ORCA – Online Research @ Cardiff

Authors

Geraldine Titeca[1], Laetitia Goudetsidis[2], Bernard G Francq[3], Francesca Sampogna[4], Uwe Gieler[5], Lucia Tomas-Aragones[6], Lars Lien[7], Gregor B.E. Jemec[8], Laurent Misery[9], Csanad Szabo[10], Dennis Linder[11], Andrea W.M. Evers[12], Jon Anders Halvorsen[13], Flora Balieva[14], Jacek Szepietowski[15], Dmitry Romanov[16], Servando E. Marron[17], Ilknur K. Altunay[18], Andrew Y. Finlay[19], Sam S. Salek[20], Jörg Kupfer[21], Florence J. Dalgard[22], Françoise Poot[23]

[1,2]Department of Dermatology, Clinique Notre-Dame de Grâce, Gosselies, Belgium;

[3]Institute of Statistics, Biostatistics, and Actuarial sciences, Université Catholique de Louvain;

[4]Clinical Epidemiology Unit, IDI-IRCCS, Rome, Italy;

[5]Department of Dermatology, Justus Liebig University, Giessen, Germany;

[6]Department of Psychology, University of Zaragoza, Aragon Health Sciences Institute, Zaragoza, Spain;

[7]Department of Public Health, Hedmark University College, Elverum, Norway;

[8]Department of Dermatology, Zealand University Hospital, Roskilde, University of Copenhagen, Copenhagen, Denmark;

[9]Department of Dermatology, University Hospital of Brest, Brest, France;

[10]Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary;

[11]Section of Biostatistics, University of Oslo, Oslo, Norway;

[12]Institute of Psychology Health, University of Leiden, Leiden, Netherlands;

[13]Department of Dermatology, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo, Oslo, Norway;

[14]Department of Dermatology, Stavanger University Hospital, Stavanger, Norway;

[15]Department of Dermatology, Wroclaw Medical University, Wroclaw, Poland;

[16]Department of Psychiatry and Psychosomatics, I. M. Sechenov First Moscow State Medical University, Mental Health Research Center, Moscow, Russia;

[17]Department of Dermatology, Alcaniz Hospital, Alcaniz, Spain;

[18]Department of Dermatology, Sisli Etfal Teaching and Research Hospital, Istanbul, Turkey;

[19]Department of Dermatology, Cardiff University School of Medicine, Cardiff, UK;

[20]Department of Pharmacy, Pharmacology and Postgraduate Medicine, School of Life & Medical Sciences, University of Hertfordshire, Hatfield, UK;

[21]Institute of Medical Psychology, Justus Liebig University, Giessen, Germany;

[22]National Center for Dual Diagnosis, Innlandet Hospital Trust, Brumundal, Norway;

[23]Department of Dermatology, Hôpital Erasme, Brussels, Belgium.

Abstract

Background: Hair diseases place an important burden on patients' lives, causing significant emotional and psychosocial distress. However, the impairment due to different hair conditions, such as alopecia areata (AA) and androgenetic alopecia (AGA), has rarely been compared.

Objective: The aim of this study was to assess the psychological burden of sub-groups of patients with different hair diseases and to compare them to a healthy population.

Methods: This study is part of a large multicenter study including 3635 adult dermatological out-patients and 1359 controls from 13 European countries.

In the sub-group of patients with hair diseases, we analyzed the sociodemographic characteristics, the stress level, and the impact of hair diseases on quality of life (QoL),

anxiety, and depression and we compared them among patients with AA, AGA, and healthy controls.

Results: The study population included 115 patients (77% women, 23% men) with hair diseases. Patients with hair diseases had a lower education level than healthy controls (medium educational level: 43% vs 28%). Overall, 41% of the patients reported stressful life events during the last 6 months compared with 31% of the controls. Patients with the same age, sex, depression level and comorbidities had a worse QoL when suffering from AA than from AGA (Mean DLQI score: 5,8 vs 2,5).

Conclusion: Patients with hair diseases are more anxious, depressed and have a worse QoL than controls. These results suggest that a psychotherapeutic and psychopharmacological approach should be proposed when necessary.

INTRODUCTION:

In humans, hair is predominantly considered as an aesthetic concern, however hair diseases may lead to an important burden on patients' lives, causing significant emotional and psychosocial distress (1). The most common hair diseases are alopecia areata (AA) and alopecia androgenetica (AGA).

It has been observed that AA significantly reduces patients' quality of life (QoL) (2). In addition, AA patients have a high prevalence of psychiatric comorbidities, such as anxiety, depression, social phobia, and personality disorders (3, 4). It is therefore difficult to know to what extent the impact of this impairment is, comparable to other skin diseases.

In an Indian study of alopecia with a wide range of etiologies including chemotherapy related alopecia, Sellami et al have shown that alopecia patients were more anxious and depressed than controls (5). In 50 AA patients, 62% had symptoms of anxiety and 38% of depression (5). These percentages were significantly higher than in the control group. In patients with AGA a significant impact on QoL was found, particularly when associated with high severity, a longer duration, younger age, having received previous non-medical hair care, and hospital visits for AGA treatment (6).

Compared to other skin conditions, which may be accompanied by itching, pain or other sensations that provide distinctive symptoms, in most hair diseases the patients generally only experience the symptom of "hair loss" Considering this mono-symptomatic aspect of hair

diseases, it is interesting to investigate other associated aspects that may differentiate the impact of different hair diseases (AA, AGA, other diseases).

The aim of this study was to assess the psychological burden of patients with hair diseases in a large European sample. For this purpose, we compared different subgroups of patients with hair diseases with a healthy control population, regarding the level of anxiety, depression, stress, and QoL impairment.

METHODS:

Study population

A multicenter, observational, case-control study was conducted in 13 European countries. The details have been described previously (7). In brief, in the dermatology clinics of each country, all patients with dermatological diseases were consecutively recruited. Controls were recruited in all centers among the hospital staff who did not currently have or previously had any dermatological disorder. Both cases and controls had to complete questionnaires on QoL and psychological comorbidities. Data were complete for 3635 patients and 1359 controls. In the present study, we have included patients with hair diseases and healthy controls.

Questionnaires

The first part of the questionnaire recorded socio-demographic variables including age, gender, marital status, and self-reported socio-economic status. Ethnicity was self-reported by each participant referring to their own country of birth.

The presence of symptoms of depression and anxiety was assessed with the HADS, a well-validated instrument showing good psychometric properties, aimed to assess symptoms of anxiety disorders and depression in somatic, psychiatric, and primary care patients, as well as in the general population. HADS includes seven items assessing anxiety and seven assessing depression, each with four possible answers. For each dimension of anxiety and depression a score from 0 to 7 is considered normal, from 8 to 10 a borderline case, and from 11 to 21 a case in need of further examination or treatment. This instrument was used in the validated translations relevant to the study countries.

To assess health related quality of life (HRQoL), we used two different self-rated questionnaires: the Dermatology Life Quality Index (DLQI) and the EQ-5D-3L. The DLQI is a dermatological specific, ten-item questionnaire used to measure the impact of skin disease on the QoL of an affected person. The ten questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex and treatment. Each question is scored from 0 to 3, giving a possible total score range from 0 (no impact of skin disease on QoL) to 30 (maximum impact on QoL). The EQ-5D-3L essentially consists of 2 parts: the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels: no problems, some problems, extreme problems. The respondent is asked to indicate his/her health state by ticking (or placing a cross) in the box against the most appropriate statement in each of the 5 dimensions. The EQ VAS records the respondent's self-rated health on a vertical, visual analogue 100-degree scale (0= "worst imaginable health state"; 100= "best imaginable health state").

This information can be used as a quantitative measure of health outcome as judged by the individual respondents. Stress was assessed with the item "Have you had any stressful life event during the last 6 months?" (yes/no).

Patients completed all the questionnaires, while controls did not complete the DLQI.

Statistical analysis:

Analyses were performed with R version 3.1.0. Baseline characteristics were compared between groups (controls versus any hair diseases; controls versus AA and AGA; men versus women; different age groups) by Fisher's exact tests for categorical variables and t-tests or ANOVA for continuous variables (or Wilcoxon tests if needed). The categorical scores were compared by Fisher's exact tests between groups. The DLQI scores and EQ5D scores, considered on continuous scales, were also compared (separately) by multivariate regressions after a logarithmic transformation for DLQI (to fulfill the normality assumption) with the groups, age, sex, depression and comorbidities as predictors (adjusting variables). The HADS scores, considered on a continuous scale, were compared between groups with t-tests or ANOVA (the normality assumption has been checked with QQ plot). The EQ5D scores were compared by Wilcoxon tests, or Kruskal-Wallis non-parametric ANOVA between gender and

categorized age, while their five components were compared by Fisher's exact tests. The population was adjusted by linear model for age, sex, depression and comorbidities. Some results are presented using box-plots which are a convenient way of graphically depicting groups of numerical data through their quartiles. Box plots may have lines extending vertically from the boxes (*whiskers*) indicating variability outside the upper and lower quartiles, hence the terms box-and-whisker plot and box-and-whisker diagram.

RESULTS:

Details of participants' characteristics have been previously published (7). In this study, we included 115 patients with hair diseases and 1359 controls. In the group of patients with hair diseases, there were 37 patients with AA, 20 patients with AGA, and 58 patients with other hair conditions such as lichen planus of the scalp, telogen effluvium, cicatricial alopecia, frontal fibrosing alopecia and others.

Table 1 shows a comparison between the characteristics of the hair diseases group and the controls. In the hair diseases group, there were more females than in the control group; 46% of the patients were educated to a medium education level (i.e., primary or secondary school) compared with 28% of the controls. Finally, tertiary (university) level education was achieved by a smaller proportion of patients than controls (29% vs 43%).

Comparing subgroups of patients with hair diseases, we observed that AA and the subgroup of other hair diseases were more likely to have achieved a medium level education than AGA patients (47% and 49%, respectively, vs. 35%), (*p=0.007*). A higher proportion of AA patients were married (70%) compared to the other hair disease population (49%), (*p=0.021*). Stress was reported by 49% of the AA patients and 35% of the AGA and 31% of controls (*p=0.061*).

HADS mean score in patients (*anxiety 7.9; depression 5.4*) was significantly higher compared to controls (*anxiety 5.6; depression 3.6*). Overall, 41% of the patients reported stressful life events during the last 6 months compared with 31% of the controls.

Patients with same age, sex and comorbidities had a higher DLQI score when suffering from AA than AGA, (Fig. 1). Figure 2 (Fig. 2) shows that patients with AA had a higher HADS score compared to the AGA population. An ANOVA Test was performed to compare

controls, AA and AGA population and confirmed the results above. *(Anxiety p<0.001; depression p=0.005).*

Females had a poorer quality of life (Fig. 3a), especially in the pain dimension (*p=0.001*) and anxiety and depression dimension (*p=0.012).* Patients aged more than 50 years old had lower EQ-5D scores (*p<0.001*) and EQ VAS scores (Fig. 3b), i.e. a more impaired QoL, than younger patients.

 Comparison between controls, AA and AGA patients showed a lower EQ-5D score in both AA and AGA patients when adjusted for age, sex, depression and comorbidities (Fig. 3c). Specifically, EQ-5D activity, pain and anxiety and depression dimensions showed lower scores in all hair patients compared to controls (*p=0.002, p<0.001, p<0.001).* Also, EQ VAS score was lower for all hair patients compared to controls when adjusted for age, sex, depression and comorbidities. AA patients reported lower self-evaluated health than AGA patients and controls when using the EQ VAS scale (fig. 3d) and had a lower EQ-5D anxiety and depression scores (*p<0.001*). All other comparisons did not show any significant differences.

DISCUSSION:

How do hair diseases affect patients' lives? In this study, we found that having any hair disease was associated with more anxiety, a more depressed mood and impaired QoL compared to a control group without skin disease. These differences were most pronounced in AA patients.

The special impact of AA is in line with previous studies. Liu et al. showed that HRQoL experienced by patients with AA is similar to that seen in patients with other chronic skin diseases including atopic dermatitis and psoriasis (8, 9). Rencz et al. have also demonstrated that patients with AA experience significant impairment in HRQoL, especially in the area of mental health (2).

AA patients may suffer more than patients affected by other hair diseases for different reasons. AA is a chronic disease and is well known for having a significant impact on the psychological sphere of patients. Indeed, AA is a burdensome medical problem because concealing the symptoms of that condition is relatively difficult, especially for women. T. Cartwright showed that QoL was significantly poorer for women with alopecia, compared

with men. There were gender differences in several of the DLQI subscales. Women were significantly more likely to feel that alopecia affected their leisure activities and personal relationships, while men scored higher on work interference than women (10).

AA also has a major impact on the social life of a patient, leading him/her to feel socially alienated and rejected. Furthermore, AA is associated with mental disorders such as depression, anxiety disorders, body dysmorphic disorders, social phobia and suicidal thoughts. These mental disorders could be primary conditions which declare themselves in medical problems associated with the skin or these could be a result of this serious and disfiguring condition (11).

An interesting result was the significant difference of marital status between the AA patients and other hair disease patients. In fact, 70% of AA patients were in a relationship compared to 49% of the others. In a previous study, we demonstrated that there are more dysfunctional families in AA patients (12). Those dysfunctions could be fusions and ruptures, generational repetition of behaviors of dependence or vulnerability and unsolved mourning if traumatic events are experienced. We could hypothesize that not resolving these problems could lead to increasing the perceived stress and consequently to more anxiety and depression. Moreover, these patients have a lower education level, which is usually correlated with earlier partnerships (13,14). Further studies should be done to confirm this hypothesis.

Concerning the AGA patients, we also found an impact on HRQoL. Their level of anxiety and depression was also higher than for the controls. In previous studies, it has been shown that the HRQoL of male and female AGA patients is altered, in particular in younger patients (6,13,15). This should not be underestimated and psychological support could be helpful for these patients.

The weakness of this study is that several generic and dermatology-specific HRQoL instruments have been used, but no specific instruments for AA were used. The newly developed AA-specific measures seem very promising, however, a more extensive assessment of validity and reliability is needed.

In conclusion, patients with hair diseases experience a considerable impact on their QoL and may benefit from a psychological assessment. We recommend the use of anxiety and depression questionnaires such as HADS, which is specific and user-friendly. Some caution

remains warranted: we must take into account the risk of biases such as underestimation with self-administered questionnaires; moreover AA patients are often alexithymic (16) and therefore have problems in articulating their affections. We therefore recommend letting the patient complete the questionnaire on his own and evaluate the answers with the dermatologist. Also, the observation of patients' nonverbal behavior is an invaluable tool to assess the presence of depression. Finally, once an adequate psychological assessment has been performed, psychotherapeutic and psychopharmacological support should be offered to patients whenever such support appears to be conducive to a better outcome.

References:

1 Janković S, Perić J, Maksimović N et al. Quality of life in patients with alopecia areata: a hospital-based cross-sectional study. *J Eur Acad Dermatol Venereol* 2016; 30: 840-846.

2 Rencz F, Gulácsi L, Péntek M et al. Alopecia areata and health-related quality of life: a systematic review and meta-analysis. *Br J Dermatol* 2016; 175: 561-571.

3 Chu SY, Chen YJ, Tseng WC et al. Psychiatric comorbidities in patients with Alopecia areata in Taiwan. Br J Dermatol 2012; 166: 525-531.

4 Hunt N, McHale S. The psychological impact of alopecia. *Br Med J* 2005; 22: 951-953.

5 Sellami R, Masmoudi J, Ouali U et al. The relationship between alopecia areata and alexithymia, anxiety and depression: a case-control study. *Indian J Dermatol* 2014; 59: 421.

6 Han SH, Byun JW, Lee WS et al. Quality of life assessment in male patients with androgenetic alopecia: result of a prospective, multicenter study. *Ann Dermatol* 2012; 24: 311-318.

7 Dalgard FJ, Gieler U, Tomas-Aragones L et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatological out-patients in 13 European countries. *J Invest Dermatol* 2015; 135: 984-991.

8 Balieva F, Kupfer J, Lien L et al. The Burden of common skin diseases assessed with the EQ5D: an European multi-centre study in 13 countries. *Br J Dermatol 2017*; 176: 1170-1178.

9 Liu LY, King BA, Craiglow BG. Health-related quality of life (HRQoL) among patients with alopecia areata (AA): a systematic review. *J Am Acad Dermatol* 2016; 75: 806-812.

10 Cartwright T, Endean N, Porter A. Illness perceptions, coping and quality of life in patients with alopecia. *Br J Dermatol* 2009;160:1034-9.

11 Kuty-Pachecka M1. Psychological and psychopathological factors in alopecia areata. *Psychiatr Pol* 2015; 49: 955-964.

12 Poot F, Antoine E, Gravelier M et al. A case-control study on family dysfunction in patients with alopecia areata, psoriasis and atopic dermatitis. *Acta Derm Venereol* 2011; 91: 415-421.

13 Berrington A, Pattaro S. Educational differences in fertility desires, intentions and behaviour: A life course perspective. *Adv Life Course Res.* 2014; 21: 10-27.

14 Addo FR, Sassler S, Williams K. Reexamining the association of maternal age and marital status at first birth with youth educational attainment. *J Marriage Fam*. 2016;78: 1252-1268.

15 Ramos PM, Miot HA. Female Pattern Hair Loss: a clinical and pathophysiological review. *An Bras Dermatol* 2015; 90: 529-543.

16 Willemsen R, Roseeuw D, Vanderlinden J. Alexithymia and dermatology: the state of the art. *Int J Dermatol* 2008; 47: 903-910.

Table 1: Comparison between hair diseases groups and controls. Mean values given with standard deviation (SD)

VARIABLE	LEVEL	N (%) Hair diseases	N (%) controls	P-value
Sex	Male	27 (23%)	453 (33%)	P=0,03
	Female	88 (77%)	903 (67%)	
Educational level	Medium	49 (46%)	375 (28%)	P<0,001
	High	26 (25%)	399 (30%)	
	University	31 (29%)	577 (43%)	
Stressful life events reported during the last 6 months		47 (41%)	412 (31%)	P=0,02
		Mean values (SD)	Mean values (SD)	P-value
Age		41.6 (SD)	41.1 (SD)	P=0,732
HADS Anxiety		7.9 (SD)	5.6 (SD)	P<0,001
HADS Depression		5.4 (SD)	3.6 (SD)	P<0,001

		Median	Median	
EQ-5D		0.8	1	P<0,001

Figure 1: Median scores of quality of life as assessed with the DLQI in alopecia areata (AA) and androgenetic alopecia (AGA) (*p= 0,022*)
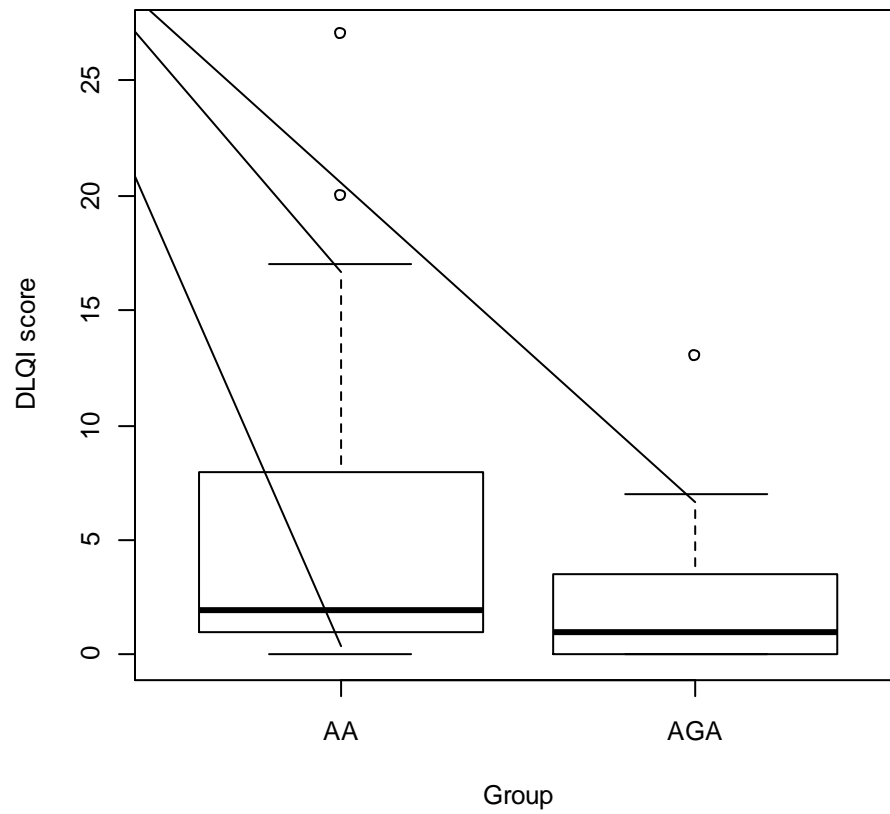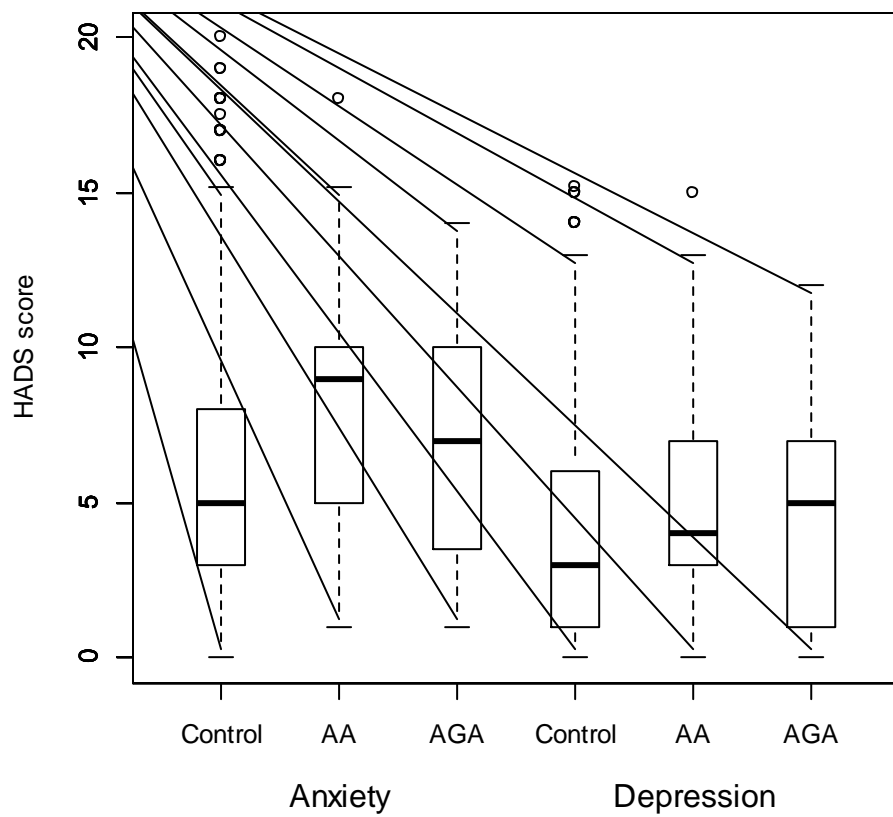
Figure 2: Score of Anxiety and Depression (HADS) in Control - AA–AGA patients (*Anxiety p< 0,001; depression p=0,02*)

Figures 3a: Median scores for Health Related Quality of Life (HRQoL) as assessed by the (EQ5D) in male versus female patients (*p=0,001*)
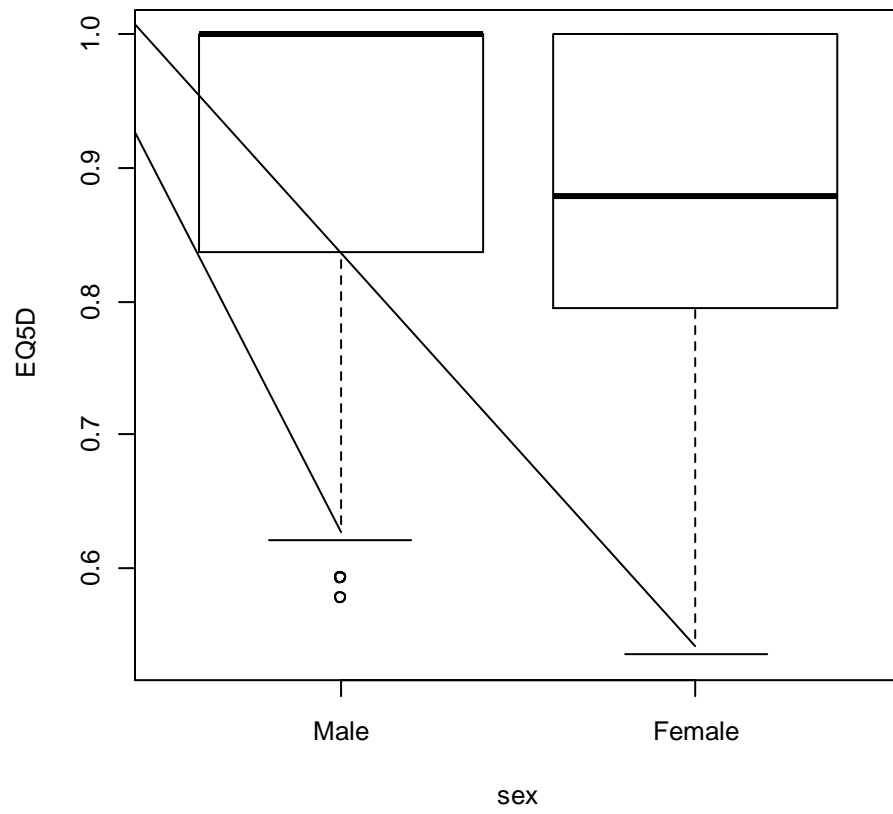
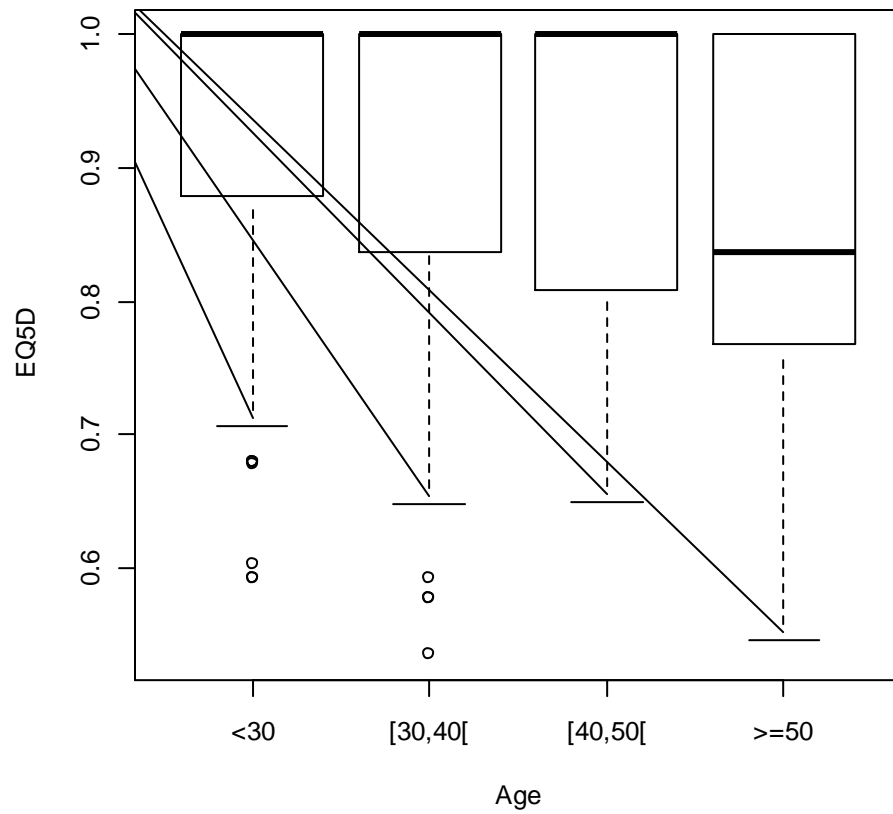Figure 3b: HRQoL as assessed by the EQ5D in different age groups (*p<0.001*)

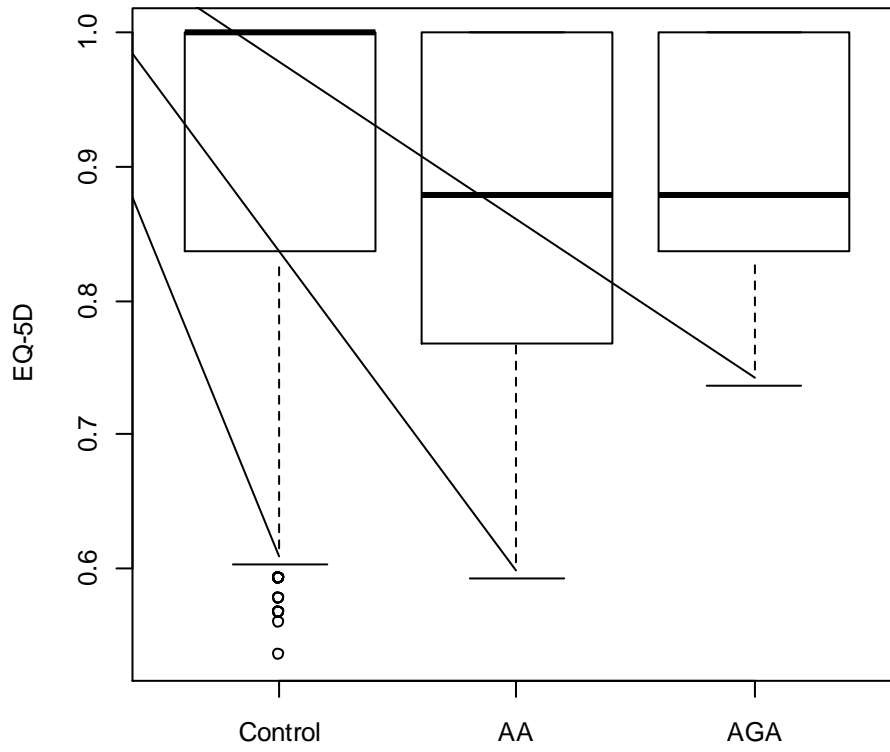Figure 3c: HRQoL in general health (EQ5D) in control- AA-AGA patients (*p=0,003*)

Figure 3d: HRQoL with visual analogue score (EQ VAS) in control - AA-AGA patients (*p<0,001*)