons. PRP, an autologous concentration of human platelets in a small volume of plasma has a higher platelet concentration (4-7 times) above the baseline. It is obtained from the patient's own blood

after processing in an automated centrifuge and it is injected subcutaneously into the area of Alopecia. PRP includes (and releases through degranulation) several different growth factors and other cytokines that stimulate healing of bone and soft tissue (103).

Ubel in 2005 conducted a study on 23 patients who undertook hair transplant after enriching the hair root grafts with PRP and without PRP. Two areas (2.5 cm2) each were marked on the scalp and planted with 20 grafts/cm2, and after 1 year, the area implanted with the PRP-enriched grafts demonstrated a yield of 18.7 FU/cm2 versus 16.4 FU/cm2 of that without PRP, an increase in follicular density of 15.7%(104) . Li *et al*. , *In vivo* study, where mice received subcutaneous injections of PRP, and their results were compared with control mice showing that activated PRP increased the proliferation of dermal papilla (DP) cells and stimulated extracellular signal regulated kinase and Akt signaling. Both fibroblast growth factors 7 (FGF-7) and beta-catenin are potent stimuli of hair growth, where upregulated in the DP cells. The injection of mice with PRP induced faster Telogen-to-Anagen transition than that in control mice (105).

Thus, the beneficial effects of PRP in Androgenic Alopecia can be attributed to various platelet-derived growth factors causing improvement in the function of hair follicle and promotion of hair growth. It is also safe, cheap, and non-allergic and it appears to be a useful adjuvant in the management of Androgenic Alopecia (106).

There are contradictions between the wish of hair re-growth and willingness to perform a therapeutic regimen. Thus, the limited efficacy, poor tolerance, fear and lack of information on treatment duration and possible adverse events lead to disappointment Androgenic Alopecia. Mainly the individual therapeutic concepts are still based on

physicians' personal experiences ignoring the current evidence-based knowledge regarding the efficacy of the therapies (107).

The compliance of the patients is most important in the individual response on a therapeutic concept. Good compliance is not only related to a balance of benefits, costs and adverse effects, but also requires informed patients. Response rates and satisfaction will increase with the increase of the level of the patients' knowledge about the optimal use of each therapy. So it's possible that patients' compliance, and information on administration and adverse reactions should serve to eliminate or reduce these and therefore will additionally improve compliance (34).

In routine clinical practice the individual decision for a particular treatment of Androgenic Alopecia do not depend only on the efficacy, but also on practicability, risks and costs. The assessment of cost effectiveness has to be undertaken by balancing the costs with the benefit attained. So, expensive therapeutic options can also be cost-effective, if they are highly effective. While the patient usually has to bear the full costs of the treatment, consideration of patient-relevant benefit is essential. The benefit attained from the therapy of Androgenic Alopecia is not only stabilization, prevention of progression and induction of hair growth, but leads also to an improved Quality of Life (51).

## 2.9 Quality of life after using Finastride

Although the etiopathogenesis is not completely understood yet, it has been noted that, while many of the side effects are directly related to the drug, the others may not be at all.

They are usually minimal or reversible, but may alter the patient's Quality of Life or even reduce compliance to treatment. Press reports, internet websites, and misinformation by alternative medicine practitioners, have contributed to an incorrect image of the drug, and led to patients' psychological apprehension (108).

Yamazaki et al conducted a study on twenty-seven male Androgenic Alopecia patients aged 19-76 years (average, 33.8) who answered the Visual Analog Scale (VAS), Dermatology Life Quality Index (DLQI), WHO/Quality of Life-26 and State-Trait Anxiety Inventory (STAI) questionnaires before and after the administration of Finasteride (1 mg/day) for 6 months. The physicians assessed the patients as "excellent" or "good" and were defined as "high responders"; those who were assessed as "moderate" or "no change" were defined as "low responders". The changes in Quality of Life before and after the treatment were statistically analyzed, and the improved value of each Quality of Life index of the high responders and low responders from baseline were compared. There was a statistical difference in the VAS ($P < 0.0001$) and DLQI ($P < 0.01$) indices before and after the administration of Finasteride. No significant changes occurred in the WHO/Quality of Life-26 and STAI indices. Comparison of the high responders (11 cases) and low responders (16 cases) revealed no statistical difference in the improvement of VAS and DLQI scores. Oral Finasteride improves the Quality of Life of these patients, and VAS and DLQI are useful for the evaluation of patients' Quality of Life because of the high sensitivity of these tests(35). However, oral Finasteride did not alleviate the patients' anxiety nor did its efficacy correlate with the level of reported anxiety.

Finasteride is well tolerated because the side effects are extremely rare, and even when they occur due to increased Oestrogen levels, caused by partial conversion of testosterone in estradiol through the aromatase enzyme, they become easily reversible after suspension of the drug. The increased Oestrogen levels can lead to problems like water retention, adiposity, Gynecomastia and increased risk of breast cancer infection, while low levels of DHT can lead to sexual dysfunction (reduced libido, reduction in amount of ejaculated semen and erection problems). Depression, ocular symptoms, alterations in lipid metabolism and increased cardiovascular risk, have also occasionally been reported (108).

### 2.9.1 Sexual dysfunction

Since the approval of Propecia for Androgenic Alopecia by FDA, there has not been any large-scale study on a bigger population (61). The most recent and only review that investigate consideration the efficacy of Propecia therapy and sexual disorders in Androgenic Alopecia was published in 2010 by Mella et al. (87). It contained controlled randomized trials, but did not completely consider the incidence of global sexual disturbances. Actually, not all the clinical trials reported a precise incidence of global sexual disturbance. Based on the 12 clinical trials, collected by Mella, Propecia increased hair count while increasing sexual dysfunction risk, but, due to the contradictions of data, this could not be certainly identified. Kaufman et al. and Leyden et al illustrated that 4,2% and 2% respectively of adverse effects incidence in patients treated with Propecia, with regression of symptoms(6)(74). McClellan and Markham reported an incidence of 3,8% of sexual dysfunction disappeared after suspension of therapy(109). In 2001 Tosti

et al. indicated the presence of sexual dysfunctions in 0.5% of patients treated with Finasteride 1 mg, but he made no reference to their reversibility (110). Yet, later Tosti et al. (2004) asked 186 patients with Androgenic Alopecia to complete a questionnaire regarding erectile function domain before (IIEF-5) at baseline and 4 to 6 months after beginning Finasteride treatment and found that the patients' sexual functions remained stable during treatment.

Whiting et al found a bit higher percentage of Finasteride-treated patients (8.7%) compared to placebo-treated patients (5.1%) who experienced a drug-related sexual adverse experience (70). It was reported that higher incidence of drug-related sexual adverse experiences in Finasteride-treated patients more than in placebo-treated patients by Olsen et al and Rossi et al described an incidence of 5.9%, but the reversibility was not reported(111)(78). The findings of Irwig and Kolukula showed after conducting standardized interviews with healthy men aged 21–46 years that they reported onset of sexually related side effects associated with the temporal use of Finasteride in which symptoms persisted for at least three months after suspension of use(88). Limitations to the study included the small number of patients, reserving bias before Finasteride data, and there was no serum hormone analysis (108). The efficacy and safety of oral Finasteride 1 mg was examined on Androgenic Alopecia of 3177 Japanese men and the Incidence of adverse reactions was 0.7%. (79).

### 2.9.2 Depression

Rahimi-Ardabili et al. used Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS) on 128 men who were prescribed Propecia to treat Androgenic Alopecia in order to evaluate their depressed mood and anxiety. Participants completed BDI and HADS questionnaires before beginning treatment and two months after. Treatment increased both depression scores significantly (112) Dihydroprogesterone (DHP), produced from progesterone by 5α-reductase, is further converted to allopregnanolone, that is a modulator of gamma amino butyric acid type A receptor (GABA-A) and has anti-convulsant, anaesthetic and anxiolytic effects (113).

Bitran et al. boosted that changes in levels of allopregnanolone could be considered a cause of depressive disorders (113). Barrett-Connor et al showed that BDI scores were inversely associated with bioavailable testosterone and DHT levels, suggesting that high serum DHT levels, is inversely associated with depression. In agreement with Rahimi-Ardabili et al(114)(112), Altomare and Capella reported the case of 19 patients who developed a mood disturbance during treatment with Finasteride, 1 mg/day. Depression was associated to marked anxiety in some cases, developed after 9–19 weeks of treatment and resolved after suspension of therapy (115)

Rogers and Pies published all the drugs that could induce depression and Finasteride was mentioned (99). Irwig assessed depressive symptoms and suicidal thoughts in former users of Finasteride, who developed persistent sexual side effects despite the

discontinuation of Finasteride (84). Clinicians and potential users of Finasteride should be aware of the potential risk of depressive symptoms and suicidal thoughts. That is the reason all patients/candidates should complete a BDI-II test, before starting Finasteride therapy for Androgenic Alopecia. Moreover, depression could have an influence on the onset of side effects (nocebo effect) (108).

### 2.9.3 Metabolic Effects

Recent studies showed that DHT could play a role in the metabolism of visceral fat (108). Duskova et al analysed the relationship between drug assumption in the treatment of Androgenic Alopecia and improvement of some characteristics of metabolic syndrome, which is often associated to this condition. The examination of twelve men affected by Androgenic Alopecia, undergoing Finasteride 1mg/day therapy for 12 months were examined, to monitoring hormonal and lipid profile after 4, 8 and 12 months of treatment showed a reduction of DHT and an increase of testosterone and androstenedione. They found an early increase of total cholesterol, LDL and HDL, that tended to stabilize with pursuance of therapy, in addition to a significant reduction of glycosylated hemoglobin and insulin resistance.(116)

Various authors have investigated the relationship between male Androgenic Alopecia and cardiovascular involvement over the past few decades. Cotton et al. and Hirrso et al reported an increase in cardiovascular risk (117)(118) . Ellis et al did not find any connection (14). Lotufo et al showed an association between severity of baldness and coronary artery. This fact could be justified, as reported in the given literature, by the presence of 5α-reductase and DHT receptors on blood vessels, inducing a proliferation of

vessel smooth-muscle cells (119). Moreover, patients affected by Androgenic Alopecia present an increase in sensitivity to andogens not only in the scalp, but also in the vessels, promoting atheroma development (120)

## 2.10 Role Of Androgens In Pattern Hair-loss And Sexual Function

Pattern hair loss in males is Androgenic in etiology therefore, Anti-androgens such as Finasteride are useful in the management of the condition. Androgens, especially testosterone increases the libido. So any drug, which interferes with the action of androgens, is therefore assumed, by the layperson, to induce impotence. However, the precise role of androgen in penile erection needs to be fully elucidated (121)(122). Even an individual with low testosterone levels can achieve erection, also, androgens, visual, olfactory, tactile, auditory, and imaginative stimuli influence the libido. The penile erection is mainly under the control of parasympathetic nervous system. Ejaculation and detumescence require an intact sympathetic system (122)(123).

The androgens testosterone and dihydrotestosterone (DHT) have nearly different actions. The enzyme, 5α-reductase converts testosterone to DHT and exists in two isoenzyme forms:type I is predominant in liver and type II is predominant in prostate, seminal vesicles, epididymes, hair follicles, and liver (122).The two types have a different distribution within the hair follicle too. Type I 5α-R, is present in the sebaceous gland, while type II 5α-R is found on the outer root sheath of the hair follicles and dermal papillae. At all these sites, the testosterone is converted to DHT (124). Although the type II 5α-R enzyme has a more significant role in pattern hair-loss (and therefore mechanism of action of Finasteride) than the predominantenzyme in scalp skin, it is mainly because

of localization to the sebaceous glands, which are large and plenty in scalp. Finasteride is a specific and competitive inhibitor of Type II 5—AR, and has, therefore a selective action on hair follicles. Scalp skin DHT levels fall by more than 60% after administration of Finasteride, thereby suggesting that a significant amount of DHT found in scalp skin is derived from both local DHT production and circulating DHT. Thus, the effect of Finasteride on scalp DHT is likely because of its effect on both local follicular DHT levels as well as serum DHT levels. This explains why relatively small dose of Finasteride may be adequate therapeutically (81).

### 2.10.1 Side Effects of Finasteride Related To Sexual Function

A number of studies have investigated the problem of side effects caused by Finasteride. Such studies reveal that sexual adverse effects occur at the rates of 2.1% to 3.8%, erectile dysfunction (ED) being the commonest followed by ejaculatory dysfunction and loss of libido. These effects occurred early in the therapy and returned to normal on stopping or over a time on continuous use of the drug. The only causal relation between Finasteride and sexual adverse effects is decreased ejaculatory volume because of predominant action of DHT on prostate (125).

A comprehensive review was conducted on total of 73 papers on medical therapies for BPH and focused on the effects of different pharmacological agents on sexual function (126). The review revealed that Finasteride is infrequently associated with problems of ejaculation (2.1-7.7%), erection (4.9-15.8%), and libido (3.1-5.4%).

The role of nocebo effect in the causation of ED due to Finasteride has been investigated by (127). Nocebo effect refers to: an adverse effect that results from the psychological

awareness of the possibility of the side effect, however, it is not a direct result of the specific pharmacological action of the drug. In this study, the group informed about the sexual adverse effects of Finasteride reported increased incidence of ED, when compared to the group without information (127). The side effects were completely reversible in 5 days when the medicine was discontinued, confirming that nocebo effect has an influence in causation of side effects and suggesting the role of psychological factors.

Two studies in 1999 showed that the incidence of these side effects with Finasteride therapy was generally comparable to that was observed with the treatment with placebo (128)(74), and there was no evidence of dose dependency or increased incidence with longer therapy out to 12 months. Besides , the side effects ceased in patients although they continued to receive Finasteride.

A long term study showed that drug-related sexual side effects such as decreased libido, ED, and ejaculatory disorders occurred in <2% of men (9). These side-effects disappeared not only in all men who stopped the drug, but also in most of those who continued therapy. The incidence of each side effect mentioned decreased to ≤0.3% by the fifth year of treatment with Finasteride. The incidence of side effects were comparable to that of placebo both at one year and at 5 years.

A large prospective study on 17,313 patients was conducted to investigate the effects of Finasteride and other covariates on sexual dysfunction as part of the analysis of The Prostate Cancer Prevention Trial (PCPT) (129). Sexual dysfunction was assessed in the 17,313 PCPT participants who received Finasteride 5 mg during a 7-year period. Finasteride increased sexual dysfunction only slightly even at 5 mg dosage (which is

much higher than the 1 mg administered in pattern hair loss) and its impact diminished over time. The authors concluded that the effect of Finasteride on sexual functioning is minimal for most men and should not impact the decision to prescribe or take Finasteride. A recent review of the available literature too reached similar conclusions (130).

However, there are more recent studies, which documented contradicted findings (88). There is a study has been widely reported findings after conducting standardized interviews with 71 healthy men aged 21-46 years.Those men reported new onset of sexual side effects associated with the temporal use of Finasteride in which the symptoms persisted for at least three months despite stopping the drug. The study revealed that the subjects reported new-onset persistent sexual dysfunction (low libido, ED, and problems with orgasm) associated with the use of Finasteride. The mean number of both sexual encounters per month dropped, and the total sexual dysfunction score increased before and after Finasteride use ($P< 0.0001$ for both). The mean duration of Finasteride use was 28 months and the mean duration of persistent sexual side effects was 40 months from the time of Finasteride cessation to the interview date. However, there were many limitations in the study such as: small numbers of patients, selection bias, recall bias for before Finasteride data, and no serum hormone analysis. The study recommended that physicians who treat Androgenic Alopecia should discuss the potential risk levels with patients while prescribing the drug.

An important study by Mella et al. conducted a systematic review of twelve randomized trials, which evaluated the efficacy and safety of Finasteride therapy in 3927 male patients. Moderate-quality evidence was found from an increase in erectile dysfunction and a possible increase in the risk of any sexual disturbances however, the risk of

discontinuing treatment because of sexual adverse effects was similar to that of placebo (87)

A number of isolated case reports have also been published on the effect of low dose Finasteride on DNA changes in sperms (131), on motility, and sperm counts (132). Such patients were under investigation for Oligospermia (lower sperm count) and infertility when these findings were discovered. It is obvious that these parameters improved after stopping the drug.

Another small study (133) on three cases of young men, who had used Finasteride for five years, investigated male Infertility. Semen quality was checked by light microscopy to evaluate sperm concentration and motility sperm morphology by transmission electron microscope (TEM), presence of Y micro-deletions by PCR, and meiotic segregation by fluorescence *in, situ* hybridization (FISH). TEM analysis revealed that altered sperm morphology is consistent with necrosis and FISH data revealed elevated diploid and sex chromosome deformity frequencies.

One year after the men had stopped the use of Finasteride without receiving any other treatment, they were recovered from spermatogenetic. Motility and morphology improved whereas the meiotic pattern did not change.

Traish et al conducted a review of different published studies and concluded that altered sexual functions such as erectile dysfunction and diminished libido are reported by a subset of men receiving Finasteride, raising the possibility of a causal relationship (97). The review suggested discussion with patients on the potential sexual side effects and possible alternate treatments before administration of the drug.

In the light of the conflicting and continuing, and importance of the subject, the International Society of Hair Restoration Surgery (ISHRS) established a Task Force on Finasteride Adverse Event Controversies to evaluate published data and make recommendations. The taskforce posted their initial update on the subject as follows:“To date, there is no evidence-based data substantiating the link between Finasteride and persistent sexual side effects in the numerous double blinded, placebo controlled studies using Finasteride 1 mg for hairloss". Reports of persistent sexual side effects resulted from a variety of sources with some Internet sites attracting individuals claiming to have sexual and psychological issues related to Finasteride. While the continued difficulty having erections after discontinuing Finasteride has been reported in post-marketing surveillance, yet the incidence of this problem remains unknown (81).

The persistence of sexual side effects appears to be a rare event, and it has not been determined whether in these recent reports that represent a true causal relationship, or if they are simply coincidental and related to other factors such as: the high incidence of sexual dysfunction in the general population, and/or the placebo effect. Just a few data is available concerning the medical and psychological work-up of these patients to exclude other potential causative factors. At the present time, the mechanism of interaction among the brain, 5 alpha-reductase metabolism, and hormones on sexual dysfunction is speculative and poorly understood. Obviously, this is a complicated issue, which overlaps with other disciplines in medicine such as Endocrinology, Urology, and Psychiatry. More research are needed to assess the actual incidence of side effects to determine if there is a true causal relationship among persistent side effects and if so, how to identify who may be at risk (81).

In view of this, it is very important to properly counsel patients about the treatment. Particularly, the following facts need to be stressed: The drug is probably the best available to treat Androgenic Alopecia and the only one to address the root of the problem; its effects are proven; several studies have shown its safety over long duration of administration (the dosage given (1 mg) is small and unlikely to cause side effects. Even in those cases where side effects were reported, the changes were found to be reversible). There are very few effective alternatives to the drug and it is therefore important for the patient not to stop the drug unless he experiences any side effect. The patient should contact the doctor for any advice, especially when he experiences a side effect; most importantly, the administration of the drug is totally voluntary, as male pattern hair loss is only a cosmetic condition and it is entirely up to the patient to take or not take the drug. The treating physician should provide full information about the drug to enable the patient to make an informed decision; and it is better to avoid the drug for any patient who has prior history of Oligospermia, infertility, particularly if he is newly married and is trying to raise a family (81).

## 2.11 Saudi Arabia and Androgenic Alopecia

We could not complete our literature review about assessing the Quality of Life of Androgenic Alopecia patients using Propecia without elaborating more about the county our study took place in. We were not able to find publications regarding the prevalence or the incidence of Androgenic Alopecia in Saudi Arabia and subsequently we were not able to find studies about the Quality of Life of the Androgenic Alopecia patients in general and the ones who are seeking medical intervention in specific.

However, we find the need to emphasize on certain facts that would affect the perspective of the study. We found those facts related to the topic of our study because it is part of the country's culture, traditions and even governmental rules and regulations.

We first have to explain the traditional wear that Saudi Arabians prefer to wear most of the time over wearing the regular western clothing of pants and shirts. According to the official website of the Royal Saudi Arabian Embassy in D.C and the official website of the Saudi Commission for Tourism and National Heritage, Saudi Arabia's men's national dress is an-ankle- long shirt, usually white, that covers the whole body except the head. Also On their heads, they wear a large folded piece of cloth called (Shemagh or Ghutra), and held in place with a cloth-made-wire-like called (Igal).(136)(137).

Men wear that garment almost in every social and formal occasion including marriage proposals and job interviews. (137)Even though we did not find any solid statistics regarding the percentage of Saudi Arabian men wearing it, we can firmly say that wearing it is mandatory in any governmental institution according to the Saudi Arabian law and it is the formal dress code among Saudi Arabians.(138) We also found out that 90% of Saudi men actually work for the Saudi Arabian government. Also according to a recent report of a survey that was conducted on 2,500 Saudis of over 15 years of age between 2013 and 2015, 75% of Saudi Arabian men actually prefer to work in the government sector. That makes wearing the Shemagh an essential part of the Saudi Arabian lifestyle.(139)

Based on that fact and the covering nature, to the body and head, of the Saudi Arabian traditional wear, we can say that the body image in general among Saudi men is not as

apparent or critical in comparison to men in other countries, where the daily clothing shows more of the body features.

In this case in specific, the hair would be even less important playing a role in the body image and self-esteem of the Saudi Arabian man. And because of that, the Quality of Life of Androgenic Alopecia patients in Saudi Arabia would be rather higher than the Quality of Life in Androgenic Alopecia patients in other countries, where the symptom of the Androgenic Alopecia would be clear.

Even though there is an absence in the literature regarding the Quality of Life of Androgenic Alopecia patients seeking medical intervention to improve their situation, we can easily expect the baseline of the Quality of Life of those patients in Saudi Arabia would be high in general, unless it got effected by a another medical condition or a side effect of a certain drug.

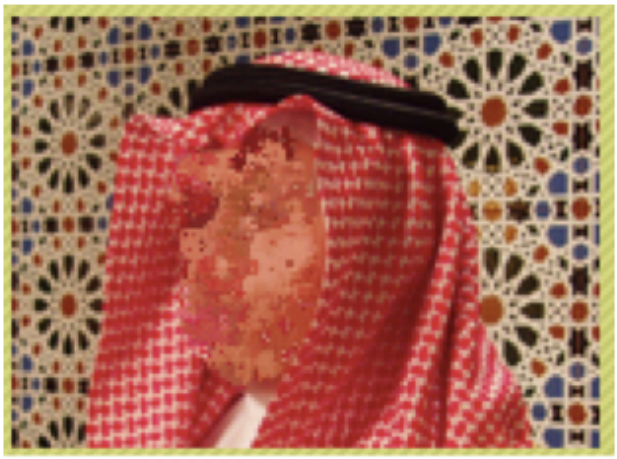

**Figure 2 Saudi Arabian Man's Head Garment**

# CHAPTER III

## 3. METHODOLOGY

### 3.1 Place of the Study

At the initial attempts and observations of the study, patients were meant to be interviewed at the dermatology clinic hoping to get a good scope regarding the study. Unfortunately, patients were only visiting the dermatology clinic to get diagnosed and get started on the medication and almost never come back to be re-assessed. The reason for that is because once the condition improved, patients find no reason to come back to the clinic and just continue on the medication. Such a scenario puts the patient at risk of developing the side effects of the drug without knowing its correlation to Propecia even though it is mentioned in the drug's label

For that reason, the Propecia dispensing pharmacies were a good alternative of the study location. Patients were asked to take part in the study when they show up to refill their prescriptions. That scenario gave us a more general view of to assess the participants Quality of Life. Also that would give us access to patients who have been on the treatments for longer periods of time and stopped going to the dermatology clinic.

An advantage for the pharmacy as an institution to collect data regarding the side effects of certain medications over the clinic is the fact that pharmacies out number clinics and clinical institutions in general, and dermatology clinics in specific. Patients might not be in the city or region where they are following up their cases, yet they would still refill their prescription.

Another advantage for conducting the study in pharmacies is the working hours and days of the pharmacies, which are more than the working hours and days of dermatology clinics. That gave us the chance of collect more data

Another observation was notice regarding collecting the data from pharmacies instead of clinics, is that patients felt more comfortable filling the measurement tool in the pharmacy more than the clinic for the reason of that Propecia is an over-the-counter medication, in Saudi Arabia, that mean it does not require any sort of formal prescription from a dermatologist and subsequently does not need a formal identification in order to get the drug. That put the patients more at ease to fill the questionnaire instead of the clinic where he felt that the staff might have access to his record, even after explaining to the patient his privacy rights.

Also conducting the study in pharmacies made us notice an important observation. Some patients came to the pharmacy asking for the drug Proscar (Finastride 5 mg). Those patients are using the drug Proscar as a cheaper alternative to propecia after splitting the pill into 5 small pieces and then taking one piece everyday, as the Propecia is instructed to be taken.

## 3.2 Data Collection

The Medical College of The University of Northern Boarders of Saudi Arabia has been contacted to help collecting the questionnaires from random pharmacies in the northern region of Saudi Arabia where the study took part.

Data collectors were instructed to collect our questionnaire from Androgenic Alopecia patients who are using Propecia only to treat their condition and came to the pharmacy to refill their prescription of Propecia, which is an over the counter medication in Saudi Arabia.

We have decided that Androgenic Alopecia patients using Minoxidil only who came to the pharmacy to refill medication, which is an over the counter medication in Saudi Arabia, to be our control group. We based our decision on the assumption that both, Propecia-only-patients and Minoxidil-only-patients have had the same baseline of Quality of Life level before seeking medical intervention to improve it.

From that point, studying each group's Quality of Life level gave us a picture of how much of an effect Propecia has on the Quality of Life of Androgenic Alopecia users versus the Quality of Life of Androgenic Alopecia patients who did not use the Propecia and instead used Minoxidil only.

Another reason we have chosen to use Propecia-only as our study group versus studying patients who are on combined therapy is the fact that Minoxidil itself has some side effects that might also impact the Quality of Life of the Androgenic Alopecia patients who are using Propecia as part of their therapy. So including patients who are used combined therapy would effect the result by the probability of that side effects from both medications might overlap. Even though each side effect is different, our measurement tool is generalized and not specific to a certain physical or emotional illness.

The collected data was clean as we instructed the data enterer not to enter any forms that were not fully answered from the participants. And after we received the data, was used the data-cleaning functions in one of the software we used in processing the data.

## 3.3 Measurement tool

**Main tool**: As mentioned, SF-36 has been validated and proved to be a very reliable tool to assess the Quality of Life of patients. The SF-36 is a quite comprehensive tool that gives a clearer picture about the Health Outcome of the patient's experience.

The tool is made of 36 questions. Each question's answer is scaled from 0 to 100 making the perfect score of 3,600 implies that the patient is at a 100% level of Quality of Life on the SF-36 scale. The 36 questions are sub-grouped. Each sub-group covers a certain health component and used to evaluate the patient's health in that component as the following:-

1- Physical Functioning: covers the patient's ability to perform his daily activities such as walking up a flight or several flights, taking care of himself, moderate and vagarious physical exercises.

2- Role Limitations Due to Physical Problem: questions based on the nature of the question. The questions are to assess whether the physical condition of the patient has impacted his production in general and getting his desired work accomplished.

3- Role Limitations Due to Emotional Problem: The questions are to assess whether the emotional and mood conditions has limited the patients production in general and restricted his daily activities.

4- Energy: The assessment is based on how much of pep the patient had and if he was

feeling tired and worn out, how bad was it according to his own view.

5- Mental Health and Emotional Well-being: this part of the questionnaire covers the patient's mental stability whether he has any general symptoms of depression or anxiety.

6-Social Functioning: 2 questions to evaluate how much the physical or emotional state have interfered with the patient's social life. Such as, being active in social gathering and taking parts in social or community events.

7- Bodily Pain: if the patient feeling any physical pain and how much the pain was tolerable.

8- General Health: 5 questions to assess the patient's health in general including his own comparison to others and expectation of his health condition in the future.

9- Health Change: one question for the patient to evaluate his health status throughout last year and whether his health has improved or not.

| Health Components | Number of Questions | Details |
|---|---|---|
| Physical Functioning | 10 | Evaluating physical health of daily activities |
| Role Limitations Due to Physical Problem | 4 | The impact of physical health on daily activities |
| Role Limitations Due to Emotional Problem | 3 | The impact of emotional health on daily activities |
| Energy and Vitality | 4 | Feeling energetic and full of pep versus feeling too tired and worn out |
| Wellbeing Emotional | 5 | Evaluating mental condtion and sings of depression and anxiety |
| Social Functioning | 2 | The impact of physical and mental health of the patient on the social life the of the patient |
| Bodily Pain | 2 | Evaluating the patien's body pain if any |
| General Health | 5 | Patient's own assessment to his general health |
| Health Change | 1 | Comparing health status to last year |

Table 1 Health Components of SF-36 Quality of Life Scale

We have chosen this tool because

(1) it is a tool that scales the patients' current Quality of Life. Some other tools' results are contingent to a certain period of time, as of before and after receiving the treatment such as the Dermatology Quality Life Index.

(2) it is focused on the patient's general health and outcome, which is our focus in this study, disregarding his level of satisfaction of the treatment's result, such as in Visual Analog Scale.

(3) SF-36 is a measurement tool for the patient's Quality of Life that is not specific to a certain dermatological condition and its score is not based on the condition itself.. The Hairdex-29 for example, is a Quality of Life tool that includes the patients' dermatology condition. Some of its items and scores are based on the involvement of the patient's condition in his daily life, such as whether the condition is causing him embarrassment not.

(4)Some other Quality of Life tools that were used to assess the Quality of Life in Androgenic Alopecia patients were mainly focused on a certain impact of the condition on the patient's life. One of those tools is the Symptoms Check-List-90-R .

**Added items**

**Age**: as we learned in our literature review, age in some studies played a role in the quality of life of the Androgenic Alopecia patients. However, studies' results were not consistent. Some studies' findings showed that younger patients had a better Quality of

Life, because the condition was relatively new and did not progress yet to the severity level that would affect the patient's confidence. Other studies showed that older patients had a better Quality of Life in general because body image is not important to that age group as to the younger ones.

In our study we wanted to know whether age played a role in the Quality of Life in Androgenic Alopecia patients who already started their Propecia treatment and might have already experienced some of its side effects.

was it the older ones who had a better over all experience with the drug?

Is there a correlation between the age of the patient and the Quality of Life after using Propecia?

**Duration**: In the Rahimi study, patients', who experienced some mental and emotional side effects from the medication, their conditions have gotten worse with time. Some of the subjects needed to withdraw from the study as their conditions were not tolerable any longer after (112) years. However in the Japanese study, subject were reassessed after up to 2 years and yet the majority of the patients did not report a Quality of Life altering condition.

Based on those studies, we added duration scale by years to study the correlation between the Quality of Life and using the medication Propecia.

Did patients experienced worsen side effects as they continued their treatment?

**Compliance**: Propecia, is instructed to be taken orally as 1 mg daily and its half-life is 6-8 hours. That means the body is on a consistent exposure to the drug through out the

treatment. And because Propecia is a treatment for a persistent condition, it should not be stopped, as long the patient wants to prevent his hair shedding.

From that fact, we wanted to know whether patients who are complied to the instructions of taking the drug would have worse side effects as their exposure to Propecia would be longer than those other patients who are not complied to the instructions.

We added 3 level of compliance to our measurement tool, complied, semi-complied and not complied, respectively.

Patients were instructed to answer that based on their own judgment evaluating their own compliance throughout their whole course of treatment.

Most of our sample was below the age of 36 with a mean age of 29 men between the age of 26-36 were slightly higher than the younger group. That can be explained by the financial ability to effort the medication when compared to the younger subjects, yet still care more about their image in comparison to the older subjects. The mean score for Quality of Life for our sample was found to be 3027 out of 3600 as a Quality of Life is at 84% level. On the other hand, our control group mean age was 30 with a mean score of 3533 meaning their Quality of Life level is at 98%.

The following table shows the differences in Quality of Life scores in the sub-groups of health aspects among our study and control group.

## 3.4 The Hypotheses

1. Patients using Propecia have lower Quality of Life than patients using Minoxidil (control group).

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

2. Age is a factor in effecting the Quality of Life in Androgenic Alopecia patients using Propecia.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

3. Duration of using Propecia has an impact on the Quality of Life in Androgenic Alopecia patients.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

4. Patient's compliance to the medication Propecia, has an effect on their Quality of Life.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

5- Combining variables of age of the patient and the duration of using Propecia, has an affect on the Quality of Life of Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

6- Combining the variables of age of the patient and the patient's compliance to the medication Propecia has an effect on the Quality of Life of the Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

7- Combining the duration of using Propecia with the compliance of the patient to taking the medication has an effect on the Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

8 – Combining the 3 variables of age, duration and compliance of using Propecia as one factor would have an effect on the Quality of Life of the Adrogenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$

## 3.5 Software Tools

The questionnaires were collected and entered into 2 Microsoft Excel 2011 files. A file for the Propecia users (study group), and another file for the Minoxidil users (control group, separately. We used Microsoft Excel because its familiar environment and simplicity of data entry.

Then the data was imported to IBM SPSS Vr23. We used this software because of its user-friendly interface and easy steps to process the imported data.

## 3.6 The sample

247 participants took part in our study. 90 Propecia users (study group) and 157 Minoxidil users (control group). The mean age of our sample was 30, where most of the patients fell under the age group between 25 and 36. The sample was normally distributed among the age of the patients. Both the study group and the control groups were normally distributed across the age.

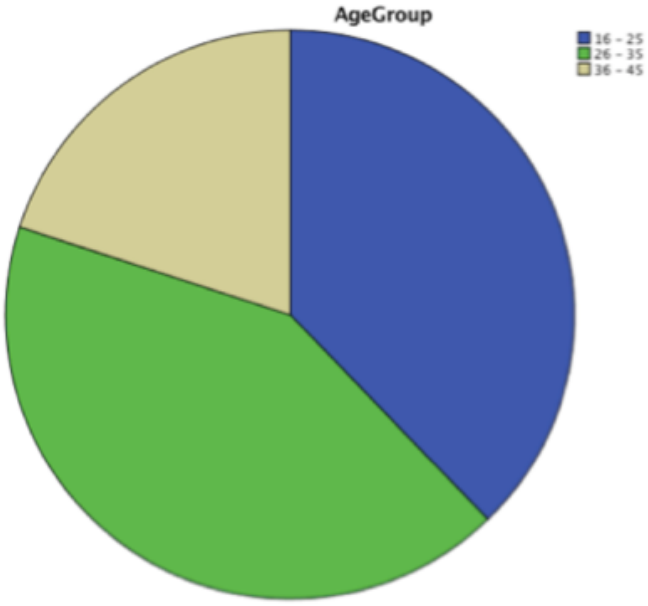


Figure 3 Age Groups of the Sample

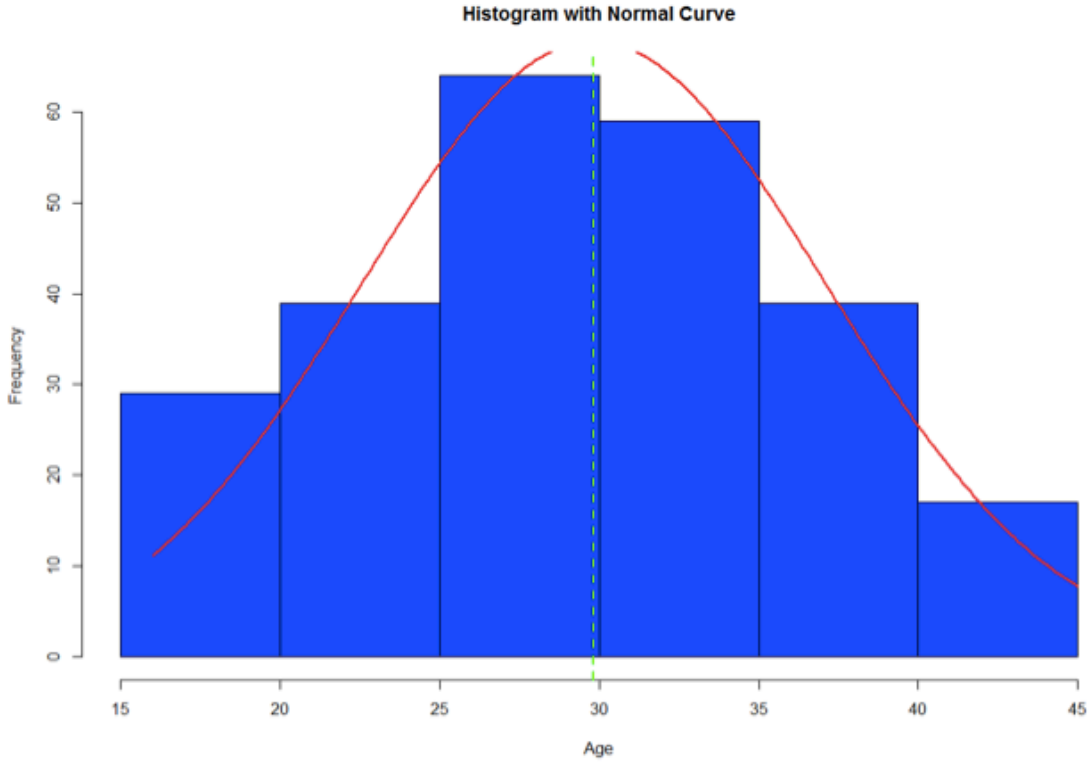


Figure 4 Age Distribution in the Sample

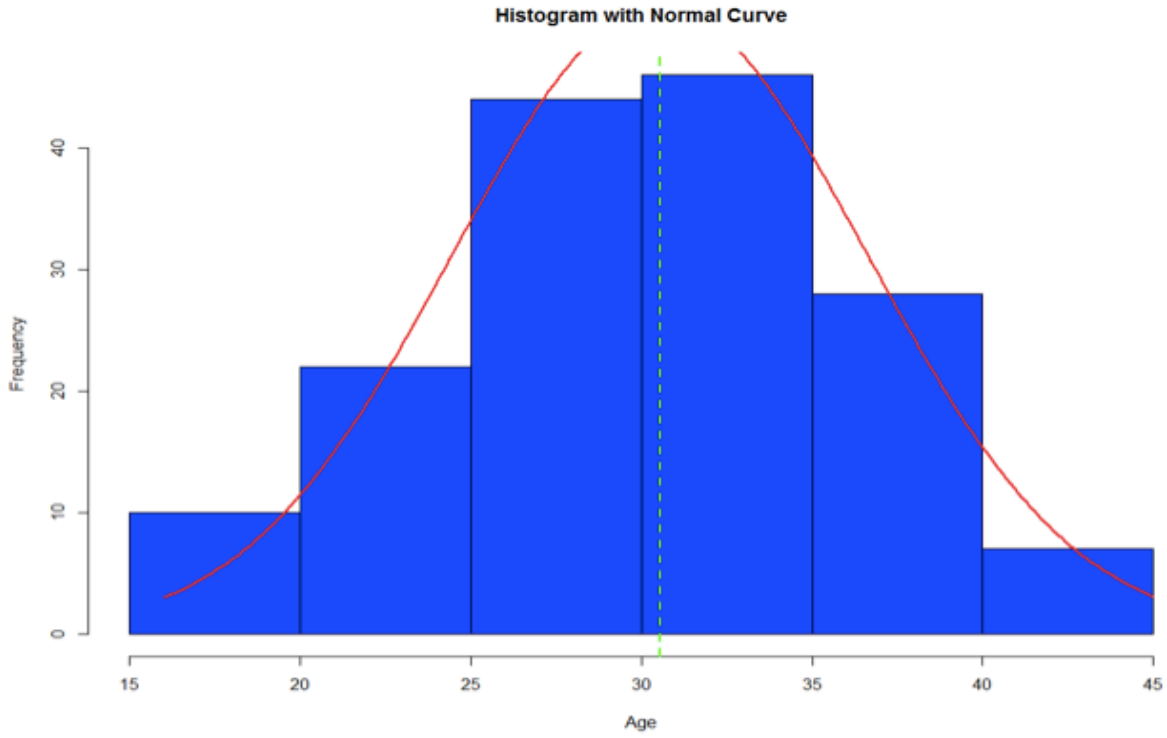


Figure 5 Age Distribution in Minoxidil Group (Control Group)

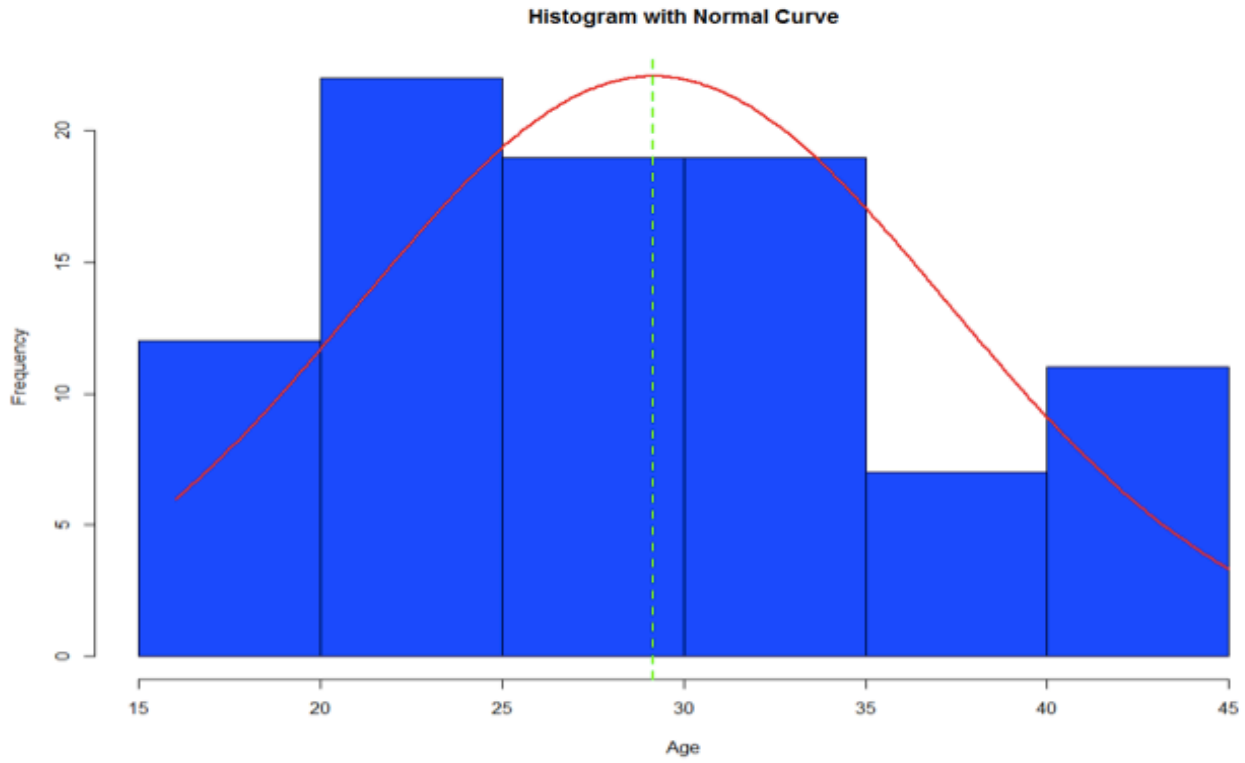


**Figure 6 Age Distributions in Propecia Group (Study Group)**

The mean of total score of the Quality of Life of our sample was 3281 (91%) however the score was not normally distributed in that term. But the scores were normally distributed once graphed separately among each group of the study, Propecia and Minoxidil. The mean score for Quality of Life for the Minoxidil group (study group) was 3533 out of 3600, also explained as their Quality of Life is at 98% level. Our Minoxidil group (control group) had a mean score of 3027 meaning their Quality of Life level is at 84%.

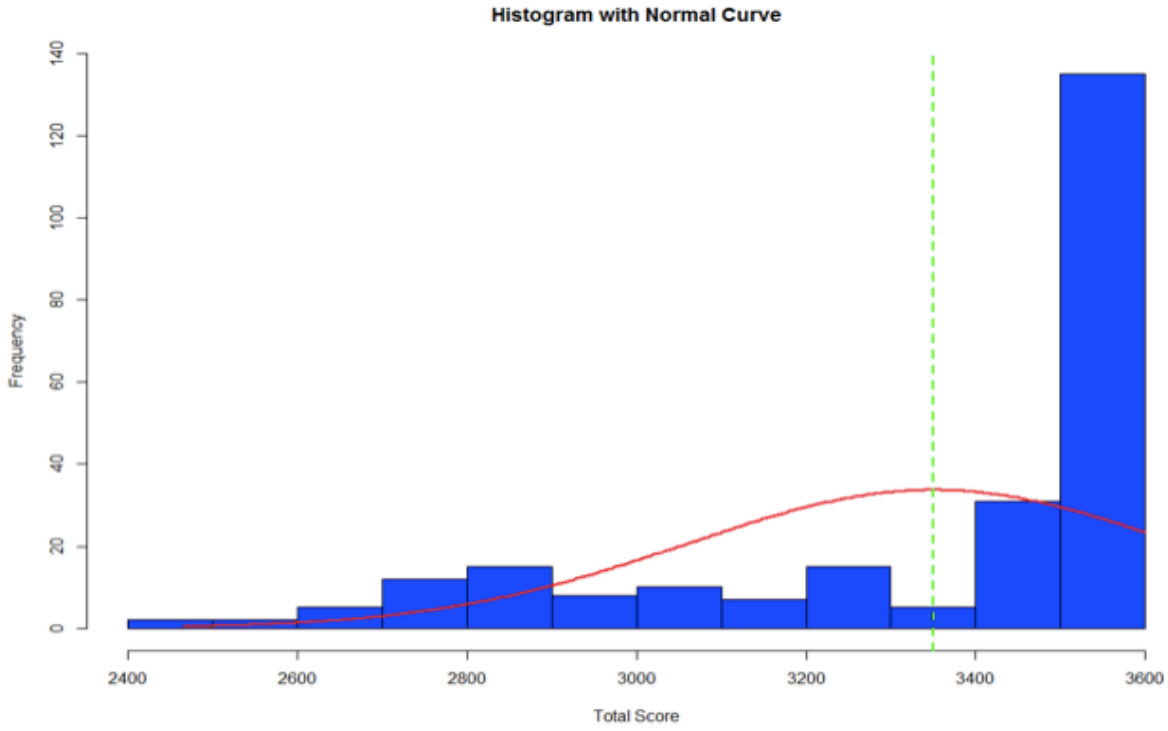


**Figure 7 Quality of Life Score Distribution in the Sample**

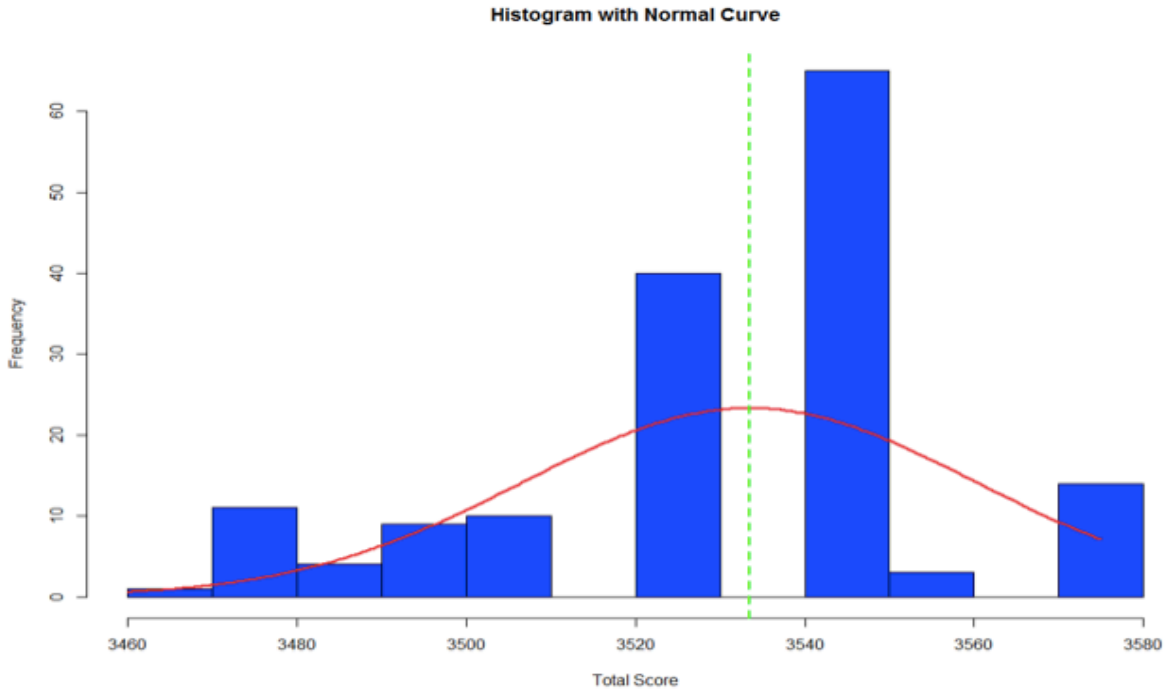


**Figure 8 Quality of Life Distribution in Minoxidil Group (Control Group)**

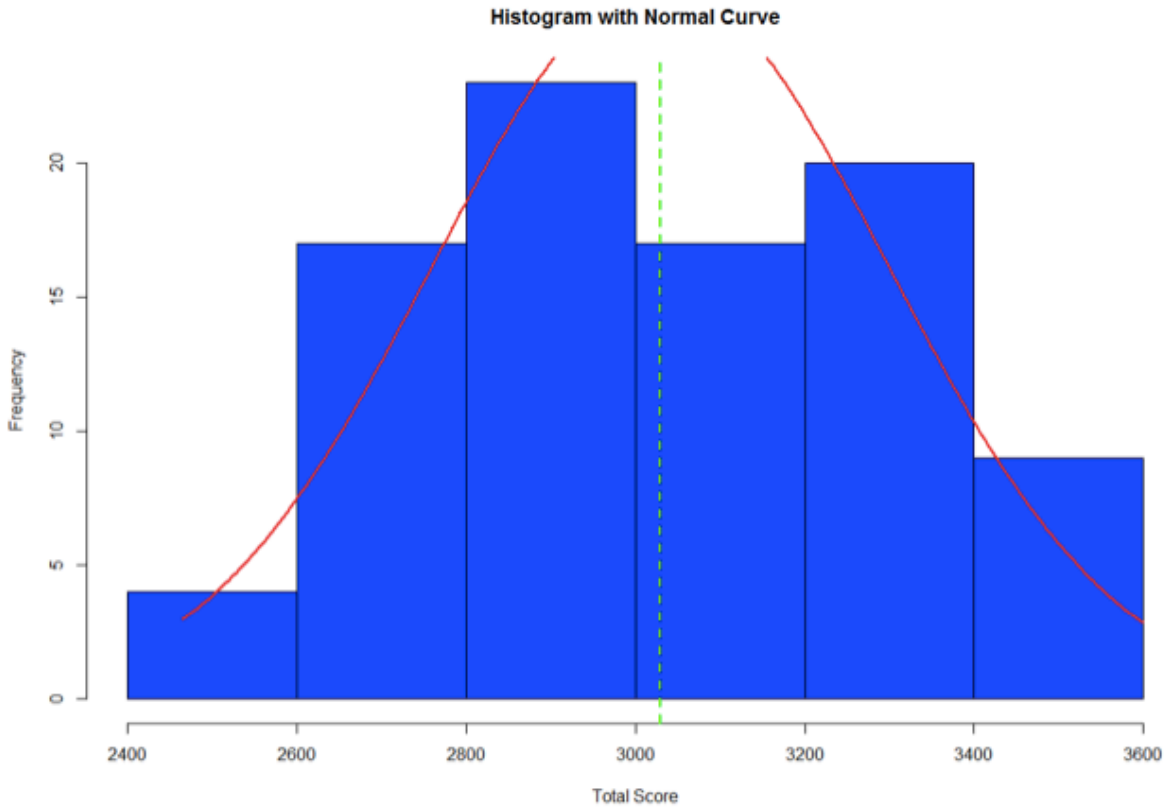


**Figure 9 Quality of Life Distribution in Propecia Group (Study Group)**

We added up the values of each health component among each group (study and control) to have an idea which health compontet in each group had the highest score and which one had the lowest score accodring to the following table.

| Health Component | Perfect Score | Propecia (study group) QoL Score | Standard Deviation | Propecia (study group) QoL | Minoxidil (study group) QoL Score | Standard Deviation | Minoxidil (study group) QoL |
|---|---|---|---|---|---|---|---|
| Physical Health | 1000 | 996 | 14 | 99% | 993 | 15.5 | 99% |
| Role Limitations Due to Physical Problem | 400 | 332 | 87 | 83% | 400 | 0 | 100% |
| Role Limitation Due to Emotional Problem | 300 | 182 | 116 | 61% | 300 | 0 | 100% |
| Energy | 400 | 307 | 43 | 77% | 397 | 8 | 99% |
| Emotional well-being | 500 | 373 | 60 | 74% | 500 | 0 | 100% |
| Pain | 200 | 200 | 0 | 100% | 194 | 13 | 97% |
| Social Functioning | 200 | 154 | 36 | 77% | 197 | 8 | 98% |
| General Health | 500 | 428 | 46 | 86% | 496 | 11 | 99% |
| Health Change | 100 | 57 | 13 | 57% | 55 | 12 | 55% |

Table2: Quality of Life Health Components' Scores of Minoxidil and Propecia Groups

## 3.7 Statistical Analysis Approach

We tested our hypothesis using the *t-test* to compare the means of the Quality of Life of the Propecia (study group) and the Minoxidil (control group), according to the SF-36 scale. After that we broke down the health components of the SF-36 scale and compared the means of each health component of the Propecia group (study group) to its parallel on the Minoxidil (group control).

Using the Analysis of Variance, we analyzed the effect age of the patients on the total score of the scale and because our age range was wide, we have decided to group the ages of the patients to 3 groups (16-25 \ 26-35 \ 36-45) to see whether a certain group had a different statistical significant over the others in each health component.

Once we established that, we analyzed the Quality of Life of Androgenic Alopecia patients using Propecia according to the duration of using the drug since other studies shave already proved it on different scales. We studied the correlation between the total scores of the patients, and then we broke down each health component and studied its correlation to the duration of use. Then had made the same approach with the compliance of using Propecia. We studied each health component according to the compliance of using the drug.

We also studied whether there was a correlation between the Quality of Life of the patients and the duration of using the drug if that variable was combined with the age of the patient.

Then again we studied the Quality of Life of patients using Propecia's score and its correlation to the duration if we combined it with the compliance of using the drug.

Also combining the age of the patient with the compliance was worth studying since we did not come across a similar study about the both independent variables combined.

And finally we combined the 3 variables to see if there is a statistical significance on the Quality of Life of the Androgenic Alopecia patients once applied all together.

## 3.8 Results

### 3.8.1 Propecia (study group) vs Minoxidil (control group)

We compared the means of the total scores of both groups then we broke them down to their 9 health components and compared them according to those components.

#### 3.8.1.1 Study Group vs Control Group Total Score

Running a t-test between the means of the 2 groups gave us a significant result with a *p-value* = < 2.2e-16. That indicates there a difference between the total scores of the 2 groups.

#### 3.8.1.2 Study Group vs Control Group in Physical Health

Comparing the means of the scores for the ability of the patient to do his daily physical activities like walking and exercising came with an insignificant *p-value*=0.21.

#### 3.8.1.3 Study Group vs Control Group in Role Limitation Due to Physical Problem

This health component indicates how much the patient daily production and accomplishment got affected by his health condition. We found a statistical significance between the means of the 2 groups at *p-value*=8.16e-11

#### 3.8.1.4 Study Group vs Control Group in Role Limitation Due to Emotional Problem

The importance of the emotional status of the patient might reflect o his job and production. And we compared the means of our control and study group with found a clear difference with a *p-value*=1.6e-15

#### 3.8.1.5 Study Group vs Control Group in Energy

Effect of using Propecia on the Androgenic Alopecia patient's patient was statistically significant according to our sample. The *p-value* once we compared their energy mean to the control group who are using Minoxidil was = < 2.2e-16

#### 3.8.1.6 Study Group vs Control Group in Emotional Well-being

Depression and anxiety were found to one of the most documented side effect from using Propecia. With = < 2.2e-16 we can say that there is a significant difference in the emotional well-being of the patients using Propecia in comparison to those who used Minoxidil instead

#### 3.8.1.7 Study Group vs Control Group in Pain

*P-value* = 4e-8 was the result of analyzing the mean scores of the Pain component between our 2 groups, indicating there was a significant difference between them.

#### 3.8.1.8 Study Group vs Control Group in Social Functioning

When we compared the means between the Propecia group and the Minoxidil group in terms of the interference of the drug's side effect with the patient's social life and being active in his community, we found a significant statistical difference between the two groups at a p=value of = < 2.2e-16.

#### 3.8.1.9 Study Group vs Control Group in General Health

This health components of the scale is the General Health assessment is important because the questions cover the patients' self-view on his health in comparison to the community around him. The p-value= < 2.2e-16 resulting from comparing the means of this health component between our study and control group, indicates a significant difference between the two.

#### 3.8.1.10 Study Group vs Control Group in Health Change

When comparing the scores of the 2 groups when comes to the patient's self assessment about his health change during the last year, we found that both group had a close scoring on the scale with a p-value = 0.3923

### 3.8.2 The Effect of Age on the Quality of Life

We first analyzed the total score of the Quality of Life of the study and control group and its correlation to the age. Then we sub-grouped the ages of the patients and analyzed them according to the total scores of the Quality if Life of the patients. Then we broke down the Quality of Life scale into its 9 health components and studied each component's scale and its correlation to the age groups we have sub-grouped our patients to, (16-25\26-35\36-45)

#### 3.8.2.1 Total Score with Age

Analyzing the association of age to the total score of the SF-36 did not show a statistical significance to the patient using Propecia group where the *p-value* was 0.23. The same case was found in our Minoxidil group resulted in a *p-value* of 0.24.

#### 3.8.2.2 Total SF-36 Score Among Patients' Age Groups

Once we grouped our Propecia and Minoxidil groups into 3 age groups of (16-25 \ 26-35 \ 36-45), the insignificance of the of the correlation of those age groups to the total Quality of Life score was clear with a *p-values* of 0.059 and 0.45.

#### 3.8.2.3 Physical Health Score Among Patients' Age Groups

Our Propecia group did not show a significant correlation to any age group with *p-value* =0.33 under the health component of Physical Health. When we looked up the same analysis with our control group of Minoxidil, we also did not a significant correlation *p-value* =0.9.

#### 3.8.2.4 Role Limitations Due to Physical Problem Score Among Patients' Age Groups

We were not able to point out a certain age group that was correlated to the score of the health component covering the physical limitations the patients have experienced among Propecia users. The *p-value* was 0.08 marking the insignificance. The control group of Minoxidil, neither showed a significant effect related to the patients' age group *p-value*= 0.69.

#### 3.8.2.5 Role Limitations Due to Emotional Problem Score Among Patients' Age Groups

Even though there was a clear change in the Quality of Life in this health component among Androgenic Alopecia patients using Propecia, we were not able to find a correlation between the that change among a certain age group when the *p-value* =0.11. Same scenario with our control group, none the age groups showed a superior, or inferior score in this health component as the *p-value*=0.69.

#### 3.8.2.6 Energy Score Among Patient's Age groups

Usually younger men would have more energy than older ones, however we did not find a statistical significance in this health component when we analyzed our Propecia users according to their age. The *p-value* = 0.16 clearly does not show a correlation between any age group and the score of the Energy on the SF-36 scale. Also the *p-value* of 0.48 among our control group shows that the correlation is absent.

#### 3.8.2.7 Emotional Well-being Score Among Patient's Age Groups

*P-values* of 0.28 and 0.69 shows there is not significant correlation between the score of Emotional Well-being component of the SF-36 Quality of Life scale among patients' age groups in both the study and control group respectively.

#### 3.8.2.8 Pain Score Among Patient's Age Group

The significant difference between the study and control group in the Pain component, was not found to correlate to any age group in our sample. With *p-values* of 0.5 and 0.61, there is not a statistical significance.

#### 3.8.2.9 Social Functioning Score Among Age Groups

Propecia users had a lower Quality of Life score in comparison to the Minoxildil users in the health component of Social Functioning. However that decrease was not correlated to any age group with the *p-value* of 0.56. Even though our control group of Minoxidil scored high in this component, there was not a correlation to a certain age group, *p-value*=0.47.

#### 3.8.2.10 Health Change Score Among Age Groups

Analyzing the score of the Health Change component on the SF-36 in relation to the age groups in our study and control group did not show any statistical significance. The *p-value* was 0.089 for the study group and 0.62 in the control group.

#### 3.8.2.11 General Health Score Among Age Groups

There was not a significant correlation between the age group of the Propecia user and their General Health score on the Quality of Life scale*, p-value*=0.79. However we were able to find a correlation between our control group of Minoxidil users and the age groups of the patients, p-value=0.0044. The age group of 16-25 scored the lowest of 450 out of 500, as 90% level of Quality of Life in comparison to other Minoxidil users' age groups, as show in the following plot.

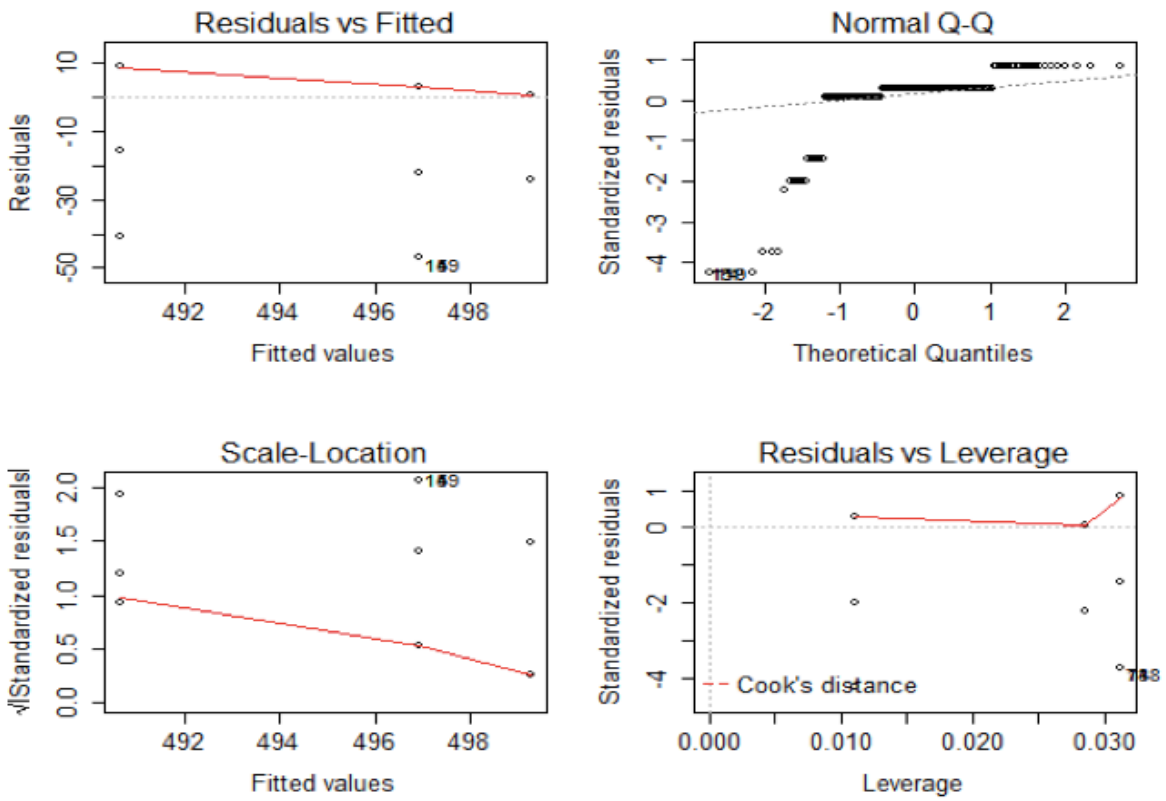


Figure 10 Correlation Plot: General Health and Minoxidil (Control Group) Age Group 16-25

### 3.8.3 The Effect of Duration on Androgenic Alopecia Patients Using Propecia

As we mentioned in our hypotheis that the duration of using the Propecia has an effect on the Quality of Life of the patient, unlike the Minoxidil users. For that reason, we have decided to analyze the patients using Propecia  according to their score on the Quality of Life scale and the duration of using the medication. We analyzed the association between the two variables. Once the total score of the the Quality of Life and then we broke down each health compenent to study whether it is linked to the duration or not.

### 3.8.3.1 Total Score of Quality of Life of Propecia Users and the Duration of using Propecia.

We were able to find a an association between the total score of the patients and the duration of using Propecia. The *p-value*<2.2e-16 indicates a significance link between them. The following plot shows the association between the total score of the Quality of Life of the patient and the duaration of using Propecia

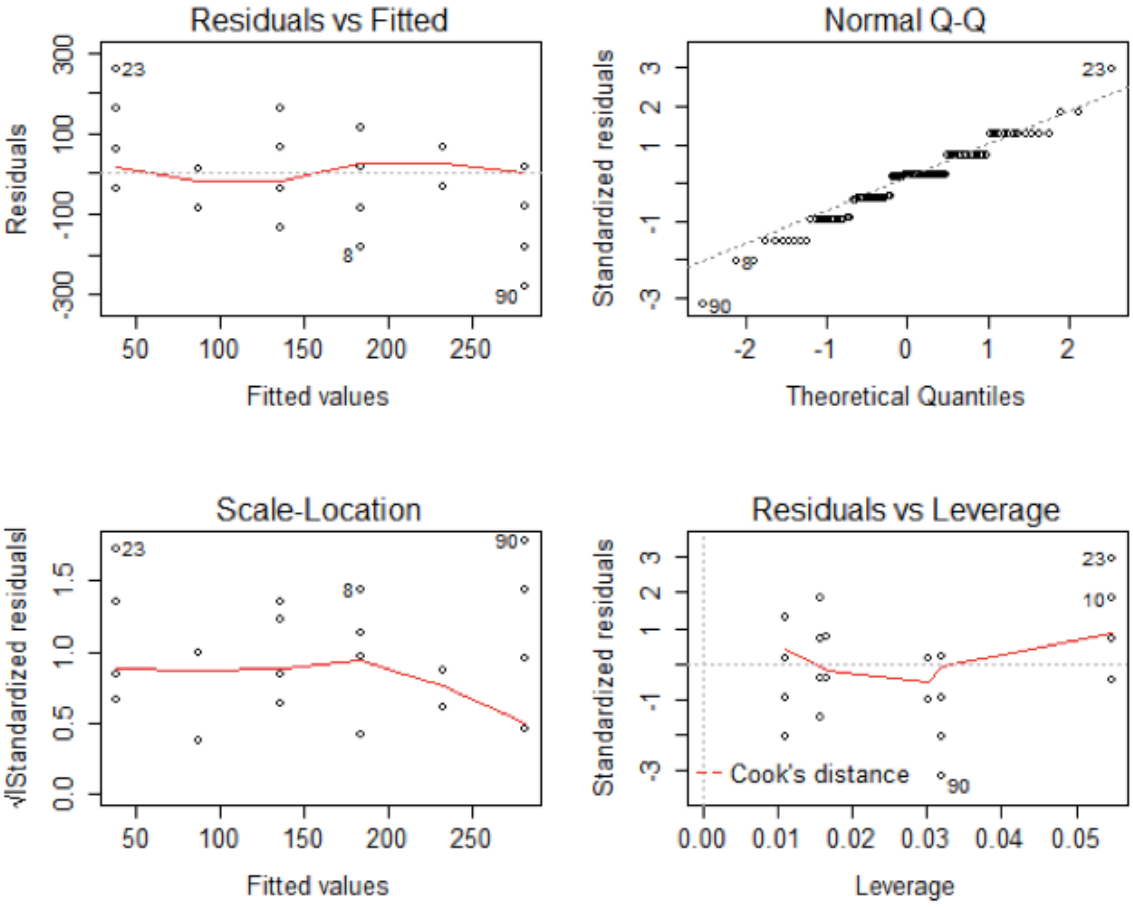


Figure 11 Correlation Plot: Total Quality of Life Score and Duration in Propecia Users

#### 3.8.3.2 Physical Health Score of Propecia Users and the Duration

There was not a statitical significance when analyzed the association between the duration of using Propecia and the health compenent regarding the patient's Physical Health.

#### 3.8.3.3 Role Limitations Due to Physical Problem Score of Propecia Users and Duration

With a p-value of <8.5e-9, a clear statistical significance stating the link between the patient's score when it comes to be limited due to a physical health and the duration of using Propecia.

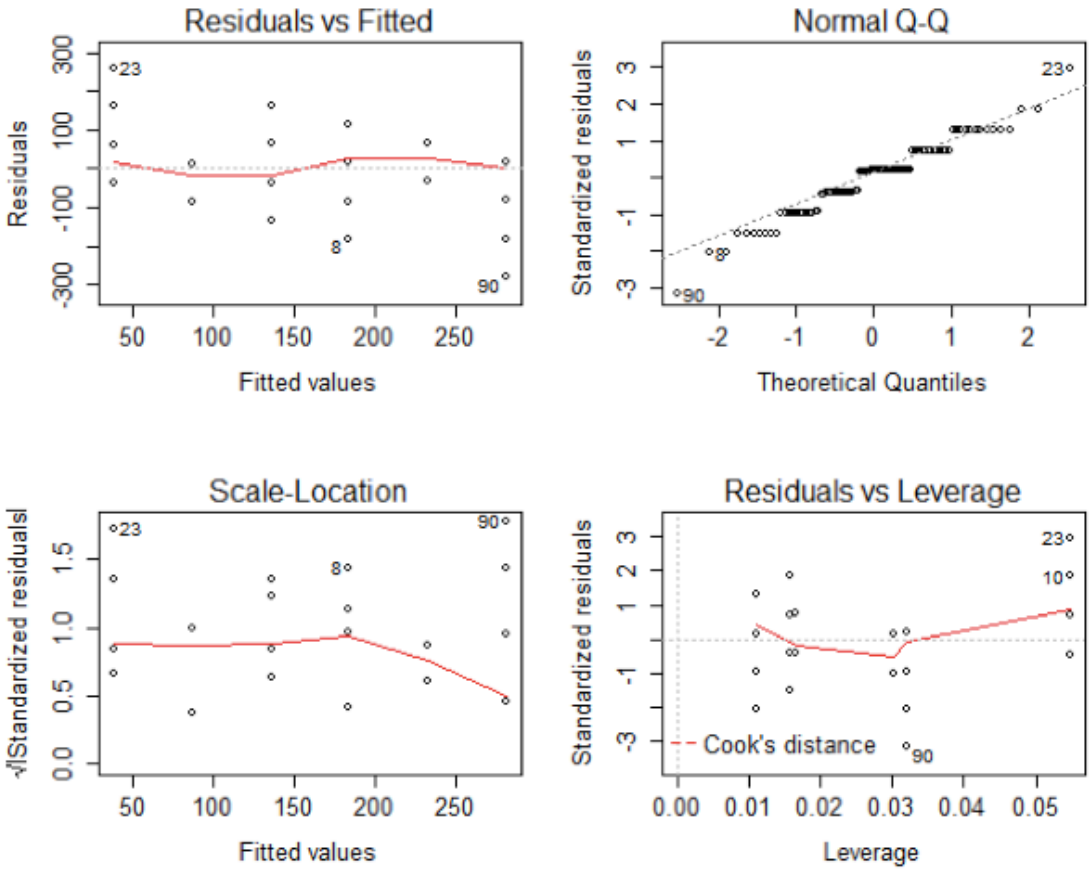


**Figure 12 Correlation Plot: Role Limitation Due to Physical Problem Score and Duration in Propecia Users.**

### 3.8.3.4 Role Limitations Due to an Emotional Problem Score of Propecia Users and Duration

When it comes to the association between using Propecia and its involvment in limiting the patients' daily acitivities because of their mental health status, we found a clear significant link. P-value<2.7e-11.

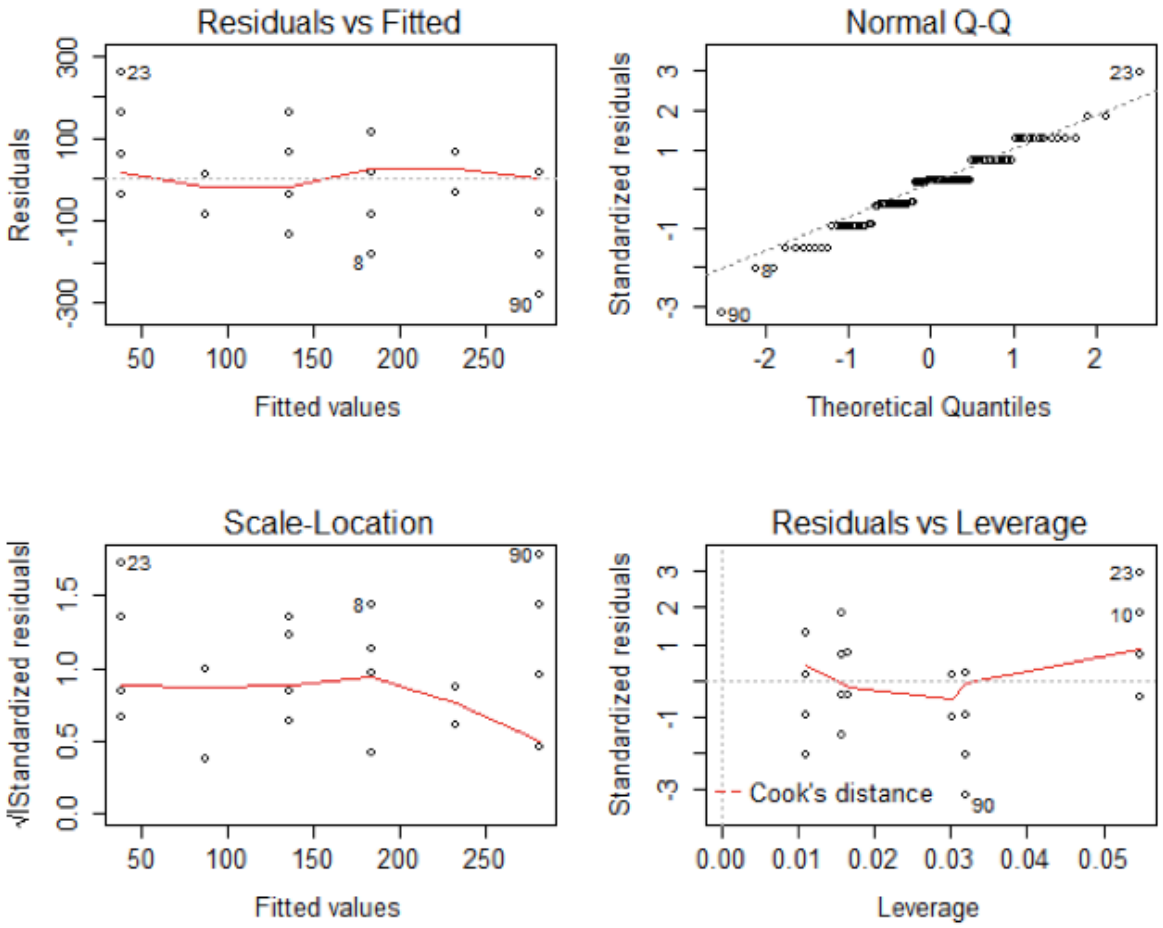


**Figure 13 Correlation Plot: Role Limitation Due to an Emotional Problem and Duration in Propecia Users.**

### 3.8.3.5 Energy Score of Propecia Users and Duration

Patients' scores showed a relation to the duration of using Propecia in temrs of the Energy health component of the SF-36 scale. The statistical significance of *p-value*=2.5<6 proves this relation among our sample.

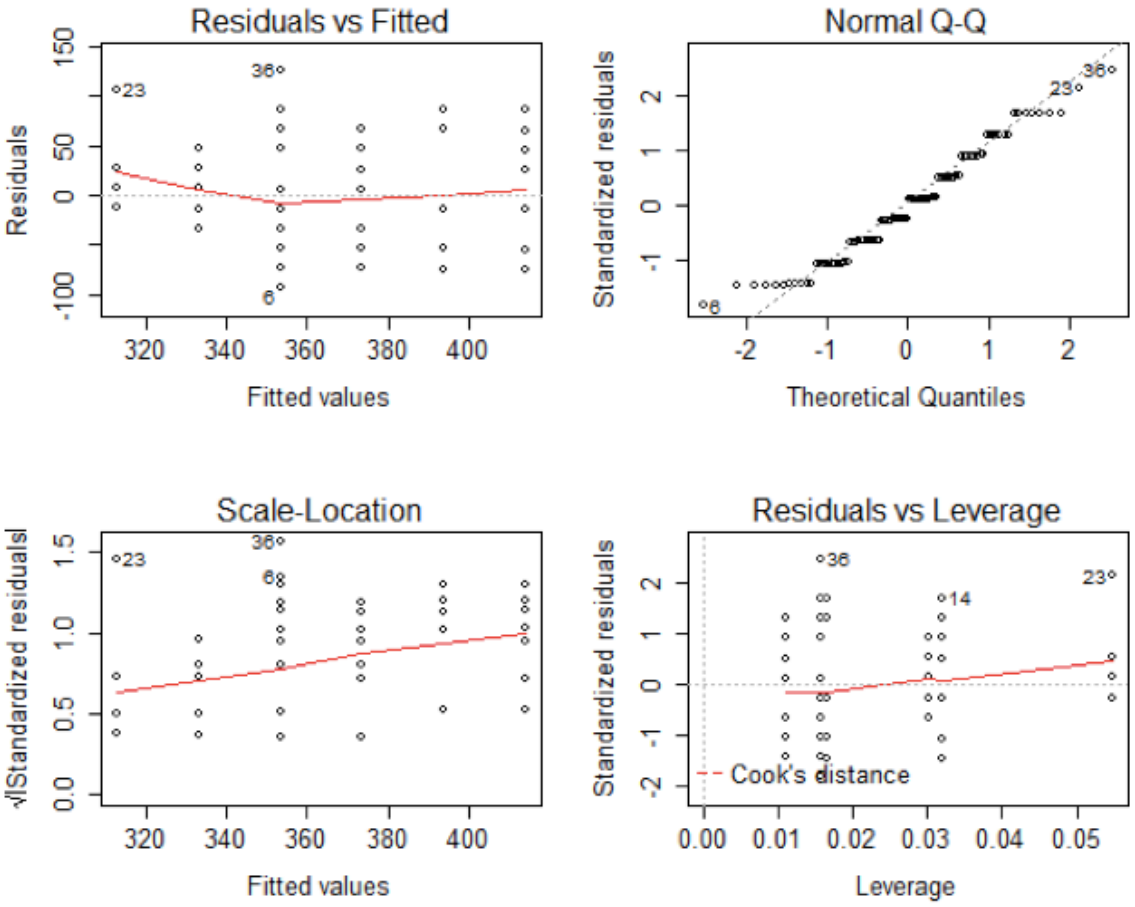


**Figure 14 Correlation Plot: Energy Score and Duration in Propecia Users**

### 3.8.3.6 Emotional Well-being Score of Propecia Users and Duration

The significance of the link between the the score the patients reported in the Emotional Well-being health compoenent has been statitically anaylzed with a *p-value*<3.4e-7.

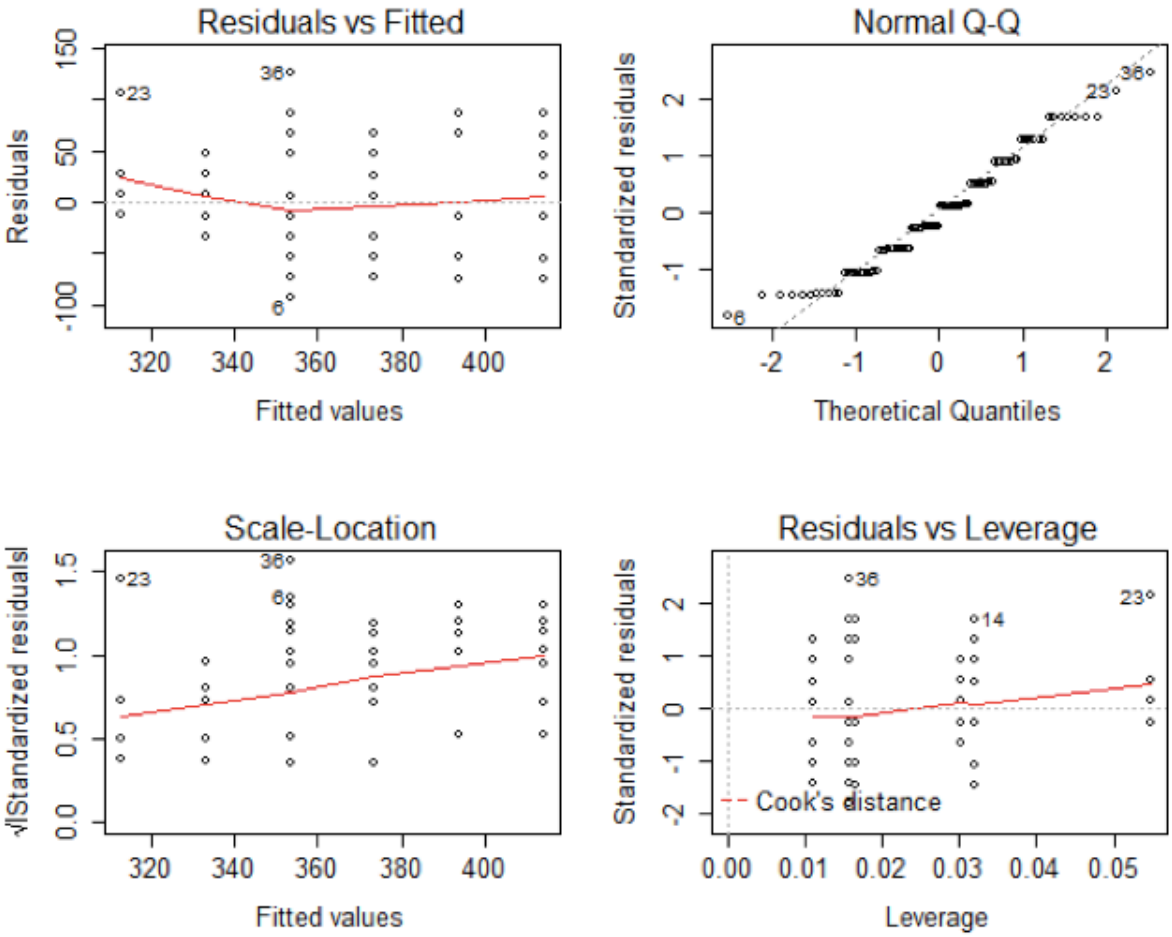


**Figure 15 Correlation Plot: Emotional Well-being Score and Duration in Propecia Users.**

### 3.8.3.7 Pain Score of Propecia Users and Duration.

The durtion of using Propecia did not show any significant relation to the Pain score on the Quality of Life scale.

### 3.8.3.8 Social Functioning Score of Propecia Users and Duration

The social activities of the patients who happened to be using Propecia, were found to be affcted by the paeriod of time they been on the medication. The *p-value* <4.3e-6

Shows the significance of that effect and the following plot demonestrates i

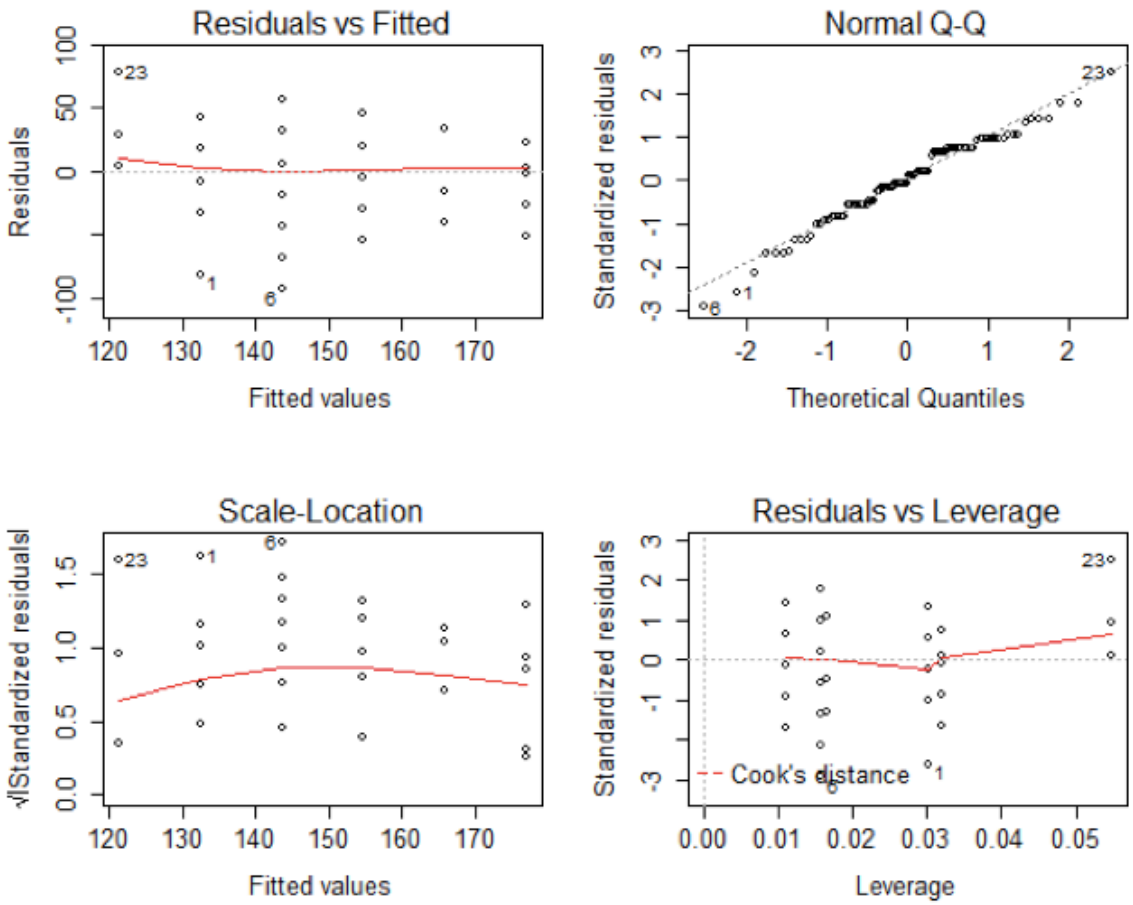


**Figure 16 Correlation Plot: Social Functioning and Duration in Propecia Users.**

### 3.8.3.9 Health Change Score and Duration

A *p-value*=0.07 was the statistical result when analyzing the score of the Health Change component among Androgenic Alopecia patients using Propecia in association to the duration of use. That value makes the relation between the two variables statistically insignificant.

### 3.8.3.10 General Health Score and Duration

When analyzing the score of our study group according to the duration of using Propecia, there was a statistical significance at a *p-value* <3.4e-6. We can see that link from the following plot

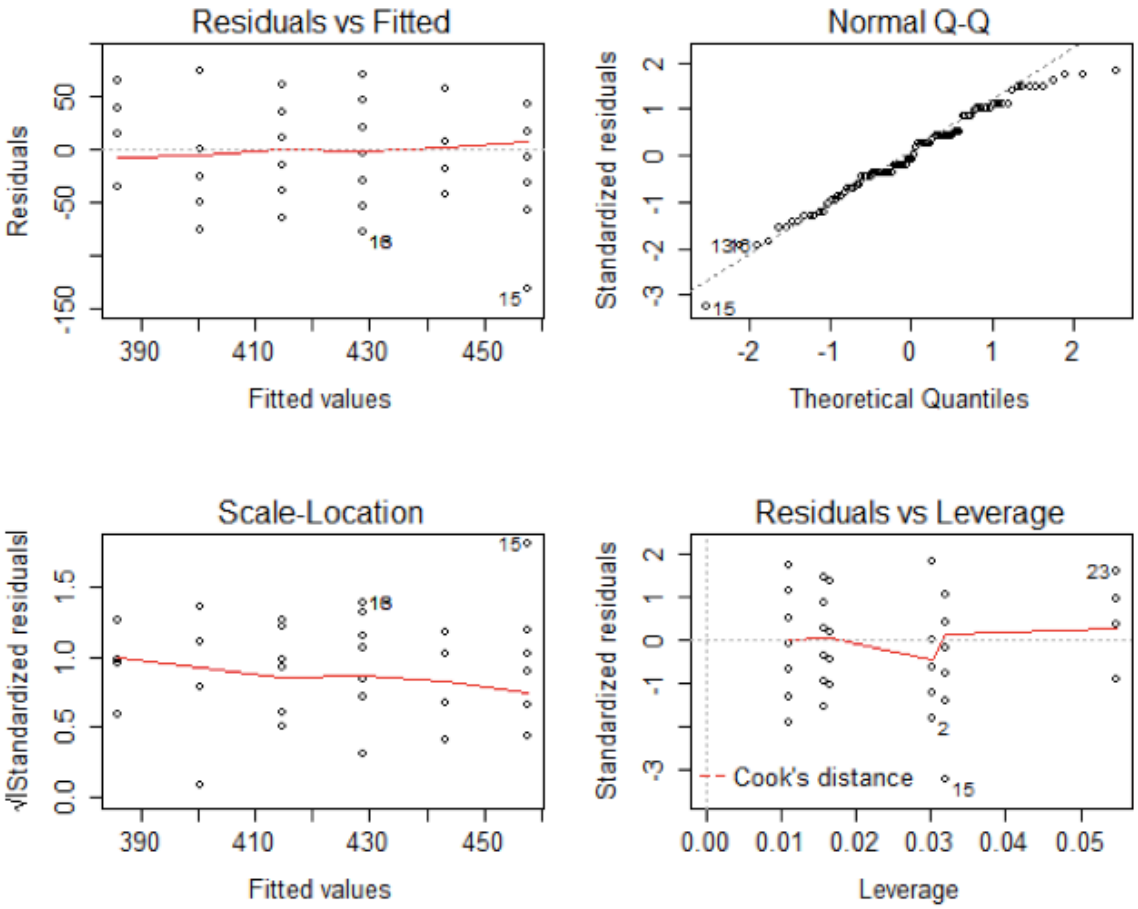


**Figure 17 Correlation Plot: General Health Score and Duration in Propecia Users.**

### 3.8.4 The Effect of the Compliance of the Patient Using Propecia on their Quality of Life Score.

We analyzed the connection between the score of Androgenic Alopecia patients who are using Propecia according to their compliance of using the drug. The compliance responses we got were either complied or semi-complied, and none of the participant responded as not-complied to using Propecia. Once we got the data we studied its link to the Quality of Life's total score then analyzed each health component.

#### 3.8.4.1 Total Score of Quality of Life of Propecia Users and the Compliance of Using the drug.

On the contrary of our expectation, the connection between the total score collected from the patients was found to be not significant *p-value =0.23,* when it came to the duration of using Propecia.

#### 3.8.4.2 Physical Health Score of Propecia Users and the Compliance of Using the drug.

We could not find a statistical significance in relation to the association of the patient's Physical Health score and as the *p-value* came up as 0.07

#### 3.8.4.3 Role Limitations Due to Physical Problem Score of Propecia Users the Compliance of Using the drug.

Unlike the duration of using Propecia, the compliance of using the drung wan not found to have relation to the score of the patient in this health component. *P-value*=0.2

#### 3.8.4.4 Role Limitations Due to Emotional Problem Score of Propecia Users the Compliance of Using the drug.

At a p-value of 0.34, there was not a significant association between the limitation of the patient's daily activities due to some emotional problem and his compliance to using Propecia.

#### 3.8.4.5 Energy Score of Propecia Users and the Compliance of Using the drug the Compliance of Using the drug.

When we analyzed our sample in regard to the link between their compliance and there Energy score, the result came with a *p-value*= 0.7 indicating an insignificance between the two.

#### 3.8.4.6 Emotional Well-being Score of Propecia Users and the Compliance of Using the drug.

The compliance of using Propecia, according to our sample, does not have a signifance relation to the score of this health compoenet. *P-value*=0.68

#### 3.8.4.7 Pain Score of Propecia Users and the Compliance of Using the drug.

Just like the age and duration of use among Propecia users, the compliance did not have a connection to the Pain component on the Quality of Life score, *p-value*=0.33

#### 3.8.4.8 Social Functioning Score of Propecia Users and the Compliance of Using the drug.

When the *p-valu*e of 0.7 came up from analyzing our sample, the statitical relation between the Social Functioning score of the patient did not have a significant connection to the compliance of the usnig Propecia

#### 3.8.4.9 Health Change Score and the Compliance of Using the drug.

The complinace of using Propecia was not a factor determing the patient's own view about his health change throughout the last year. The *p-value* came as 0.18 from our sample stating the insignificance.

#### 3.8.4.10 General Health Score and the Compliance of Using the drug.

According to our sample's score in the health component that measures the patient's self-assessment about his General Health in relation to the patient's compliance to Propecia, we did not find a statistical significance between the two. The *p-value* once we analyzed the patient's records came as high as 0.8 showing that the compliance did not have an effect on the General Health score of the patient.

### 3.8.5 Quality of Life Score of Patients Using Propecia in Relation to Duration and Age Combined

After we confirmed the relation between the duration of using Propecia and the Quality of Life score, we added the age factor to the equation, which did not have a statistical significance on its own.

Interestingly, the result of combining the two factors did not have an effect on the Quality of Life of the patient. The *p-value* came as 0.89 implying that insignificance.

### 3.8.6 Quality of Life Score of Patients Using Propecia in Relation to Duration and Compliance Combined

Duration and compliance, separately, were found to be important factors affecting the Quality of Life of the patients using Propecia according to our literature review. However, our sample only showed that affect from the duration of using the drug, while the compliance did not show an effect.

We combined the two factors and analyzed the patients' Quality of Life according to that. The *p-value* of 0.41 shows that there is an insignificant connection between the two factors combined the score of the Quality of Life of the patients using Propecia.

### 3.8.7 Quality of Life Score of Patients Using Propecia in Relation to Age and Compliance Combined

We decided to combine the age of the patient with the compliance of using the drug. We did not find a statistical link between the variables combined and score of the Quality of Life of the patient. *p-value*=0.63

### 3.8.8 Quality of Life Score of Patients Using Propecia in Relation to Duration, Age and Compliance Combined

In our review, we found that several factors affected the Quality of Life of the patients independently. Same thing was noted that in our sample but only with the duration factor. When we combined 2 of the factors and analyzed their effect on the total score of the Quality of Life, we did not find solid connection.

The next step was to combine all the three factors, age, duration and compliance, and study their combined effect on the Quality of Life of Androgenic Alopecia patient using Propecia.

We found out that the statistical result was insignificant. The p-value of our analysis of our sample is 0.43. For that reason, we can say that there is no effect of the three-combined factors on the Quality of Life according to our sample.

## 3.9 Discussion

The overall study has showed a decreased level of Quality of Life in Androgenic Alopecia patients who are using Propecia in comparison to Minoxidil patient. Even though we assumed the Quality of Life of the patient prior to starting both medications, Propecia and Minoxidil, was not as low as what we have found in the literature because

of the tradition head garmet (the shemagh)(136)(137), we can see that it got effected negatively after starting the medication Propecia because our control group scored higher on all health components in comparison to the study group, except in the Physical Health, where the scores were not significantly different and the Pain components, where the control group score was found to be significantly lower.

The statistical significance of decreased total score of Quality of Life result implies and confirms the hypothesis of a lower Quality of Life in patients who are using Propecia to treat Androgenic Alopecia versus Minoxidil.

Such a result solidates the studies that reported the side effects after using Peropecia. It also suggests that participants, who took part in the studies that were focused on a certain side effect, such as impotence and low libido (88), might suffered from other side effects, such as anxiety and depression, during the study but did not report that since the study did not cover the mental condition of the participants.

Looking at the levels of Quality of Life scores among the health components, we can see that the Role Limitation Due to Emotional Problem was the most effected part of the scale among Propecia users at a score of 61%. This scale is supposed to measure how much the mood and mental status of the patient effected his production and work. Consistently, we noticed that the second lowest score was the Emotional Well-being at a 74% for the scale that implies whether the patient has a mental or mood issue or not, or if the patient might be suffering from depression-anxiety-like symptom. Those symptoms are corresponding with another health component, the Social Functioning. As mentioned in the literature (112) depression and anxiety were found to affect the patient's social life.

That shows the intervention of Propecia to improve the patient's confidence in social settings has backlashed on the patients on our sample.

However we found out that patients have contradicted their answers when it came to the Physical Health. We did not find a statistical difference between the study and control group in the Physical Health components but there was a difference in the Role Limitation Due to Physical Problem and Energy level. Because of this contradiction, we looked more into the scenario and came with a possible explanation. Even though the patients' physical status was not very negatively effected, from the high score of 99% on physical health, their physical abilities to perform (83%) and their level of energy and vitality (77%) got effected by their mood and mental status. It was found that mood disorders such as depression and anxiety, have an effect on the patient's physical activities. 8 studies involved a meta-analysis of the correlation between mood disorders and level of physical exercise. There was a clear statistical significance that depression has decreased the physical performance of the patients who do not have any physical illness. This confirms the results from our sample making one of the potentials of the side effects of Propecia is mood-induced limitation of physical activities.

We need to mention that we found a statistical difference among the health component of Pain between the 2 groups. Except that in this case it was the control group, Minoxidil users, that scored lower. But because the SF-36 is a general Quality of Life health assessment, we were not able to point out in which part of the body the pain was and other related pain characteristic. If we made of an assumption according to our literature review, the pain we found associated with Minoxidil would be from the skin irritation (53) on the area the medication was used on. However, we were not able to confirm that

since the scale did not include any details else that the pain's presence and severity. Future studies must clear out any physical illness in both groups to avoid that bias or include the symptoms of  scalp irritation due to using Minoxidil.

**Age**

According to the literature review,age has been reported to play a role in the Quality of Life of Androgenic Alopecia patients. Yet again, that role got contradicted. A study reported that younger patients had a better Quality of Life, as they have expressed better coping with the condition based on the fact that the severity has not occurred much enough to alter a patient's Quality of Life making their older peers have a lowered score.On the other hand, other studies showed that the older patients had better coping with the condition based on the fact that by the age they have reached, they have already established their lives and body image is not as important as to the young patients.(20)(27).

With that we have decided to study the correlation between the age of the patient and the Quality of Life score and made a hypothesis based on it. However that hypothesis was rejected because we did not find a statistical significance between the two. The same result came out when we looked up the association between the total scores of the Quality of Life and any age group among our sample. Actually, we did not find any association between any of the health components with any age group, except for the control group who happened to be between the age of 16 and 25. That age group has shown an association with a lower General Health component compared to other age groups in the control group.

We were not able to point out the exact reason for that score because our study was about the effect of Propecia on the Quality of Life, not Minoxidil, which has actually shown a good scoring in its group.

The questions for General Health component included the following :-

"How TRUE or FALSE is <u>each</u> of the following statements for you.

- I seem to get sick a little easier than other people
- I am as healthy as anybody I know
- I expect my health to get worse
- My health is excellent
- In general, would you say your health is excellent.

The answers for this question were scored as [100 – 75 - 50 - 25 – 0]. The values were assigned to the following answers [Definitely true, Mostly true, I don't know, Mostly wrong, Definitely wrong] depending on the nature of the question.

Based on this way the answers are presented, a probable explanation for the nature-lowered score among the youngest age group of the control group. Most participants have answered "I don't know" to some of the last three questions making their score to be lower than other age groups. Yet that explanation cannot be confirmed because the other age groups from the control group answered it perfectly.

However, we should emphasize on the fact that the un-relatable link between the age and the score of the Quality of Life among all health components findings corresponds with the contradiction between the studies we have covered in our literature review.

But it is worth mentioning that we were expecting younger patients in our sample to have a lower Quality of Life in the Propecia users groups. The reason behind that is the fact younger patients would expect to be more sexually active than the older ones. And considering the negative side effect of Propecia on the patient's sexual life, the impact on the patients' Emotional Well-being would be worse in that young age group as sex plays a more major of a role in their lives. Especially because the younger age group in specific are expected to be looking for their life spouse by that age, or have recently got into wedlock. The side effect of erectile-dysfunction or loss of libido leave the patient with the feeling of inability to live up to the expectation from their spouse or to face the pressure by their families to get married knowing they would not be able to sexually perform and subsequently have their own offspring's. Probably that expectation was not confirmed because in a previous study about Propecia's efficacy, better results were noted in younger patients (78). So the good results of the hair regrowth and patients' satisfaction might have been neutralized by the side effects of the drug.

**Duration**

Our study also found statically significant correlation between the duration of using Propecia and the total score of the Quality of Life of the Androgenic Alopecia's patients. We can understand from this finding that the patients' side effects got worse with time, which can be interpreted as a sign of inability of the patients' bodies to adapt to the side

effect of Propecia and build tolerance in order to bring the body's condition back to normal as prior to starting the medication.

We confirmed that finding when we studied the correlation of the medication to each health component of the SF-36 Quality of Life scale. All the components that were affected by taking Propcia, were found to be correlated to the duration of using the drug. Also the expected result was found in the health components, which were not affected by the drug. Pain, Physical health and Health Change scores' were not correlated to the duration of using Propecia.

Worth mentioning, that according to the American Hair loss Association, Bradley Wolf stated Propecia's therapeutic effect of preventing hair-shedding, was found to be decreasing with time. In a 5-year follow up study, Propecia has proven to slow down the hair loss process but the team conducting the study has documented that there was a progressive level of hair loss also (139). We cannot determine whether the patients in that study have built a tolerance to Propecia's effect or not. Also let us not forget Rossi's 10-year study that shows that the hair regrowth has improved with the time using Propecia. If the information from the American Hair Loss Association was confirmed by adequate proof from mort studies, that will make choosing Propecia as a long term solution a bad decision since patients have expressed a correlation between the time period of using it and the worsening of the Quality of Life, and also its therapeutic use has shown decrease in Propecia's efficacy.

**Compliance**

Propecia's half life in the blood lasts from 6-8 hours, for that reason the drug is prescribed to be taken once a day to maintain its level in the blood. Being not complied means that the targeted drug level will not be constant in order to get the desired result. We can also say it means that the not-complied patient's exposure to the drug will be less than the exposure in complied-patients. Based on that, we wanted in our study to know whether the compliance of the patient to taking the drug as instructed, once daily, would negativity of the Quality of Life's score and made a hypothesis on that correlation. We were expecting patients who were not complied with the medication i.e. the body's exposure to Propecia was not as high as in patients who were complied, will have a better Quality of Life. In our measuring tool we have added a compliance item that included 3 levels of compliance as: complied, semi-complied and not-complied.

None of our study-group of Propecia users has chosen the option of not-complied which left us with 2 groups to compare their mean, complied and semi-complied.

As the result came with a high *p-value =0.*23, our hypothesis should be rejected. That can be interpreted as that Propecia's side effects has the same impact on the patients Quality of Life regardless of his compliance and the side effects signs might have been irreversible as some cases were reported. Even though that we were not able to find a correlation between the patient's compliance to the medication and the score of the Quality of Life, we raised the question why some patients were more complied to the medication more than others. The instruction of using Propecia is simpler than using other Androgenic Alopecia treatments, such as Minoxidl which requires twice topical application of the drug on a cleaned hair, and the laser comb that require at least 20 minutes of the combing the hair daily. Some studies suggested that the expectations of

the patients' regarding the results of some medications made them more complied than others (140). Meaning those who were complied had a better understanding of the drug's efficacy and subsequently they were more satisfied about the treatment than the ones who were semi-complied. On the down side however, both Propcia groups (complied and semi-complied) did not have significance different in score of the Quality of Life scale. That makes non-complied patients have the worst experience of using Propecia between the two groups since they suffered from the same severity of the side effects of the drug and yet did not have the desired results from using Propecia.

But we cannot firmly state that because our measurement to the compliance was not detailed. This should be taken in consideration in further trails because our sample seemed to be obligated to chose between just 3 levels of compliance, where scaling the compliance to different level would give a clearer answer about the patient's compliance to the medication.

**Combined Factors**

After establishing the correlations' main hypotheses, the Quality of Life score in relation to age, duration and the compliance of the patient separately, we decided to go further in our study and combine the variables together and analyze our data according that.

Some studies in different health conditions proved that between the age of the patient and the duration of the illness and a certain medication is a correlation to the outcome of the treatment (141). And since according to several studies relating the age and duration, separately(20)(27)(78), to the health outcome, in our study, we had a hypothesis suggesting a correlation between the combined factors and the score of the Qaulity of

Life. That hypothesis however is rejected, as we did not find a strong correlation between the Quality of Life score and the combined factor of duration and age.

Another combined factor we expected the Quality of Life to have a correlation with, is combining the duration of using Propecia with the patients' compliance to the drug. We built our hypothesis on the idea of the implication of the patients who been complied to using the medication for a longest period of time, would have a worst Quality of Life score than the other patients because those are the ones who got exposed the most to the drug. But after analyzing our data according to this hypothesis, we did not find a link between the Quality of Life score and combining the duration and compliance together and the hypothesis got rejected.

We also analyzed our sample based on combining the age of the patients with their compliance level. The hypothesis was there would be an effect once we study their value according to the score of the Quality of Life. But we rejected that hypothesis as the result was insignificant.

Lastly we added up all the three variables, age, duration and compliance of the patient to the medication, and analyzed the newly formed factor, made out of the three, according to the Quality of Life score on the SF-36 scale. The result came statistically insignificant in our sample. Even though the duration of using Propecia was found to have an effect on the Quality of Life score, the its effect diminishes as we combined it with the statistically insignificant factor of age and the statistically insignificant compliance of using the drug. We can tell based on our sample, this result of using Propecia to treat Androgenic Alopecia was a negative medical intervention. And based on the reports from the studies suggesting the effects of the drug are irreversible in some cases, Propecia should be

classified as bad first line of treatment by dermatologist. Especially in mild cases of Androgenic Alopecia, Propecia should not be considered part of the initial treatment plan. Even if the patient's complaint gave the impression of a serious decrease of his Quality of Life because of loss of confidence and the interference of the condition with the patient's social life, according to our sample, Propecia is considered a less favorable treatment for number of reasons such as (1) the overall treatment might worsen the case as what we have gathered from our sample (2) the patient might have some initial symptoms that are similar to some of the Finasteride side-effects and starting the Propecia treatment might superimpose those symptoms. Dermatologist must discuss the all alternative treatment options with the patient before deciding to proceed with the Propecia and inform the patient about all efficacy levels of each option and its side effects.

Our finding suggests dermatologists are strongly advised to assess the patients for symptoms that are similar to the known side effects of Propecia. Also it is important for the dermatologist to clearly educate the patients about the side effects of the medication. That importance is critical because once the patient starts experiencing the Propecia side effect, he would be able to understand that it is drug-related rather than another health abnormality.

That makes continues assessment of the patient's general health an essential clinical practice. The clinician should emphasize on follow-up appointments and explain to the patient that those appointments are as important not only to assess the progress of the treatment but also to maintain the patient's Quality of Life.

**SF-36 as a measurement tool**

After conducting our study we noticed different downfalls for the SF-36 measurement tool being used in Saudi Arabia and specially in our targeted area. The main downfall was the Arabic words describing the scale levels of some questions and the value given to these questions. Even though SF-36 has been validated in different regions in Saudi Arabia, the Northern Region participants showed some bias in their answers that might contradict other answers, which subsequently impacted the result.

For example, our control group's mean score level for Physical Functioning was 99% that matches their level of Role Limitation Due to Physical Problem which was 100%. However, our study group scored same as 99% on the Physical Functioning but their results came up as 82% for Role Limitation Due to Physical Problem. The un-matched scores raises the question of did the patients fully understood the question. Because the exact translation of the question is "were you unable to achieve your daily work because of you're a physical problem?". That statement might have confused the patient with feeling fatigue and tired since it is a physical state. As matter of fact their answers' score was consistent with their answers to the health component of Energy. The Energy component measured the level of pep the patients had in order to perform their daily activities, both physical and social. Because of that, we believe the Energy component was consistent with the Social Functioning score, which according to the patients' understanding might be connected to the Role Limitation Due to an Emotional Problem. The lowest score was actually documented in the latter's component.

The explanation we mentioned about the effect of depression on the physical activity was based on out own view on about the scenario. For that reason, in future studies, there

must be a more clear question stating whether the patient had a limitation in his daily physical activities due to specific physical illness in order not to confused it with a result of the mental health problem.

Another result that is worth analyzing is the Health Change components. We found out that both groups, Propecia and Minoxidil have scored interestingly low as of 57% and 55% respectively. And that was the lowest scores from both groups.
We realized that that scale was rather confusing to most of the patients. The question for the Health Change component goes as the following

"Compared to last year, my general health is:

1. Much better now than a year ago.
2. Somewhat better now than a year ago.
3. About the same as a year ago.
4. Somewhat worse than a year.
5. Worse than a year ago.

Answer number 1 was valued as 100, answer number 2 was valued as 75, answer number 3 was valued as 50, answer number 4 was valued as 25 and answer number 5 was valued as 0.

From the mean score of 57-55 out of 100, we can confidently say that most of the patients answered “About the same as last year”, which made sense to them because the wording was not specific to mental or physical problem.

That kind of bias would have been avoided if there was a different way of wording the scale in Arabic. As we noticed an unclear bias in the question about the General Health components, the same situation is applied here on the Health Change component. The answers as “I don’t know” and “About the same” seem to be more favorable in some patients because of their neutral nature.

## 3.10 Summery of Results' Hypotheses

1. Patients using Propecia have lower Quality of Life in comparison to other patients using Minoxidil.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(ACCEPTED HYPOTHESIS)**

2. Age of Androgenic Alopecia patient using Propecia affects his Quality of Life score.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

3.Duration of using the Propecia affects the Quality of Life score of Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(ACCEPTED HYPOTHESIS)**

4.Compliance of Androgenic Alopecia patient to the drug Propecia affects the Quality of Life score.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

5. Combining the 2 variables of age and duration affects the level of Quality of Life score in Androgenic Alopecia patients using Propecia.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

6-Combiing the 2 variables of age and compliance affects the level of Quality of Life score in Androgenic Alopecia patients using Propecia.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

7.Combining the 2 variables of compliance and duration of using Propecia affects the Quality of Life score of the Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

8- Combining the 3 variables of age, duration and compliance affects the Quality of Life score of the Androgenic Alopecia patient.

Null Hypothesis: $H_0 = H_1$

Alternative Hypothesis: $H_0 \neq H_1$ **(REJECTED HYPOTHESIS)**

# 4. Conclusion

For Androgenic Alopecia, Propecia has proven its efficacy as well Minoxidil. However according to our study, the overall outcome and Quality of Life of the patients in general had been altered after using Propecia in comparison to the patients who used Minoxidil. On the SF-36 Quality of Life scale, patients has scored the least on the Role Limitation Due to Emotional Problem. Lower scores were registered, from our study group, in health components that are related to the psychological status of the patients, Emotional Well-being, Social Functioning.

We also found a decreased level of Role Limitation Due to Physical Problem even though the patients scored high in Physical Health. That made us consider that the patients' mental health has impacted the level of activities that patients usually capable of performing.

Our study concluded that the longer time the patients used the drug, the lower score of Quality if Life is reported. Meaning there is a clear correlation between the duration of using the medication Propecia and the Quality of Life.

Unlike the duration of use, the age of the patient was found not to play a role in altering the Quality of Life. The hypothesis of the correlation between the two variables was rejected.

The compliance of the patients to use the medication Propecia was found not to be correlated to the score of the Quality of Life. Even though complied patients were expected to have a lower score than the semi-complied because of their exposure to the medication was higher, comparing the scores of the two groups did not have a statistical significant.

We also expected the patients to have a significant correlation once combining the duration of use with the compliance because of the increased exposure of the patient to the drug, both dose-wise and time-wise, yet we did not find a strong correlation once adding the two variables.

We also analyzed the sample to find whether combining the duration of using Propecia to the age of the patient would have an effect on the Quality of Life. The result was statistically insignificant. Same result was found when combining compliance of the patient with the age. No correlations were found in both scenarios.

# 5. Recommendations and Further Studies

Even though Propecia have been proven to be a good treatment for hair shedding in Androgenic Alopecia patient, the obvious alteration of the Quality of Life is a serious matter to be considered before prescribing the medication. Instead of improving patients' lives, the medication can worsen it making the ultimate outcome to be negative.

So it is very important for physicians to emphasis on instructing the patient to come back to assessing his condition. Regardless of how the hair regrowth has improved, calling back the patient to assess his Quality of Life is very essential with this medication.
Our study has shown the longer the patient is on the medication, the worse level of Quality of Life has become, and making periodic assessment is a must throughout the treatment.
Both, the patient and the dermatologist must consider all that, before choosing this kind of treatment disregarding the patient's age.

We noticed certain complications and difficulties in the course of our study that should be taken in consideration for future studies.

1- Country of study: we found out that Saudi Arabia lack many important elements when it comes to conducting a study regarding Androgenic Alopecia. We were not able to find any studies that cover the incidence and prevalence of Androgenic Alopecia in Saudi Arabia and subsequently the Quality of Life in Androgenic Alopecia. Adding to that we could not find a similar study covering the Quality of Life among Androgenic Alopecia seeking medical intervention in Saudi Arabia.
2- The Shemagh : If a similar study is to be conducted in Saudi Arabia, the Saudi Arabian head garment, the Shemagh, should be considered when conducting such a study in Saudi Arabia. Because the Shemagh is a basic piece of clothing that essentially all Saudi men wear it throughout their professional and social

activities. It would obviously make a difference assessing the Quality of Life in Androgenic Alopecia patients and the coping mechanism they practice.

3- A more validated SF-36 Arabic version based on our population of Androgenic Alopecia seeking medical intervention: The current Arabic SF-36 had a confusing health component to our population, Role Limited Due to Physical Problem, which made the answers of the patients' regarding physical health components inconsistent.

4- Patient's marital status: From our literature review, we found that one of the reasons the Androgenic Alopecia patient's Quality of Life is lowered is because his ability to find a life partner. It would be worth studying in the future whether the Quality of Life of the Androgenic Alopecia patient who is using Propecia has a different scoring than the single ones. That can be a 2-way path because guaranteeing a life companion might improve the Quality of Life but also, because of the sexual side effects of the patient,the Quality of Life might get affected negatively.

5- Compliance: Even though we have included compliance in our study, we did not scale compliance in a good regressional manner, especially for a medication like Propecia, where good compliance means taking the medication once daily. We suggest scaling the compliance as a percentage as (0\20\40\60\80\100)%. That scale would give a better insight about how the compliance to Propecia would affect the score of Quality of Life in Androgenic Alopecia patients.

6- Finastride Splitters: We were not able to truly assess the Quality of Life among our targeted group because many of the users were buying the cheaper version of

the medication, the ovther the counter 5 mg Finastride, which is used to treat Benign Prostate Hypertrophy and split it to 4 quarters and just take one part of the pill everyday. That action made us miss a good number of patients who their Quality of Life score could have altered the results.

7- Clinic-Pharmacy Coordination: At the first trial of the study, we have chosen the dermatology clinic assuming it is the location where patients would come to be assessed about their progress in the treatment. However, the patients barely showed for their follow-up appointment. The problem here is that patients, who are not assessed after starting the treatment, might suffering from the side effects mentioned and have no clue that it is caused by the medication. Hence pharmacies must be instructed to advise any patient who comes to re-fill his prescription, to follow-up with his physician to clear out any occurring side effects.

8- Mood-induced physical limitation: further studies should take in consideration that the patients might score low on their Role Limitation Due to Physical Problem health component because of the impact of their mental health on their physical activities.

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To whom it may concern

This is with reference to data required for Dr.Naif Alanazi who is currently pursuing his PhD Dissertation work at the Department of Health Informatics, Rutgers, Newark, NJ 07107-3001. We are providing herewith completely de-identified data pertaining to the Quality of Life Among Propecia and Minoxidil Users acquired by collaborating with our associate pharmacies for his analysis and use for interpretation and reporting towards his PhD Dissertation work.

Please note that this is secondary data that contains only the responses for the Quality of Life Measurement Tool SF-36 among the targeted group and cannot be used for identifying any participant.

Vice dean of Faculty of Medicine for Academic Affairs

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