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COMPARISON OF COPING, QUALITY OF LIFE AND PSYCHOSOCIAL WELL-BEING IN CHILDREN AND ADULT PATIENTS WITH VITILIGO BEFORE AND AFTER TREATMENT WITH PSEUDOCATALASE PC-KUS

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PhD

2009

COMPARISON OF COPING, QUALITY OF LIFE AND PSYCHOSOCIAL WELL-BEING IN CHILDREN AND ADULT PATIENTS WITH VITILIGO BEFORE AND AFTER TREATMENT WITH PSEUDOCATALASE PC-KUS

A questionnaire-based investigation into social anxiety, helplessness, anxious-depressive mood, quality of life and depression before and after treatment with pseudocatalase PC-KUS depending on demographic characteristics and experiences

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2009

Abstract

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COMPARISON OF COPING, QUALITY OF LIFE AND PSYCHOSOCIAL WELL-BEING IN CHILDREN AND ADULT PATIENTS WITH VITILIGO BEFORE AND AFTER TREATMENT WITH PSEUDOCATALASE PC-KUS

Keywords: Vitiligo, quality of life, social anxiety / avoidance, helplessness, anxious-depressive mood, depigmentation, depression, children, pseudocatalase PC-KUS

Vitiligo is an idiopathic, non-contagious and often familial depigmentation disorder affecting both sexes equally. The mostly progressive and patchy loss of the inherited skin colour is not only a cosmetical problem, it has a profound impact on the patient's well-being. Stigmatisation and rejection often causes depression, self-consciousness, sexual problems and an impaired quality of life.

To further substantiate earlier investigations and to introduce new aspects, we utilised the Dermatology Life Quality Index (DLQI), the Beck Depression Inventory (BDI) and the Adjustment to Chronic Skin Disorders Questionnaire (ACS) with its sub-scales on Social anxiety / avoidance, Helplessness and Anxious-depressive Mood in 422 patients and 55 healthy controls. We also included 103 children, their parents and 18 controls by using the Children's Dermatology Life Quality Index (CDLQI) and an adapted version of the ACS.

We found that patients with vitiligo experience high levels of stigmatisation. They have an impaired quality of life and are more socially anxious / avoidant, helpless and (anxious-) depressive compared to healthy controls. The results correlate with disease severity, avoidant behaviour / hiding of vitiligo and the belief that psychological stress influences the disease. Female patients are generally more affected. Treatment with pseudocatalase PC-KUS improves quality of life and reduces anxious-depressive mood.

Children also suffer from stigmatisation and an impaired quality of life. Parents are more socially anxious and helpless compared to the control group.

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1.3 List of abbreviations

$6BH_4$	- 6 Tetrahydrobiopterin
ACS	- Adjustment to Chronic Skin Disorders Questionnaire
AIS1	- Autoimmune susceptibility 1 gene
BDI	- Beck Depression Inventory
bFGF	- Basic fibroblast growth factor
CDLQI	- Children's Dermatology Life Quality Index
CMV	- Cytomegalovirus
DLQI	- Dermatology Life Quality Index
DNA	- Deoxyribonucleic acid
FOXD3	- alias of AIS1
FT-Raman	- Fourier transform Raman spectroscopy
GHQ	- General Health Questionnaire
GM-CSF	- Granulocyte-macrophage colony-stimulating factor
H_2O_2	- Hydrogen peroxide
HVC	- Hepatitis C virus
IFPD	- Institute for Pigmentary Disorders
IL-6	- Interleukin-6
KUVA	- Khellin plus ultraviolet A light
mM	- Milli molar
NB-UVB	- Narrow-band ultraviolet B light
PC-KUS	- Pseudocatalase developed by Prof KU Schallreuter
PAUVA	- L-phenylalanine plus ultraviolet A light
PUVA	- Psoralens plus ultraviolet A light
PUVASOL	- Psoralens with sunlight
QoL	- Quality of life
SF-36	- Short Form (36) Health Survey
TNF-α	- Tumor negrosis factor alpha
UV	- Ultraviolet
UVA	- Ultraviolet light A
UVB	- Ultraviolet light B
VAS	- Visual analogue scale
µM	- Micro molar

1.4 List of publications and presentations

Publications / Published abstracts

C. Krüger, J.W. Smythe, A. Panske, K.U. Schallreuter (2007). "*Evidence for elevated stress and anxiety in stable vitiligo*." **J Invest Dermatol 127** Suppl. 2 (Abstracts of the 37th Annual European Society for Dermatological Research Meeting in Zürich, Switzerland, 5-8 September 2007): p29.

K.U. Schallreuter, C. Krüger, H. Rokos, S. Hasse, C. Zothner, A. Panske (2007). "*Basic research confirms coexistence of acquired Blaschkolinear Vitiligo and acrofacial Vitiligo.*" **Arch Dermatol Res 299**(5-6): 225-30.

K.U. Schallreuter, C. Krüger, B.A. Würfel, A. Panske, J.M. Wood (2008). "*From basic research to the bedside: efficacy of topical treatment with pseudocatalase PC-KUS in 71 children with vitiligo.*" **Int J Dermatol 47**(7): 743-53.

K.U. Schallreuter, C. Krüger, B. Würfel, G. Chiuchiarelli, A. Panske (2009) *"Childhood- vitiligo: what can we do?"* (abstracts of the EADV spring symposium 23-26 April 2009 in Bucharest, Romania), **JEADV** in press

C. Krüger, K.U. Schallreuter (2009). "*Eingeschränkte Lebensqualität und Vitiligo.*" (conference abstract) **J German Soc Dermatol 7** (Suppl): p118

K.U. Schallreuter, C. Krüger, B. Würfel, G. Chiuchiarelli, A. Panske (2009) *"Kindervitiligo - Was tun und zu welchem Zeitpunkt?"* (conference abstract) **J German Soc Dermatol 7** (Suppl): p118

Presentations

23/07/2007 *„Evidence for elevated stress and anxiety in stable vitiligo“* at the annual Bradford Club conference, held in Greifswald, Germany

06/09/2007 *„Evidence for elevated stress and anxiety in stable vitiligo“* including poster at the annual conference of the European Society for Dermatological Research (ESDR) in Zürich, Switzerland

16/04/2008 *“Psychosocial Implications of Vitiligo”* at the Department of Biomedical Sciences at the University of Bradford, UK

01/05/2009 “*Eingeschränkte Lebensqualität und Vitiligo” (Impaired quality of life and vitiligo)* at the annual conference of the German Society of Dermatology in Dresden, Germany

2 Acknowledgements

First and foremost I am very grateful to Professor Schallreuter for making it possible that I could start a PhD study at the University of Bradford, especially for me as somebody educated in Social Science. Luckily, the subject I could work on linked natural and social science. Prof Schallreuter has always been encouraging, supportive and enthusiastic about this project. Also, it was thanks to her that I had the chance to add pieces to my work in parts of the world I had never dreamt about seeing so soon, i.e. USA and Jordan. Professor Schallreuter has opened an opportunity that has changed my life profoundly.

Secondly, I am thankful to have met Professor John Wood, who was a true scholar with an impressive scientific history, and still a very humble and humorous Yorkshire man. I was impressed by his knowledge and ability to turn complicated scientific stuff into simple words. Many of his often funny statements will stay with us.
Both John Wood and Professor Schallreuter generously shared not only their home on many occasions with their students, but also their experiences, for which I am grateful.

Special thanks are deserved by Angela Panske who has always been supportive of my work in Bradford from the Institute in Greifswald, Germany, be it the office part or my study by distributing and collecting questionnaires. Being reliable and warm-hearted, Angela often found the right words in difficult times.

It was a pleasure to share office space and, sometimes, pints with “the group” as there are (in alphabetical order): Bhaven Chavan, Souna Elwary, Nick Gibbons, Johanna Gillbro, Stephanie Iwanek, Elke Marsch, Samantha Murphy, Mohamed Salem, Omid

Shalbaf, Jennifer Overton née Spencer and Carsten Zothner, not to forget Susan Gledhill and hubby Richard. I also like to thank Dr Hartmut Rokos for all his advice and support regarding technical issues.

I am particularly grateful to all the patients, both adults and children, for their support by filling out all the long questionnaires and giving saliva samples. It was very impressive and often fun to meet so many interesting people from literally all *inhabited* continents and so many different countries. It is certainly a very special community.

Stella Pavlides and Marilyn Giordano of the American Vitiligo Research Foundation have always been supportive, i.e. by making it possible that I could distribute questionnaires during their annual AVRF meeting in June 2005. Both do an incredible job not only in supporting children with vitiligo, but also for the whole vitiligo community.

I like to thank Klaus Ferber and Dr Jürgen Weser, the former for placing an announcement to children to take part on the website of the German Vitiligo-Bund and the latter for distributing the children's questionnaires to the control group in his paediatric practice in Greifswald, Germany.

I am grateful to the German Vitiligo Association (*Deutscher Vitiligo Verein*) in Hamburg and Stiefel Laboratories for their financial contributions towards my studies.

Professor AY Finlay kindly permitted the use of the DLQI and CDLQI questionnaires.

Last but not least, all this work would not have been possible without the support and endless patience by my family and especially my wonderful wife Sybille, who was one of the reasons for me to come to England. Not to forget my son Jannis who supports me by being an easy-going nice little guy.

3 Introduction

3.1 Definition of vitiligo

Vitiligo is an acquired, non-contagious, idiopathic, often familial and worldwide common depigmentation disorder. The prevalence is approximately 0.5-1% (Howitz et al. 1977; Mosher et al. 1979).

Symptoms are the progressive loss of the inherited native skin or / and hair colour affecting the human epidermis, mucosa and the hair. As a result, white spots of depigmented skin occur at different locations. The whole body can be white without any or only little pigmentation left (Mosher et al. 1979; Hann 2000).

This disease can be distinguished from other leukodermas by using Wood's light (UVA 351nm wavelength). Vitiligo spots show a yellow / green or blueish fluorescence, which is not the case in other depigmentation disorders. This specific fluorescence has been attributed to the presence of oxidised pterines in the skin (Schallreuter et al. 1994c).

Although there are occasional reports about vitiligo in mainstream media (**Figure 1**), the disease is not well-known in the general population, sometimes not even in the medical community (McLeod 2004). Clearly education and campaigns to raise awareness are needed (Olasode and George 2008).

Figure 1: Stories about vitiligo in British tabloids and other media

1- **www.bbc.co.uk** website (7/1/2006)
2- **The Sun** (24/11/2005)
3- **The Times** (25/06/2005)
4- **Daily Mail** (06/05/2003)
5- **The Sun** (21/02/2008)
6- **The Sun** (09/04/2008) – taken from www.thesun.co.uk

3.2 Prevalence of vitiligo according to population-based studies

3.2.1 Review of the literature

There are numerous studies of two different kinds available aiming to establish the prevalence of skin diseases in the general population.

On one hand it is possible to study patients in dermatological clinics and on the other hand one can investigate the general population in geographically determined locations or use certain population groups not defined by dermatological criteria (e.g. school classes or statistically representative samples of a country). Both ways have advantages and pitfalls.

It seems to be more common to use data from dermatological clinics, because it can be expected that the skin diseases are accurately diagnosed. Moreover, it is possible to review patients' charts in retrospective analyses. However, it is difficult to conclude from these data the true prevalence in the general population since not everybody with a skin disease seeks medical treatment.

The ideal way to get a more detailed picture would be a survey on all inhabitants in a large geographically enclosed area by experienced dermatologists. There are a few studies available regarding skin diseases in general (Lomholt 1964; Abdel-Hafez et al. 2003) including one for vitiligo (Howitz et al. 1977). The thorough physical examination of a large representative sample from a country's population can be equally exact (Johnson and Roberts 1978; Massarrat and Tahaghoghi-Mehrizi 2002).

3.2.2 Prevalence of vitiligo in children / adolescents

Most of the studies have been carried out on school children. Only a few concerned enclosed geographical units (e.g. villages) or were part of investigations on all age groups. Here it is of interest that the prevalence rates are lower than those in the total population, except from India. The prevalence rates in children populations range from 0.04 to 2.16% (**Table 1**).

3.2.3 Prevalence of vitiligo in the total population

The results of various studies from geographically enclosed areas, on samples representing the total population, on self-reported diseases and also on examinations of populations not defined by skin diseases (young males for military draft purposes, female housekeepers in Asia for work permit purposes etc) are shown in **Table 2**. The prevalence rates range from 0.06 to 2.28%.

These numbers show that the often cited prevalence of 8.8% (Ortonne et al. 1983) is far too high, because this obviously referred to the prevalence of patients with vitiligo *within one skin institute* in Delhi (Behl and Bhatia 1972).

%	Country	[n]	Age (years)	*Comments*	Authors
0.04	Brazil	9955	6-16	*School children examined in Purus Valley, Amazonia*	(Bechelli et al. 1981)
0.05	China	8,532	10-19	*Part of a survey on representative sample of population of Shaanxi Province*	(Lu et al. 2007)
0.09	Taiwan	3,273	6-11	*All children of classes within age group were examined in 4 schools (71.87% of schoolchildren in Magong area)*	(Wu et al. 2008)
0.12	Denmark	14,824	0-19	*Part of a survey on the Isle of Bornholm*	(Howitz et al. 1977)
0.17	India	12,481	4-15 (?)	*65.8% of all pupils examined of 97 government and 13 private schools*	(Valia et al. 1991)
0.22	Egypt	1356	5-16	*636 disabled students from 3 caring institutions in Mansura, Egypt + 720 matched healthy controls from nearby schools*	(Fathy et al, 2004)
0.23	Mali	1729	<15	*All children examined in two villages in a rural area of West Africa*	(Faye et al. 2005)
0.24	USA	20,749[1]	1-17	*Survey on representative sample of population*	(Johnson and Roberts 1978)
0.27	Romania	1114	6-12	*All children from selected schools in Bucharest*	(Popescu et al. 1999)
0.4	Tanzania	820	6-19	*Children of two primary schools in Ifakara were examined (one complete, 62% of other)*	(Ferié 2006)
0.4	Sweden	8298	12-17	*86.3% of all school children of that age examined in Västerbotten county, Northern Sweden*	(Larsson and Liden 1980)
0.4	Saudi Arabia	2239	6-17	***Female** pupils only from selected schools in Al-Khobar*	(Al-Saeed et al. 2006)
0.43	Saudi Arabia	230	6 – 18+	*All students of special schools for deaf and blind dermtologically examined in Asir region*	(Abolfotouh and Bahamdan 2000)
0.59	Turkey	682	14-25	*All **male** students from 2 boarding schools were examined by dermatologists*	(Tuncel and Erbagci 2005)
0.6	India	666	0-14	*House-to-house study in 5 villages of Wardha district in Maharastra (Central India)*	(Vikas 1997)
0.67	Italy	3125	12-17	*Caucasian schoolchildren from 13 areas in Northern, Middle and Southern Italy, examined by dermatologists for atopic dermatitis – vitiligo found in 21 /3125 children*	(Naldi et al. 2009)
0.9	India	3835	2-14	*Skin examination of children in semi-urban Gorimedu region*	(Kumar et al. 1988)
0.94	India	531	n.d.	*Volunteering elementary & higher secondary students of two schools in Pachai Malai (Tamil Nadu) examined for various diseases*	(Walter 1999)
1.0	India	201	11-19	*School children examined from high altitude tribunal area of Himachal Pradesh*	(Sharma and Sharma, 1990)
1.51	India	3697	5-14	*Children from 4 urban schools were examined by a group of junior doctors*	(Sharma et al. 1986)
1.65	India	2,613	0-15	*Part of a population survey in Surat area*	(Mehta et al. 1973)
2.16	India	12,586	6-14	*Children from selected schools in Chandigar, Northern India*	(Dogra and Kumar 2003)

Table 1: Prevalence of vitiligo in children populations
(Review of the literature)

[1] Size of total sample examined including adults. The number of children could not be concluded from the paper

%	Country	[n]	Age (years)	*Comments*	Authors
0.06	Faeroe Islands	10,984	all ages	*Population survey on all inhabitants of the 7 northern islands*	(Lomholt 1964)
0.09	China	42,833	all ages	*Survey on representative sample of population of Shaanxi Province*	(Lu et al. 2007)
0.10	USA	136,816	Mean 59.8	*Retrospective analysis of a control group in an investigation on Hepatitis C cases using a database of the Department of Veteran Affairs (control group: no HCV cases, 97% males, all army personnel)*	(El-Serag et al. 2002)
0.13	Mozambique	appr 780	all ages	*251 families (of 345 who reported a skin disease) visited by dermatology students in a slum in Beira,* ***one*** *case of vitiligo found*	(Chhaganlal et al. 2007)
0.15	Romania	2021	all ages	*Survey on all inhabitants of 5 villages surrounding 2 isolated other villages where high a prevalence of vitiligo was found*	(Birlea et al. 2008)
<0.17	Ethiopia	3979	all ages	*House-to-house survey on 827 households in two rural communities in Illubabor province (Southwest), people with self-reported diseases examined by dermatologists* **(0.17% "mainly chloasma and vitiligo")**	(Figueroa et al. 1998)
0.17	Italy	34,740	18 years only	***18 years old males*** *only from coastal regions in Southern Italy when examined by the Draft's Council Medical Unit*	(Ingordo et al. 2007)
0.2	USA	423	1-40	*Relatives of patients from a dermatology and paediatric clinic + patients + volunteers from community through advertisements*	(Vanderhooft et al. 1996)
0.21	Mexico	50,000	all ages	*Survey on inhabitants of 41 representative communities of Guerrero province*	(Estrada Castañón et al. 1992)
0.27	Tanzania	1114	all ages	*Inhabitants of two villages in rural Ngara district were visited*	(Gibbs 1996)
0.28	France	18,137	all ages	*Estimation after survey on representative sample of French population*	(Wolkenstein et al. 2003)
0.32	Saudi Arabia	1520	18-45	***Female*** *housekeepers of foreign (i.e. Asian) nationalities were examined for work permit issue*	(Kubeyinje and Belagavi 1997)
0.38	Denmark	47,033	all ages	*Population survey on the Isle of Bornholm*	(Howitz et al. 1977)
0.46	India	15,685	all ages	*Population survey in Calcutta*	(Das et al. 1985)
0.49	USA	20,749	1-74	*Survey on representative sample of population*	(Johnson and Roberts 1978)
0.51	Iraq	6,666	all ages	*Survey on 1080 houses in two areas of Basrah City, Southern Iraq (questionnaires and home visits)*	(Al-Rubiay and Al-Rubiay 2006)
0.57	Germany	350	14-86	*Prevalence in a group of healthy persons serving as control group for a Vitiligo-Melanoma study*	(Schallreuter et al. 1991a)
0.6	Iran	61,137	all ages	*Survey on 8776 urban and 4719 rural families representing one thousandth of Iran's population (questionnaires and family visits by physicians)*	(Massarrat and Tahaghoghi-Mehrizi 2002)
0.7	Italy	3660	>44	*Self-reports of representative sample of population*	(Naldi et al. 2004)
0.9	Nepal	878	1-80	*39% of all inhabitants of 5 randomly chosen villages examined*	(Walker et al. 2007)
1.13	India	9065	all ages	*Population survey in Surat area*	(Mehta et al. 1973)
1.2	Denmark	584	>50	*All individuals examined who were living in an municipal old people's home*	(Weismann et al. 1980)
1.2	Sri Lanka	1806	all ages	*Survey on 418 out of 6000 households in several villages of a suburban area*	(Perera et al. 2000)
1.22	Egypt	8008	all ages	*Survey on inhabitants of rural areas of Assiut Governorate*	(Abdel-Hafez et al, 2003)
1.2	Australia	1037	adults	*Survey on adults as part of long-running health study in the south-west coastal town of Busselton*	(Quirk 1979)
1.7	Uzbekistan	16,398	all ages	*Survey on inhabitants of 4 rural areas*	(Arifov et al. 2004)
1.9	China	47,490	all ages	*Survey on sample of population in Anhui province*	(Xu et al. 2002)
2.28	Romania	1710	all ages	*Survey on all inhabitants of one small isolated rural community*	(Birlea et al. 2003)

Table 2: Prevalence of vitiligo in the general population

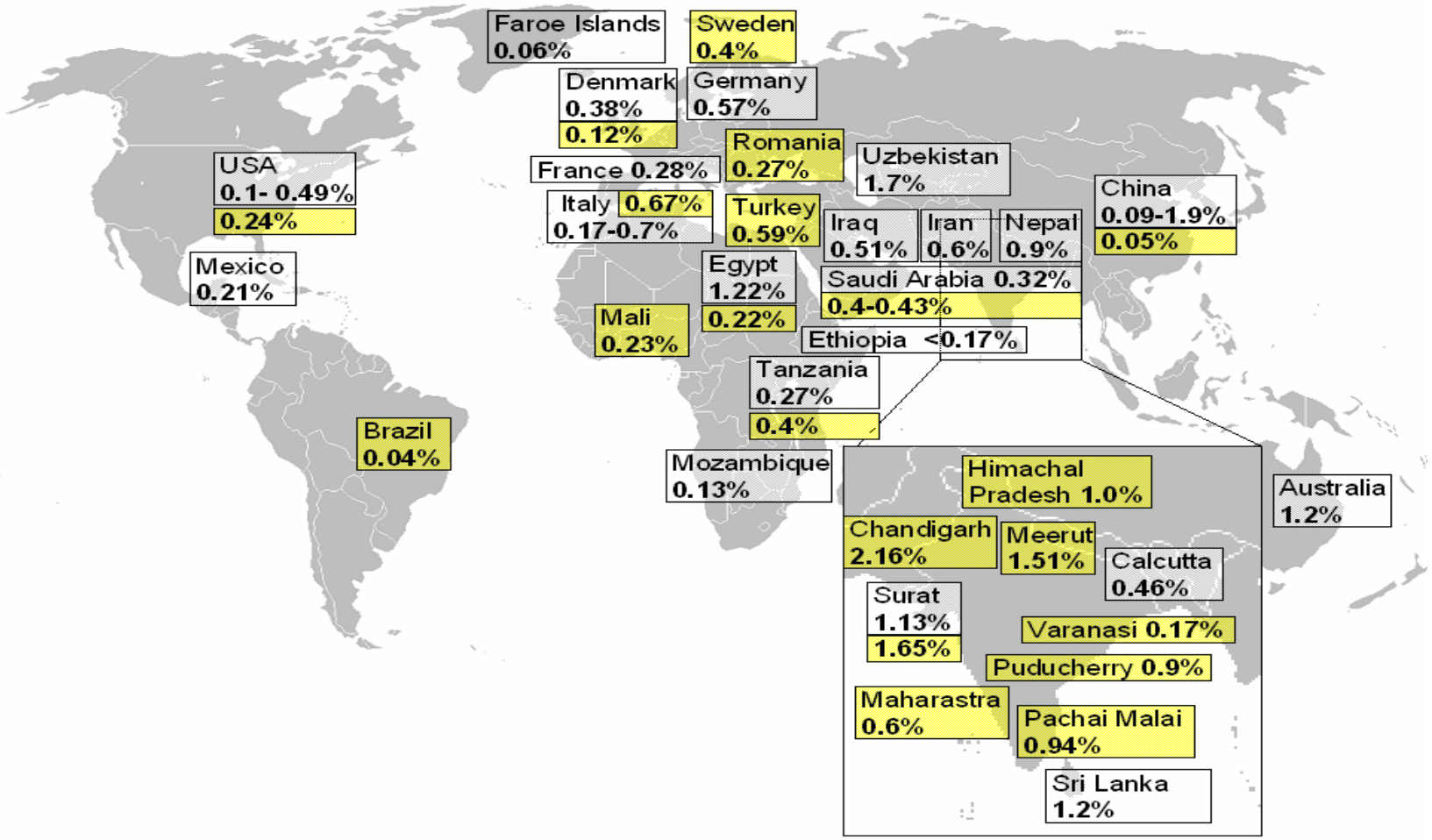


Figure 2: World prevalence rates of vitiligo
White boxes – general population, yellow boxes – children / adolescents only

3.3 Onset of vitiligo

3.3.1 Age and site of onset

Vitiligo affects people of all skin colours, both sexes and all ages and it can occur at any time in life. However, there seems to be a peak in the second decade of patients' life at about 22-24 years of age (Das et al. 1985; Alkhateeb et al. 2003). Others suggest a mean age between 10 and 30 years. In 50% of patients with vitiligo the disease started before the age of 20 years (Mosher et al. 1979).

According to a Danish study the onset of the disease was more frequent between the age of 40 to 60 years, but this study seems to be an exception (Howitz et al. 1977).

Some reports state that the onset is earlier in males compared to females (mean age 19 years respectively 24 years) (Das et al. 1985; Majumder et al. 1993). Other reports could not confirm this difference (Liu et al. 2005).

Vitiligo can occur anywhere on the skin including the mucosae. However, the onset seems to be more frequent on exposed parts including face, neck and hands (**Table 3**).

In a study from Libya there was a more pronounced involvement of exposed parts in male patients compared to females. This results could be based on the cultural background, where women are more covered compared to men (Singh et al. 1985).

Taken together, vitiligo is a disease, which is often visible from the beginning to other people due to its location in exposed areas of the body.

References↓	[n]	Country	Comments	Site of onset → Head, incl. face and lips [%]	Neck [%]	Trunk [%]	Genitalia/ perianal [%]	Arms [%]	Hands [%]	Legs [%]	Feet [%]
(Kanwar et al. 1993)	100	India	**children** <13years	**39**		15	2	10	--	30	--
(Jaisankar et al. 1992)	90	India	**children** <12 years	**39.5**		15.8	5.2	14.9	--	24.6	--
(Handa and Dogra 2003)	625	India	**children** >10 years	**1st**		3rd	--	4th	--	2nd	--
(Cho et al. 2000)	80	South Korea	**children** 8-12 years	**58.8**	26.3	--	3.8	11.3	--	--	--
(Pajvani et al, 2006)	137	USA	**children** 9-15 years	**36.5**		15.3	--	9.5		27	
(Al-Mutairi et al, 2005)	88	Kuwait	**children** < 12 years	**28.4**		20.5	8[+]	23.9		16	
(Chun and Hann 1997)	318	South Korea	non-segmental vitiligo	**39**	10.4	32.7	1.6	3.1	6.3	5.7	0.6
(Dogra et al. 2005)	182	India	onset > 50 years of age	**24.2**	--	22	(7.1)*	23	--	17.6	--
(Handa and Kaur 1999)	1463	India		**1st**	--	2nd	--	--	--	3rd	--
(Wu et al. 2008)	264	Taiwan		**79.2**		--	--	--	--	56.7	--
(Akrem et al. 2008)	60	Tunisia		16.7		15	10	25		**33.3**	
(Al-Mutairi and Sharma 2006)	612	Kuwait		17.97		16.35	7.85*	25.65		**32.19**	
(Shajil et al. 2006)	424	India		24.74	--	12.03	5.19	8.96	3.54	**45.52**	--
(Mehta et al. 1973)	66	India		16.7	--	7.6	--	10.6	--	**65.1**	--
(Sarin and Kumar 1977)	771	India		26.7	3.6	19.9	2.2	12.1	--	**32.4**	--
(Ramaiah et al. 1988)	52	India	inbreeding SSK*** community, Bangalore	25**	1.92	11.53**	--	1.92	13.46	**26.9****	17.31
(Jaigirdar et al. 2002)	200	Bangladesh		32	2	21.5	1.5	22		**30**	
(Schallreuter, unpublished data)	118	Germany		23.7	6.8	20.3	3.4	5.1	**24.6**	8.5	5.1
(Lerner 1959)	200	USA		10	11	10	3	11	**28**	6	--
(Arycan et al. 2008)	113	Turkey		24.8		15	8.8	**38.1**		13.3	

Table 3: Frequencies of disease onset on different body sites

Frequencies are shown either in percent of total number of patients (n) or in order of frequency. Sites with highest frequency of onset are bold.

*was part of *'oral / genital mucosae'*

***abbreviation of *Somavamsha Sahasrarjuna Kshatriya*

** calculated from this author according to details provided in the publication

[+] mentioned as *Genitalia (extramucosal)*

3.3.2 Possible trigger factors

For a long time it has been suggested that stress or distressing events might trigger the onset of vitiligo or that those could worsen the disease (Robert 1941; Barbee and Sumner 1951; Mosher et al. 1979). Many patients believe that stress plays a major role in this disease (Gieler et al. 2000; Firooz et al. 2004).

Recently this topic has been analysed in several studies containing a considerable number of patients. The results showed clear differences between patients and control groups (see **Table 4**).

Several trigger factors have been documented ranging from hormonal changes and physical problems to stressful life events. Moreover, some chemical agents have been identified. Some studies included control groups in order to mark the differences to patients with vitiligo. The results showed indeed that there are significant differences in stress-related experiences between patients with vitiligo and controls supporting the perception of the patients that stress has contributed to their disease (**Table 4**).

	Perceived trigger factor	total [n]	% patients	% control group	References
	Unremarkable events	41	78.0	n/a	(Mason and Gawkrodger 2005)
		482	78.6	n/a	(Sehgal et al. 1976)
		200	60.0	n/a	(Lerner 1959)
		117	32.0	n/a	(Salzer and Schallreuter 1995)
		650	24.0	n/a	(Dutta and Mandal 1969)
		33	21.0	n/a	(Gieler et al. 2000)
Hormones	***Hormonal changes***	117	39.0	n.d.	(Salzer and Schallreuter 1995)
	Pregnancy	200	30.0[2]	n.d.	(Lerner 1959)
		400	8.0	n.d.	(Behl and Bhatia 1972)
		41	7.3	n.d.	(Mason and Gawkrodger 2005)
		650	2.5	n.d.	(Dutta and Mandal 1969)
Psychological causes	***Loss of or separation from a close person***	88	**41.0**	**4.0**	(Papadopoulos et al. 1998)
		72	≈33.0[3]	n.d.	(Manolache et al. 2004)
		117	30.0	n.d.	(Salzer and Schallreuter 1995)
		n.d.	23.0[4]	n.d.	Harper 1992 cited in (Papadopoulos et al. 1998)
	Parents' separation	91	14.3*	n.d.	(Montes 2008)
	Stress at work	117	17.5	n.d.	(Salzer and Schallreuter 1995)
		33	15.2	n.d.	(Gieler et al. 2000)
	Relocation	88	**26.0**	**13.6**	(Papadopoulos et al. 1998)
		117	16.0	n.d.	(Salzer and Schallreuter 1995)
	Stressful life events	32	**65.0**	**22.0**	(Manolache and Benea 2007)
		54	**60.0**	**20.0**	(Manolache et al. 2004)
	(Psychological) trauma	65	57.0*	n.d.	(Barišíc-Druško and Rucević 1997)
		365	3.8	n.d.	(Shah et al. 2008)
	Stress	30	60.0	n.d.	(Elgoweini et al. 2003)
		21	**57.1***	**23.8**	(Manolache et al. 2009)
		87	**54.0**	**39.3**	(Al-Rubaiy and Al-Rubaiy 2006)
		1000	41.0	n.d.	(Behl et al. 1994)
		33	27.3	n.d.	(Gieler et al. 2000)
		400	7.5	n.d.	(Behl and Bhatia 1972)
	'Nervousness' 'Emotional undertones' or 'upset'	200	15.0	n.d.	(Lerner 1959)
		482	12.2.	n.d.	(Sehgal et al. 1976)
		650	8.3	n.d.	(Dutta and Mandal 1969)
		365	2.2	n.d.	(Shah et al. 2008)
	≥3 uncontrollable life events	31	**16.7**	**2.8**	(Picardi et al. 2003)
Physical causes	***Physical stress / trauma***	650	40.8	n.d.	(Dutta and Mandal 1969)
		65	30.7*	n.d.	(Barišíc-Druško and Rucević 1997)
		200	15.0	n.d.	(Lerner 1959)
		41	14.5	n.d.	(Mason and Gawkrodger 2005)
		33	9.1	n.d.	(Gieler et al. 2000)
		400	5.0	n.d.	(Behl and Bhatia 1972)
		998	5.0	n.d.	(Tawade et al. 1997)
		482	1.5	n.d.	(Sehgal et al. 1976)
		365	0.8	n.d.	(Shah et al. 2008)
	Chemical agents	400	5.0	n.d.	(Behl and Bhatia 1972)
		998	0.4	n.d.	(Tawade et al. 1997)
	Medication / Antibiotics	400	32.5	n.d.	(Behl and Bhatia 1972)
		41	2.4	n.d.	(Mason and Gawkrodger 2005)
	Other illnesses	88	**26.0**	**0.0**	(Papadopoulos et al. 1998)
		21	**9.5**	**0.0**	(Manolache et al. 2009)
		33	9.1	n.d.	(Gieler et al. 2000)
		650	5.5	n.d.	(Dutta and Mandal 1969)
		200	3.0	n.d.	(Denman et al. 2006)
		998	0.3	n.d.	(Tawade et al. 1997)

Table 4: Possible trigger factors (Review of the literature)
Bold numbers are from case-control studies

[2] only regarding exacerbating effect
[3] stated as '*one third*'
[4] unpublished work by J. Harper (1992) cited in Papadopoulos et al 1998, no case number given and no control group used, *bereavement* was the most commonly reported life event,
* in children only

3.4 Clinical subtypes

Vitiligo can be divided into several subtypes according to extent and location of the white spots.

3.4.1 Generalised vitiligo

3.4.1.1 Vitiligo vulgaris

Vitiligo vulgaris is the most common subtype of the disease. It appears with symmetrical distribution of white maculae, affecting about 40-80% of all patients (Mosher et al. 1979; Handa and Kaur 1999; Dogra et al. 2005; Liu et al. 2005). However, in one study only 10.5% of all patients had vitiligo vulgaris (Onunu and Kubeyinje 2003). The course of generalised vitiligo is unpredictable (Liu et al. 2005) (**Figure 3**).

3.4.1.2 Acrofacial vitiligo

Acrofacial distribution includes involvement of distal extremities (hands, feet and ano-genital area) and the face. This subset has been documented in about 3-16% of all patients with vitiligo (Schallreuter et al. 1994b; Parsad et al. 2004; Zhang et al. 2004; Dogra et al. 2005; Liu et al. 2005).

Recently it has been suggested by Liu et al that acrofacial vitiligo changes rather rarely to vitiligo vulgaris. These authors reported that acrofacial vitiligo remains stable in approximately 74% of all cases (Liu et al. 2005).

3.4.1.3 Vitiligo universalis

Vitiligo universalis is a clinical subset where more than 80% of a patient's body surface is depigmented. Rarely, patients can be totally depigmented mimicking clinically albinism. Although this form is one of the least common subsets, it still occurs in 1.6%-7% of all patients (Schallreuter et al. 1994b; Kar 2001; Zhang et al. 2004; Liu et al. 2005; Mason and Gawkrodger 2005) (**Figure 3**).

However, in the inbreeding *Somavamsha Sahasrarjuna Kshatriy* community in India, where a high prevalence of a positive family history (90.4%) exists, vitiligo universalis was found in 15.4% of 54 patients (Ramaiah et al. 1988).

3.4.2 Localised subtypes

Localised vitiligo is characterised by the appearance of one or more white maculae in a non-symmetrical and rather scattered manner. Depending on location of the appearance, localised vitiligo can be divided into the segmental and focal form including lip-tip vitiligo (Hann and Im 2004).

3.4.2.1 Segmental vitiligo

Segmental vitiligo appears unilaterally as localised single maculae in nearly definite dermatomes. Hence, a connection to nerves has been suggested. Sites most often affected are face and neck, followed by trunk and extremities (Koga and Tango 1988; Hann and Lee 1996; Hann and Im 2004) (**Figure 3**).

In some cases, segmental vitiligo can also occur in association with vitiligo vulgaris resulting in mixed vitiligo (Schallreuter et al. 2008b).

A review of the literature shows that about 5% or more of all patients are affected by segmental vitiligo (Hann and Im 2004), although some reports showed prevalences as high as 10-14% (Kar 2001; Parsad et al. 2004; Zhang et al. 2004). The distribution among children, however, is usually more frequent (up to one third) and the onset normally earlier than non-segmental vitiligo (Handa and Kaur 1999; Cho et al. 2000; Grimes and Billips 2000; Prćić et al. 2002; Silverberg et al. 2004; Zhang et al. 2004).

Interestingly, it has been shown that the cutaneous blood flow and adrenoceptor response differ in segmental vitiligo compared to other clinical subsets of the disease and normal healthy controls. Wu et al found a threefold increase in cutaneous blood flow compared to normal skin, whereas non-segmental vitiligo showed a 1.5-fold increase only. The authors suggest that this is caused by a dysfunction of the sympathetic nerves (Wu et al. 2000).

Finally, the progression of segmental vitiligo has been described as different from the vulgaris type of vitiligo. While in the majority non-segmental vitiligo can spread on the entire body surface during life, the segmental form spreads more frequently on the dermatome only and ceases often after about one year and remains stable for the rest of the life (Koga and Tango 1988; Hann and Lee 1996; Hann and Im 2004). However, as mentioned above, segmental vitiligo can occur together with vitiligo vulgaris (Schallreuter et al. 2008b).

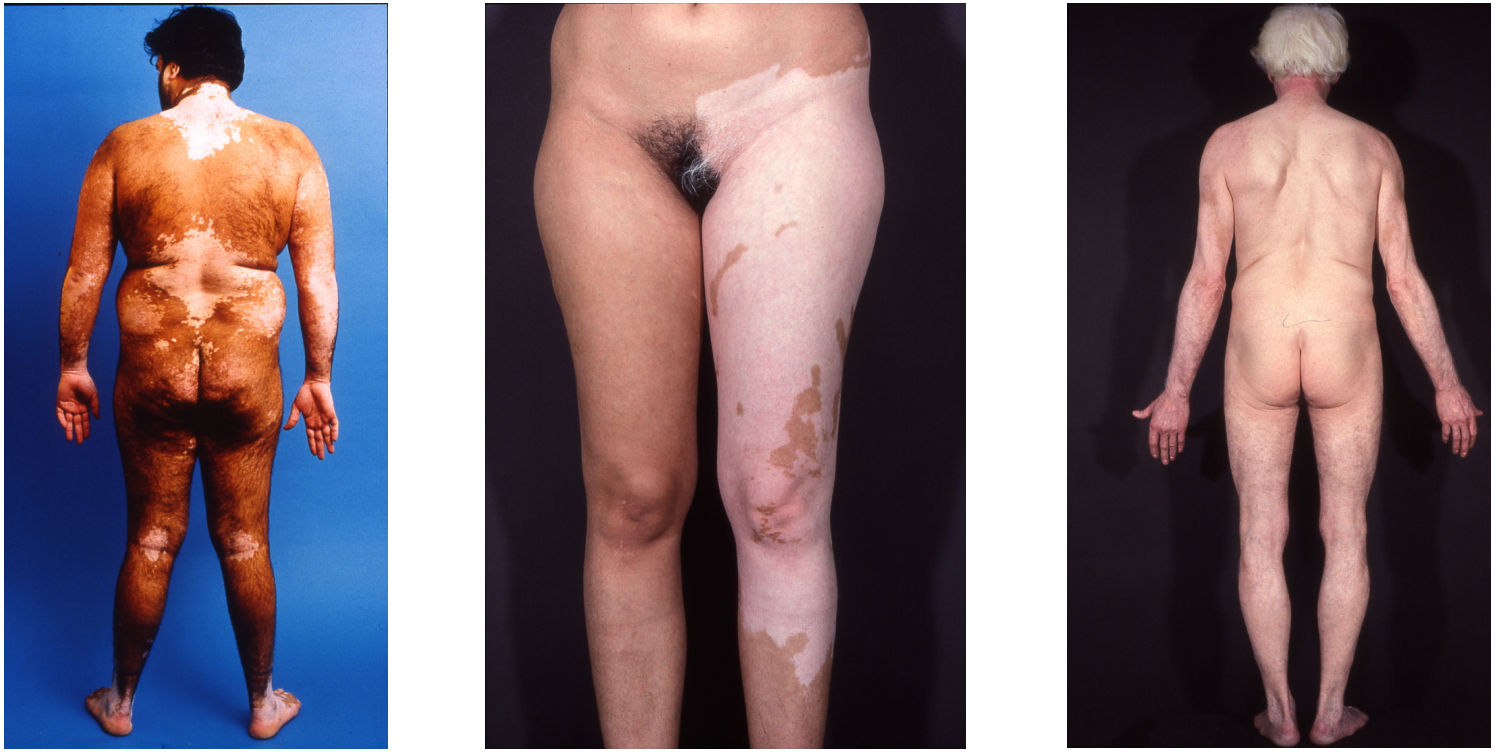


Figure 3: Clinical subtypes of vitiligo
Left: vitiligo vulgaris with clearly visible symmetrical pattern.
Middle: vitiligo segmentalis. Note the distinctive border at the midline of the body.
Right: vitiligo universalis with no remaining pigmentation visible
(with courtesy from KU Schallreuter)

3.4.2.2 Vitiligo focalis

This subset refers to cases where one or more patches appear in a single area in random distribution. About 15-35% of all patients with vitiligo are affected (Schallreuter et al. 1994b; Handa and Kaur 1999; Zhang et al. 2004; Liu et al. 2005). For some authors, focal vitiligo seems to be more an intermediate state rather than a distinct subtype as more than half of all cases develop other clinical subtypes. Recently it was reported that 75% of vitiligo vulgaris cases start as focal vitiligo (Liu et al. 2005).

3.4.2.3 Blaschko-linear vitiligo

There are many skin diseases (genodermatoses, congenital and acquired disorders) that follow Blaschko's lines. This pattern was first described by the German dermatologist Alfred Blaschko (Blaschko 1901) and it is thought to be a marker in development and growth of two unlike cell populations in the skin tissue, also called *mosaicism* (**Figure 4**). The existence of two different cell populations may be the result of *lyonisation*, i.e. spontaneous inactivation of certain chromosomes during embryogenesis (Happle 1985).

There have been single case reports of vitiligo occurring in linear or Blaschko-linear patterns (El Mofty 1968; Punshi 1975; Schallreuter et al. 2007) (**Figure 5**), but not all of them seem to follow exactly these lines (Bolognia et al. 1994). Khaitan found a blaschkoid pattern in 49.6% of 141 patients with segmental vitiligo (Khaitan et al. 2007).

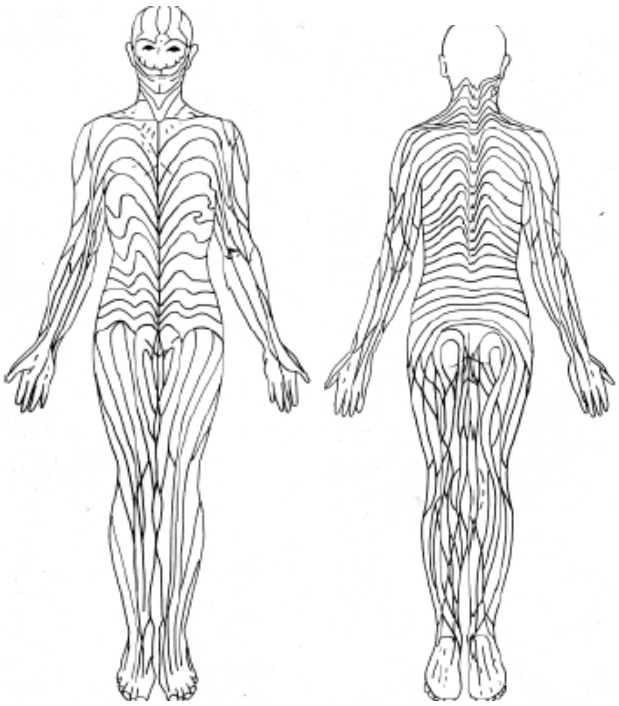


Figure 4: **Blaschko's lines on the human body (Jackson 1976)**

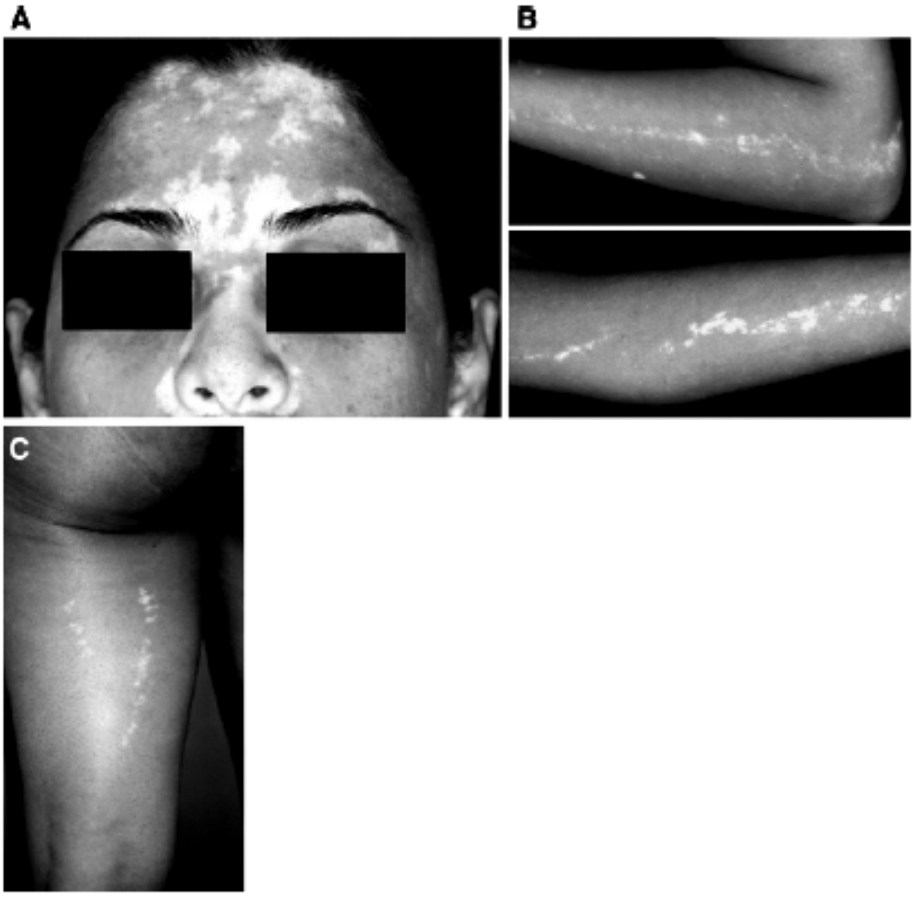


Figure 5: Blaschko-linear vitiligo on arms (B) and legs (C) co-existing with acrofacial vitiligo (A)
(Schallreuter et al. 2007)

3.4.3 Special forms

3.4.3.1 Trichrome / quadrochrome vitiligo

This form shows clinically more than two skin colours ranging from hyperpigmented, hypopigmented to depigmented areas. **Figure 6** shows one example of *trichrome* or four colours *(quadrochrome)* vitiligo.

The importance of this phenomenon is not yet clear. It might be either a transitional stage in the development of active spreading vitiligo (Schallreuter, personal observation) or just an unusual pattern of depigmentation (Mosher et al. 1979; Hann and Im 2004).

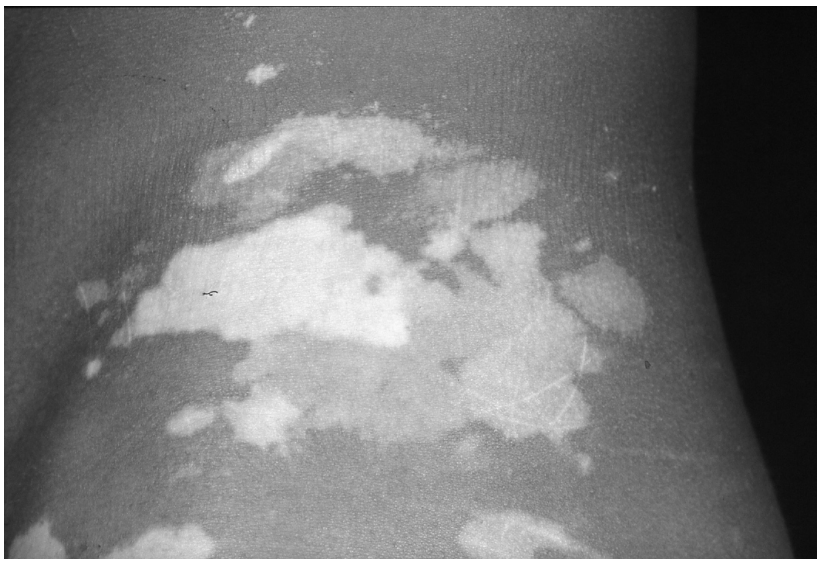


Figure 6: Trichrome vitiligo
(with courtesy from KU Schallreuter)

3.4.3.2 Inflammatory vitiligo

Sometimes, the borders of vitiligo patches can be red, raised and even scaly as an expression of an inflammatory process. At the same time, a mild pruritus (itching) can be noticeable. Eczema-like changes, the absence of melanin and the presence of lymphocytic and histocytic infiltrates can be observed (Hann and Im 2004).

The significance of these raised and red borders is not yet known. It has been suggested that this phenomenon is an expression of the normal inflammatory process in the development of vitiligo (Hann and Im 2004; Sharquie et al. 2004).

3.5 Aetiology of vitiligo

Vitiligo has generated a lot of interest and, consequently, research is ongoing worldwide to find the cause for this devastating disease. There are many theories trying to explain vitiligo including autoimmune, genetic, neural, autocytotoxic, biochemical, and oxidative stress mechanisms. However, a satisfying explanation for what causes the sudden mostly progressive loss of the inherited skin colour has not yet been found (Grimes 2004; Schallreuter et al. 2008a).

3.5.1 Autoimmune hypothesis

A possible autoimmune reaction of the human body against its own melanocytes is currently still the most popular hypothesis to explain the cause for vitiligo. It is thought that antibodies in a majority of patients with this disease are directed against melanocytes, but also against thyroid, adrenal and parietal mucosa tissue. As a result, melanocytes are absent after being destroyed in lesional skin of these patients (Naughton et al. 1983; Schallreuter et al. 1994b; Farrokhi et al. 2005; Le Poole and Luiten 2008).

Antibodies are observed in 30-80% of patients (Naughton et al. 1983; Farrokhi et al. 2005), but sometimes they cannot be detected at all (Schallreuter et al. 1994b).

However, recent findings have questioned the idea that melanocytes are completely destroyed or absent in white patches of long-standing vitiligo. It was shown that

melanocytes are not only still present even after long duration of the disease, but also started to produce melanin again under certain conditions (Tobin et al. 2000). These findings raised the question whether subpopulations of melanocytes actually survive but are in fact not functioning.

In summary, there are conflicting reports whether autoimmunity plays a major role in this disease.

3.5.2 Genetic hypothesis

In about every third patient, a positive family history of vitiligo can be documented. This finding suggests a possible involvement of genes in the development of vitiligo (Mosher et al. 1979; Majumder et al. 1993). Reports on a positive family history in affected individuals vary from 1.5-48% (Singh et al. 1985; Schallreuter et al. 1994b; Al-Khawajah 1997). Based on the presence of vitiligo in families, there is an ongoing interest since the 1960‘s to find genetic evidence involved in this disease. During this course the role of certain blood groups was investigated, but these studies were inconclusive (Nordlund 1997).

More recent studies tried to identify certain candidate genes or chromosomes which could be involved in the development of vitiligo. Recently, certain candidate genes have been implicated in vitiligo. However, it is clear no simple Mendelian genetics exist for vitiligo, but rather multiple susceptibility loci and genetic heterogeneity with possible differences between ethnic groups (Schallreuter 2004; Chen et al. 2005; Laberge et al. 2005; Zhang et al. 2005).

One of the genes involved is the catalase gene. This data supports both the genetic and oxidative stress hypotheses (see chapter on oxidative stress) (Casp et al. 2002; Wood et al. 2008). Such genetic predisposition might be the reason for a higher susceptibility of melanocytes to exogenous or endogenous enviromental factors (chemicals, food ingredients, etc) (Nordlund 1997).

Other susceptibility genes have been put forward including the PTPN22-1858C>T[5] (Laberge et al. 2008), the NALP1[6] (Jin et al. 2007), AIS1 (Fain et al. 2003) or the FOXD3[7] gene (Alkhateeb et al. 2005), most often in connection with autoimmune diseases. Since the data vary between patients, it is possible that different subtypes of vitiligo may exist.

3.5.3 Neural hypothesis

This hypothesis is based on that both melanocytes and neuronal cells derive from the neural crest during embryogenesis. A link between the nervous system and vitiligo as well as other skin diseases has been discussed for a long time (Crooker 1884). This hypothesis was supported by some observations in vitiligo patients. One example is segmental vitiligo which often follows dermatomal pattern. Moreover, depigmentation has been described in connection with neural diseases such as multiple sclerosis, syphilis or physical damage to nerves. It is thought that cutaneous nerve endings and their neurotransmitters influence the functionality of melanocytes (Lerner et al. 1966; Del Bianco et al. 2004; Hautmann et al. 2004). Increased levels of catecholamine

[5] encodes lymphoid protein tyrosine phosphatase (Laberge et al. 2008)
[6] encodes NACHT leucine-rich-repeat protein 1, a regulator of the innate immune system (Jin et al. 2007)
[7] melanoblast developmental regulator gene in autosomal dominant vitiligo (Alkhateeb et al. 2005)

metabolites in urine have been documented by several groups (Morrone et al. 1992; Schallreuter et al. 1994d)

However, segmental vitiligo does not always strictly follow a dermatomal pattern and many other clinical phenomena of vitiligo cannot be explained by this hypothesis. Consequently, the neuronal hypothesis can only add in parts to the pathogenesis of vitiligo (Nordlund and Ortonne 1998).

3.5.4 Autocytotoxic hypothesis

The essential part of this hypothesis is that certain precursors of melanin or chemicals similar to melanin can inhibit the process of melanogenesis or even destroy melanocytes. A severe imbalance could cause a loss of protection against such chemicals which in turn especially affects melanocytes (Hann and Chun 2000; Hautmann et al. 2004).

Slominski et al suggested that melanocytes in vitiligo are destroyed by a cascade of reactions initiated by a dysregulation of melanogenesis in connection with activation of the melatonin receptor. These authors suggested that an uncontrolled production of free radicals and toxic products of melanogenesis could provoke an autoimmune response against exposed surface antigens leading in turn to the destruction of melanocytes (Slominski et al. 1989).

3.5.5 Oxidative Stress hypothesis

This hypothesis is based on a discovery made by Schallreuter et al who showed *in vivo* by FT-Raman spectroscopy, that patients with vitiligo have increased levels of hydrogen peroxide (H_2O_2) in the lesional and non-lesional skin leading to oxidative

stress in the entire epidermis in association with low epidermal catalase levels (Schallreuter et al. 1991b; Schallreuter et al. 1999).

Physiological H_2O_2 levels in the epidermis are in the *micromolar* [µM] range. However, once H_2O_2 reaches high levels (*millimolar* [mM] range), a number of mechanisms in the skin can be altered leading to destruction / dysfunctionality of melanocytes.

This also includes accumulation of oxidised pterins, because $6BH_4$, a cofactor involved in melanogenesis is oxidised to 6-L-biopterin. The latter is cytotoxic to melanocytes (Schallreuter et al. 1994a). The presence of oxidised pterines in the skin of patients with vitiligo is the reason why Wood's light can be used for diagnosis of this disease, because the observed fluorescence is caused by oxidised pterins (Schallreuter et al. 1994c).

At the same time epidermal catalase, thioredoxin reductase and systemic glutathione peroxidase levels are significantly decreased. These anti-oxidant enzymes normally degrade high levels of H_2O_2. The low level of catalase is caused by oxidative degradation of the active site of this enzyme (Aronoff 1965; Schallreuter et al. 1991b; Schallreuter 2004; Maresca et al. 2006; Wood and Schallreuter 2006; Wood et al. 2008).

Others authors also reported that there is an imbalance in the anti-oxidant system in vitiliginous melanocytes (Maresca et al. 1997) as well as an increased sensitivity of vitiliginous melanocytes to oxidative stress, associated with the abnormal expression of tyrosinase-related protein TRP1 leading to early cell death (Jimbow et al. 2001).

As mentioned above, recently the catalase gene has been implicated as a most likely susceptibility candidate, which would support this hypothesis (Casp et al. 2002; Wood et al. 2008).

An indirect proof for this hypothesis is also that vitiligo can be treated with a topical application of a narrow-band UVB activated pseudocatalase (PC-KUS) leading to

removal of H_2O_2 from the epidermis. With this modality progressive de-pigmentation can be stopped and re-pigmentation can be achieved with good success rates (Schallreuter et al. 1995; Schallreuter et al. 2008b).

Whether oxidative stress can fully explain the cause of vitiligo needs yet to be shown. However, all data generated so far revealed that the entire epidermis of patients is involved (i.e. lesional and non-lesional skin) in the disease process and not only melanocytes. Moreover, the possible connection with the catalase polymorphism strongly suggests that H_2O_2 is one of the major players in this disease (Schallreuter et al. 2008a).

3.5.6 Viruses and vitiligo?

Besides the above-mentioned hypotheses, there have been some other suggestions to explain the pathogenesis of vitiligo including viral infections. It is believed that viruses could play a part in some autoimmune diseases like Hashimoto's thyroiditis, which is more frequent in patients with vitiligo compared to healthy controls (Castanet and Ortonne 1997).

Implicated viruses are for example the human cytomegalovirus (CMV) (Grimes et al. 1996; Galarza et al. 2004) or the hepatitis C virus (HCV). However, the results are controversial, because no significant connection could be found by other groups (Würfel 1999; Akbayir et al. 2004; Schallreuter 2004; Jadali et al. 2005).

In the majority of patients only a rather weak direct link can be documented between viral infections and the development of vitiligo. At this time, molecular mimicry cannot be ruled out. More investigations are necessary to support or dismiss this hypothesis (Schallreuter 2004).

3.5.7 Vitiligo and hormones

There have been several reports that the onset of vitiligo is often associated with hormonal changes. In a report by Salzer and Schallreuter, 39% of all patients examined associated the beginning of their disease with hormonal changes, such as puberty, pregnancy, birth and menopause. This association was significant (Salzer and Schallreuter 1995).

In this context it has been shown only recently that oestrogens can contribute to oxidative stress due to elevated H_2O_2 and semiquinone and orthoquinone levels in lymphocytes, finally leading to DNA damage in these cells (Anderson et al. 2003).
Since oestrogens can be produced in the human epidermis, it was proposed that hormone-induced oxidative stress could add to the H_2O_2 pool contributing to the depigmentation process (Schallreuter et al. 2006).

3.5.8 Other hypotheses

Another hypothesis is based on the idea that melanocytes are part of the so-called epidermal melanin unit which includes melanocytes and keratinocytes (Fitzpatrick and Breathnach 1963). It was shown that stimulatory cytokines are low in the skin of patients with vitiligo, by contrast with inhibitory cytokines, which were significantly increased (Moretti et al. 2002; Hautmann et al. 2004). It is thought that these cytokines and / or growth factors cause an alteration of the microenvironment within this melanin unit leading to apoptosis of melanocytes. Therefore, vitiligo could be seen as a result of such alteration.

No difference was found between melanocytes from non-lesional skin and melanocytes from healthy controls regarding apoptotic mechanisms (Tobin et al. 2000; Van den Wijngaard et al. 2000). Furthermore, as described above, Tobin et al could show that melanocytes are still present in lesional skin even after long duration of vitiligo (Tobin et al. 2000). Moreover, when these melanocytes were established in cell culture, they showed normal growth and morphology. These results suggested that recovery of a normal homeostasis / environment is important for melanocyte function in vitiligo (Tobin et al. 2000). The absence of apoptosis was further confirmed in two recent PhD theses by Shalbaf and Abou-Alloof (PhD at the University of Bradford, 2009).

3.6 Treatment

Vitiligo is a disease known for more than 1000 years. Similar old are attempts to treat this depigmentation disorder (Kopera 2000). In some old medical books from India, a plant mentioned to be useful is named as *Bavachee* (or *psoralea corylifolia*). Later is was found that it contains psoralene, a photo-sensitizing chemical compound (Morrone 2004; Njoo and Westerhof 2004). Psoralens have been used since ancient times and they are still in use today in combination with UVA light or natural sun light known as PUVA and PUVASOL.

In a review on vitiligo from the 1940s, Robert mentioned other treatment modalities reported in the literature at that time, including:

- *Kromayer's lamp* (a quartz lamp of mercury vapour with actinic rays),
- *Re-injection of patient's own blood*,
- *Sensitizing with acriflavine (an antiseptic) followed by quartz lamp irradiation,*
- *Sun light exposure,*
- *X-rays* (Robert 1941).

It is obvious that already in earlier time doctors tried to treat vitiligo with irradiation or light exposure, a principle that is still true for today. In his own clinic the author apparently used several different tablets (e.g. *Histamin*) without observing any significant improvements (Robert 1941).

In 1948 El Mofty was the first in modern times to investigate the efficacy of oral psoralen combined with sunlight, which was apparently the most effective treatment for vitiligo at that time (El Mofty 1968).

Nowadays there is a broad range of more or less successful treatment modalities available often following the mentioned hypotheses about possible causes of the disease. **Table 5** summarises the various methods.

	Treatment modality	Possible action mechanism	Side effects	Success rates	[n]	Reference
Photo-chemo therapies	Psoralens + UVA **(PUVA)**	Stimulates hypertrophy (enlargement), proliferation and enzymatic activity of melanocytes	Risk of skin cancer increased	8 out of 97 (nearly) complete pigmented **(8.3%)**, 59 out of 97 had moderate to extensive repigmentation of different qualities, 30 showed none or only little improvement.	97	(Kwok et al. 2002)
	Khellin + UVA **(KUVA) -** active principle of the plant a*mmi visnaga*	Activates melanocyte proliferation and melanogenesis	Mild nausea, impaired liver functions	**41%** of patients showed good response (>70% repigmentation) after a mean of 194 treatments	28	(Hofer et al. 2001)
	L-phenylalanine + UVA **(PAUVA)**	Stimulates migration of melanocytes from adjacent areas	Not stated	Half of patients satisfied with results, 11 out of 25 patients (44%) still repigmented 5 years after treatment	25	(Greiner et al. 1994)
	Pseudo-catalase + narrow-band UVB **(PC-KUS) -** (*bis-(Mn)(EDTA) bi-carbonate*)	Reduction of millimolar levels of epidermal H_2O_2 leading to recovery from oxidative stress and repigmentation	None	**92%** of patients had excellent repigmentation (>75%) in face, 79% on trunk, 73% on extremities, 9% on hands / feet after one year of daily treatment	71	(Schallreuter et al. 2008b)
	Combined climato-therapy with PC-KUS at the Dead Sea	Weak pseudocatalase activity of Dead Sea water supports PC-KUS treatment	Exposure to sunlight	Repigmentation initiated already after 10-16 days compared to 8-14 weeks with PC-KUS alone	59	(Schallreuter et al. 2002)
	Melagenina - a hydroalcoholic extract from the human placenta	Accelerates the formation of melanin from dihydroxy-phenylalanine (DOPA) as part of melanogenesis	Not stated	62 out of 366 paediatric patients (**16.9%**) showed 71-100% repigmentation	366	(Mal'tsev et al. 1995)
Phototherapies	Narrow-band **UVB** (311nm wavelength)	Induces immuno-supression, increases melanocyte-stimulating hormones, melanocyte proliferation and melanogenesis	Increased risk of skin cancer	**53%** of treated children had at least 75% of their vitiligo repigmented, in 6% (n=3) it was even complete	51	(Njoo et al. 2000)
	Climato-therapy at the **Dead Sea**	Salty water rich in minerals, filtered sunlight to stimulate pigmentation	Sun-induced skin cancer	n.d.	n.d.	(Even-Paz 1996)
	Excimer laser Targeted mono-chromatic light 308nm	Similar to narrow-band UVB	Increased risk of skin cancer	23 patches from 12 patients achieved about 57% repigmentation, whereas 11 patches from 6 patients received all 12 treatments and gained appr. 82% pigmentation back	18	(Spencer et al. 2002)
Local therapies	**Steroids -** synthetic analogues of hormones of the adrenal cortex	Anti-inflammatory and immunosuppressant effects	Atrophy weight gain, insomnia, acne, menstrual disturbances	In various studies good to excellent repigmentation has been reported in **9-92%**	Var.	(Stratigos and Katsambas 2004)
	Calciopotriol - a synthetic analogue of vitamin D_3	Influence on growth and differentiation of melanocytes and keratinocytes	Mild irritation of the skin possible	55% had marked to complete repigmentation, moderate repigmentation in 4, rest showed only minimal or no improvement, none developed new patches	21	(Parsad et al. 1999)
	Topical immuno-modulators Tacrolimus & Pimecrolimus	Limiting activation and maturation of T-cells by inhibiting calcineurin function.	Site burning, pruritus, cancer	76-100% repigmentation in **47%** of patients on head and neck, 25% of patients with involvement of trunk and / or extremities	57	(Silverberg et al. 2004)
	Skin grafting	Pigmentation up to 8mm around each graft	Scarring, hypo- or hyper-pigmentation, infections	**84%** of participants with segmental vitiligo showed excellent repigmentation (95-100%), 6% good results (65-94%), only 10% showed poor repigmentation (0-24%)	67	(Mulekar 2004)

Table 5: Selection of common treatment modalities and their success rates in the literature

3.7 Psychosocial impact of vitiligo - limitation of available data

Until the end of the 1970's only little research had been conducted on the psychosocial impact of vitiligo on patients' life (Barbee and Sumner 1951). Starting with the pioneering work of Porter's group, several aspects of vitiligo such as its influence on children, sexual relationships, self-esteem and the role of skin colour, age and patients-doctor relationships were covered (Porter et al. 1978; Porter et al. 1979; Porter and Beuf 1988; Porter et al. 1990; Porter and Beuf 1991; Porter and Beuf 1994). Numerous publications have followed since on the emotional well-being of patients and not only on medical aspects.

However, in this context it is noteworthy that all data originate from patients who were associated with dermatological clinics or self-support organisations, because this is the easiest way to get hold of patients.
Moreover, it can be expected that patients who seek medical treatment and / or support are psychosocially more affected and more desperate compared to those who do not bother. Therefore, the critical question was whether numbers from the literature form a realistic basis for the general patient population.

One indication that individuals, who are members of support groups, are more affected was shown by Ongenae et al who investigated the impact of vitiligo and psoriasis on quality of life. Patients of those groups scored significantly higher compared to non-members indicating a greater impairment of quality of life in these patients (Ongenae et al. 2005b).

To the best of our knowledge there is only one study available in the literature providing a hint about how many patients with vitiligo care about their disease at all. In the 1970's a health examination survey was conducted in the USA to obtain data on skin conditions and their related medical care. This study included 20,749 persons aged 1-74 years, who were examined by dermatologists. Vitiligo was found in **0.49%** of the population, a result which is in agreement with the reports in the literature (**Table 2** and **Figure 2**). This number confirms other data on the prevalence in the population. However, after the dermatologists asked for '*skin conditions of concern'*, vitiligo was mentioned by only **0.14%** of the group (Johnson and Roberts 1978). Based on these data, it can be concluded that only **29%** of all patients with vitiligo are actually concerned about their disease. This information is a big surprise. If the above study is representative, it is tempting to conclude that most likely all available data originate from *concerned* sufferers only.

3.8 The world of patients with vitiligo

3.8.1 'What is beautiful is good'

The skin is not only the largest organ of a human being; it also provides the boundary between the body and the external environment. Hence this organ plays an important part in people's communication with others, as mirrored for example by blushing as a reaction to somebody, hair-rising or getting pale (Van Moffaert 1992).

The skin is important for tactile communication and interaction, for instance between children and parents or between adults. In the early years of life some emotions are learned partly by skin contact, for instance bonding to the parents (Griesemer and Nadelson 1979; Van Moffaert 1992; Walker 2005).

Taken together, the skin has not only biological functions, but it is also important in people's social interactions playing a major part in our physical appearance.

Physical appearance and its influence on other people's opinion about strangers have been the subject of many earlier investigations revealing that people attribute physically attractive strangers:

- as socially more desirable, better spouses and having happier marriages (Dion et al. 1972),
- as more likable, especially by men (McKelvie and Matthews 1976),
- as more intelligent (Zebrowitz et al. 2002).

Dion summarised this phenomenon with '*What is beautiful is good*' (Dion et al. 1972). Based on these concepts a link between vitiligo and and its influence on social life can

be made. Since our skin is important for our self-confidence and appearance, vitiligo and other skin diseases can significantly alter this and thus influence personal relationships.

By contrast to the wide range and long history of research on skin diseases including biochemical backgrounds and treatment modalities there was very little research done on the psychosocial impact of skin diseases until the beginning of the 1980's. Nowadays, a connection between skin diseases and psychosocial problems has been established opening the field of *psychodermatology* (Van Moffaert 1992; Walker 2005).

3.8.2 Stigmatisation

Stigma is a negative evaluation of a certain feature or behaviour by society. It reduces the affected individual to a tainted, discredited person leading to disapproval, negative comments, discrimination and exclusion (Goffman 1968; Bruce 2000; Chaturvedi et al. 2005).

Stigmatisation may occur as reaction to either *tribal* identity based on race, gender or religions, character blemishes including addiction and mental illness or *alterations of the physical appearance* of somebody, for example by vitiligo (Kent 2005).

Stigmatisation may be encountered by the affected person in several ways. Besides open negative reactions and rejections, it is also possible to sense that other people with the same disease are stigmatised. Not always are all reactions negative, but it is important to realise than being the centre of unwanted attention as curiosity leads to the same effect (Kent 2005).

There are several theories why stigmatisation takes place among humans:

- Altered appearances or behaviours are examples for deviations from predictability which may pose a threat to the smooth running of a society (Albrecht et al. 1982).

- If a certain condition or behaviour is believed to be controllable (e.g. alcohol addiction), they are more likely to cause stigmatisation (Albrecht et al. 1982; Kent 2005) → *'Just World hypothesis':* people have certain conditions, because they must have deserved it, for example acne must be caused by bad food (Kent 2005).

- An unknown skin condition could be a threat to the physical health of other people, because this condition could be contagious. Therefore contacts are avoided. Here an evolutional origin is suspected since avoidance of potential threats is seen as advantage for survival (Hornstein et al. 1973; Kent 2005).

Baumeister developed the *Social Exclusion Theory*, which implies that humans have a fundamental motive not to be excluded by their fellows. Moreover, this theory emphasises that our social behaviour often reflects the attempts to enhance our chances of social inclusion. In fact, there are negative effects including depression, if we do not achieve our goals in psychosocial interaction (Baumeister and Leary 1995; Kent 2005).
Stigmatisation is often associated with vitiligo, because other diseases appear clinically similar. This is also the case with leprosy which is by far more dangerous due to possible infection from the affected individual (Kopera 2000). One example is presented in **Figure 7**.

Figure 7: Leprosy of the face
Note the striking similarity of the white spot to vitiligo (source: **www.who.int/lep/en)**

In India, for example, people with vitiligo experience the same abuses and negative reactions, because it is believed that they have "*Sweta Kushta*" (white leprosy). Some Indian people believe that vitiligo sufferers must have "*insulted teacher*" (Chaturvedi et al. 2005) or that they must have done something punishable in their past lives (Weiss et al. 1992).

A confusion of vitiligo with leprosy has also been reported from other countries, for instance in Nigeria resulting in stigmatisation (Onunu and Kubeyinje 2003; Olasode and George 2008).

An overview of published data on the subject of stigmatisation is presented in **Table 6**.

Stigmatisation experiences	% of [n]	[n]	Reference
Subject to questions about disease	**72**	62	(Porter et al. 1979)
Staring by other people	**67**	62	(Porter et al. 1979)
	57	326	(Porter et al. 1987)
'Negative comments, teasing or bullying'	**49**	45	(McLeod 2004)
Rude remarks	**50**	326	(Porter et al. 1987)
	16	62	(Porter et al. 1979)
Avoided interactions	**13**	62	(Porter et al. 1979)
Rejection	**13**	78	(Ongenae et al. 2005a)
Negative effects on education and job opportunities	**33**[8]	77	(Borimnejad et al. 2006)
Discrimination at work	**13**	62	(Porter et al. 1979)
	8	326	(Porter et al. 1987)

Table 6: Frequencies of stigmatising experiences in vitiligo (review of the literature)

Importantly, it was shown by Porter and Beuf that perceived stigmatisation leads to lower self-esteem and a higher degree of disturbance in patients with vitiligo. This result stresses the deep impact of stigmatisation on the affected persons (Porter and Beuf 1991). In this context it is noteworthy that perceived stigmatisation was the most influential factor accounting for 39% of variance in the assessment of quality of life (Kent and Al-Abadie 1996a). There are no differences in experiencing stigmatising encounters between both genders in a group of 45 patients with vitiligo (McLeod 2004).

[8] Calculated by this author using numbers provided in the publication (21 out of 53 females, 4 out of 24 males)

3.8.3 Vitiligo - a non-predictable disease

For a long time vitiligo has been recognised as a disease with a rather unpredictable character. Although normally progressing with time, spreading of the disease can stop at any time or progress even faster. Rarely, spontaneous re-pigmentation has been observed (Mosher et al. 1979; Chun and Hann 1997).

This lack of predictability makes it more difficult for patients to cope with the disease. Porter et al reported that the majority of the population investigated (n=62) were concerned about the progressive character of vitiligo (Porter et al. 1979). In another report this was 41% of 326 patients (Porter et al. 1987).

It was shown that after diagnosis '*the predominant reactions were worry about being different from others and finding, because vitiligo has no cure, that they were unable to control this difference*' (Thompson et al. 2002).

3.9 Psychological reactions to Vitiligo

3.9.1 Depression

Depression is one of the most common psychiatric disorders in patients with skin diseases. It can be defined as a mental disorder characterised by persisting low mood, change in appetite, loss of interest / pleasure in usual activities involving one or more episodes of such changes (Gupta and Gupta 2003).

In one of the earliest investigations on psychosocial wellbeing of patients with vitiligo it was found that 40% of 62 participants were depressed using the Coppersmith Self-Esteem Inventory. Depression was associated with acute and chronic embarrassment. The depressed patients tried "heroically" to hide their vitiligo (Porter et al. 1979).

Several later publications investigated whether patients with vitiligo were more depressed compared to healthy controls. The results varied from none to significant differences.

No differences were found between patients and controls in a German study with 33 patients using the Beck Depression Inventory (BDI) (Gieler et al. 2000).
The same outcome was confirmed for children / adolescents (n=13, 10-15 years old) with the Birleson Depression Scale (Prćić et al. 2006). Moreover, the depression scores tend to decrease with duration of vitiligo (Gieler et al. 2000).

There was also no significant difference between patients and healthy controls or between genders using the BDI (n=21). Neither age, the presence of progressive

vitiligo, visibility of lesions nor the duration of the disease did seem to influence depression levels (Lee et al. 2000).

Other authors, however, stressed that there are differences between patients and controls. Kökçam and colleagues compared 11 patients with vitiligo to sufferers from alopecia areata and healthy controls using the Zung Depression Scale and Symptom Check-List 90-R (SCL-90-R). Manifest depressive symptoms were found in 55% of the vitiligo group, in 36% of the alopecia group, but only in 15% of the control group (Kökçam et al. 1999).

This difference was even more pronounced in an investigation from Iran, where the Hamilton Rating Score for Depression (HRSD) was used in 52 patients with vitiligo and the same number of healthy controls. 46.2% of the patients, but only 6% of the controls were depressed (Maleki et al. 2005). Similar results were obtained with the Minnesota Multiphasic Personality Inventory where scores in the subscale *depression* were higher in patients with vitiligo (n=30) compared to healthy controls (Elgoweini et al. 2003).

3.9.2 Anxiety

Gieler et al used the Intercations Anxiety Questionnaire for measuring the individual degree of anxiety in eight specific situations. Patients with vitiligo were more anxious in three out of the eight situations including *fear of deviation from standard, fear from self-assertion* and *fear of challenging situations*, whereas evaluating of *fear of physical injury, fear of performance* and *hypochondriac fear to get a disease* yielded no differences (Gieler et al. 2000).

Kökçam et al compared 11 patients with vitiligo with sufferers from alopecia areata and healthy controls using the Zung Depression Scale and SCL-90-R with one subscale being on anxiety. Here, patients with vitiligo were more anxious than healthy controls (Kökçam et al. 1999). Similar results were obtained by Manolache et al who compared patients with vitiligo (n=54) to those with alopecia areata (n=72) and healthy controls (Manolache et al. 2004). Furthermore, after the introduction of the Adjustment to Chronic Skin Disorders Questionnaire, it was shown that female patients (n=23) were more socially anxious than males (n=10) (Stangier et al. 2003).

There are a number of contradictory reports in the literature. No differences in anxiety between adolescents with vitiligo (n=33) and healthy controls (n=60) were found utilising the Spielberger's Scale (Prćić et al. 2006). The same result was reported for adult patients (n=22) using the Spielberger's State and Trait Anxiety Inventory (STAI). No significant differences could be observed between female and male patients, between the age groups of younger and older than 30 years of age, and with regards to disease progression and visibility (Lee et al. 2000).

Using one subscale of the Adjustment to Chronic Skin Disorders Questionnaire, men (n=79) and women (n=284) with vitiligo showed equal levels of *social anxiety / avoidance* (Schmid-Ott et al. 2007).

3.9.3 Reduced Self-esteem

Self-esteem is "*a personal judgement of worthiness that is expressed in the attitudes the individual holds toward himself. It is a subjective experience which the individual conveys to others by verbal reports and other overt expressive behaviour*" (Coopersmith 1967).

In 1986, Porter et al showed that patients with vitiligo scored significantly lower on the Coopersmith Self Esteem Index indicating a lower self-esteem compared to healthy controls (Porter et al. 1986). In another study 58% of patients (n=80) *believed* that vitiligo had strongly affected their self-esteem (Firooz et al. 2004).

High self-esteem before the onset of vitiligo led to less difficulties in coping with the disease (Porter et al. 1979). Already 30 years earlier and based on interviews with 13 patients it was suggested that vitiligo "*does not induce a change in the basic structure of the personality but accentuates already present personality traits*" (Barbee and Sumner 1951).

A positive correlation between self-esteem (measured by Rosenberg Self Esteem Scale - RSES) and Quality of Life (measured with the Dermatology Life Quality Index - DLQI) was documented in 614 patients with vitiligo (Kent and Al-Abadie 1996a). The same correlation was found between self-esteem and perceived stigma (n=614) (Kent 1999).

Low self-esteem in patients with vitiligo improved significantly by cognitive-behavioural therapy (CBT) as demonstrated by Papadopoulos et al with 16 patients with vitiligo measured utilising the Rosenberg Self Esteem Scale (RSES). After 8-weeks of therapeutic counselling the mean RSES score of 30 decreased to approximately 13, compared to the control group where RSES scores hardly changed (Papadopoulos et al. 1999).

A build-up of appearance-independent competencies to improve self-esteem leads to better coping with this skin disease in children (Hill-Beuf and Porter 1984).

3.9.4 Embarrassment

In 1979 Porter et al investigated psychological reactions of 62 patients to chronic skin disorders, using vitiligo as a model disease. Two thirds of the patients felt embarrassed by their disease. Approximately 53% stated that they felt socially uncomfortable, ugly or forced to hide their white spots by certain clothes. Younger people (<40 years) felt more embarrassed. There was no gender-related difference compared to older people, where men are less affected (Porter et al. 1979).

Seventy eight percent of 109 Saudi-Arabian patients with vitiligo felt embarrassed by the disease. Women were more affected than male patients (Al Robaee 2007). The percentage of Nigerian patients embarrassed by their vitiligo was with 90% even higher (Olasode and George 2008).

From these data it can be concluded, that embarrassment is common in patients with vitiligo.

3.9.5 Limited personal and sexual relationships

Vitiligo can influence the patients' sexual relationships profoundly at all levels. Many patients find it difficult to socialise and / or to establish relationships at all (Porter et al. 1990).

Approximately 10-15% of patients stated that vitiligo has limited either sociability or their potential to enter relationships (Porter et al. 1990). In a later investigation it was shown that vitiligo affecting the genital area has a negative effect on socialising and

meeting potential sexual partners. Half of the participants reported stress and general embarrassment in the presence of strangers and people of the opposite sex (Porter et al. 1990).

Another study regarding quality of life evaluated 30 patients with vitiligo who received treatment with narrow-band UVB light over the last 4 years. On the one hand, thirteen patients of this group had never experienced any problems with relationships or with starting new ones, and 17 patients had never had any sexual problems due to their vitiligo. On the other hand, these data reflect that half of the group must have had experienced such problems in the past (Tjioe et al. 2005).

In an investigation on differences between the sexes regarding quality of life in Iranian patients (n=77), it was found that females were more affected in the DLQI sub scores '*interpersonal and social relationships'* and *'sexual activity'* (Borimnejad et al. 2006).

25 – 30% of all patients with vitiligo reported that their sex lives were strongly affected (Porter et al. 1979; Porter et al. 1990).

It was documented that males and especially persons

- with low self-esteem,
- with higher rating of appearance as important factor
- who are unmarried

had more difficulties. Self-esteem was the most influential factor (Porter et al. 1990).

However, several investigations could not confirm the difference between married and unmarried patients. Kent and Al-Abadie found no differences in DLQI measurements comparing patients with vitiligo living in stable sexual relationships (n=446) to those who were separated, divorced or who had never lived with a sexual partner at the time of the survey (n=167) (mean scores 4.67 vs. 5.24, $p>0.1$) (Kent and Al-Abadie 1996a).

The same result was reported in Iranian patients where no differences between married patients and singles were found (n=70) (Aghaei et al. 2004).

Sukan and Maner compared vitiligo and chronic urticaria patients with healthy controls (each group n=50) to assess sexual functions using the Arizona Sexual Experience Scale (ASEX). The authors found that both disease groups experienced significantly more difficulties in sexual arousal and higher failure in attaining and maintaining sexual excitement. Females in the vitiligo and chronic urticaria groups had more difficulties in reaching orgasm compared to healthy controls. More than 60% of females, but only 11.5% of male patients with vitiligo showed sexual difficulties compared to 16% in the control group (Sukan and Maner 2007).

3.9.6 Impaired quality of life

In recent years much research has been conducted on how patients with skin diseases might be affected regarding parts of their emotional lives, such as self-esteem or depression. However, for daily management and guidance of those patients in clinical routine, these parameters were not sufficient to get a glimpse of how this disease affects the daily lives. Thus, quality of life research was introduced into dermatology in the middle of the 1990's by Finlay and Khan (Finlay and Khan 1994).

When developing their questionnaire, Finlay and Khan asked 120 patients which parts of their daily life were affected by their skin diseases. In the end six important dimensions were identified:

- *symptoms and feelings*
- *daily activities*
- *leisure*
- *work and school*
- *personal relationships*
- *treatment* (Finlay and Khan 1994).

Based on the results of this study a subsequent questionnaire was developed called Dermatology Life Quality Index (DLQI), which evaluates all the dimensions as stated above. Quality of life is assessed by adding up each question's score which leads to a maximum score of 30. The higher the score, the more the quality of life is impaired (Finlay and Khan 1994).

Besides the DLQI there are other instruments to measure quality of life in dermatology, for instance the Skindex (Chren et al. 1996), Freiberg Life Quality Assessment (Augustin et al. 2004) and the Dermatology QoL Scales (Morgan et al. 1997).

Consequently, numerous studies on quality of life have been published investigating patients with vitiligo. These studies clearly show that patients with this disease have an impaired quality of life compared to healthy controls (Finlay and Khan 1994; Papadopoulos et al. 1999; Aghaei et al. 2004; Lewis and Finlay 2004; Hartmann et al. 2005), and even compared to some other skin diseases (Mechri et al. 2006).

Based on the results of the DLQI it was suggested that training in assertiveness and assistance with building up self-confidence could have a positive effect on quality of life. Support in the development of social skills and confrontation with their difficulties were proposed to improve psychological well-being (Kent and Al-Abadie 1996a).

3.9.7 Other possible reactions

Salzer and Schallreuter investigated the personality structure and a possible association with an impaired catecholamine metabolism. The results revealed no specific personality pattern. Importantly, 75% of the patients said that they felt **moderately to intolerably disfigured** and **psychologically disturbed** (Salzer and Schallreuter 1995).

Patients with vitiligo have not less positive thoughts compared to the healthy population, but rather an **increase in "*irrational*" negative thoughts**. This was concluded from a study using the Body Image Automatic Thoughts Questionnaire, which includes a subscale on positive and one on negative thoughts (n=16) (Papadopoulos et al. 1999).

In a study by Kökçam et al it was found that patients with vitiligo (n=11) were more **paranoid** compared to healthy controls (n=20) as measured with a subscale of the Zung Depression Scale and Symptom Check List 90-R (SCL 90-R) (Kökçam et al. 1999).

Elgoweini et al found patients with vitiligo (n=30) **more obsessed** and **hypochondriac** compared to healthy controls as measured with the Minnesota Multiphasic Personality Inventory (MMPI) (Elgoweini et al. 2003).

Mouzas et al reported that patients with vitiligo (n=116) suffered more frequently from **sleep disturbances** (sleepwalking, nocturnal enuresis, nightmares) compared to healthy controls (n=48) prior to the manifestation of the disease. The authors also claim a correlation between parasomnias in earlier life and the later development of vitiligo (Mouzas et al. 2008).

3.10 Factors influencing psychosocial reactions to vitiligo

3.10.1 Gender

Since vitiligo alters the physical appearance of the affected individual, it has been of interest whether there are any gender differences. There are numerous publications showing indeed such differences.

More female than male patients with vitiligo are affected in terms of

- **Quality of life** (Abeni et al. 2005; Ongenae et al. 2005b; Borimnejad et al. 2006; van Geel et al. 2006; Gajur et al. 2007; Schäfer and Augustin 2007; Sampogna et al. 2008),
- **Psychiatric morbidity** in general (Abeni et al. 2005),
- **Helplessness** (Rehme 2002; Schmid-Ott et al. 2007)
- **Retreat** (Schmid-Ott et al. 2007)
- **Embarrassment** (in older patients only) (Porter et al. 1979)
- **Sexual dysfunctions** (Sukan and Maner 2007).

However, there are also some reports which could not confirm differences regarding quality of life (Kent and Al-Abadie 1996a; Aghaei et al. 2004; Al Robaee 2007), psychiatric morbidity (Ahmed et al. 2007) or depression (Lee et al. 2000; Maleki et al. 2005). Interestingly, perceived stigma is also independent of gender (Kent 1999; McLeod 2004).

With regards to composure, men (n=79) seem to be more affected than female patients (n=284) as measured with a questionnaire about experiencing skin complaints (Rehme 2002).

In general, women are more likely to visit a doctor because of their vitiligo (Ongenae et al. 2004), to use cosmetics or to receive support from others (Porter and Beuf 1994), whereas male patients seem to be more analytical and likely to attribute external and internal causal factors towards their vitiligo (Papadopoulos et al. 2002).

3.10.2 Skin colour

For a long time it has been of interest whether the inherited skin colour may influence people's psychological reaction to vitiligo.

In this context it was hypothesised that the increased visibility of vitiligo in black people due to the sharp contrast may lead to an increased degree of disturbance (Barbee and Sumner 1951). Additionally, turning white threatens black identity. Obviously, this phenomenon does not apply for white people (Porter and Beuf 1991).

The same authors examined 158 patients (60% white / 40% black) to establish whether or not there is indeed a difference in disturbance among black and white people by measuring self-esteem, visibility of vitiligo, perceived stigmatisation, age, gender and importance of appearance. The results could *not* establish that race, visibility, age or gender is significantly and directly associated with disturbance through vitiligo, but it was found that some of the factors mentioned have an indirect influence. Blacks are more likely to perceive stigmatisation (Kent 1999) which in turn has a significant effect on disturbance indicating that race is indirectly associated with disturbance by vitiligo.

Moreover, visibility is indirectly associated with disturbance, because low visibility means lower levels of perceived stigmatisation and higher self-esteem leading to less disturbance (Porter and Beuf 1991). The same authors also stress the importance of coping resources, for example self-esteem, which in turn prevents black people from being more disturbed than white people. In this study, most of the black participants came from a city where the majority of inhabitants were black, Therefore, supporters such as friends and doctors would empathise with the specific identity problem of dark skinned people turning white (Porter and Beuf 1991; Porter and Beuf 1994).

McLeod and Kent and Al-Abadie reported that people with darker skin are more likely to experience stigmatisation than people with fair skin (Kent 1999; McLeod 2004). Non-Caucasians (n=46) showed higher DLQI means cores than Caucasians (n=567) (7.78 vs 4.59, $p<0.001$) (Kent and Al-Abadie 1996a).

This result was also confirmed in a recent study. From all patients with various skin diseases, African Americans showed higher DLQI and Skindex-29 scores compared to white patients. This difference, however, is not detectable when comparing the disease severities. Based on this study it can be concluded that the African-American group is more affected, despite having the same disease severity, than Caucasians (Hackett et al. 2008).

3.10.3 Age

One other important question was whether age has any effect on experiences and coping with vitiligo.

Younger people (<40 years) felt more embarrassed because of their vitiligo with no gender-related difference compared to older people, where men were less affected (n=62) (Porter et al. 1979).

A study on 269 patients assessed patients' disturbance using self-esteem, severity of the disease and perceived discrimination as variables for determination. The results showed that older people are better adjusted to vitiligo compared to younger people, because physical appearance was not so important anymore. Thus, age has a direct and significant effect (Porter and Beuf 1988).

Kent and Al-Abadie found that 59% of 614 patients with vitiligo were affected in their life during the last 3 weeks. When compared to those who did not report any influence, the affected persons were younger, their quality of life was more influenced, they had a lower self-esteem and perceived more stigmatisation (Kent and Al-Abadie 1996b).

However, the published data are conflicting. One report by Ongenae et al showed no significant relationship between age and the impact of vitiligo (n=102) compared to psoriasis (n=162) (Ongenae et al. 2005b). Uesseler could not show a correlation between age and social and emotional problems as measured with the Skindex-29 (n=362) (Uesseler 2002).

3.10.4 Duration of the disease

Duration of the disease could affect quality of life. Several studies showed that long duration had a negative effect.

A direct correlation has been reported by Gajur et al (n=1023) and Schäfer and Augustin who found that with longer duration there were higher mean DLQI scores indicating a more impaired quality of life (Gajur et al. 2007; Schäfer and Augustin 2007). Elgoweini reported a direct significant correlation between duration of vitiligo and obsession as measured with the Minnesota Multiphasic Personality Inventory (MMPI) (n=30) (Elgoweini et al. 2003). Finally, Uesseler found a positive correlation of duration with Skindex-29 scores (socially and emotionally affected) in 362 patients with vitiligo (Uesseler 2002).

However, other studies could not confirm this correlation.

Gieler et al found in 33 patients with vitiligo that the longer they had the disease the *less* depressed the patients became as assessed with the Beck Depression Inventory (BDI) (Gieler et al. 2000). Stangier et al found no statistical correlation between duration of the disease and mean scores in the subscales of *social anxiety / avoidance, helplessness* and *anxious-depressive mood* using the Adjustment to Chronic Skin Diseases (ACS) for assessment (n=33) (Stangier et al. 2003). Kent and Al-Abadie could also not confirm that higher scores in DLQI measurements correlate with time since diagnosis (n=614, $p>0.05$) (Kent and Al-Abadie 1996a).

3.10.5 Severity of the disease

In many investigations it was of interest whether the severity of vitiligo correlates with an improvement or worsening of emotions.

In a study by Njoo et al, 51 children with vitiligo underwent one year of narrow-band UVB monotherapy. The Children's Dermatology Life Quality Index (CDLQI) was

utilised in the beginning and at the end of the therapy. The results revealed that the better the repigmentation rate, the better was the improvement in quality of life (Njoo et al. 2000).

Other authors also concluded that anything reducing the size and visibility of vitiligo is very likely to improve psychological wellbeing (Kent and Al-Abadie 1996a; Innocenti et al. 1997).

Stangier found that in 33 patients with vitiligo there was a positive correlation between severity of the disease and mean scores in the Adjustment to Chronic Skin Diseases Questionnaire's subscales *social anxiety / avoidance, helplessness* and *anxious-depressive mood* (Stangier et al. 2003). Similar results were reported for the Skindex-29 (n=362) (Uesseler 2002).

In a thesis from Manchester University / UK, 45 patients with vitiligo were investigated about their disease-related social experiences. The participants were divided into four groups according to the severity of the disease (first group 1-25% of skin affected, followed by 25-50%, 51-75% and 76-100%). The majority (18 out of 23) of the group with least severity did not experience negativity. Based on these results it was concluded that the more vitiligo is visible, the more likely is the person to experience stigmatisation by others (McLeod 2004).

The same has been confirmed by others who also found that patients with visible lesions experienced more stigmatisation (Schmid-Ott et al. 2007).

In this context it is noteworthy that the objective '*severity of a general disfigurement'* is not always a reliable predictor for the level of psychological adjustment, compared to the subjective view on the own disfigurement where a linear relationship exists (Moss 2005; Ongenae et al. 2005a). Poorer adjustment to a visible difference is mainly

relevant in people with moderate severity, whereas patients with less and, surprisingly, more severe disease were better adjusted ("*inverted U relationship*"). This was explained by the fact that in the case of severe and minor disfigurement other people's reactions to the appearance are relatively consistent or trivial, whereas in the case of moderate severity the reactions might differ more. It was concluded that it is more difficult to develop an adaptive strategy (Rumsey and Harcourt 2004; Moss 2005).

Again, the results in the literature are not conclusive. Gieler et al found *no* correlation between the size of the affected areas and levels of depression as measured by the Beck Depression Inventory. On the one hand, this does not necessarily support Moss' finding of an inverted U relationship, but on the other hand, it is not a confirmation of a linear relationship (the more extended the vitiligo the more affected the patient) either (Gieler et al. 2000).

3.10.6 Combination of medical and psychological treatment

Considering that psychological factors such as stress or life events may influence the onset or course of vitiligo, it has been of interest to find out whether a combination of medical treatment and psychological counselling could actually improve the medical outcome. Several studies have addressed this issue.

Koshevenko reported that a combination of photochemotherapy with "*correction of psychologic abnormalities*" in 49 patients with vitiligo with impaired sociopsychological adaption lead to an by 20% increased repigmentation and to shorter periods of time necessary to achieve marked pigmentation (Koshevenko Iu 1989).

A positive influence of cognitive-behavioural therapy on impaired self-esteem, body image and quality of life was also shown in 16 patients with vitiligo[9] (Papadopoulos et al. 1999). These authors found that self-esteem, body image and quality of life have been significantly improved into the normal range after the latter mentioned variables were compared after ending the treatment 5 months later. Interestingly, vitiligo lesions of three participants in the experimental group were reduced by up to 35%, whereas the vitiligo of two control group members worsened by up to 50%, the rest remained more or less stable. The authors suggest that medical treatment together with cognitive-behavioural therapy may lead to better cosmetical results than medical treatment alone (Papadopoulos et al. 1999). However, this study can only count as a pilot study as the case number is very low.

Parsad et al treated 150 Indian patients with vitiligo in their clinic and after finishing a course of medical treatment the authors grouped the patients according to whether their repigmentation was successful or not. The authors found that the mean DLQI score in the 'successful' group was significantly lower than that of the 'failed' group *in the beginning of the trial* (7.06 vs. 13.12). Therefore the authors suggested that additional psychological approaches might be very helpful (Parsad et al. 2003; Parsad and Kanwar 2006). Other authors have reported similar effects (Muller 2005).

[9] these 16 patients were randomly allocated into either the test group or the control group

3.10.7 Vitiligo in children

As shown above, a considerable number of studies on the psychosocial impact of vitiligo have been published. However, these studies mainly concerned adult patients or the entire patient group. There are still few data available on psychosocial aspects in children, although many researchers argue that childhood vitiligo is a distinct subset of this disease. These reports mainly concern:

- *distinct clinical features of vitiligo in children in contrast to adults*

  (Jaisankar et al. 1992; Kanwar et al. 1993; Behl et al. 1994; Barišić-Druško and Rucević 1997; Cho et al. 2000; Prćić et al. 2002; Prćić et al. 2004; Kakourou et al. 2005; Martin et al. 2005),

- *childhood vitiligo and its treatment possibilities*

  (Halder et al. 1987; Halder 1997; Grimes and Billips 2000; Njoo et al. 2000; Herane 2003; Lepe et al. 2003; Schaffer and Bolognia 2003; Kanwar et al. 2004; Silverberg et al. 2004; Choi et al. 2008; Pagovich et al. 2008; Schallreuter et al. 2008b; Sehgal 2009).

The psychosocial burden for children with vitiligo was first investigated by Hill-Beuf and Porter more than 20 years ago (Hill-Beuf and Porter 1984), but until now this remained one of the rare pure psychosocial investigations. The authors found children are indeed affected by their altered physical appearance. They emphasised that age is highly influential on how children can cope with the disease and that this is particularly difficult when they are in Junior High School age (11-14 years old) or when they move to another town or school. It was recommended to build up self-esteem by developing competencies that do not depend on appearance (Hill-Beuf and Porter 1984).

Prćić et al compared 33 adolescent patients with vitiligo (aged 10-15 years) to 60 healthy controls of the same age regarding clinical symptoms, depression, anxiety and frequency of stressful events. The authors could not find any differences between cases and controls as measured with the Birleson Depression Scale, Spielberger's Scale (State-Trait Anxiety Inventory) and Risk Scale. This result was explained by pre-pubertal age and that these patients were not yet focussed on their physical appearance (Prćić et al. 2006).

Schwartz and Sepulveda did also not find any differences between children with vitiligo and healthy controls using the Junior Temperament and Character Inventory (JTCI) apart from its *harm avoidance* domain. This result indicates that young patients are more passive, pessimistic, cautious and insecure. In addition, they also have a higher tendency to be easily fatigued. In another questionnaire (Qualitative Psychosocial Development Survey) the same group was found to be more fearful of strangers compared to healthy controls. Children with vitiligo reported an average of 3.2 negative experiences in the year before the disease onset (Guttman 2007)[10].

Interestingly, one study investigated whether childhood vitiligo had any impact on adult life lead by the sufferers later on. Participants were 232 patients with vitiligo who developed the disease before the age of 20 years and 201 healthy controls. Both groups were asked to fill out several questionnaires[11] and to answer questions about any negative experiences due to vitiligo during childhood.

[10] Unpublished study cited by Guttman 2007
[11] the Course of Life questionnaire, the Skindex-29 (quality of life questionnaire specific to skin diseases), and the Dutch-language version of the SF-36 (short form health survey)

The data showed no differences between patients and controls in any of the questionnaires used. However, when comparing patients with negative experiences (n=91) to the remaining ones, patients who had more frequently vitiligo on their arms, feet and genitals, scored lower in the '*social development'* domain, and reported significantly poorer health-related quality of life as measured with the SF-36 and Skindex-29. These patients avoided intimacy and social activity and tended to do things alone.

Most importantly, patients with negative experiences wished, that they had had more information about the disease and its treatment, more coaching and contacts with fellow sufferers and also more psychological support (Linthorst Homan et al. 2008).

It has been of interest whether there are any factors probably triggering childhood vitiligo. There are some hints in the literature such as *parents' separation* (Montes 2008), *stress* (Manolache et al. 2009), *psychological trauma* (Barišíc-Druško and Rucević 1997), but also *physical stress / trauma* (Barišíc-Druško and Rucević 1997). Others have also recognised and mentioned the psychosocial impact of vitiligo on children (Halder 1997; Herane 2003), but it is evident that more research needs to be done.

Recently, the introduction of the Children's Dermatology Life Quality Index (Finlay and Khan 1994; Lewis-Jones and Finlay 1995) as an easy-to-use instrument created more possibilities for research in childhood vitiligo. However, only a few reports on this entity have been published, for example one on the effect of NB-UVB treatment (Njoo et al. 2000) or one comparing children with vitiligo to healthy controls (Guttman 2007).

4 Aim

By contrast with the plethora of biochemical and biological research data, little had been done on the psychological problems related to vitiligo until the end of the 1970's. Since then, many aspects have been targeted, for example problems regarding self-esteem, depression, body image, quality of life, age, sexual relationships and skin colour.
Surprisingly, anxiety and helplessness have hardly been explored. The latter is clearly important, because reduction of helplessness was highly rated by 1023 German patients with vitiligo associated with self-support organisations (Gajur et al. 2007).

In this situation it was tempting to fill some of these gaps by introducing the Adjustment to Chronic Skin Disorders Questionnaire which has rarely been used in vitiligo and which evaluates social anxiety / avoidance, helplessness and anxious-depressive mood. Also, since there is no agreement in the literature on the role of depression in these patients, we decided to follow up this aspect with appropriate tools. Moreover, since the DLQI scores in the literature vary to a great deal, we wanted to examine this parameter in a controlled environment, i.e. in the Institute for Pigmentary Disorders in Greifswald / Germany and Bradford / UK.

To address these questions in more detail, we decided to use several questionnaires to be answered by adult patients, children patients, their parents and healthy controls.

Patients were enrolled with the Institute for Pigmentary Disorders (IFPD) in Greifswald in association with the Ernst Moritz Arndt University of Greifswald / Germany and the University of Bradford / UK, at the annual meeting of the American Vitiligo Research Foundation and by a German self-support group for vitiligo.

Both the latter groups filled out their questionnaire anonymously. The patient group from the IFPD is rather unique because these patients have to travel to Greifswald in Germany, and they do have to pay their fees for enrolment and treatment. Considering these circumstances, it is tempting to conclude that those patients are clearly determined to combat their vitiligo, because they should have experienced severe stress or stigmatisation due to course of their disease.

- One study group were children and adolescents and their parents. We wanted to investigate the impact of vitiligo on quality of life in children, and to explore children's experiences, behaviour and demographic features.
- The second group were adult patients. Our aim was here to explore experiences, behaviour, demographic features and the impact of vitiligo on quality of life, on possible depression and their coping with the disease in adults.

5 Materials and methods

5.1 Questionnaires

This study was designed as a cross-sectional and case-control study.

We utilised three different questionnaires. For the evaluation of the impact on quality of life we used the **Dermatology Life Quality Index** (DLQI) for adults and the **Children's Dermatology Life Quality Index** (CDLQI) for patients between 8-14 years old. In order to follow coping with chronic skin diseases, we utilised the **Adjustment to Chronic Skin Disorders Questionnaire** (ACS). For assessment of depression we utilised the **Beck Depression Inventory**.

These validated questionnaires were chosen, because they are

- widely used (DLQI, CDLQI, BDI),
- available in the English and German language (DLQI, CDLQI, BDI)
- recommended for measurement of coping with chronic skin diseases (ACS) (Augustin et al. 2000).

Importantly, while DLQI, CDLQI and BDI offer many opportunities to compare our results with those from the literature, there are only a few publications using the ACS in vitiligo. Therefore, it was expected that those data could introduce new insights into the psychosocial influence of vitiligo. To the best of our knowledge, the dimensions *helplessness* and *anxious-depressive mood* (both ACS sub-scales) have not been explored so far.

Each questionnaire used in this investigation was made available either in a German or an English language version as required. The English versions of the ACS have been translated from German into the English language in a cooperation between two native German speakers living in the UK, and one native English speaker with knowledge of the German language. All translators had a scientific background. The first draft of the questionnaire was tested on some patients regarding English-language problems and comprehensibility, and subsequently necessary changes were made. With regard to the Children's Dermatology Life Quality Index, both the English and the German version have been used as provided from the original authors (Lewis-Jones and Finlay 1995). Besides the main standard questionnaires as mentioned above, some other questions were included:

- *Demographical* questions

  Age of the patient, age at disease onset, gender, skin phototype and status of patient (enrolled or not enrolled with the Institute for Pigmentary Disorders).

- *Disease-related* questions

  Family history, self-assessment of disease severity on dominant body parts, where the first spot appeared, the presence of grey hair on scalp or in eyelashes / eyebrows, state of disease (spreading, stable, re-pigmenting).

- *Beliefs*

  What could influence vitiligo? (psychological stress, other diseases or injuries)

- *Behaviour and experiences*

  Typical stigmatising experiences including being asked questions by others, having been picked on or being subject to nasty comments, avoidance of situations, hiding of the white spots in front of other people, activities including hobbies or sport.

The DLQI, BDI and also some single questions were added later on to the questionnaire. Consequently the numbers of patients analysed differ between the scores and sub-scores.

5.1.1 Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index was developed by Finlay and Khan in the beginning of the 1990's. The authors aimed for an easy-to-use questionnaire sufficient for daily medical practice.

In the beginning of its development, 120 Patients at a Welsh dermatological clinic were asked to identify essential parts of everybody's daily life that will most certainly be affected by a skin disease. The following items emerged:

- *Symptoms* (itching, irritation, pain, sore…),
- *Feelings (*self-consciousness, embarrassment…),
- *Daily activities* (shopping, gardening…),
- *Leisure activities* (swimming, social life…),
- *Work or school* (career affected, colleagues make fun…),
- *Personal relationships* (making new ones, sexuality…),
- *Treatment* (messy, smelly, makes clothes greasy).

(Finlay and Khan 1994).

The subsequently created Dermatology Life Quality Index consists of 10 questions, all of them related to the parts mentioned above. Each item has four choices to answer:

Very much	- scores **3**
A lot	- scores **2**
A little	- scores **1**
Not at all (or *Not relevant)*	- scores **0**

The sum of the total score can range from 0 to 30. The higher the score, the more quality of life is impaired within the preceding 7 days.

Thirteen years after its introduction, the DLQI had been translated into at least 55 languages, validated several times and had widely been used in more than 33 different

skin disorders (Lewis and Finlay 2004; Basra et al. 2008). The use of the DLQI offers therefore many possibilities to compare obtained data.

Recently Gajur suggested to group the DLQI scores to evaluate the subgroups in more detail (Gajur 2008). These cut-offs allow more insights into the quality of life of patients (**Table 7**).

DLQI scores	Outcome of quality of life
0-1	Not influenced
2-5	Little influenced
6-10	Moderately influenced
11-20	Severely influenced
21-30	Extremely influenced

Table 7: Levels of impaired quality of life (Gajur 2008)

5.1.2 Adjustment to Chronic Skin Disorders Questionnaire (ACS)

For measuring the impact of vitiligo on adults, a slighty adapted version of the Adjustment to Chronic Skin Disorders Questionnaire has been employed.

The original questionnaire was developed to evaluate specific dimensions (see below) for coping with chronic skin diseases by using in total 51 items (Stangier et al. 1996). We extended this questionnaire by demographic and disease-related questions such as age, sex, duration and severity of the disease.

The patients rate the validity of each item / statement by choosing one of five possibilities as answer, *1 = not at all, 2 = hardly ever, 3 = quite, 4 = mostly* and *5 =*

totally. The specific coping behaviour of the participants is based on the sum of marked answers which are compared to validated scales provided in the manual or to other publications (Stangier et al. 1996).

The Adjustment to Chronic Skin Disorders questionnaire contains 6 main sub-scales, but we used only three in this project. The other scales (*itch-scratch cycle, seeking information* and *limitation of quality of life*) were excluded. The itch-scratch cycle and seeking information were regarded as irrelevant for vitiligo. The quality of life scale is redundant because this was explored with the DLQI. The excluded questions were mostly left blank and only in a few cases replaced by others to keep the whole questionnaire as short as possible.

The remaining scales used for this project were:

- *Social anxiety / avoidance (15 items):* concerns mainly coping with the visibility of the skin disease, especially emotional and social anxiety, cognitive and behavioural reactions to the experiences in social interaction. Increased scores in this scale indicate social anxiety and avoidance of situations where negative reactions or comments are expected by the patients, but also feelings of loss of attractiveness or feelings of disfigurement.

- *Helplessness (9 items)* means feelings of loss of control regarding course of disease, and also hypochondriac worries that the disease might get worse. This is expressed by increased scores within this dimension.

- *Anxious-depressive mood (8 items)* concerns emotional and physical symptoms, which are not directly linked to the skin disease. Increased scores indicate depressive and anxious symptoms in terms of an adjustment disorder (Stangier et al. 1996).

5.1.3 Beck Depression Inventory (BDI)

The Beck Depression Inventory was developed in 1961 as a 21-question multiple choice questionnaire to measure depression levels (Beck et al. 1961). The evaluation is based on self-reports about specific symptoms of depression. Each of the 21 items consists of four possibilities to answer graded from 0 to 3. Participants have to mark those adequately to their situations. All scores are added up and the total sum of up to 63 can be compared with standard cut-offs, which are

0-9 - *no depression*
10-18 - *mild-moderate depression*
19-29 - *moderate-severe depression*
30-63 - *severe depression.*

Since it is possible to mark more than one statement in each item, it is recommended to use the highest score.

The BDI has been widely employed and validated since its introduction. Hence it offers many possibilities to compare the scores from this thesis to the literature.

5.1.4 Children's Dermatology Life Quality Index (CDLQI)

The questionnaire used for the evaluation of children contains 32 items, including the 10 unchanged questions taken from the Children Dermatology Life Quality Index (CDLQI).

The CDLQI was chosen because

- it contains 10 questions only and is easy to use, even for younger children, because there is a cartoon version available of this questionnaire (Holme et al. 2003),

- it has been validated in children with skin diseases (Lewis-Jones and Finlay 1995),
- it is widely used in different countries (Njoo et al. 2000; Chuh 2003) and diseases and, thus, provides many possibilities to compare the results.

The complete children questionnaire contains four parts.

1. General information

In the first part the child is asked to give some general information about its person including gender, age, skin colour, the most preferred season of the year and whether it has a hobby or it is involved in sportive activities. Especially the sportive activities are expected to give an indication, whether the children hide their vitiligo or not. Wearing certain sport dresses, changing clothes or having a shower in the sport facilities might reveal to others that the child has something different to others. Similar is the question concerning the season. If a child likes the summer, this indicates that it is not afraid to show the spots or to avoid summer-typical clothes.

2. Characteristics of the child's vitiligo

The second part is to find out some characteristics of the child's vitiligo such as duration of disease, family history and whether any treatment has been tried before. Furthermore, this section contains a drawn shape of the human body where the child is asked to mark the location and size of their vitiligo, which in turn provides an indication of the severity of the disease.

3. Children's Dermatology Life Quality Index

This part contains the complete and unchanged Children's Dermatology Life Quality Index as developed by Lewis-Jones and Finlay (Lewis-Jones and Finlay 1995).

This questionnaire measures the impact of the skin disease on the quality of life within the last week using the dimensions of: *symptoms and feelings, leisure, school or holidays, personal relationships, sleep* and *treatment*. It is not only possible to find out how much the quality of life is impaired compared to healthy controls or other skin diseases, it also gives an indication which part of the daily life is disturbed by the disease.

The CDLQI contains 10 questions, with four graded options to answer: *very much* (scores 3), *quite a lot* (2), *only a little* (1) and *not at all* (0). The CDLQI is calculated by adding up each item's score resulting in a maximum score of 30. The higher the score, the more the quality of life is impaired (Finlay and Khan 1994).

Dimension	**Questions**	**Questions in original CDLQI**	**Maximum score**
Symptoms and feelings	12, 13	1, 2	6
Leisure	15, 16, 17	4, 5, 6	9
School or holidays	18	7	3
Personal relationships	14, 19	3,8	6
Sleep	20	9	3
Treatment	21	10	3

Table 8: Evaluation of CDLQI, related questions and maximum score (Lewis-Jones and Finlay 1995)

4. Feelings and experiences

Since the CDLQI explores influences within the last week, we have included questions about feelings and experiences of the child in general and also of earlier periods than one week ago. This part concerns feelings of disturbance, certain behaviour patterns such as hiding of the white spots in front of other people or avoidance of situations, furthermore, experiences such as stigmatising encounters, bullying and also who gave support in such situations and who would be the first person to seek support from.

The non-CDLQI questions are mostly to be answered by ticking the cycle at the answer, which suits most the child's feeling and experiences. It is either a yes-no-answer or a variety of options completed sometimes by an open possibility to answer. The questionnaire contains only a few items where the answer has to be written down, such as age, hobbies / sport and alternative options in experiences and feelings. The evaluation is not to be done with a scoring system, instead the aim is to get results for every single item, which then can be related to other factors such as the scoring in the CDLQI.

The first drafts of this questionnaire were tested on a limited number of children. Some changes were made to improve the comprehensibility, especially with regard to the English language. Once this was done, no difficulties in understanding for children older than 7 years have been observed. Average time for filling in was as short as 5 to 15 minutes.

Taken together, the children’s questionnaire measures how much the quality of life of an affected child is impaired by vitiligo. This is completed by demographic data and knowledge about disease-related experiences and feelings.

5.1.5 Parents' questionnaire

Our investigation of the parents of children with vitiligo was based on an adapted version of the *Adjustment to Chronic Skin Disorders Questionnaire.* The itching-scratching-circle dimension has been replaced by additional questions, for example to evaluate the frequency of how often parents examined their child for new white spots.

Moreover, all questions of the original survey, where participants had to rate feelings toward their own disease were changed, allowing analysis of the parents feeling toward their children's vitiligo. All items of the *anxious-depressive mood* dimension remained completely unchanged, because this dimension concerns feelings and emotions in general.

The interpretation of the entire questionnaire needs caution since the mentioned items were changed. The results could reveal an indication in terms of the dimensions of the original questionnaire including *social anxiety / avoidance, helplessness, anxious - depressive mood.* However, the evaluation included also single item analysis.

Some more questions have been added regarding demographic data not only on the parents but also on the child's disease including age, gender, site of onset, duration, observed features (poliosis, Koebner phenomenon), possible trigger factors for their child's vitiligo and family history.

5.2 Participants

For this thesis it was possible to include an international patient population:

- All new patients of the German and UK Institute for Pigmentary Disorders, which is specialised on research and patient care for the pigmentation disorder vitiligo, were asked to take part voluntarily in this investigation. This institute offers its service to patients from all over the world. Therefore the study included not only German patients, but also individuals from the UK, the US, and from other countries as far as India and Australia. It is obvious that these patients are very determined to treat their vitiligo because they make a huge effort by travelling long distances and by paying all expenses themselves in order to start the treatment modality offered. Importantly, the patients are asked to fill in the questionnaire before they are seen by the doctor and before they are introduced to the treatment modality. This procedure enables us to compare the results to those patients who were already enrolled in the institute and who were already undergoing treatment for their vitiligo with narrow-band UVB activated pseudocatalase PC-KUS.

- As already indicated, during clinic sessions patients who were already enrolled and who had started their treatment were also asked to take part.

- We also asked at their annual meeting members of the American Vitiligo Research Foundation. This included children, their parents and adults.

- Finally, an announcement source was published on the website of a German patient-support organisation (Vitiligo-Portal). Everybody (children and their parents) who were willing to take part and had contacted the organisation was sent a questionnaire by the secretary of this organisation in a pre-stamped envelope, which was then returned anonymously.

Parents were normally asked to let their children fill in the questionnaire on their own and not to interfere with them.

This wide-ranging patient / parent population gives the opportunity to compare not only the possible influence of nationality / language and skin colour, but also the influence of treatment and its duration.

5.3 Control group

Healthy controls were most often friends or partners of patients when the latter were seen for an appointment at the Institute for Pigmentary Disorders. They were asked to fill out the same basic questionnaires, with only some slight changes in the demographic section.

5.4 Statistical analysis

The following statistical tests have been used in this thesis:

- *Independent Sample T-Test* (also called *Student's T-test*) has been used to measure for differences between means of two groups within the population

- *Mann-Whitney-U-test* compared two groups within a population when there was no normal distribution of scores

- *One-way analysis of variance (ANOVA)* test was used to measure differences between two or more independent groups

- *Kruskal-Wallis-test* was utilised to compare two or more groups within a population when there was no normal distribution of scores

- *Paired sample T-Test* compared two (related) samples

- *2-tailed Wilcoxon signed-rank test* compared two related (paired) samples when there was no normal distribution (non-parametric)

- *Pearson Chi-Square test* tested a null hypothesis for the frequency distribution of certain events (e.g. distribution of patients or experiences) observed in a sample consistent with a particular theoretical distribution

- *Pearson correlation analysis* measured linear correlation between two variables

For statistical analysis SPSS 14.0 for Microsoft Windows has been used (SPSS inc, Chicago, Illinois, USA).

Before starting evaluation of all the questionnaires main and sub-scores, it is necessary to find out whether to use mean or median. For this, skewness analysis has been employed and the following skewness coefficients and subsequent appropriate standard tendencies have been established:

- DLQI 1.351 → Median
- ACS (Adults)
  - Social anxiety / avoidance 0.408 → **Mean *possible***
  - Helplessness 0.094 → **Mean *possible***
  - Anxious-depressive Mood 0.417 → **Mean *possible***
- BDI 1.114 → Median
- CDLQI 2.109 → Median
- ACS (Mothers)
  - Social anxiety / avoidance 0.864 → Median
  - Helplessness 0.605 → Median
  - Anxious-depressive Mood 0.730 → Median
- ACS (Fathers)
  - Social anxiety / avoidance 0.920 → Median
  - Helplessness 1.096 → Median
  - Anxious-depressive Mood 1.195 → Median

6 Results

6.1 Adult patients and control population

6.1.1 Control group

The study included 55 healthy controls. Fourty one were males (74.5%) and 14 were females (25.5%). The mean age was 48.2 years, the median was 45.0 years ranging from 21 to 79 years. Thirty three controls (60.0%) used the German-language questionnaires and 22 used the English-language questionnaire (40.0%).

The vast majority of the control group had fair skin, only 6 had darker skin phototypes IV and V (10.9%) (**Figure 8**).

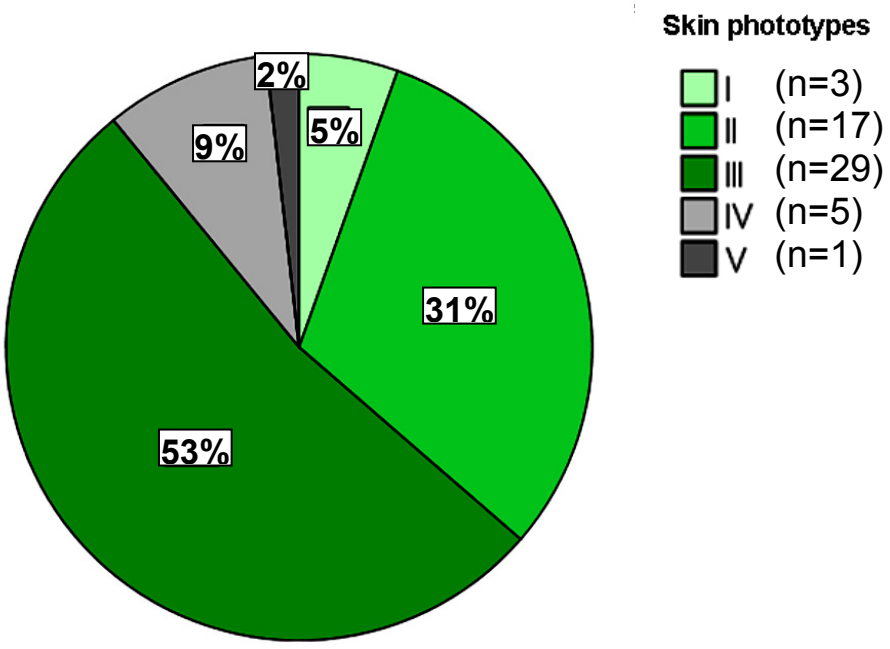


Figure 8: Distribution of skin phototypes in the control group (n=55)

The control group was dominated by males, whereas the adult patient group had more females (***p<0.001, Pearson Chi-Square test). Controls were also older (*p=0.005, 2-sided Independent Sample T-test). Both groups were matched with regards to skin phototype groups (I-III vs. IV-VI) and language of questionnaires used (all p>0.05, Pearson Chi-Square test).

Since the DLQI and ACS questionnaires were designed to assess the impact of skin diseases in general and not just vitiligo, it was important to evaluate the presence / absence of any skin diseases in the control group. The results revealed that 24% (n=11) of our healthy controls had a skin disease. Moreover, 46% (n=5) of those controls with a skin disease also said that their condition was visible to others.

6.1.2 Available data

Our study included a total of 422 adult patients with vitiligo. However, this number only applies to the Adjustment to Chronic Skin Disorders Questionnaire and basic socio-demographic questions (age, gender, skin colour, enrolled / not enrolled with the IFPD, age of disease onset, disease severity), because these had been used from the beginning of this project.

Some of the questions were included from the start, but were not answered by all the patients or their answers could not be used due to incomplete marking. These parts include family history as well as influence of psychological stress, other diseases and injuries.

Two important parts were added later to this project: the Dermatology Life Quality Index (n=164)[12] and the Beck Depression Inventory (n=123). The same applies to the questions about prevalence of grey hair, site of disease onset, hobby / sport, stigmatisation experiences, avoidant behaviour.

For all the above reasons, the numbers of patients differ between the parts of this thesis and also between the questionnaires.

6.1.3 Patients

This study included 422 adult patients with vitiligo. 136 were males (32.2%) and 286 were females (67.8%). The mean age of the group was 43.1 years, the median age 43.0 years (SD 12.2) ranging from 17-70 years. More than half of the patients were middle aged (57%, 30-49 years old, n=241), only a few were younger than 20 years (n=17, 4%). The distribution of different age groups is shown in **Figure 9**.

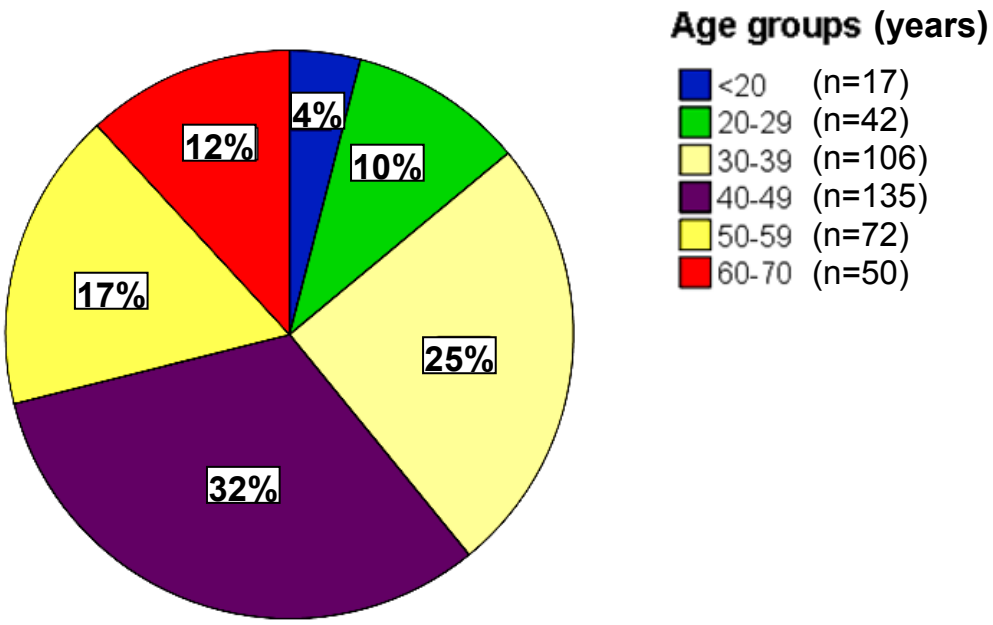


Figure 9: Distribution of age groups in our patient population (n=422)

[12] The total score is available for 164 questionnaires, whereas the single items' scores were included for 90 patients

The duration of the disease was 18.7 years (mean), median was 16.0 years (SD 12.73). More than half of the patients used the German-language version of the questionnaires (n=243, 57.6%), while 42.4% (n=179) used the English-language version.

258 patients (61.1%) were already enrolled with the Institute for Pigmentary Disorders and were undergoing treatment with narrow-band UVB activated pseudocatalase PC-KUS, whereas 164 patients visited the institute for the first time (38.9%).

The vast majority of our patient population had fair skin phototypes II and III (85%, n=354). The remaining 68 patients had darker skin (skin phototypes IV-VI) (**Figure 10**).

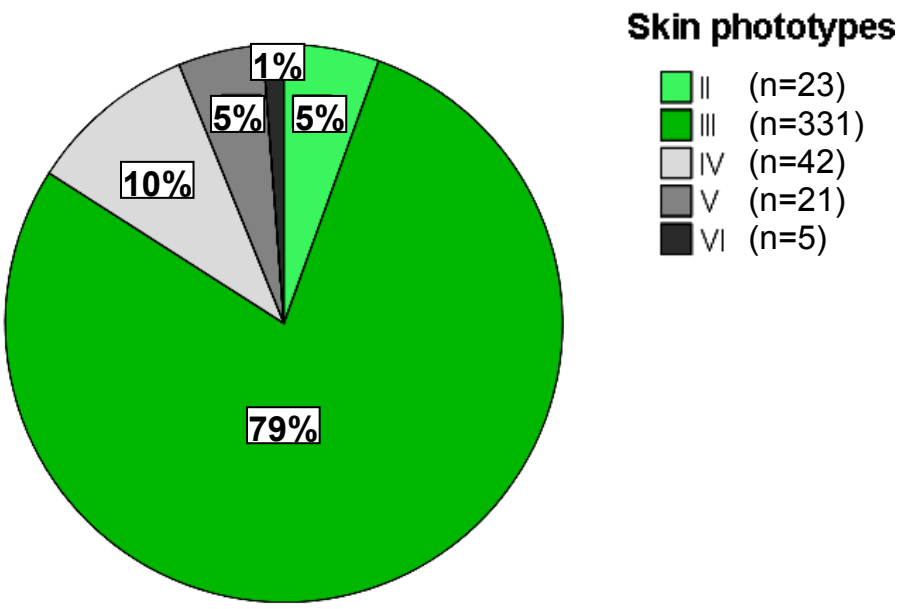


Figure 10: Distribution of skin phototypes (Fitzpatrick classification) in the adult patient population (n=422)

6.1.4 Disease status and severity

Since the progression of vitiligo is rather unpredictable, it was important to establish the status of vitiligo in our patient population, i.e. whether the white spots were currently actively spreading, re-pigmenting or remaining stable at the time when the study took place. We found that the disease was progressing in nearly half of the patients (46%, n=120). One third of the group (33%, n=84) had stable vitiligo, whereas 54/258 (21%) were re-pigmenting (**Figure 11**).

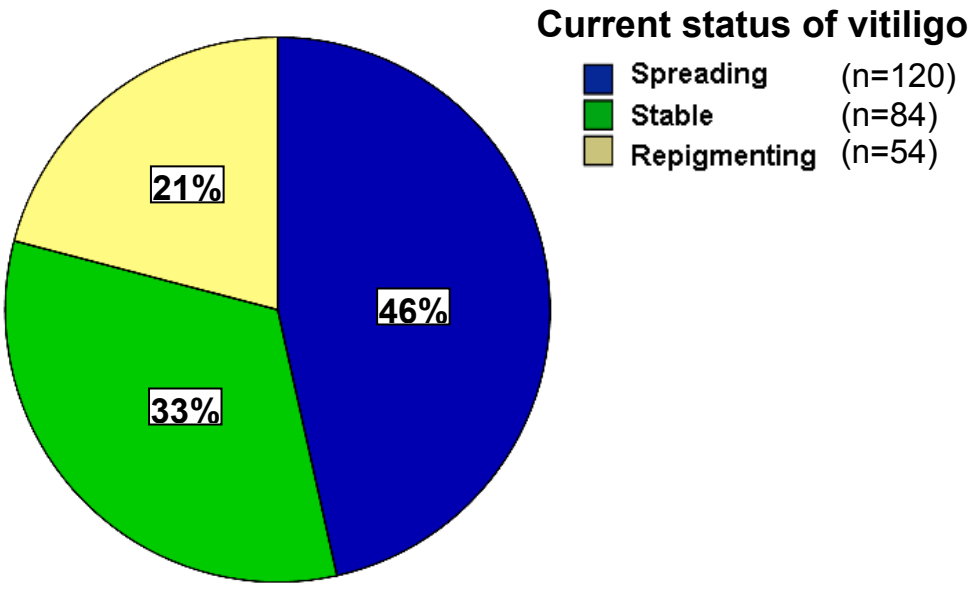


Figure 11: Disease status in our patient population (n=258)

Next we wanted to know whether there were less patients with actively spreading vitiligo in the group already treated at the Institute for Pigmentary Disorders compared to new patients. Crosstabulation shows that indeed patients undergoing treatment had

less frequently progressive vitiligo. These differences were borderline significant (2-sided Pearson Chi-Square test, p=0.059, **Figure 12**).

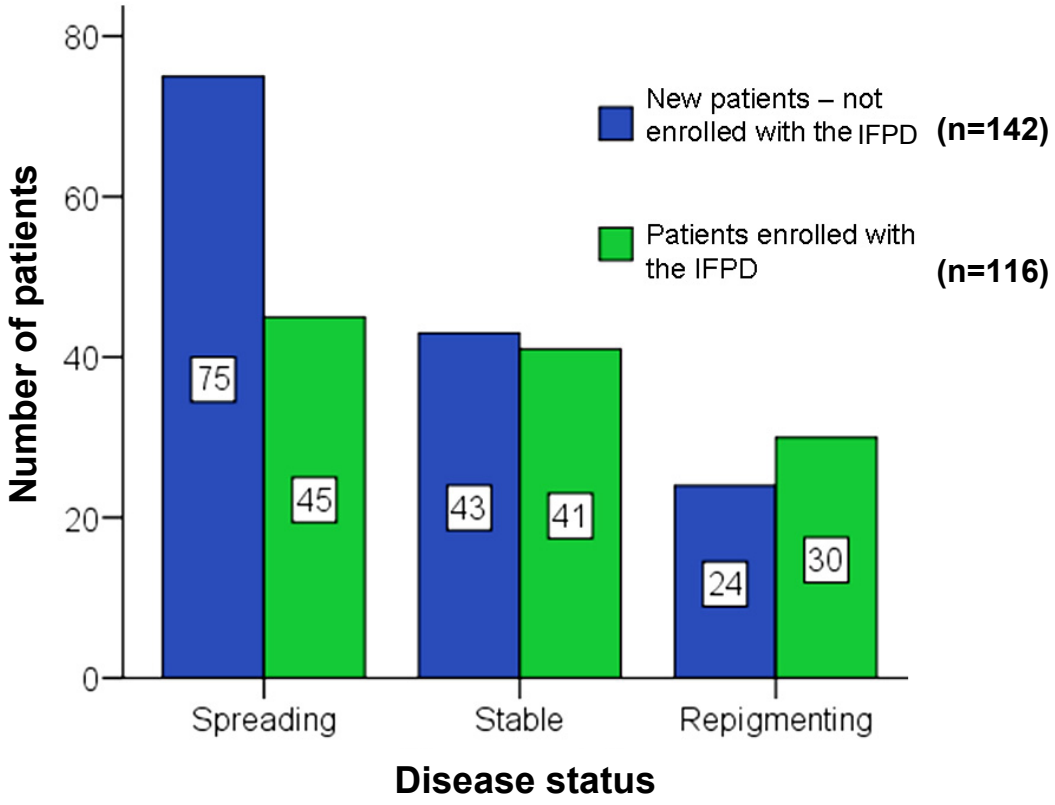


Figure 12: Frequencies of disease status in patients enrolled and not enrolled with the Institute for Pigmentary Disorders (IFPD)

To further characterise our patient population, we asked the patients to self-assess the severity of vitiligo on six dominant body parts. If the disease was present on the mentioned parts, then they could chose between *slightly* and *severely* affected. Self-assessment of all the body parts with vitiligo revealed that the *face* was the least often *severely* affected part in this patient population, whereas *hands* were most often chosen as *severely* affected (**Table 9**).

Body area	Disease severity	N	%
Face (n=365)	1	262	71.8
	2	103	28.2
Neck (n=293)	1	145	49.5
	2	148	50.5
Hands (n=376)	1	89	23.7
	2	287	76.3
Arms (n=343)	1	172	50.1
	2	171	49.9
Trunk (n=340)	1	174	51.2
	2	166	48.8
Legs (n=352)	1	208	59.1
	2	144	40.9

Table 9: Self-assessed disease severity on different body parts
Disease severity: 1 - little, 2- severe

6.1.5 Family history and affected family members

Evaluation of a family history for vitiligo and exact information on who has / had the disease in the family is helpful to follow a genetical pattern of the disease. Perhaps, in the end of the day this information might add more information to what could cause vitiligo.

In our adult patient group there was a positive family history of vitiligo in **37.8%** (n=107 out of 283 who answered this question). **Table 10** shows a break-down of who else in the family had vitiligo. In correlation to other family members, the *mother* was most often affected (23 out of 101, 22.8%) followed by the *father, siblings* and the *grand-parents*.

Relatives	N	%
Mother	23	22.8
Father	11	10.8
Brother	7	7.0
Grandmother	7	7.0
Grandfather	6	5.9
Uncle	6	5.9
Sister	5	5.0
Son / daughter	5	5.0
Aunt	4	4.0
Great-grandmother/-father	4	4.0
Cousin	4	4.0
Grandmother + brother	3	3.0
Aunt + cousin	3	3.0
Uncle + cousin	3	3.0
Sister + cousin	2	1.9
Son + grandmother	2	1.9
Grand aunt + grand uncle	2	1.9
Mother + aunt	2	1.9
Grandfather + uncle	1	1.0
Niece	1	1.0
Total	**101**	**100.0**
Missing	**6**	

Table 10: Frequencies of family members with vitiligo

6.1.6 Age of disease onset

The mean age of disease onset in the literature is often around the 20th year of age (Das et al. 1985; Alkhateeb et al. 2003). In our adult patient group the mean age was 24.4 years (n=422) ranging from 0.5 to 63 years. The frequency of disease onset in different age groups is shown in **Figure 13**. According to our results, vitiligo occurred in all age groups, but there is a peak in the age group between 10-19 years.

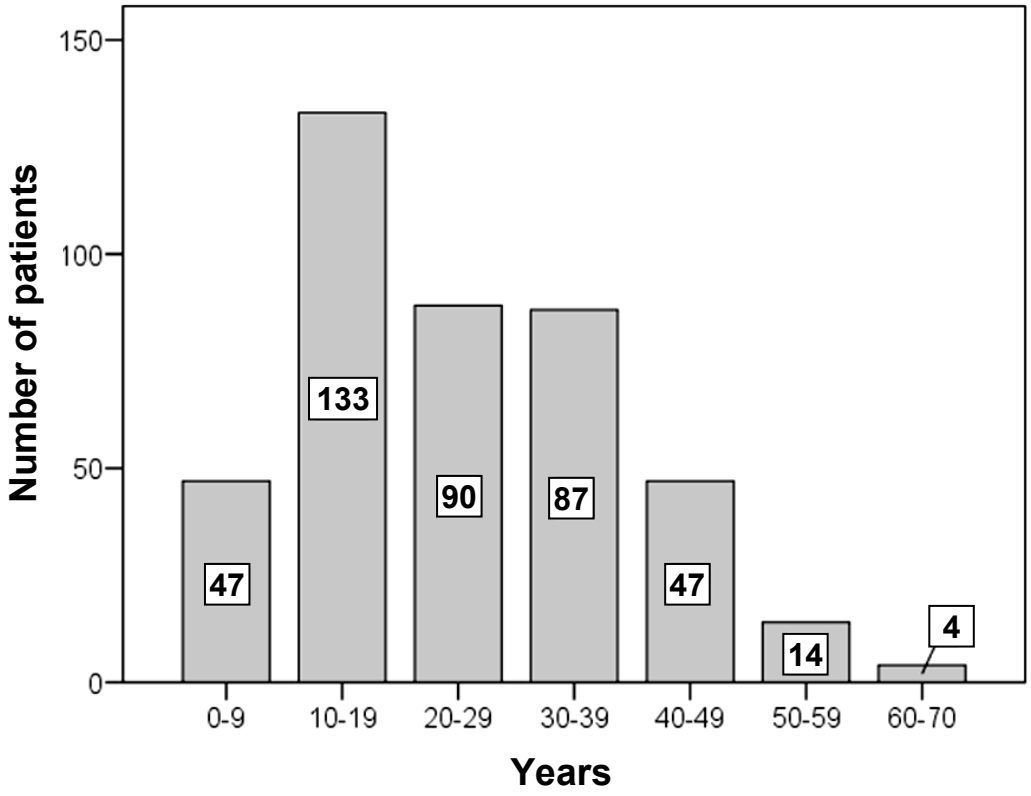


Figure 13: Age groups according to disease onset (n=422)

It has been reported that the mean age of disease onset might differ between genders (Majumder et al. 1993). We found indeed that the age of disease onset is significantly earlier in *male* patients compared to females (means 22.4 vs. 25.3, *p<0.05, Independent Sample T-Test, **Table 11**).

At the same time it was tempting to explore other socio-demographic subgroups of our adult patient group as well. In some cases we found significant differences regarding age of disease onset:

1. Patients who *do not believe* that *psychological stress* or *other diseases* are involved in vitiligo, were younger when the disease started (**p<0.005 and *p<0.05 respectively).

2. Patients who developed vitiligo earlier in life are more likely to avoid certain situations because of their vitiligo (**p<0.005). All differences were measured with a two-sided Independent Sample T-Test and a Mann-Whitney-U-test (**Table 11**).

Subgroups		N	Mean age of onset (years)	Median age of onset (years)	SD	p value
Gender	Male	136	***22.4****	21.0	11.96	**0.038**(1)
	Female	286	***25.3****	24.0	14.07	>0.05 (2)
Skin phototype fair skin	I-III	354	24.5	22.0	13.68	>0.05
dark skin	IV-VI	68	23.9	24.0	12.45	
Positive family history	Yes	107	22.2	18.0	13.90	>0.05
	No	176	24.5	23.5	13.46	
Psychological stress	Yes	214	***25.5****	***25.0*****	12.4	**0.003**(1)
	No	82	***20.4****	***16.0*****	13.7	**0.001**(2)
Vitiligo caused by injuries (Koebner phenomenon)	Yes	59	20.7	18.0	12.8	>0.05
	No	98	24.7	24.0	13.4	
Vitiligo caused by other diseases	Yes	24	***27.7****	25.5	13.1	**0.049**(1)
	No	112	***21.4****	20.5	12.5	0.056(2)
Language of questionnaire	German	97	24.9	21.0	14.61	>0.05
	English	70	22.7	20.5	12.75	
Have you ever avoided certain situations because of your vitiligo?	Yes	79	***21.5****	***20.0****	11.65	**0.002**(1)
	Never	40	***29.1****	***29.0****	14.04	**0.004**(2)

Table 11: Age of disease onset in socio-demographic subgroups of the patient population
(1) two-sided Independent Sample T-Test; (2) Mann-Whitney-U-test

6.1.7 Location of onset

Some earlier publications reported that the initial sites of onset are often exposed parts of the body, i.e. face, neck or legs (Singh et al. 1985). Therefore, we wanted to find out whether this also applied to our study group. The most frequent sites of onset in our adult patient group were *hands* (26%, n=68/262). If *face* and *neck* are counted as one part, as often done in in the literature (Akrem et al. 2008; Wu et al. 2008), then this would be the most common site of onset (26.7%, n=70/262) (**Table 12**).

Initial site of onset	N	%
Hands	68	26.0
Face	49	18.7
Neck	21	8.0
Genitals	16	6.1
Legs	15	5.7
Stomach	13	5.0
Arms	11	4.2
Feet	11	4.2
Knees	10	3.8
Back	9	3.4
Chest	9	3.4
Arms + face	6	2.3
Hands + face	6	2.3
Hips	5	1.9
Hands + legs	4	1.5
Neck + genitals	3	1.1
Hips + hands	2	0.8
Neck + hands	2	0.8
Chest + arms	2	0.8
Total	**262**	**100.0**

Table 12: Frequency of body areas where the first spot appeared

6.1.8 Progressive vitiligo can itch

Pruritus is often related to disease progression on sites where vitiligo will be developed shortly after (Schallreuter et al. 2008b). From 111 patients who answered this question there were 38 (34.3%) who had experienced pruritus in our adult group (**Table 13**).

	Answers	**N**	**%**
My skin itches sometimes before a new spot appears	Not at all right	54	48.6
	Hardly ever right	19	17.1
	Quite right	23	20.7
	Mostly right	11	9.9
	Totally right	4	3.7
	Total	**111**	**100.0**

Table 13: Frequency of pruritus before the development of new spots

6.1.9 Patients' perceptions of trigger and worsening factors for vitiligo

Many factors have been implicated as a trigger or as a worsening factor in vitiligo. Our interest was focussed on what patients think regarding involvement of *psychological stress, other diseases* or *injuries* (Koebner phenomenon) in their vitiligo. The results are shown in **Figure 14**.

Almost three quarters of patients (n=214, 72%) felt that *psychological stress* is involved in their vitiligo. Sixty patients (38%) related their vitiligo to *injuries* (Koebner phenomen) and 25 patients (18%) connected their vitiligo to *other diseases*.

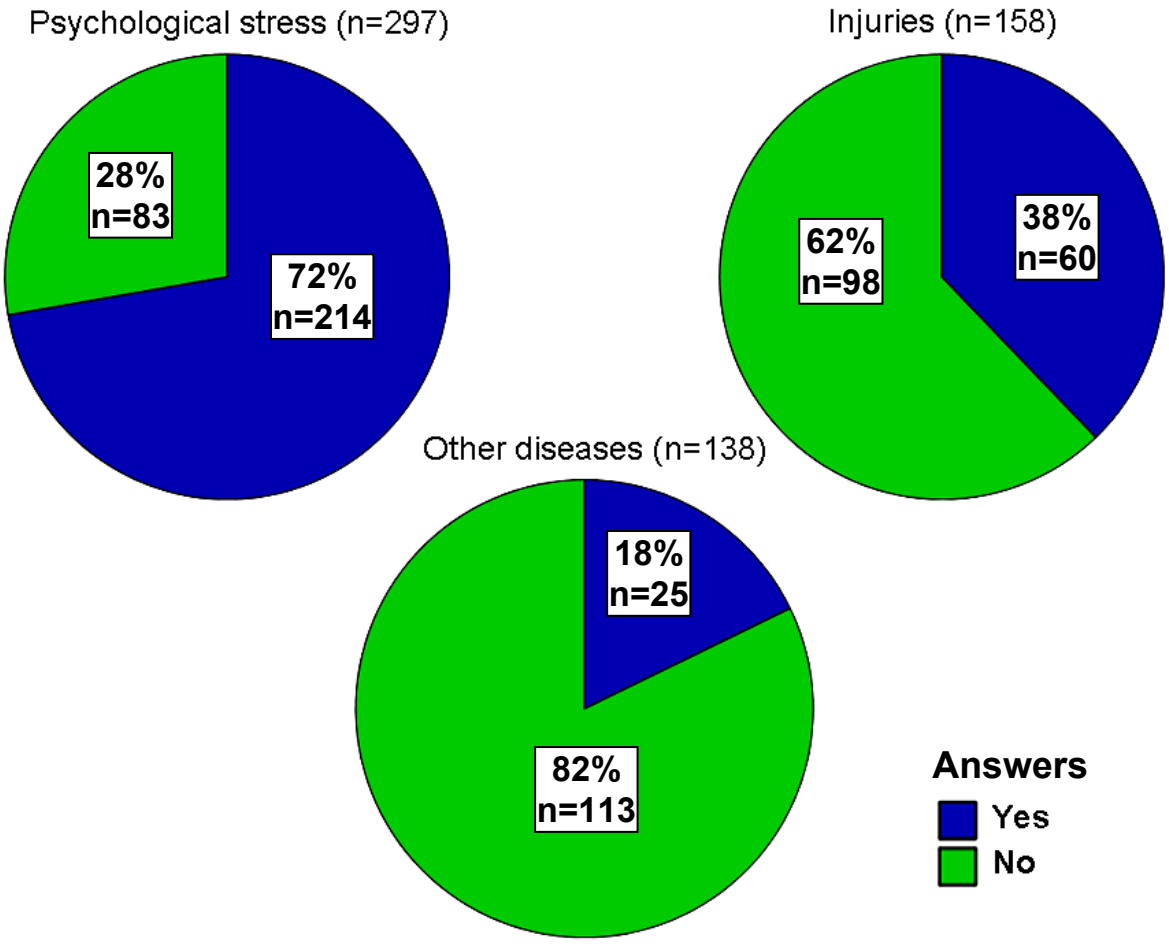


Figure 14: Perceived trigger / worsening factors

6.1.10 Prevalence of grey hair on the scalp and in eyelashes / eyebrowes

Premature greying of the scalp hair *(canities praecox)* is characterised by the onset of greying before the age of 25 years (Mosher et al. 1979). Lerner associated this early greying with vitiligo. He suggested self-destruction of melanocytes by melanin precursors (either a phenol or a catechol derivative or the phenol-tyrosinase complex) as the common cause (Lerner 1971). In addition, the complete loss of hair colour in a bundle of scalp hair *(poliosis)* was also assessed.

The prevalences of *canities praecox* and *poliosis* are shown in **Table 14** and **Table 15**. Crosstabulation shows that about one third of patients <30 years did have grey hair on their scalps (33.3%, n=3 in the group <20 years; 37.5%, n=12 in the group of 20-29 years old patients). The numbers for older age groups are less important as it becomes normal with age to have grey hair.

The numbers for *poliosis* are similar. One third of the patients <20 years had poliosis on the eyelashes / eyebrows (33.3%, n=3), whereas this was 41.9% of the 20-29 years old (n=13). The frequency of poliosis does not significantly differ between age groups. Hence, this phenomenon seems to be a general symptom in vitiligo.

Grey scalp hair		Age groups (years)						Total
		<20	20-29	30-39	40-49	50-59	60-70	
Yes	N	3	12	47	64	25	22	**173**
	% of age group	**33.3***	**37.5***	67.1	68.1	64.1	81.5	**63.8**
No	N	6	20	23	30	14	5	**98**
	% of age group	66.7	62.5	32.9	31.9	35.9	18.5	**36.2**
Total N		**9**	**32**	**70**	**94**	**39**	**27**	***271***

Table 14: Prevalence of *grey hair* on the scalp in different age groups of patients (n=271)
**Canities praecox* as this phenomenon concerns people younger than 25 years only by definition

Poliosis		Age groups (years)						Total
		<20	20-29	30-39	40-49	50-59	60-70	
Yes	N	3	13	26	35	11	11	**99**
	% of age group	**33.3**	**41.9**	44.8	41.2	34.4	44.0	**41.3**
No	N	6	18	32	50	21	14	**141**
	% of age group	66.7	58.1	55.2	58.8	65.6	56.0	**58.8**
Total N		**9**	**31**	**58**	**85**	**32**	**25**	***240***

Table 15: Prevalence of *poliosis* in eyelashes / eyebrows in the patient population (n=240)

6.1.11 Evaluation of leisure time activities

Since daily activities may influence the psychological strength and the coping process in patients' life, we used *sport* and *hobbies* as representative parameters for further analysis.

The data from 124 patients revealed that 77% (n=96) are involved in sport or had hobbies (**Table 16**). However, 23% (n=28) were neither doing any sport nor did they have any hobby.

Taken together, the majority of our patient group had no difficulties with an active leisure time.

Question	Answer	N	%
Do you do any sports or do you have a hobby?	Yes	96	77.4
	No	28	22.6
	Total	**124**	**100.0**

Table 16: Frequency and percentage of patients with active leisure time

6.1.12 Stigmatisation experiences

Stigmatisation has been shown to be an influential factor in coping with skin diseases. Therefore, we included two questions to find out how often our patient population had experienced typical situations of stigmatisation. These questions concerned *approaches / questions* and *nasty comments* by other people.

Figure 15 shows that 89% (n=110) of our patients were approached by other people and / or were asked questions about the disease, whereas only 11% (n=13) lacked these experiences.

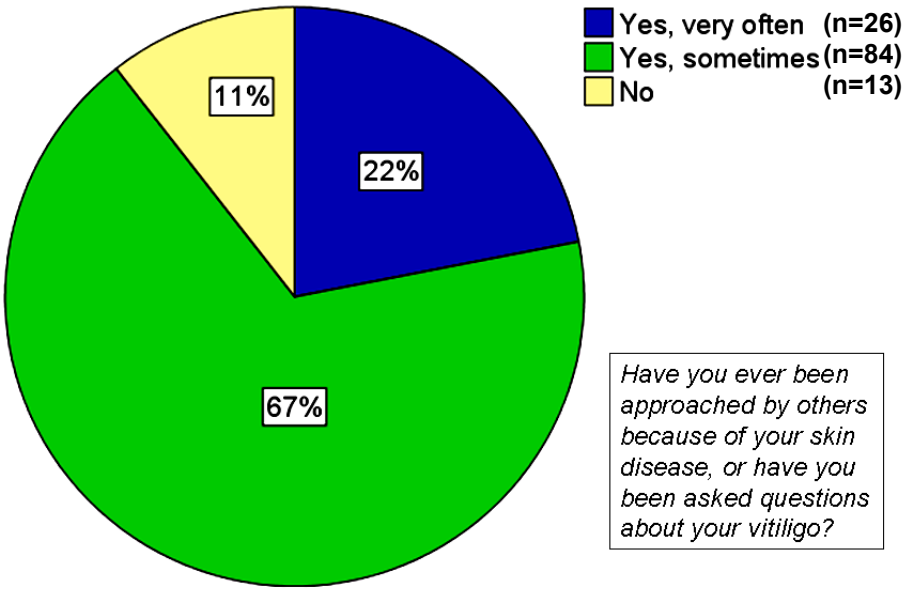


Figure 15: Frequency of patients who experienced approaches and questions by other people about their vitiligo (n=123)

The picture regarding *nasty comments* is different. One quarter of our patients (24%, n=31 out of 123) had experienced other people picking on them or making nasty comments. Only one patient had experienced this even very often.

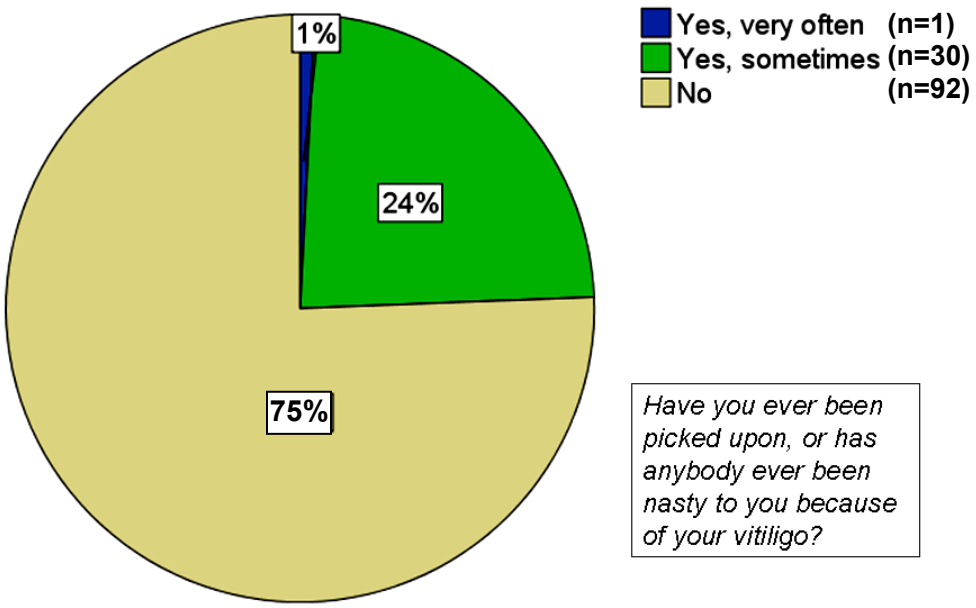


Figure 16: Frequency of patients who had been picked on because of their vitiligo (n=123)

6.1.12.1 Stigmatisation differs between patient groups

At this point it was tempting to further analyse these data about which socio-demographic subgroups were more strongly affected by stigmatisation and which factors played a role when patients were stigmatised. **Table 17** summarises our findings regarding *approaches / questions* by strangers and other people.

Our results show a significant difference between female and male patients. Female patients are much more likely to experience such approaches / questions *very often,* whereas our male patients reported more often that they were *never* asked questions about the disease (**Table 17**).

Moreover, the severity of vitiligo on legs and hands is influential on how often such stigmatisation was experienced. Patients with severly affected legs and hands are more likely to become subjects to questions and remarks by other people, whereas patients with only minor vitiligo are targeted less often. Neither disease severity on any of the other body parts nor language of questionnaire were influential. Interestingly, even skin colour did not play a role as reported earlier (Porter and Beuf 1991) (**Table 17**).

Question	Answer		Subgroups of patient population													
			Language		Gender		Skin phototypes		Face affected		Hands affected		Arms affected		Legs affected	
			German	English	male	female	I-III	IV-VI	Slightly	Severely	Slightly	Severely	Slightly	Severely	Slightly	Severely
Have you ever been approached by others, or have you been asked questions about your vitiligo?	1	N	19	7	*5*	*22*	24	2	14	10	*3*	*22*	8	16	*9*	*14*
		%	25.0	14.9	*10.2*	*28.9*	22.6	11.8	17.3	32.3	*12.5*	*26.2*	15.7	33.3	*15.8*	*35.0*
	2	N	51	34	*35*	*50*	73	12	57	20	*16*	*57*	38	29	*41*	*25*
		%	67.1	72.3	*71.4*	*65.8*	68.9	70.6	70.4	64.5	*66.7*	*67.9*	74.5	60.4	*71.9*	*62.5*
	3	N	6	6	*9*	*4*	9	3	10	1	*5*	*5*	5	3	*7*	*1*
		%	7.9	12.8	*18.4*	*5.3*	8.5	17.6	12.3	3.2	*20.8*	*5.9*	9.8	6.3	*12.3*	*2.5*
	Total	**N**	**76**	**47**	*49*	*76*	**106**	**17**	**81**	**31**	*24*	*84*	**51**	**48**	*57*	*40*
	p value		p>0.05		p=0.007		p>0.05		p>0.05		p=0.05		p>0.05		p=0.035	

Table 17: Stigmatising experiences (approaches, questions) in patient subgroups
All significances were measured by a Pearson Chi-Square test.

1 - Yes, very often, **2** - Yes, sometimes, **3** - No

A second typical stigmatisation experience is that strangers make *nasty comments* or *pick on* individuals with vitiligo. We found that this kind of stigmatisation is hardly influenced by demographic characteristics. One significant difference was found between patients with *severly affected arms* and those with only minor vitiligo on their upper extremities. The latter group was less likely to become subject to nasty comments *very often* or *sometimes* (**p<0.005, Chi-Square test, **Table 18**). There was no significant difference between any of the other subgroups investigated (age groups, gender, skin colour, all p>0.05, Pearson Chi-Square test) (**Table 18**), apart from *age at disease onset*. We found that patients with a disease onset before the age of 20 years were more likely to experience nasty comments compared to patients with a disease onset later on in life (*p=0.021, 2-sided Pearson Chi-Square test) (**Figure 17**).

Taken together, stigmatisation experiences are frequent in the life of patients with vitiligo, especially in women, but also in patients with severly affected hands, legs or arms and in patients with a disease onset before the age of 20 years.

Question	Answer		Subgroups of patient population													
			Language		Gender		Skin phototypes		Face affected		Hands affected		Arms affected		Legs affected	
			German	English	male	female	I-III	IV-VI	Slightly	Severely	Slightly	Severely	Slightly	Severely	Slightly	Severely
Have you ever been picked upon, or has anybody ever been nasty to you because of your vitiligo?	1	N	1	0	0	1	1	0	1	0	0	1	*0*	*1*	0	1
		%	1.3	0.0	0.0	1.3	0.9	0.0	1.2	0.0	0.0	1.2	*0.0*	*2.1*	0.0	2.5
	2	N	22	7	10	19	23	6	16	8	4	20	*5*	*18*	8	12
		%	28.9	14.9	20.4	25.0	21.7	35.3	19.8	25.8	16.7	23.8	*9.8*	*37.5*	14.0	30.0
	3	N	53	40	39	56	82	11	64	23	20	63	*46*	*29*	49	27
		%	69.8	85.1	79.6	73.7	77.4	64.7	79.0	74.2	83.3	75.0	*90.2*	*60.4*	86.0	67.5
	Total	**N**	**76**	**47**	**49**	**76**	**106**	**17**	**81**	**31**	**24**	**84**	**51**	**48**	**57**	**40**
	p value		p>0.05		p>0.05		p>0.05		p>0.05		p>0.05		p=0.002		p>0.05	

Table 18: Stigmatising experiences (picked on, nasty comments) in patient subgroups
All significances were measured by a Pearson Chi-Square test.

1 - Yes, very often, **2** - Yes, sometimes, **3** - No

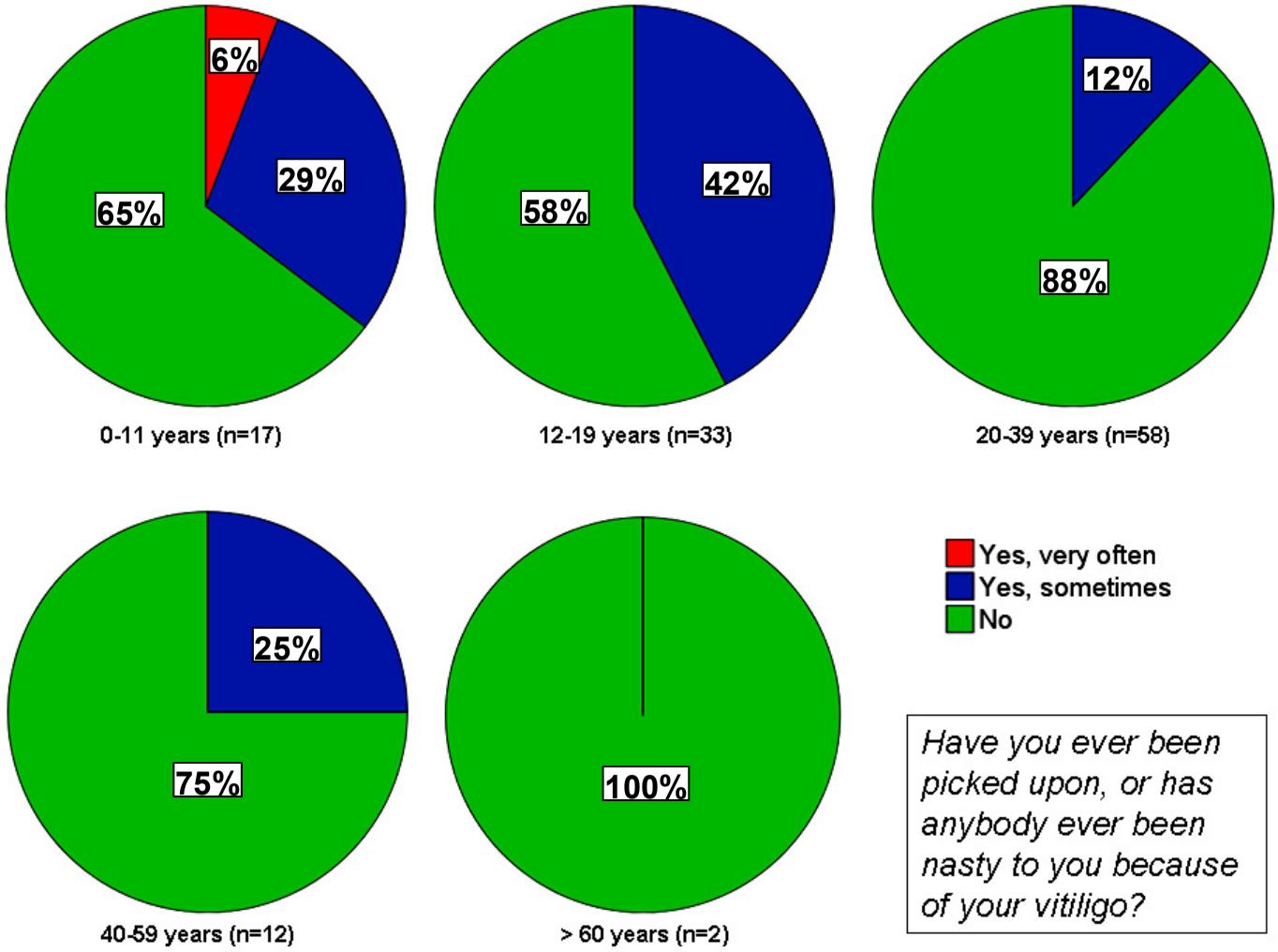


Figure 17: Frequency of stigmatisation experiences (picked on, nasty comments) in different age groups related to disease onset

6.1.13 Avoidant behaviour

Next we wanted to know whether and how often our patients hide their white spots in front of other people. We also included whether our patients would avoid certain situations because of their vitiligo. Finally, our interest was to find out whether this behaviour was different in the subgroups of our patients. Hiding white spots or avoiding certain situations can be indicators of avoidant behaviour, which in turn mirrors altered self-confidence.

With regards to frequency of hiding the white spots, our results revealed that 37% (n=45) of our patients had *never* or only *rarely* hidden their white spots. More than one third of the population (35%, n=43) had done this *quite often* and 28% (n=35) even *very often* (**Figure 18**).

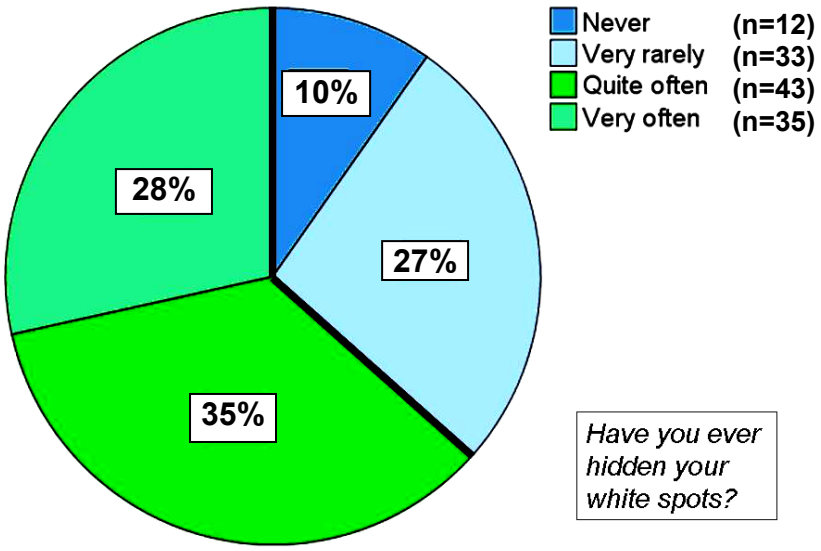


Figure 18: Frequencies of how often patients have hidden their white spots (n=123)

Further exploration of common hiding strategies revealed that almost half of them (46.4%, n=45/97) preferred a *combination* of covering by clothes and using certain body positions and camouflage. This strategy was followed by several single strategies including *hiding the white spots under clothes* (23.7%, n=23), using *camouflage* and certain *body positions*. Least often mentioned were *other* strategies, without any further specification (**Table 19**).

Our further interest was to explore whether there were any differences between the socio-demographic subgroups of our patients. The results revealed that there were no significant differences in all subgroups except for *gender* (**Table 21**). Female patients were more likely to hide their white spots *very often* (*p=0.045, Pearson Chi-Square test). Disease severity, age, age of disease onset, language, skin colour or presence / absence of a family history had no influence on avoidant behaviour of our patients (all p>0.05, Pearson Chi-Square test).

Question	Answers	N	%
How have you hidden your white spots?	Combination of clothes, positions, camouflage	45	46.4
	Under clothes	23	23.7
	Camouflage	16	16.5
	Body positions	10	10.3
	Others (not specified)	3	3.1
	Total	**97**	**100.0**

Table 19: Hiding strategies of patients with vitiligo (n=97)

While there were only 10% of our patients who had never hidden their white spots, the picture regarding *avoidance of situations* is different. We found that 35% (n=42) of our patients had never avoided any situations because of their vitiligo. However, the remaining patients mentioned several situations which they tended to avoid. Most often mentioned were *shaking hands* / *getting undressed in changing rooms* (39.8%, n=31), followed by *swimming / bathing* (24.4%, n=19) and *other situations* (11.5%, n=9). S*haking hands* alone was reported less often (**Table 20**).

As shown in **Table 22**, there were no significant differences within any of the subgroups regarding avoidance of situations (skin colour, language, family history, disease severity, age, age of disease onset - all $p>0.05$, 2-sided Pearson Chi-Square test).

Question	Answers	N	%
Have you ever avoided certain situations because of your vitiligo?	Shaking hands, undressing in changing rooms	31	39.8
	Swimming / bathing	19	24.4
	Others (not specified)	9	11.5
	Undressing in changing rooms	6	7.7
	Swimming / bathing, undressing in changing rooms	5	6.4
	Shaking hands	3	3.8
	Swimming / bathing, sports, undressing in changing rooms	3	3.8
	Swimming / bathing,sports	2	2.6
	Total	**78**	**100.0**

Table 20: Avoided situations in patients' life

Question	Answer		Subgroups of patient population													
			Language		Gender		Skin phototypes		Family history		Face affected		Hands affected		Arms affected	
			German	English	Male	Female	I-III	IV-VI	Yes	No	Slightly	Severely	Slightly	Severely	Slightly	Severely
Have you ever hidden your white spots?	1	N	8	5	*7*	*6*	11	2	2	10	8	4	2	9	5	3
		%	10.5	10.6	*14.3*	*7.9*	10.4	11.8	5.9	11.6	9.9	12.9	8.3	10.7	9.8	6.3
	2	N	18	14	*16*	*17*	29	3	11	20	24	6	7	23	15	11
		%	23.7	29.8	*32.7*	*22.4*	27.4	17.6	32.4	23.3	29.6	19.4	29.2	27.4	29.4	22.9
	3	N	26	18	*19*	*25*	37	7	12	31	30	12	9	30	19	19
		%	34.2	38.3	*38.8*	*32.9*	34.9	41.2	35.3	36.0	37.0	38.7	37.5	35.7	37.3	39.6
	4	N	24	10	*7*	*28*	29	5	9	25	19	9	6	22	12	15
		%	31.6	21.3	*14.2*	*36.8*	27.3	29.4	26.4	29.1	23.5	29.0	25.0	26.2	23.5	31.2
Total N			**76**	**47**	**49**	**76**	**106**	**17**	**34**	**86**	**81**	**31**	**24**	**84**	**51**	**48**
p values (Pearson Chi-Square test)			p>0.05		p=0.045		p>0.05		p>0.05		p>0.05		p>0.05		p>0.05	

Table 21: Hiding in patient subgroups
1 - Never, **2** – Very rarely, **3** – Quite often, **4** – Very often

Question	Answer		Subgroups of patient population													
			Language		Gender		Skin phototypes		Family history		Face affected		Hands affected		Arms affected	
			German	English	male	female	I-III	IV-VI	Yes	No	Slightly	Severely	Slightly	Severely	Slightly	Severely
Have you ever avoided certain situations because of your vitiligo?	1	N	52	27	31	49	68	11	25	51	50	20	15	54	32	32
		%	70.3	61.4	66.0	67.1	67.3	64.7	73.5	63.0	65.8	64.5	68.2	66.7	65.3	71.1
	2	N	22	17	16	24	33	6	9	30	26	11	7	27	17	13
		%	29.7	38.6	34.0	32.9	32.7	35.3	26.5	37.0	34.2	35.5	31.8	33.3	34.7	28.9
Total N			**74**	**44**	**47**	**73**	**101**	**17**	**34**	**81**	**76**	**31**	**22**	**81**	**49**	**45**
p values (Pearson Chi-Square test)			p>0.05		p>0.05		p>0.05		p>0.05		p>0.05		p>0.05		p>0.05	

Table 22: Avoided situations in patient subgroups
1 - Yes, **2** - No

6.2 Dermatology Life Quality Index (DLQI)

6.2.1 Comparison to healthy controls

In order to measure the true effect of vitiligo on the daily life of patients, it was necessary to compare the data of our patients to healthy controls under the same life circumstances[13]. The results show that patients with vitiligo (n=164) scored significantly higher in the Dermatology Life Quality Index compared to healthy controls (n=55) with mean scores of 5.5 (SD 5.27) vs. 0.7 (SD 1.98) and median scores 4.0 vs. 0.0 (both differences ***p<0.001, 2-sided Independent Sample T-Test and Mann-Whitney-U-test). The patient group also showed a wider range of scores (**Figure 19**).

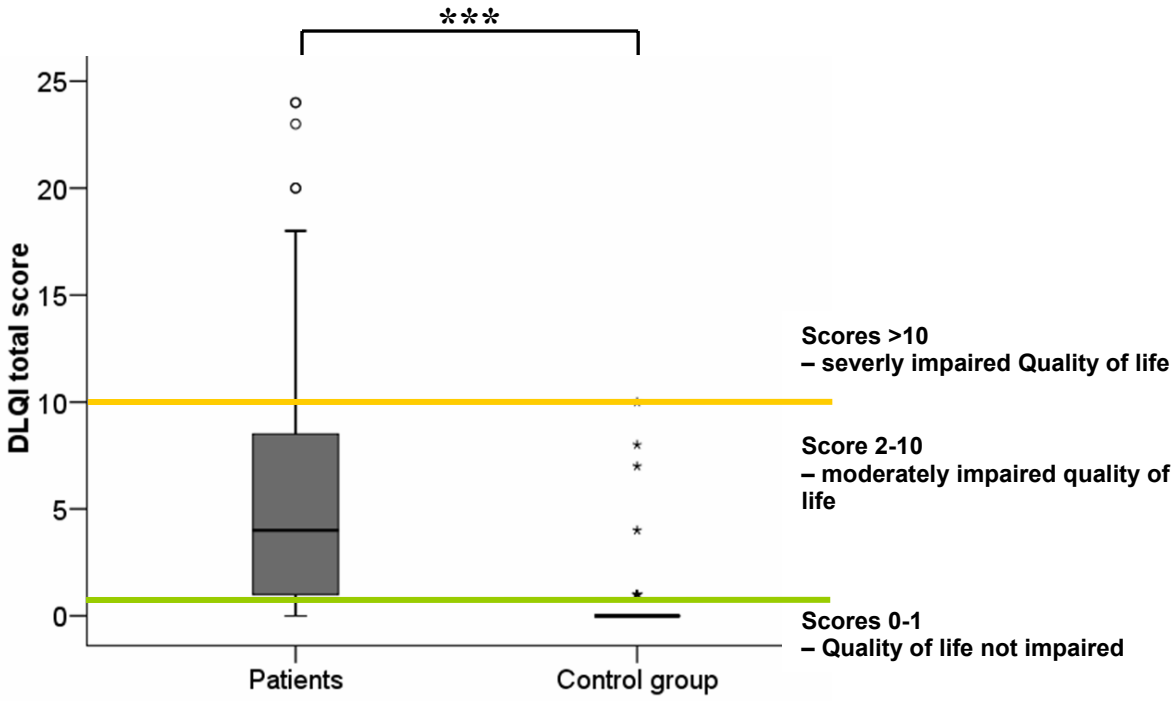


Figure 19: DLQI scores for patients (n=164) and healthy controls (n=55) (medians, ***p<0.001)

[13] as mentioned above, the control group was recruited from friends and family members of the patients

In this context it is noteworthy that members of the control group *with* a skin disease (n=11) also scored higher compared to the 44 healthy individuals without any skin disease (means 2.2 vs. 0.2, medians both 0.0, **p=0.002 with an Independent Sample T-test, p=0.046 with a Mann-Whitney-U-test). This result emphasises that a skin disease clearly influences quality of life in affected individuals.

Since the DLQI contains 10 items only, further analysis is necessary to obtain more data than just the central tendencies. Our data show that the DLQI scores are clearly positively skewed (**Figure 20**), which means that there are much more patients with low scores than one would expect considering the mean and median scores mentioned above. The skewness coefficient calculated is *1.351* confirming that there is no standard distribution.

By comparison, the DLQI scores of healthy controls are also positively skewed. However, their mean and median scores are very low, so that the high number of controls who scored zero are no surprise (**Figure 21**).

Moreover, given that a DLQI score of 0-1 indicates that quality of life is not impaired (Gajur 2008), we can conclude that 42 out of 164 patients in our group (25.6%) were not affected by their disease (**Table 23**). Furthermore, another 59 patients (36.0%) scored between 3 and 5, which is in agreement with minor impact on patients' quality of life (Gajur 2008).

DLQI scores	Impact on quality of life	N	%
0-1	None	42	25.6
2-5	Minor	59	36.0
6-10	Moderate	37	22.6
11-20	Severe	23	14.0
21-30	Extreme	3	1.8

Table 23: DLQI scores in our patient group (n=164) according to Gajur's grouping order (Gajur 2008)

This result implies that about 60% (n=101) of our patients were not or only little affected by their vitiligo. This is in sharp contrast to our personal impression that these patients had been suffering by their disease. Consequently, the question remains whether all questionnaires have really been filled out honestly.

To complete the picture, we found that only 22.6% (n=37) of the adult patient group were moderately and 15.8% (n=26) were severly affected in their quality of life by vitiligo. This results warrants further investigation and calls published data in the field in question.

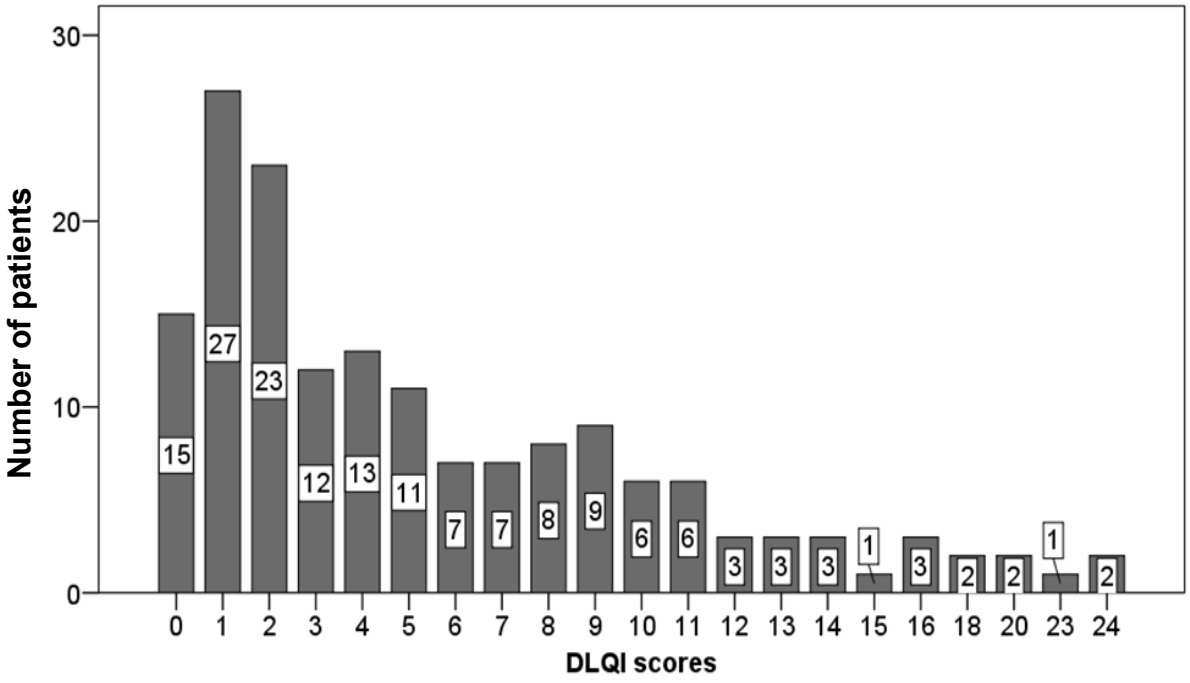


Figure 20: Distribution analysis of patients' DLQI scores (n=164)

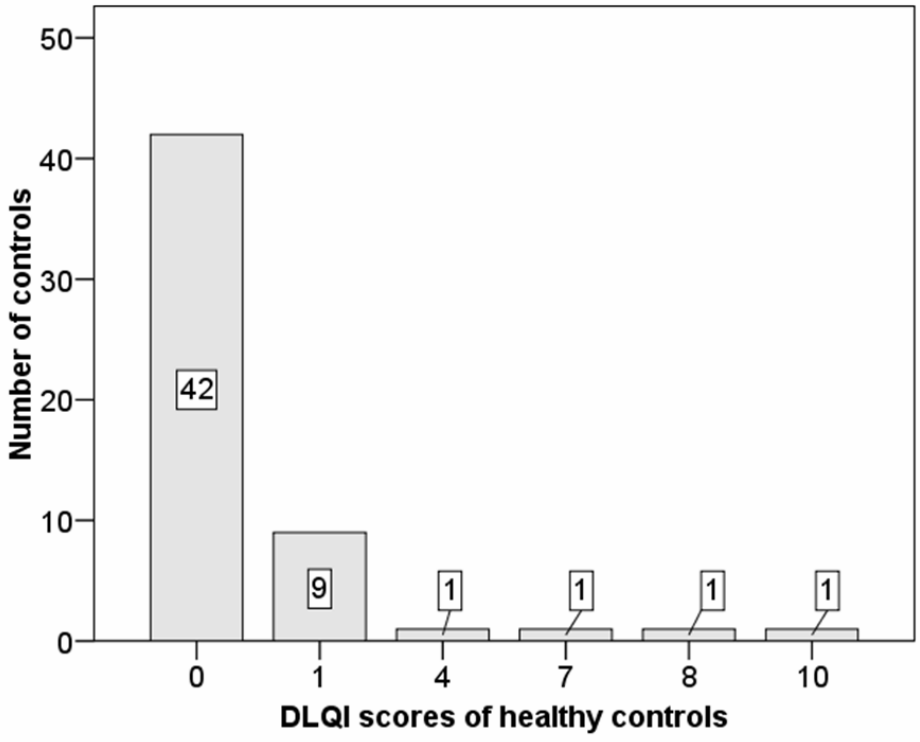


Figure 21: Distribution of DLQI scores of healthy controls (n=55)

6.2.2 DLQI scores in patient subgroups

In order to further analyse the Dermatology Life Quality Index, our interest went towards evaluation of whether there were any differences / effects between demographic or other subgroups regarding the DLQI scores.

As shown in **Table 24**, we could not find any significant differences between subgroups of our patient population. Hence, our results imply that language of the questionnaire, gender, skin colour, age group, presence / absence of a family history of vitiligo, an actively spent leisure time and disease severity on most of the body parts did not influence the DLQI outcome. There were two exceptions: patients who think that *psychological stress* is involved in triggering or exacerbating vitiligo (median 5.0, n=47) had *increased* DLQI scores compared to those who did not have this feeling (median 1.0, n=24). This difference was highly significant (**p=0.002, Mann Whitney-U-test). In addition we found that patients with extensive vitiligo on the *trunk* (n=58, self-assessment) scored significantly higher in the DLQI compared to the 65 individuals with only minor disease (medians 4.5 vs. 3.0, *p<0.05, Mann-Whitney-U-test). This result indicates an influence of disease severity on the DLQI outcome (**Table 24**).

Patients who were treating their vitiligo at home with NB-UVB activated pseudocatalase PC-KUS (n=51) scored a mean of 4.3 in the DLQI, which is lower than the mean score of 6.0 for new patients (n=113). This difference is significant (*p=0.049) but only if the mean is used. A non-parametric analysis revealed no significant difference (medians 3.0 vs. 4.0, p>0.05, Mann-Whitney-U-test). It can be concluded that treatment with NB-UVB activated pseudocatalase PC-KUS improves quality of life, albeit there is no strong effect.

Dermatology Life Quality Index **Subgroups**		N	Median	Mean	SD	p value
Language	German	95	3.0	5.2	5.413	>0.05
	English	69	4.0	5.9	5.059	
Gender	Male	61	3.0	4.6	4.573	0.077(1)
	Female	103	5.0	6.1	5.588	0.083(2)
Age	< 35 years	47	4.0	5.3	4.460	>0.05
	> 35 years	117	4.0	5.6	5.577	
Skin phototypes	I-III	137	4.0	5.5	5.380	>0.05
	IV-VI	27	4.0	5.5	4.710	
Family history	Yes	57	4.0	5.3	5.117	>0.05
	No	104	4.0	5.7	5.436	
Psychological stress	Yes	47	***5.0******	***5.8******	4.866	**0.001**(1)
	No	24	***1.0******	***2.3******	2.472	**0.002**(2)
Koebner phenomenon	Yes	32	4.0	5.2	4.930	>0.05
	No	36	2.0	4.0	4.060	
Vitiligo caused by other diseases	Yes	9	5.0	5.3	4.153	>0.05
	No	44	2.0	4.0	4.393	
Disease severity (self-assessed) Face	Little	105	5.0	5.9	5.316	>0.05
	Severe	39	2.0	4.8	5.072	
Neck	Little	59	4.0	5.9	5,388	>0.05
	Severe	47	5.0	6.5	5.324	
Hands	Little	37	4.0	5.8	5.441	>0.05
	Severe	108	4.0	5.7	5.352	
Arms	Little	69	4.0	5.1	4.392	>0.05
	Severe	58	5.0	6.6	6.087	
Trunk	Little	65	***3.0****	***4.4****	3.893	**0.017**(1)
	Severe	58	***4.5****	***6.6****	5.988	**0.047**(2)
Legs	Little	79	4.0	5.4	5.437	>0.05
	Severe	51	5.0	6.6	5.475	
Do you do any sports or do you have a hobby?	Yes	95	3.0	5.1	5.227	>0.05
	No	28	4.5	5.1	4.447	

Table 24: DLQI scores in several subgroups of patient population
All significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

Next we analysed the data of all the socio-demographic subgroups according to their *grouped* DLQI scores. Confirming our earlier findings, we could not establish any differences between the groups, including age, gender, age of disease onset, involvement of body sites, actively spent leisure time, skin colour and family history (all p>0.05, Pearson Chi-Square test).

Notably, patients who think that *psychological stress* is involved in vitiligo were more often found in the higher DLQI score groups 11-20 and 21-30 (100.0%, n=5) compared to the lower scores 0-1 and 2-5 (55.6%, n=25/45, *p<0.05, **Table 25**).

Groups of DLQI Scores		Psychological stress involved in vitiligo?	
		Yes	No
0-1	N	11	13
	%	**45.8**	**54.2**
2-5	N	14	7
	%	**66.7**	**33.3**
6-10	N	17	4
	%	**81.0**	**19.0**
11-20	N	5	0
	%	**100.0**	**0.0**
21-30	N	--	--
	%		
p value		*0.029	

Table 25: Analysis of grouped DLQI scores in adult patients
Significance was measured with a Pearson Chi-Square test.

6.2.3 DLQI and the influence of stigmatising experiences

Stigmatisation has been described as highly influential on quality of life measurements (Kent and Al-Abadie 1996a). Therefore, we wanted to know whether this applied to our patient population as well by comparing the DLQI scores regarding experiences of being *approached / asked* by others and regarding *picking on / nasty comments*.

Our results show that *approaches / questions* by others have a significant effect on DLQI (*p=0.014, one-way ANOVA test; *p<0.05, Kruskal-Wallis-test). However, there is no clear-cut tendency, because the highest DLQI score was in the group of patients who had *not* experienced *approaches / questions*, whereas the lowest score was in those who were approached / asked *sometimes.* Patients who were asked *very often* scored in the middle range (**Table 26**).

There was no significant difference within the patient group regarding experiences of *picking on / nasty comments* (p>0.05, one-way ANOVA and Kruskal-Wallis-test, **Table 26**).

Question	Answer	N	Mean DLQI	Median DLQI	SD	p value
Have you ever been approached by others, or have you been asked questions about your vitiligo?	1	27	***5.4*****	***4.0***	4.749	**0.014**(1) >0.05(2)
	2	84	***4.5*****	***3.0***	4.441	
	3	13	***8.8*****	***8.0***	7.463	
Have you ever been picked upon, or has anybody ever been nasty to you because of your vitiligo?	1	1	3.0	n.d.	0.0	>0.05(1) (2)
	2	29	6.3	6.0	5.863	
	3	93	4.8	3.0	4.729	

Table 26: Influence of stigmatisation experiences on DLQI scores
Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1 - Yes, very often, **2** - Yes, sometimes, **3** - No

6.2.4 DLQI scores and avoidant behaviour

Since dermatology quality of life measurements determine how many and how much essential daily activities are limited by a skin disease, we were interested whether there were indeed any associations between DLQI scores and avoidant behaviour. For this purpose we chose *hiding of the white spots* in front of other people and *avoidance of situations*, where the disease might be exposed.

First we analysed the correlation between frequencies of hiding vitiligo and DLQI scores. The results revealed that an increased frequency of hiding the white spots correlates with increased DLQI scores (**Figure 22**). Patients who were hiding their vitiligo *very often* showed the highest median DLQI scores (8.0, n=35), followed by *quite often* (4.0, n=43) and *very rarely* (2.0, n=33). The lowest median DLQI score was found in the group of patients who had *never* hidden their white spots (1.0, n=12). The difference between the groups is highly significant (***$p<0.001$, Kruskal-Wallis-test). This tendency is also confirmed by analysis of the grouped DLQI scores (**Table 27**).

In the groups with high DLQI scores (11-20 and 21-30), which indicate severely impaired quality of life, there were more patients hiding their white spots *quite often* and *very often* (100.0%, n=16) compared to the lower DLQI score groups (41.2%, n=14 out of 37). The difference is highly significant (**$p=0.001$, Pearson Chi-Square test) (**Table 27**).

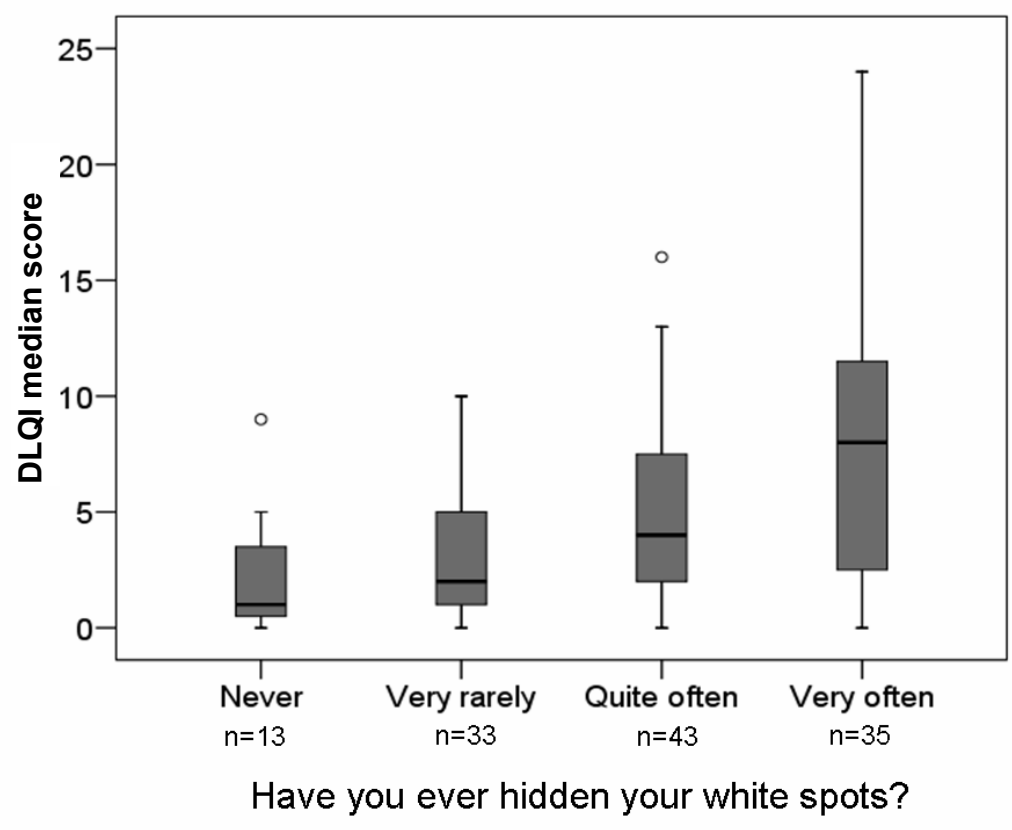


Figure 22: DLQI and hiding vitiligo (n=124, ***p<0.001)

The results regarding *avoidance of situations* were similar. Patients who had avoided situations because of their vitiligo (n=79) had much higher median DLQI scores (5.0 vs. 2.0) compared to those who never avoided anything (n=40). The difference is highly significant (***p<0.001, Mann-Whitney-U-Test, see **Figure 23**).

A comparison of patients with higher (11-20 and 21-30) and with lower DLQI score groups (0-5) yielded the same tendency. There were n=12/13 patients in the higher score groups avoiding situations because of their disease (92.3%), but this proportion was much smaller in the group with scores ranging from 0 to 5 (54.5%, n=42/77, **Table 27**). This difference was significant (*p=0.006, Chi-Square test).

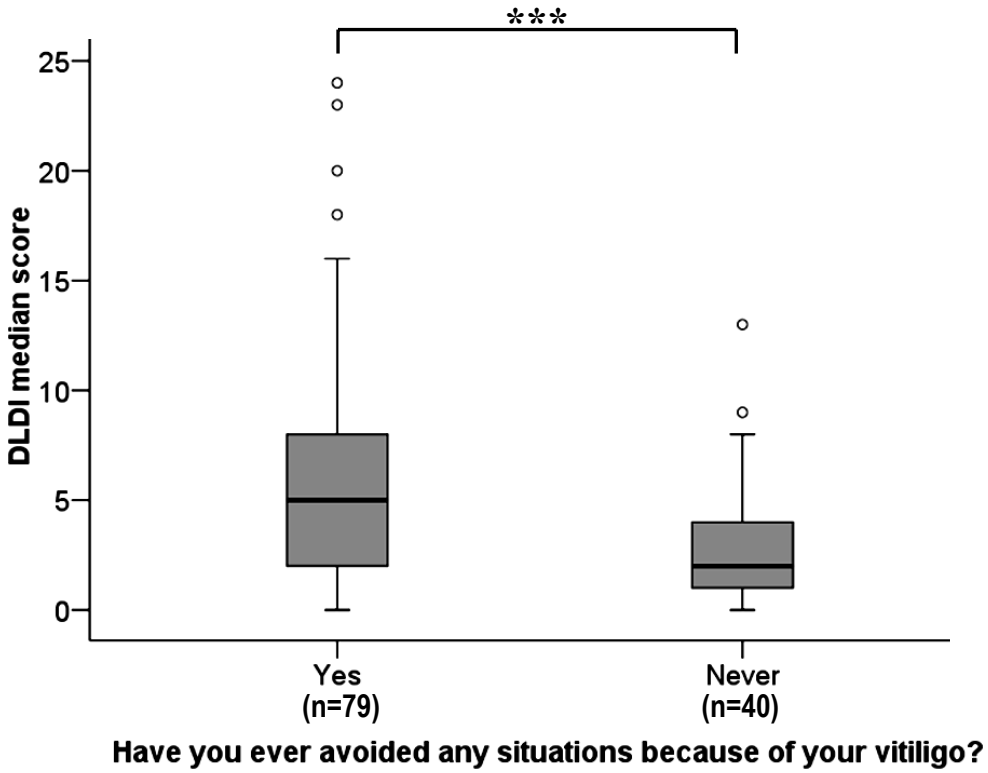


Figure 23: DLQI and avoidant behaviour (n=119, ***p<0.001)

Groups of DLQI Scores		Ever avoided situations because of vitiligo?			Have you ever hidden your white spots?				
		Yes	Never	N	Never	Very rarely	Quite often	Very often	N
0-1	N	15	19	34	7	13	10	4	34
	%	44.1	55.9		20.6	38.2	29.4	11.8	
2-5	N	27	16	43	4	12	20	8	44
	%	62.8	37.2		9.1	27.3	45.4	18.2	
6-10	N	23	5	28	1	8	8	12	29
	%	82.1	17.9		3.4	27.6	27.6	41.4	
11-20	N	10	1	11	0	0	5	9	16
	%	90.9	9.1		0.0	0.0	35.7	64.3	
21-30	N	2	0	2	0	0	0	2	2
	%	100.0	0.0		0.0	0.0	0.0	100.0	
p value		*p=0.006				**p=0.001			

Table 27: Analysis of avoidance behaviour in groups of DLQI scores
Significances were measured with a Pearson Chi-Square test

6.2.5 Influence of disease severity in male and female patients

When we analysed the DLQI scores separately for each body part for male and female patients, there were no differences between genders (data not shown, all p>0.05, Independent Sample T-test and Mann-Whitney-U-test), apart from the *face.*

The results revealed that women with severe facial vitiligo had significantly increased DLQI scores (mean 6.3, n=21) compared to male patients (3.1, n=18, *p=0.043, 2-sided Independent Sample T-test). There was no difference between male and female patients with minor facial vitiligo (**Figure 24**).

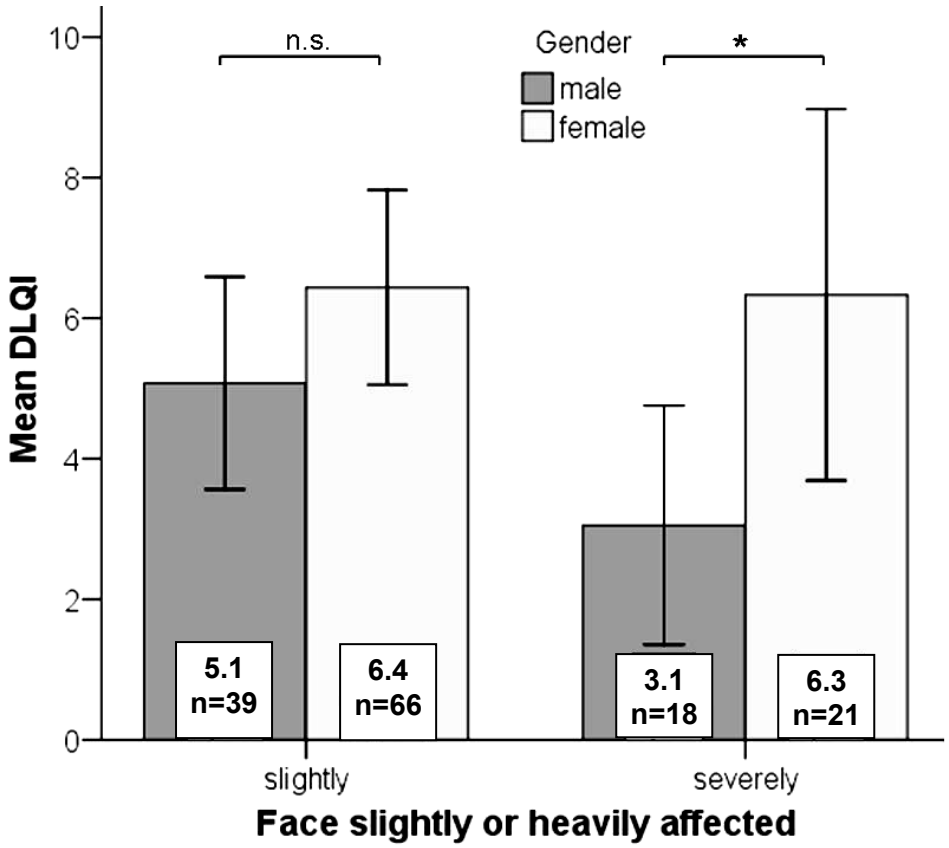


Figure 24: Mean DLQI scores and the influence of slightly or severely affected faces (self-assessment) in male and female patients with vitiligo (n=144)

6.2.6 Duration of vitiligo has no influence on quality of life

Since there is no agreement in the literature on whether duration of vitiligo correlates with total DLQI scores, we tested whether there was such correlation in our patient population.

Pearson correlation analysis yielded a correlation coefficient of 0.006 (n=164), which means that there was neither a significant positive nor negative correlation between mean total DLQI scores and duration of the disease ($p>0.05$).

Moreover, we also found that none of the single DLQI items correlated with duration of disease (n=89, all $p>0.05$), except for question 2 *(embarrassment, self-consciousness)* where a negative correlation was present (*-0.269,* *p=0.011, Pearson correlation analysis). Hence, the longer patients had vitiligo, the less embarrassed or self-conscious they were.

Taken together, we can conclude that the duration of vitiligo has no influence on quality of life of affected individuals. This is rather surprising, because patients appear frequently very disturbed at their first visit at the Institute for Pigmentary Disorders.

6.2.7 Single items analysis

Apart from differences between subgroups as measured with the *total* DLQI score, it has been of interest whether there were any significant differences in the 10 single items of this questionnaire. This analysis allowed a more detailed insight into the life of our patients. For this purpose we evaluated 90/164 randomly chosen DLQI questionnaires. The results showed no significant influence ($p>0.05$) of

- gender[(1) (3)],
- language of questionnaire[(1) (3)],
- age groups[(2) (4)],
- groups of age at disease onset[(2) (4)],
- beliefs that other diseases or injuries are involved in triggering vitiligo[(1) (3)],
- presence of grey hair on scalp or in eyelashes / eyebrows[(1) (3)],
- stigmatising experiences (having been picked on) [(2) (4)],
- self-assessed disease severity on face, neck, legs and hands[(1)(3)]

The results are based on the following tests of significance:

[(1)] 2-sided Independent Sample T-test
[(2)] one-way ANOVA test,
[(3)] Mann-Whitney-U-test or
[(4)] Kruskal-Wallis-test.

Since all the scores are rather low in each single item, evaluation using the median would yield almost only zero values. Therefore the mean has been chosen for presentation of the results.

When comparing the means of all DLQI single items, we could show that vitiligo had the strongest effect on *feelings of embarrassment / self-consciousness* (score 1.0), followed by wearing *clothes* (0.6), *social / leisure activities* (0.5) and relationships with *partners / friends / relatives* (0.5). The least affected items were *doing sports* and *work / studying* (each 0.2, **Figure 25**).

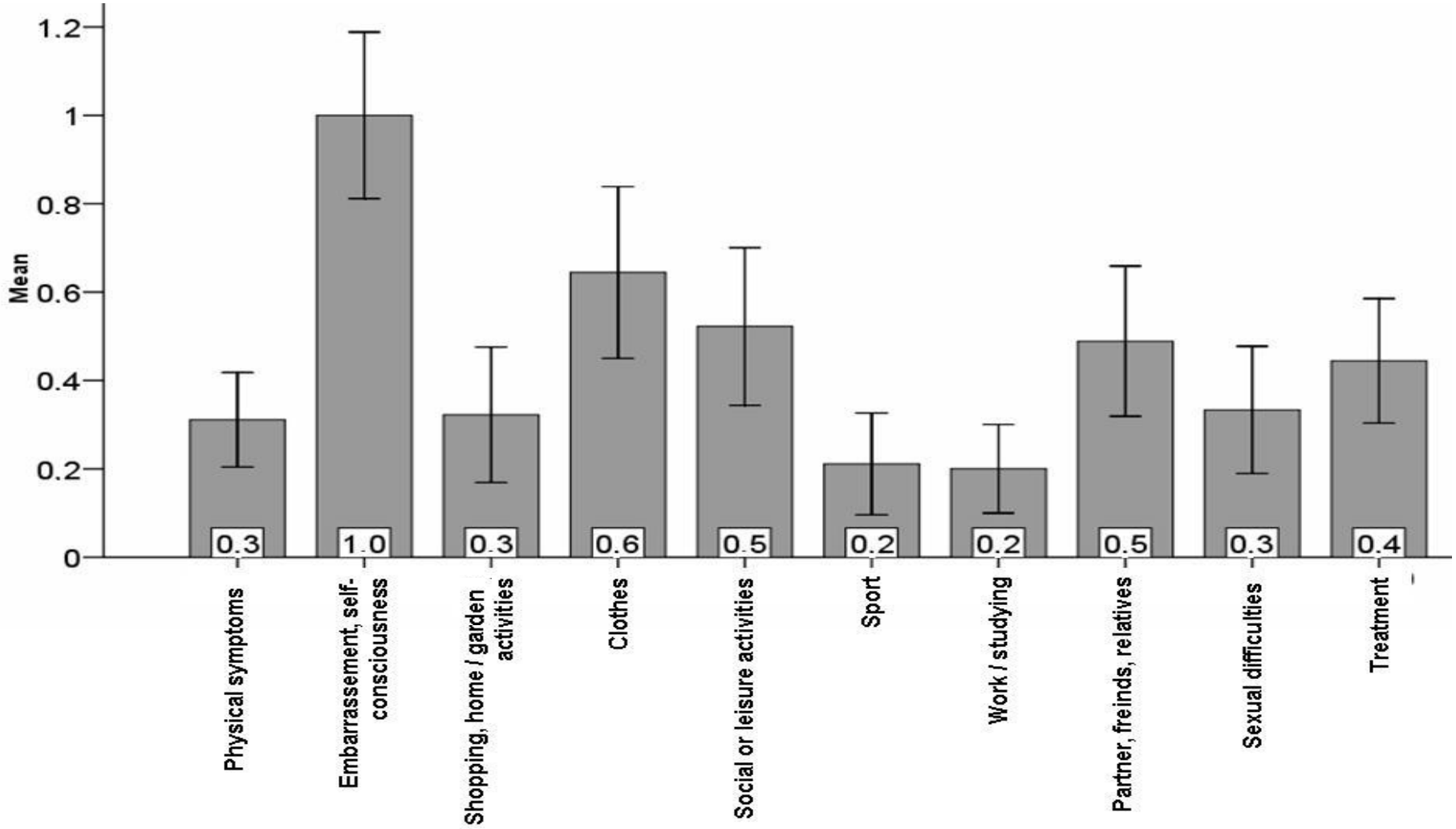


Figure 25: Single item analysis of DLQI scores (n=90)

Next we analysed whether the DLQI single items were influenced by any other demographic characteristics.

We found differences between patients undergoing treatment with NB-UVB activated pseudocatalase PC-KUS and new patients from the Institute for Pigmentary Disorders (**Table 28**). The treated group was less affected in their daily activities such as *shopping or gardening* (*$p<0.05$, Independent Sample T-test). However, the *treatment* itself (**$p<0.005$) and *physical symptoms* (*$p<0.05$, Mann-Whitney-U-test) affected patients more compared to new patients. Interestingly, there were no further significant differences ($p>0.05$, 2-sided Independent Sample T-test and Mann-Whitney-U-test).
It can be concluded that the treatment offered by the Institute for Pigmentary Disorders can improve essential parts of patients' daily life.

A comparison of patients with different skin colours revealed that those with *darker skin* felt limited in their *sportive activities* (**Table 29**, **$p<0.005$, Mann-Whitney-U-test). It is surprising that sport is harder on patients compared to *shopping / gardening* or even *sexual relationships*.

DLQI items	Patient status	N	Mean	SD	p value
Question 1	1	41	0.2	.525	>0.05(1)
Physical symptoms	2	49	0.4	.492	**0.041(2)**
Question 2	1	41	1.2	1.085	>0.05
Embarrassment, self-consciousness	2	49	0.9	.696	
Question 3	1	41	***0.5****	.978	**0.049(1)**
Shopping, home / garden activities	2	49	***0.2****	.391	>0.05(2)
Question 4	1	41	0.6	.942	>0.05
Clothes	2	49	0.7	.925	
Question 5	1	41	0.5	.951	>0.05
Social / leisure activities	2	49	0.5	.767	
Question 6	1	41	0.1	.400	>0.05
Sport	2	49	0.3	.645	
Question 7	1	41	0.2	.511	>0.05
Work / studying	2	49	0.2	.456	
Question 8	1	41	0.5	.951	>0.05
Partners / friends / relatives	2	49	0.5	.679	
Question 9	1	41	0.3	.693	>0.05
Sexual difficulties	2	49	0.3	.689	
Question 10	1	41	***0.3****	.672	**0.022(1)**
Treatment	2	49	***0.6****	.643	**0.002(2)**
Total DLQI	1	**41**	**4.5**	**5.168**	>0.05
	2	**49**	**4.5**	**3.577**	

Table 28: Comparison of DLQI scores in patients from IFPD and other sources
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

1- New patients
2- Treated patients (IFPD)

DLQI items	Skin phototype groups	N	Mean	SD	p value
Question 1	I-III	75	0.3	.514	>0.05
Physical symptoms	IV-VI	15	0.5	.519	
Question 2	I-III	75	0.9	.859	>0.05
Embarrassment, self-consciousness	IV-VI	15	1.3	.947	
Question 3	I-III	75	0.3	.684	>0.05
Shopping, home / garden activities	IV-VI	15	0.5	.660	
Question 4	I-III	75	0.6	.954	>0.05
Clothes	IV-VI	15	0.7	.855	
Question 5	I-III	75	0.5	.795	>0.05
Social / leisure activities	IV-VI	15	0.9	1.144	
Question 6	I-III	75	***0.2*** **	.456	**0.004**(1)
Sport	IV-VI	15	***0.6*** **	.870	**0.002**(2)
Question 7	I-III	75	0.2	.501	>0.05
Work / studying	IV-VI	15	0.2	.376	
Question 8	I-III	75	0.4	.738	>0.05
Partners / friends / relatives	IV-VI	15	0.7	.947	
Question 9	I-III	75	0.4	.668	>0.05
Sexual difficulties	IV-VI	15	0.3	.855	
Question 10	I-III	75	0.5	.704	>0.05
Treatment	IV-VI	15	0.3	.480	
Total DLQI	**I-III**	**75**	**4.2**	**4.145**	>0.05
	IV-VI	**15**	**5.9**	**5.257**	

Table 29: Comparison of DLQI scores in fair vs. dark skin
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

Influence of a positive family history of vitiligo on quality of life (DLQI)

Although a family history of vitiligo is present in about 38% of the patients, this has hardly been linked to quality of life in the literature. Therefore, our aim was to explore any possible differences between patients with and without somebody else in the family with the disease. Single item analysis of the DLQI showed that patients with a positive family history are less affected regarding *sexual difficulties* (**Table 30**, *p=0.04 Independent Sample T-Test, p=0.55 Mann-Whitney-U-test).

DLQI items	Family history	N	Mean	SD	p value
Question 1	Yes	24	0.3	.565	>0.05
Physical symptoms	No	61	0.3	.501	
Question 2	Yes	24	0.9	.830	>0.05
Embarrassment, self-consciousness	No	61	1.1	.939	
Question 3	Yes	24	0.3	.737	>0.05
Shopping, home / garden activities	No	61	0.3	.750	
Question 4	Yes	24	0.4	.717	>0.05
Clothes	No	61	0.7	1.015	
Question 5	Yes	24	0.4	.711	>0.05
Social / leisure activities	No	61	0.6	.903	
Question 6	Yes	24	0.1	.282	>0.05
Sport	No	61	0.3	.623	
Question 7	Yes	24	0.1	.282	>0.05
Work / studying	No	61	0.3	.545	
Question 8	Yes	24	0.4	.881	>0.05
Partners / friends / relatives	No	61	0.5	.808	
Question 9	Yes	24	***0.1****	.282	**0.04**(1)
Sexual difficulties	No	61	***0.4****	.784	0.055(2)
Question 10	Yes	24	0.5	.834	>0.05
Treatment	No	61	0.4	.620	
Total DLQI	**Yes**	**24**	**3.5**	**3.401**	>0.05
	No	**61**	**4.9**	**4.734**	

Table 30: DLQI scores in presence vs. absence of a positive family history of vitiligo (single item analysis)
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

Influence of psychological stress on quality of life (DLQI)

Earlier in this thesis, we showed that the perception of *psychological stress* influencing vitiligo has a strong effect on the total DLQI score. It was tempting to further analyse this finding to see which parts of the daily life are exactly impaired. As shown in **Table 31**, we found that those patients are more affected in almost *all* single items of the DLQI except for *physical symptoms, work / studying* and *treatment* itself (significances vary from ***p=0.001 to *p=0.05, Independent Sample T-test and Mann-Whitney-U-test).

DLQI items	Psychological stress	N	Mean	SD	p value
Question 1	Yes	45	0.3	.522	>0.05
Physical symptoms	No	24	0.3	.532	
Question 2	Yes	45	***1.2****	.960	**0.02**(1)
Embarrassment, self-consciousness	No	24	***0.7****	.761	**0.025**(2)
Question 3	Yes	45	***0.5****	.919	**0.012**(1)
Shopping, home / garden activities	No	24	***0.0****	.204	**0.006**(2)
Question 4	Yes	45	***0.9****	1.027	**0.002**(1)
Clothes	No	24	***0.2****	.482	**0.001**(2)
Question 5	Yes	45	***0.8****	.997	**0.019**(1)
Social / leisure activities	No	24	***0.3****	.532	**0.023**(2)
Question 6	Yes	45	0.3	.668	>0.05(1)
Sport	No	24	0.0	.204	**0.05**(2)
Question 7	Yes	45	0.3	.549	>0.05
Work / studying	No	24	0.1	.448	
Question 8	Yes	45	***0.8****	.908	**0.011**(1)
Partners / friends / relatives	No	24	***0.2****	.658	**0.003**(2)
Question 9	Yes	45	0.5	.757	>0.05(1)
Sexual difficulties	No	24	0.2	.565	**0.035**(2)
Question 10	Yes	45	0.5	.727	>0.05
Treatment	No	24	0.3	.550	
Total DLQI	**Yes**	**45**	***6.0****	**4.864**	**0.001**
	No	**24**	***2.2****	**2.472**	

Table 31: Single item analysis of DLQI regarding psychological stress
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

Avoidant behaviour and quality of life (DLQI)

It was also of interest to see which parts of the daily life are particularly impaired in patients who tend *to avoid situations* because of their vitiligo. It can be suspected that those activities are affected where patients fear to meet strangers or become subjects to questions. We found indeed that patients with avoidant behaviour scored significantly higher in *daily activities (shopping / gardening)*, wearing *clothes* because of vitiligo and *sport* (**Table 32**, all *p<0.05, Mann-Whitney-U-test and Independent Sample T-test). In all the other items we found no significant differences.

DLQI items	Situations avoided?	N	Mean	SD	p value
Question 1 ***Physical symptoms***	Yes	59	0.4	.517	>0.05
	Never	28	0.2	.499	
Question 2 ***Embarrassment, self-consciousness***	Yes	59	1.0	.820	>0.05
	Never	28	0.9	.956	
Question 3 ***Shopping, home / garden activities***	Yes	59	***0.4****	.763	**0.046**(1)
	Never	28	***0.1****	.262	**0.041**(2)
Question 4 ***Clothes***	Yes	59	***0.8****	.979	**0.025**(1)
	Never	28	***0.3****	.723	**0.014**(2)
Question 5 ***Social / leisure activities***	Yes	59	0.6	.929	>0.05
	Never	28	0.3	.612	
Question 6 ***Sport***	Yes	59	***0.3****	.650	**0.035**(1)
	Never	28	***0.0****	.189	**0.028**(2)
Question 7 ***Work / studying***	Yes	59	0.2	.434	>0.05
	Never	28	0.2	.568	
Question 8 ***Partners / friends / relatives***	Yes	59	0.5	.878	>0.05
	Never	28	0.4	.621	
Question 9 ***Sexual difficulties***	Yes	59	0.4	.717	>0.05
	Never	28	0.2	.548	
Question 10 ***Treatment***	Yes	59	0.5	.626	>0.05
	Never	28	0.4	.780	
Total DLQI	**Yes**	**59**	**5.0**	**4.620**	0.052(1)
	Never	**28**	**3.0**	**3.394**	**0.03**(2)

Table 32: Single item analysis of DLQI regarding avoidance of situations
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

Self-assessed disease severity and quality of life

Although the *disease severity on arms* of the patients did not influence the total DLQI score, there were some significant differences when looking at the questionnaire's single items. Our results yielded that patients who judge their own vitiligo on their arms as *severe* are more affected regarding wearing *clothes* (*$p<0.05$, Independent Sample T-test and Mann-Whitney-U-test), while all other items showed no significant differences (**Table 33**). The disease severity on the other body parts did not play a role, possibly because they are either always (trunk) or only rarely covered (face or hands).

Moreover, disease severity on the trunk did not influence the item *wearing of clothes*, but rather the one on *sexual difficulties*. Patients whose trunk was only *slightly* affected by vitiligo, had a less impaired sexual life (**Table 34**, *$p<0.05$, Mann-Whitney-U-test). This is somewhat obvious, because the trunk would only be exposed to others in intimate situations. Other situations, where this might happen would be sport or swimming, but these activities are easier to avoid.

Self-assessed disease severity ARMS		N	Mean	SD	p value
Question 1	1	34	0.3	.448	>0.05
Physical symptoms	2	32	0.3	.523	
Question 2	1	34	0.9	.851	>0.05
Embarrassment, self-consciousness	2	32	1.2	.920	
Question 3	1	34	0.2	.654	>0.05
Shopping, home / garden activities	2	32	0.4	.911	
Question 4	1	34	***0.4****	.743	**0.021**(1)
Clothes	2	32	***0.9****	1.045	**0.02**(2)
Question 5	1	34	0.4	.779	>0.05
Social / leisure activities	2	32	0.6	.801	
Question 6	1	34	**0.1**	.288	**0.053**(1)
Sport	2	32	**0.3**	.592	>0.05(2)
Question 7	1	34	0.1	.327	>0.05
Work / studying	2	32	0.3	.581	
Question 8	1	34	0.6	.985	>0.05
Partners / friends / relatives	2	32	0.5	.762	
Question 9	1	34	0.4	.779	>0.05
Sexual difficulties	2	32	0.4	.712	
Question 10	1	34	0.6	.743	>0.05
Treatment	2	32	0.3	.653	
Total DLQI	1	**34**	**4.0**	**3.717**	>0.05
	2	**32**	**5.2**	**4.568**	

Table 33: Single item analysis of DLQI regarding disease severity on arms
Significance was measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

1- Little affected
2- Severely affected

Self-assessed disease severity TRUNK		N	Mean	SD	p value
Question 1	1	34	0.3	.462	>0.05
Physical symptoms	2	24	0.4	.584	
Question 2	1	34	1.1	.977	>0.05
Embarrassment, self-consciousness	2	24	0.7	.624	
Question 3	1	34	0.4	.884	>0.05
Shopping, home / garden activities	2	24	0.2	.381	
Question 4	1	34	**0.5**	.861	>0.05(1)
Clothes	2	24	**0.9**	1.018	**0.054(2)**
Question 5	1	34	0.4	.652	>0.05
Social / leisure activities	2	24	0.5	.779	
Question 6	1	34	0.2	.359	>0.05
Sport	2	24	0.3	.608	
Question 7	1	34	0.2	.479	>0.05
Work / studying	2	24	0.2	.509	
Question 8	1	34	0.4	.786	>0.05
Partners / friends / relatives	2	24	0.5	.780	
Question 9	1	34	0.2	.521	>0.05(1)
Sexual difficulties	2	24	0.5	.722	**0.027**(1)
Question 10	1	34	0.5	.706	>0.05
Treatment	2	24	0.5	.779	
Total DLQI	1	34	4.1	3.599	>0.05
	2	24	4.6	3.599	

Table 34: Single item analysis of DLQI regarding disease severity on trunk
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

1- Little affected
2- Severely affected

Stigmatisation experiences and DLQI

Finally, it was our interest to find out which parts of the daily life are impaired if patients with vitiligo had experienced stigmatisation, i.e. *approaches* or *questions* about the disease by others. Interestingly, patients who had never been approached or asked were more affected in their *relationships to partners / friends / relatives* and *sexual relationships*. Patients who had *some* experiences, showed the lowest scores in the mentioned categories (**Table 35**, *$p<0.05$, one-way ANOVA test and Kruskal-Wallis-test). There were no further differences in any of the other DLQI single items.

Have you ever been approached by others because of your skin disease, or have you been asked questions about your vitiligo?		N	Mean	SD	p value
Question 1	1	23	0.4	.573	
Physical symptoms	2	58	0.3	.496	>0.05
	3	8	0.3	.463	
Question 2	1	23	1.2	1.043	
Embarrassment, self-consciousness	2	58	0.9	.782	>0.05
	3	8	1.1	.991	
Question 3	1	23	0.6	1.158	
Shopping, home / garden activities	2	58	0.2	.425	>0.05
	3	8	0.4	.518	
Question 4	1	23	0.7	.974	
Clothes	2	58	0.6	.862	>0.05
	3	8	1.0	1.195	
Question 5	1	23	0.4	.783	
Social / leisure activities	2	58	0.5	.753	>0.05
	3	8	1.3	1.282	
Question 6	1	23	0.3	.619	
Sport	2	58	0.1	.348	>0.05
	3	8	0.6	1.188	
Question 7	1	23	0.3	.559	
Work / studying	2	58	0.1	.395	>0.05
	3	8	0.4	.744	
Question 8	1	23	0.7	.974	>0.05(1)
Partners / friends / relatives	2	58	0.3	.664	**0.046(2)**
	3	8	1.0	1.069	
Question 9	1	23	0.5	.790	>0.05(1)
Sexual difficulties	2	58	0.2	.585	**0.019(2)**
	3	8	0.8	.886	
Question 10	1	23	0.5	.846	
Treatment	2	58	0.4	.624	>0.05
	3	8	0.5	.535	
Total DLQI	1	**23**	**5.6**	**5.080**	
	2	**58**	**3.6**	**3.283**	>0.05
	3	**8**	**7.3**	**6.902**	

Table 35: Single item analysis of DLQI regarding approaches / questions
Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1 - Yes, very often, 2 - Yes, sometimes, 3 - No

6.3 Coping with vitiligo

6.3.1 Impaired coping in adults with vitiligo

In order to test the direct influence of vitiligo on coping with this skin disease, we compared all main scores of the Adjustment to Chronic Skin Disorders Questionnaire (ACS) between patients (n=422) and healthy controls (n=55).

Patients with vitiligo scored a mean of 38.7 (SD 13.67) and a median of 37.0 for *social anxiety / avoidance*, which is much higher compared to the control group (mean 19.0, SD 7.81, median 16.0). The difference is highly significant (***p<0.001, Mann-Whitney-U-Test and 2-sided Independent Sample T-test, **Figure 26**).

The same applied to *helplessness*. The patients' mean score was 27.7 (median 27.0, SD 8.22), whereas healthy controls scored only a mean of 13.5 (median 12.0, SD 6.04), which is significantly lower (***p<0.001, Mann-Whitney-U-Test and 2-sided Independent Sample T-test).

Finally, even in *anxious-depressive mood*, the only scale not specified for skin diseases, patients with vitiligo scored much higher (mean 20.2, median 20.0, SD 6.61) than the control group (mean 14.6, median 14.0, SD 6.05). This difference proved to be significant, too (***p<0.001, Mann-Whitney-U-Test and 2-sided Independent Sample T-test) (**Figure 26**).

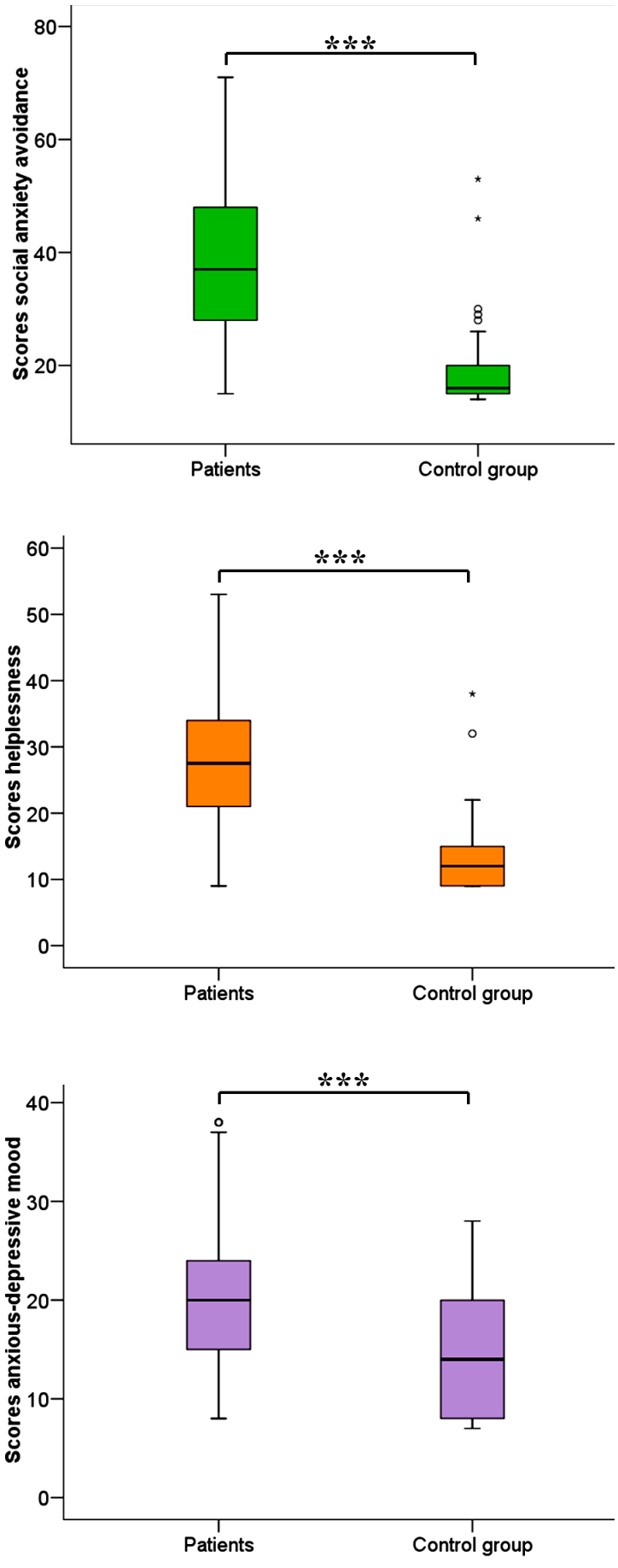


Figure 26: ACS sub-scores of patients (n=422) and healthy controls (n=55)

Patients' scores had a wider range compared to the control group (**Figure 26**). This result reflects the heterogeneity in coping strategies of patients with vitiligo.

However, there were no differences within the control group when analysed for the influence of skin diseases on coping. Members of the control group with a skin disease (n=11) and controls without any skin disease (n=33) did not differ in any subscale (all $p>0.05$, Mann-Whitney-U-test and Independent Sample T-test). This result further supports that vitiligo had a particularly strong effect on coping compared to the mix of various skin diseases present in our control group.

The following distribution and skewness analysis of the data allowed a more detailed insight. **Figure 28** shows a normal distribution for *helplessness* scores. This result is confirmed by the calculated skewness coefficient of 0.094, which is the lowest of all questionnaires used in this thesis. *Social anxietey / avoidance* and *anxious-depressive mood* are slightly more positively skewed (coefficients of 0.408 and 0.417, respectively) (**Figure 27** and **Figure 29**).

As already shown with the use of the DLQI, there are more patients with rather low ACS scores, but this tendency is not as pronounced as in the DLQI measurements. Patients with extremely high ACS scores are still a minority. Importantly, there were only 3 patients who showed the highest possible score for *helplessness,* which is 45. Nobody of the patients scored the same for *social anxiety / avoidance* or *anxious-depressive mood* (**Figure 27** and **Figure 29**).

Based on our results it is tempting to conclude that the central tendencies (median and mean) of the ACS do reflect the group's well-being better than the ones for the DLQI.

The same can be concluded after distribution and skewness analysis of the control group's scores. There are high skewness coefficients for *social anxiety* and *helplessness* (3.036 and 2.318, n=55) (**Figure 27** and **Figure 28**), whereas the one for *anxious-depressive mood* is much lower (0.58) (**Figure 29**). These results confirm that the vast majority of healthy controls do not have difficulties regarding their skin appearance. Interestingly, *anxious-depressive mood*, the only scale of this questionnaire not specified for skin diseases, seems to be more scattered, suggesting that this emotion is also relevant in healthy controls.

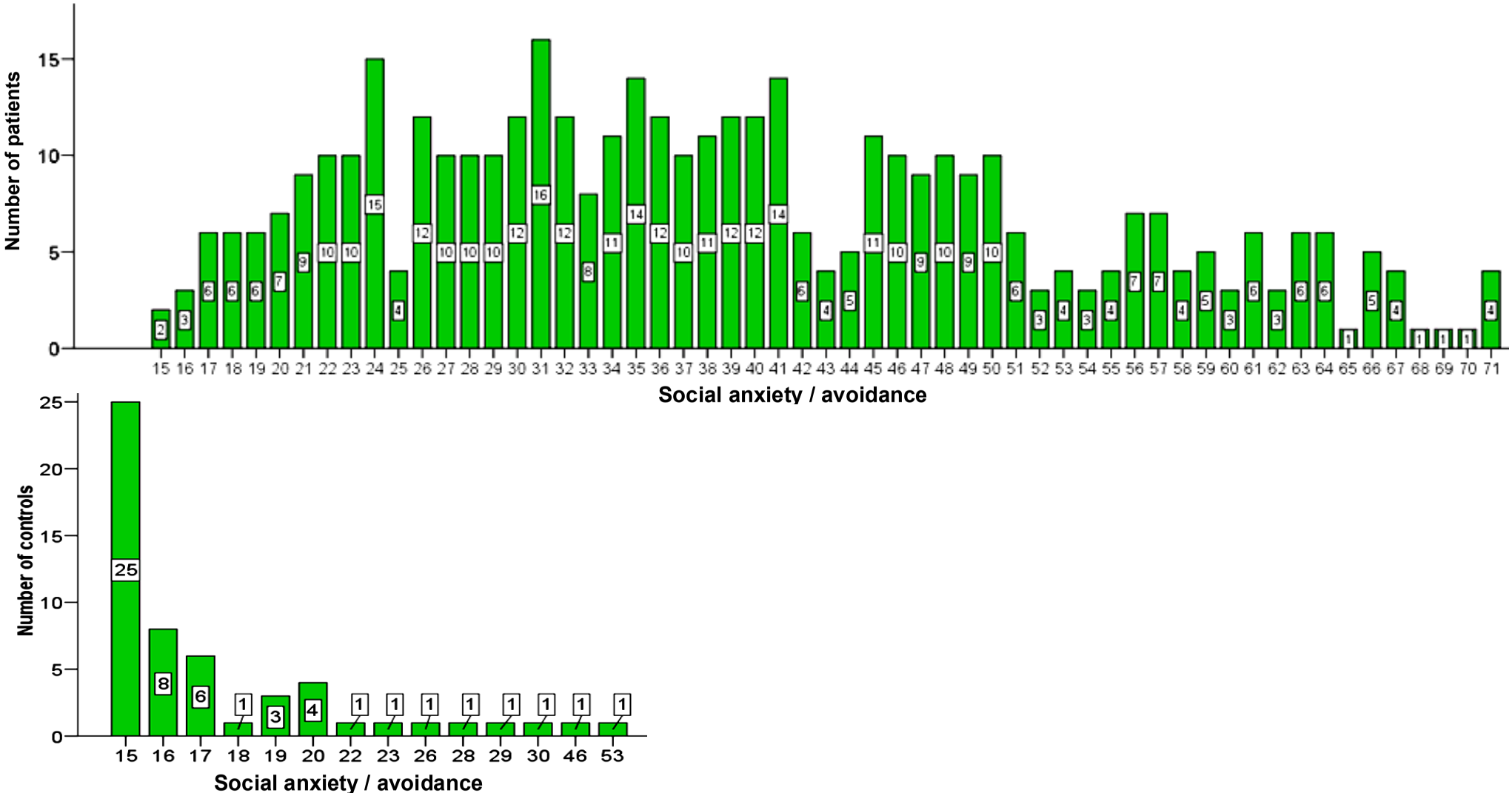


Figure 27: Distribution of social anxiety / avoidance scores in patients (n=422) and controls (n=55)

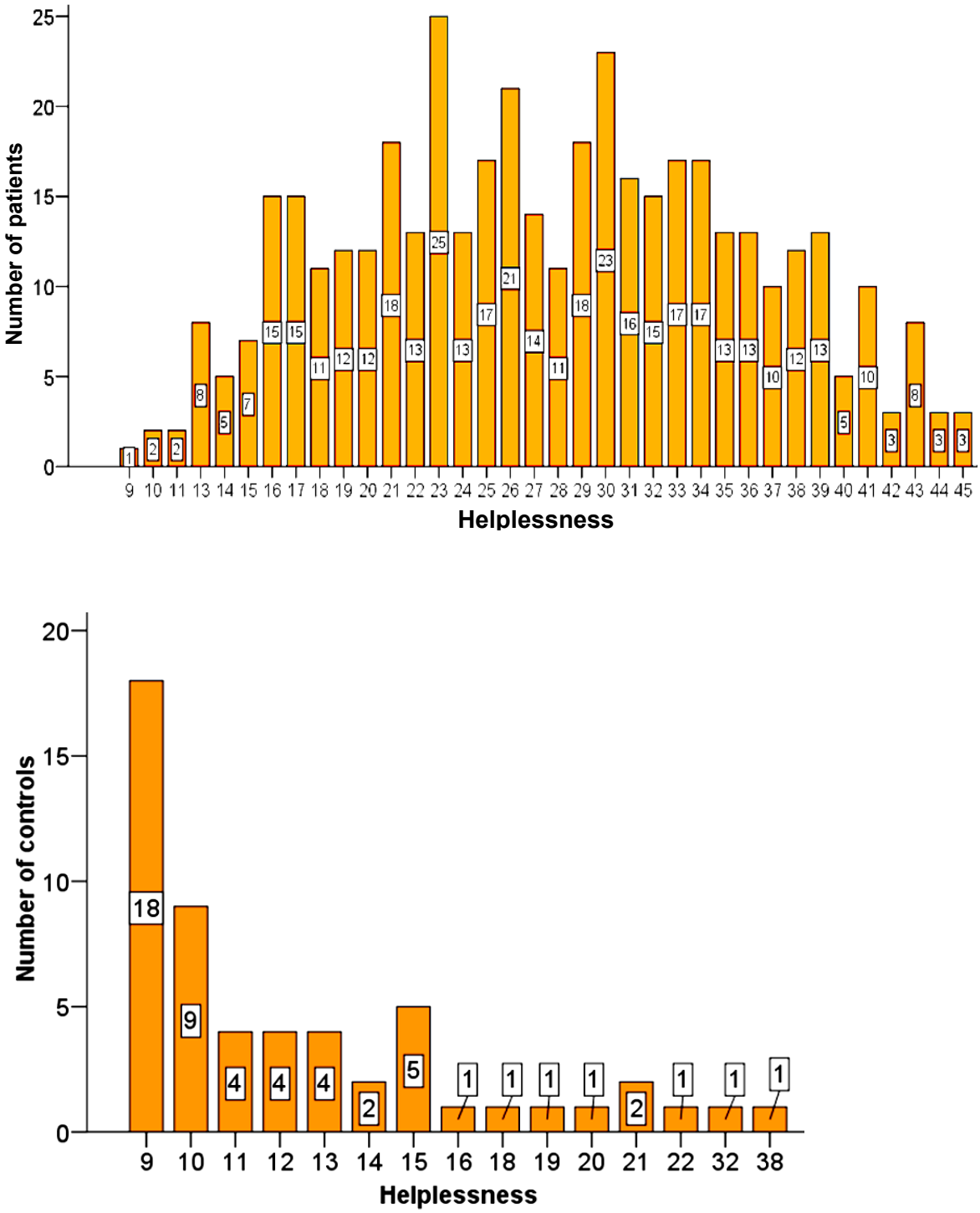


Figure 28: Distribution of helplessness scores of patients (n=422) and controls (n=55)

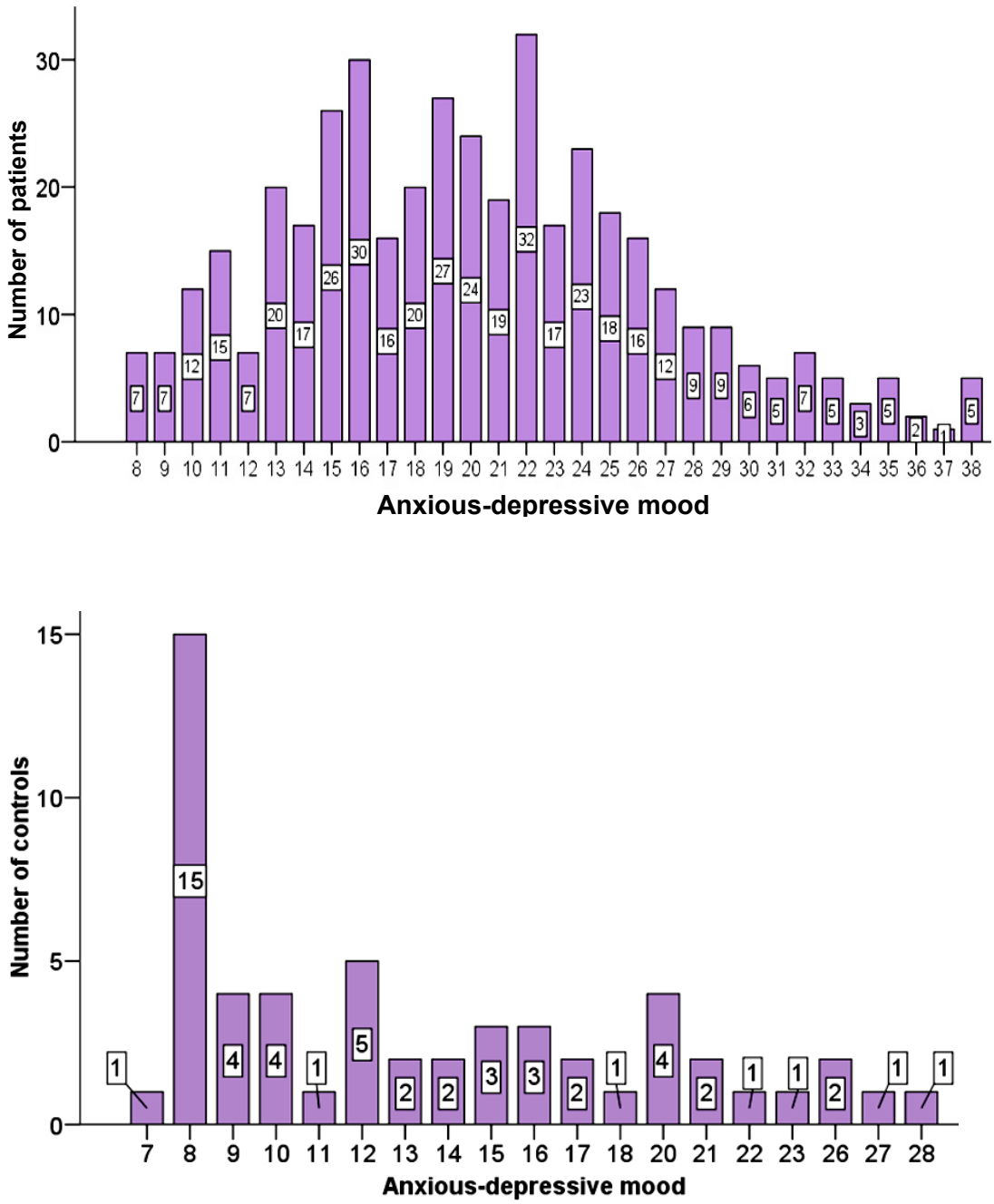


Figure 29: Distribution of anxious-depressive mood scores in patients (n=422) and healthy controls (n=55)

6.3.2 ACS sub-scores in different age groups

Since it has been described in the literature that vitiligo is less of a problem in older people compared to the younger ones, we wanted to determine if this applies to our patient group as well.

We employed Pearson correlation analysis between the ACS sub-scores and age. The results yielded the following correlation coefficients (n=422):

- *Social anxiety / avoidance* **-0.099* (p=0.042)**
- *Helplessness* **-0.126* (p=0.01)**
- *Anxious-depressive mood* **-0.103* (p=0.035)**

All sub-scores correlate significantly negatively with age, meaning that in our population the older the patients are, the less affected they are in terms of the ACS main scales. Therefore this result confirms earlier reports.

Figure 30 shows the scores for different age groups. There is a significant difference between age groups for s*ocial anxiety / avoidance* (**p=0.016), *helplessness* (**p=0.01) and *anxious-depressive Mood* (**p=0.005) as measured with a Kruskal-Wallis-test. The 20-29 years old patients showed the highest median scores, whereas they were lowest in the older group (50-59 years old).

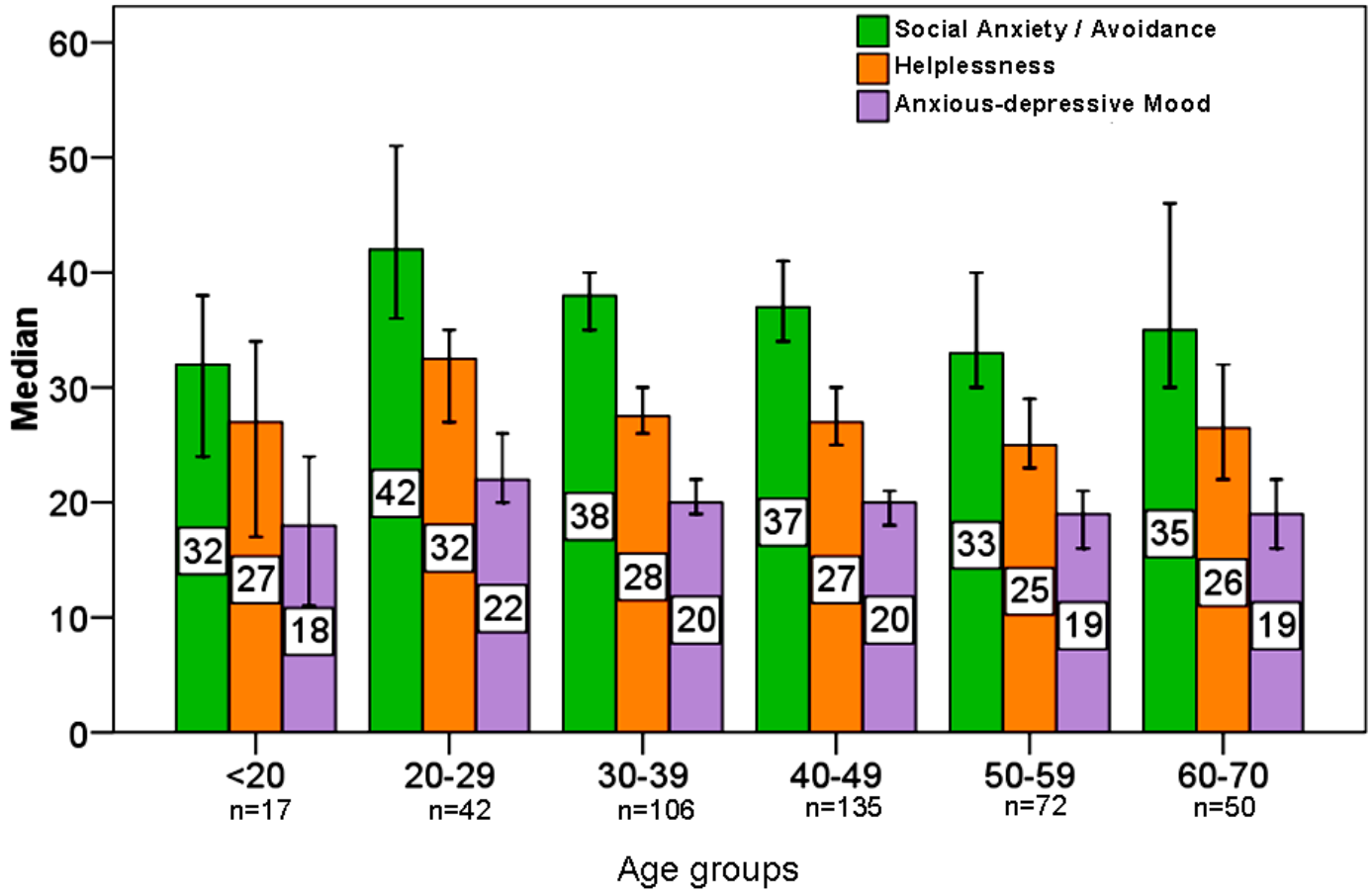


Figure 30: ACS scores in different age groups (n=422)

6.3.3 ACS sub-scores in different age groups of disease onset

It has also been of interest whether the age at disease onset was influential on the ACS scores.

Pearson correlation analysis between all ACS sub-scores and age at disease onset yielded the following coefficients (n=422):

- *Social anxiety / avoidance* **-0.199* (p=0.014)**
- *Helplessness* -0.076 (p>0.05)
- *Anxious-depressive mood* -0.079 (p>0.05)

Only for *social anxiety / avoidance* there is a significant negative correlation, which implies that the younger the age at disease onset, the higher the scores. *Helplessness* and *anxious-depressive mood* do not correlate with age of disease onset.

To complete the picture, **Figure 31** shows the scores for different age groups with regards to disease onset. There is a significant difference between age groups in *social anxiety / avoidance* (*p=0.018), *helplessness* (*p=0.035) and *anxious-depressive mood* (*p=0.007) as measured with a Kruskal-Wallis-test. Overall, the group with a disease onset between 12 and 19 years of age showed the highest median scores, whereas the lowest were found in the group >60 years.

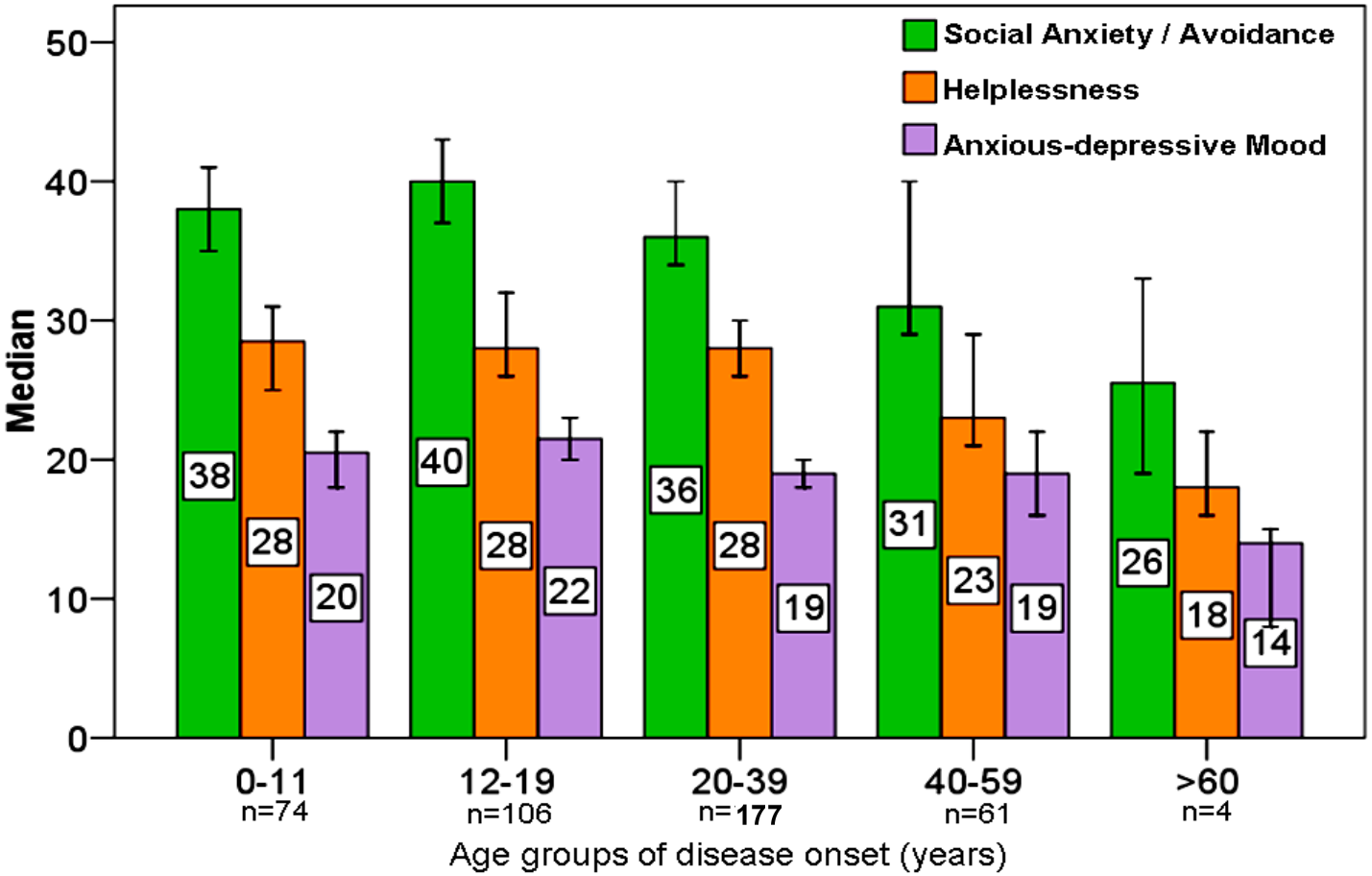


Figure 31: Sub-scores of ACS questionnaire (age groups of disease onset)

6.3.4 ACS sub-scores depending on stigmatising experiences

Stigmatisation has been described as highly influential on quality of life measurements. Therefore, we embarked to find out whether this also applied to *social anxiety / avoidance, helplessness* and *anxious-depressive mood* by comparing these scores in association with stigmatising experiences of *approaches / questions* and *nasty comments* by other people.

We found that there is a weak significant influence of *approaches / questions* on *social anxiety / avoidance* depending on whether this had happened *very often* (n=27), *sometimes* (n=83) or *never* (n=13) (*p=0.044 one-way ANOVA test, p=0.055 Kruskal-Wallis-test). However, there is no clear tendency, because the highest median score was in the *'very often'* group (41.0), followed by *'No'* (40.0) and the lowest score being in the '*sometimes*' group (33.0). These differences are not present in *helplessness* and *anxious-depressive mood* (always p>0.05, one-way ANOVA test and Kruskal-Wallis test). The results are shown in **Figure 32**.

Figure 33 shows the results regarding *nasty comments* / *picking on* individuals. Patients who had been picked on *sometimes* (n=29) showed higher median scores for *social anxiety / avoidance* compared to the 93 individuals who *never* made such experiences (39.0 vs. 33.0, *p=0.009). The same applied to *anxious-depressive mood* (medians 22.0 vs. 18.0, *p=0.042, both Mann-Whitney-U-test), but not to *helplessness* (29.0 vs. 25.0, p>0.05, Mann-Whitney-U-test). One patient had experienced this kind of stigmatisation *very often*, but this case has been left out for statistical reasons.

In summary, these results show that coping with vitiligo is clearly influenced by stigmatisation experiences.

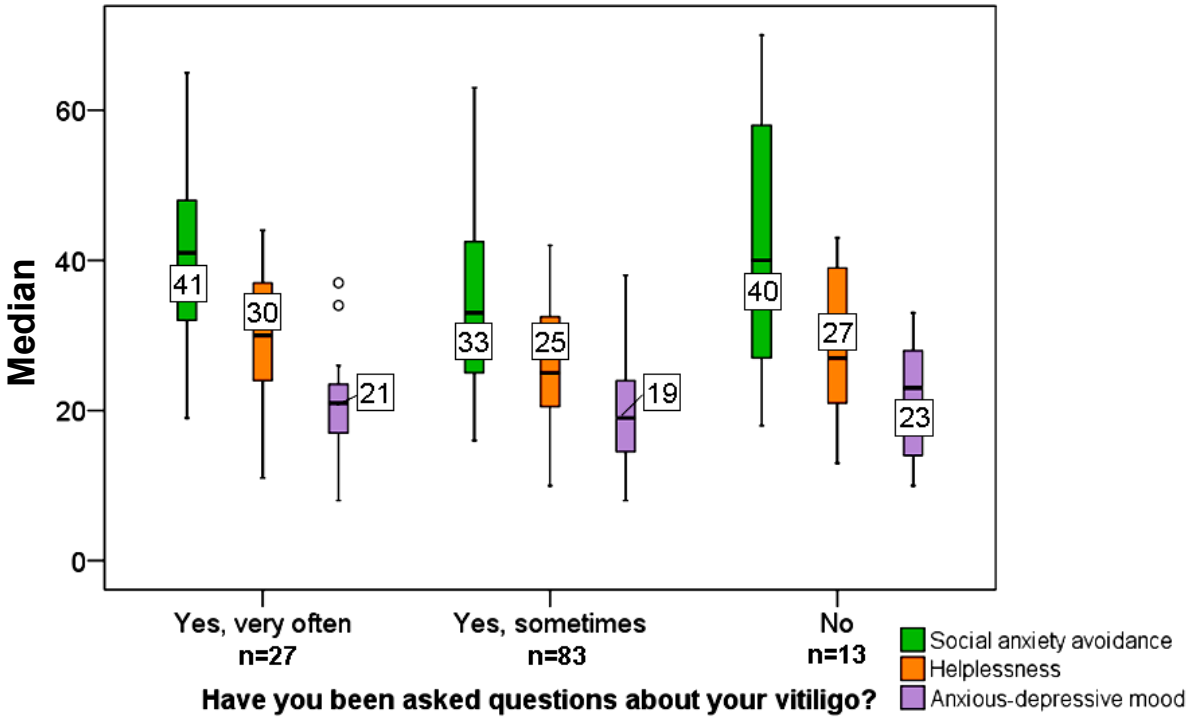


Figure 32: Median ACS sub-scores regarding frequencies of stigmatising experiences (approaches and questions by others)

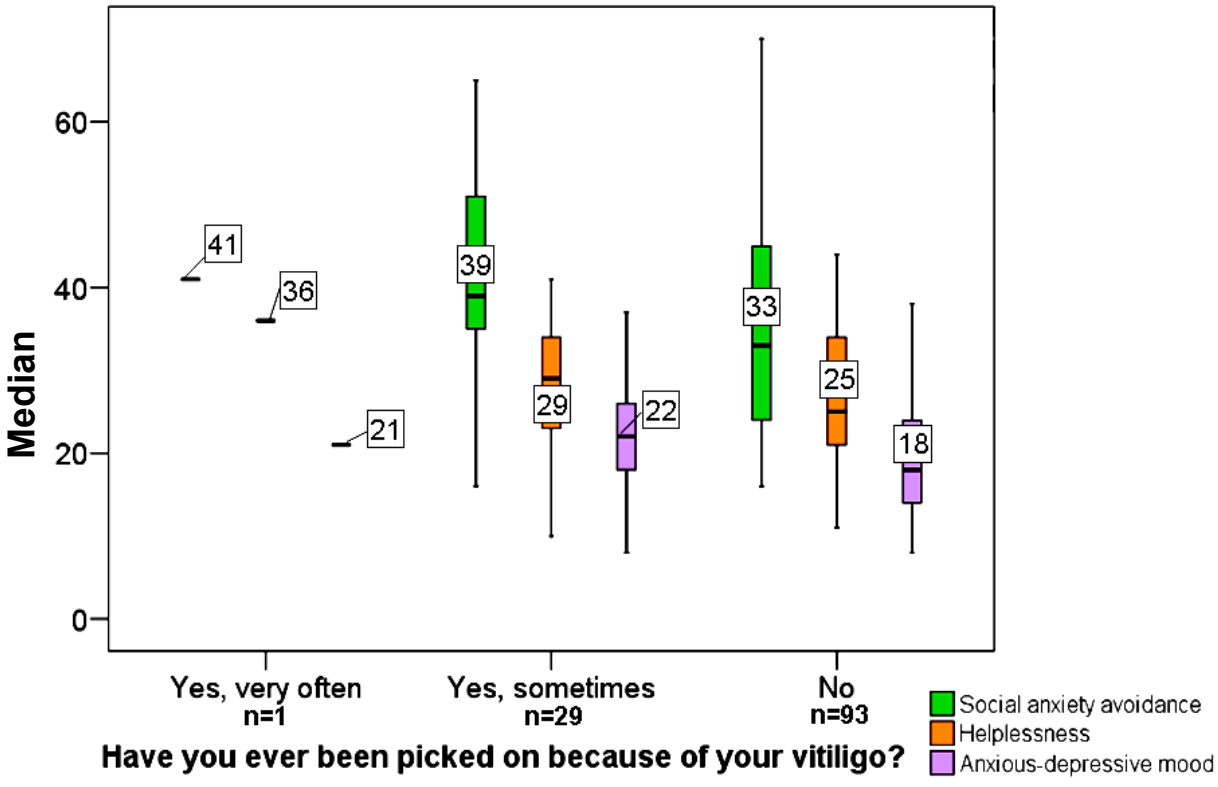


Figure 33: Median ACS sub-scores in patients with and without stigmatisation experiences (nasty comments)

6.3.5 ACS scores and avoidant behaviour

Similar to the DLQI evaluation, it was our interest to explore how those patients were coping with their disease, who tended to hide their white spots in front of other people and who had avoided certain situations.

Our results revealed that there was a highly significant and positive correlation between frequencies of hiding vitiligo and median ACS sub-scores (**Figure 34**). Patients who hide their vitiligo *very often* (n=35) scored highest in *social anxiety / avoidance* (median 50.0), *helplessness* (35.0) and *anxious-depressive mood* (22.0). This was followed by the *quite often* group (n=43, medians 39.0, 29.0 and 21.0, respectively) and patients who had *very rarely* hidden their white spots (n=33, medians 39.0, 21.0 and 16.0). The lowest scores were found in the group of patients who had *never* concealed their vitiligo (n=12, medians 20.0, 18.0 and 16.0, respectively). The difference between the four groups was highly significant in all sub-scales of the ACS (***$p<0.001$ as measured with a Kruskal-Wallis-test).

Next we wanted to know whether avoiding situations because of vitiligo makes a difference in coping with this chronic skin disease (**Figure 35**). The results showed that patients who had indeed avoided certain situations because of their vitiligo (n=79), showed much higher median scores in *social anxiety / avoidance (39.0), helplessness* (29.0) and *anxious-depressive mood* (21.0) compared to the 39 patients who had never done this (medians 27.0, 21.0 and 16.0, respectively). The difference between both groups was highly significant in social anxiety / avoidance and *helplessness* (both ***$p<0.001$) and significant in *anxious-depressive mood* (*$p=0.01$, both significances measured with a Mann-Whitney-U-test). The clear difference in the outcome of *social anxiety / avoidance* between both groups of patients provided more validation of this ACS sub-scale, because patients indeed avoided situations when they scored high.

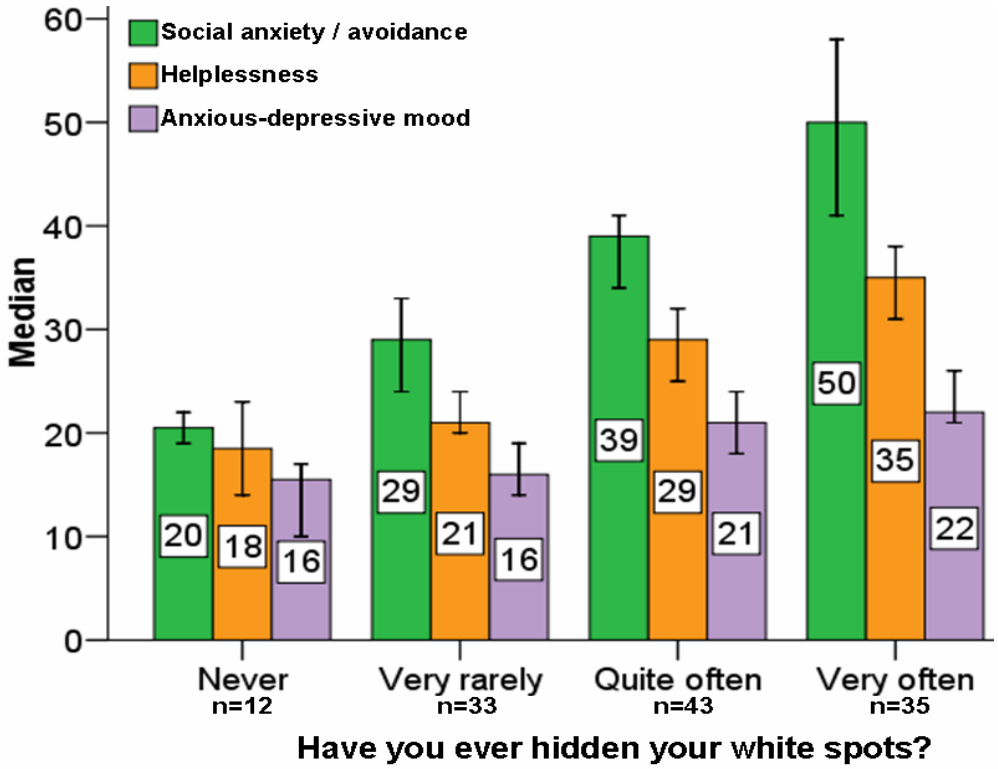


Figure 34: Influence of hiding the disease on median ACS scores

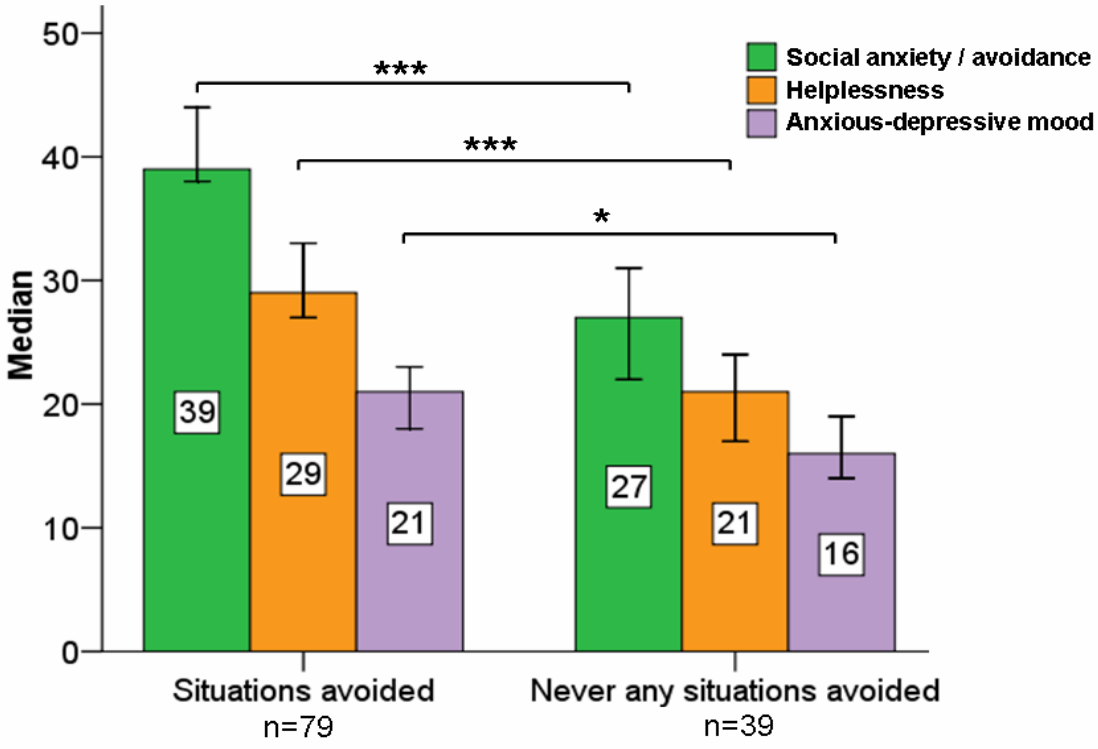


Figure 35: Influence of avoidant behaviour on median ACS scores

6.3.6 Influence of duration of disease

Similar to quality of life it was our interest to find out whether or not patients were more affected by longer duration of vitiligo.

Pearson correlation analysis yielded the following correlation coefficients between duration in years and the ACS scales for our patient group (n=422):

- *Social anxiety / avoidance* 0.03 (p>0.05)
- *Helplessness* -0.41 (p>0.05)
- *Anxious-depressive mood* -0.015 (p>0.05)

Based on these results we can conclude that none of the mentioned ACS sub-scores correlated significantly (positively or negatively) with the duration of the disease (p>0.05). Hence, coping with vitiligo is not influenced by how long the patients actually have vitiligo.

6.3.7 Median ACS scores in several subgroups of patient population

Next we analysed whether any socio-demographic or other characteristics of the patient group influenced the outcome of the ACS questionnaire. This has been done separately for each of the sub-scales.

Table 36 shows the results regarding *social anxiety / avoidance*. Our analysis of this part yielded that basic demographic features such as being younger or older than 35

years, skin colour, presence or absence of a family history of vitiligo and language did *not* influence the results of this scale ($p<0.05$, Mann-Whitney-U-test and 2-sided Independent Sample T-test).

Also, patients who were undergoing treatment with NB-UVB activated pseudocatalase PC-KUS (n=259) showed no difference in their *social anxiety / avoidance* scores compared to new patients (n=164, medians 36.0 vs. 39.0, $p>0.05$, Mann-Whitney-U-test). However, we found that female patients (n=286) scored significantly higher than male patients (n=136). The difference between their medians of 39.0 and 34.0 is significant (*$p<0.05$, Mann-Whitney-U-test).

Interestingly, we found again higher scores in patients who think that *psychological stress* influences vitiligo (n=211) compared to the remaining 81 patients, who did not think so (medians 39.0 vs. 35.0, *$p=0.018$, Mann-Whitney-U-test).

Finally, extended vitiligo on *neck, arms, trunk* and *legs* can make our patients more *socially anxious / avoidant*. Patients with a severe disease scored much higher. Facial vitiligo or heavily affected hands were not of any influence (details in **Table 36**).

Social Anxiety / Avoidance **Subgroups**		N	Mean	Median	SD	p values
Language of questionnaire	German	94	37.4	36.0	13.194	>0.05
	English	69	38.9	36.0	15.382	
Treatment status	New patient	163	39.8	39.0	14.215	>0.05
	Enrolled with IFPD	259	38.1	36.0	13.294	
Gender	Male	136	***35.9*** **	***34.0*** *	12.388	**0.004**(1)
	Female	286	***40.1*** **	***39.0*** *	14.063	**0.006**(2)
Age groups	< 35 years	107	40.0	38.0	14.357	>0.05
	> 35 years	315	38.4	37.0	13.404	
Skin phototypes	I-III	353	38.4	36.0	13.631	>0.05
	IV-VI	69	41.0	42.0	13.688	
Family history	Yes	108	39.1	38.0	13.866	>0.05
	No	176	38.9	37.5	13.884	
Psychological stress influential	Yes	211	***40.1*** *	***39.0*** *	12.702	**0.017**(1)
	No	81	***36.0*** *	***35.0*** *	13.566	**0.018**(2)
Vitiligo caused by injuries	Yes	60	37.7	36.5	12.537	>0.05
	No	97	37.8	36.0	12.983	
Vitiligo caused by other diseases	Yes	24	39.5	36.0	13.891	>0.05
	No	111	37.1	36.0	12.478	
Disease severity (self-assessed) Face	Little	258	39.0	38.0	13.490	>0.05
	Severe	101	40.6	39.0	13.754	
Disease severity (self-assessed) Neck	Little	142	***39.1*** *	***37.0*** *	13.985	**0.049**(1)
	Severe	146	***42.3*** *	***41.0*** *	13.201	**0.043**(2)
Disease severity (self-assessed) Hands	Little	88	38.2	36.0	14.227	>0.05
	Severe	281	39.6	38.0	13.554	
Disease severity (self-assessed) Arms	Little	169	***36.3*** ***	***34.0*** ***	12.875	**<0.001**(1)(2)
	Severe	167	***43.5*** ***	***43.0*** ***	13.344	
Disease severity (self-assessed) Trunk	Little	172	***36.1*** ***	***35.0*** ***	12.238	**<0.001**(1)(2)
	Severe	162	***42.9*** ***	***41.0*** ***	13.866	
Disease severity (self-assessed) Legs	Little	203	***38.1*** **	***35.0*** **	13.508	**0.002**(1)(2)
	Severe	142	***42.6*** **	***41.0*** **	13.429	
Do you do any sports or do you have a hobby?	Yes	95	36.7	35.0	12.945	>0.05
	No	27	40.3	39.0	16.186	

Table 36: Median *Social Anxiety / Avoidance* scores in several subgroups of the patient population
Significances were measured with a 2-sided Independent Sample T-test (1)and a Mann-Whitney-U-test(2).

The results regarding *helplessness* and *anxious-depressive mood* are similar. As shown in **Table 37** and **Table 38**, women with vitiligo (n=286) felt much more helpless and anxious-depressive compared to male patients (n=136). The differences between their median scores (29.0 vs. 26.0 and 21.0 vs. 16.5, respectively) are highly significant (**p<0.005 and ***p<0.001, Mann-Whitney-U-test).

Perceived *psychological stress* was again influential on well-being of our patients. Members of the group who agreed to that this factor is influential (n=211), scored much higher in *helplessness* and *anxious-depressive mood* compared to the remaining 81 patients who did not think so (medians 29.0 vs. 26.0 and 21.0 vs. 17.0). These differences are significant (***p<0.001 in *anxious-depressive mood* and *p<0.05 in *helplessness*, Mann-Whitney-U-test).

The results in **Table 37** and **Table 38** also show that disease severity on different body parts influences coping with vitiligo. Patients with severe vitiligo on their arms and trunk were more *helpless* and *anxious-depressive* compared to those patients with only minor vitiligo. Moreover, when patients had extended vitiligo on their legs, they were also more *helpless* (significances range from ***p<0.001 to *p<0.05, Mann-Whitney-U-test, details in **Table 37** and **Table 38**).

Finally, when we looked at patients who were treating their vitiligo with NB-UVB activated pseudocatalase PC-KUS (n=259), we found them less *anxious-depressive* compared to those patients not undergoing treatment (n=163). The difference between both median scores (19.0 vs. 20.5) was significant (*p<0.05), but this was not the case in *helplessness* (p>0.05, Mann Whitney-U-test).

Helplessness **Subgroups**		N	Mean	Median	SD	p values
Language of questionnaire	German	94	26.7	25.5	7.772	>0.05
	English	69	28.5	28.0	9.198	
Treatment status	New patient	163	28.3	29.0	8.102	>0.05
	Enrolled with IFPD	259	27.3	27.0	8.280	
Gender	Male	136	***25.9*** **	***26.0*** **	7.865	**0.003**(1)(2)
	Female	286	***28.5*** **	***29.0*** **	8.267	
Age groups	< 35 years	107	28.9	28.0	8.713	>0.05
	> 35 years	315	27.3	27.0	8.008	
Skin phototypes	I-III	353	27.5	27.0	8.064	>0.05
	IV-VI	69	28.8	29.0	8.910	
Family history	Yes	108	27.8	27.0	7.633	>0.05
	No	176	28.2	29.0	8.773	
Psychological stress influential	Yes	211	***28.8*** *	***29.0*** *	7.947	**0.005**(1)
	No	81	***25.8*** *	***26.0*** *	8.183	**0.013**(2)
Vitiligo caused by injuries	Yes	60	27.8	26.5	7.793	>0.05
	No	97	27.9	29.0	8.622	
Vitiligo caused by other diseases	Yes	24	29.2	30.0	8.283	>0.05
	No	111	27.1	27.0	8.500	
Disease severity (self-assessed) Face	Little	258	28.0	28.0	8.272	>0.05
	Severe	101	28.0	28.0	8.360	
Neck	Little	142	27.9	28.0	8.384	>0.05
	Severe	146	28.8	29.5	8.208	
Hands	Little	88	27.2	27.0	8.071	>0.05
	Severe	281	28.0	28.0	8.231	
Arms	Little	169	***26.7*** **	***26.0*** **	7.669	**0.002**(1)(2)
	Severe	167	***29.5*** **	***30.0*** **	8.395	
Trunk	Little	172	***26.8*** *	***27.0*** *	8.032	**0.024**(1)
	Severe	162	***28.8*** *	***29.0*** *	8.343	**0.038**(2)
Legs	Little	203	***27.3*** *	***27.0*** *	7.861	**0.04**(1)
	Severe	142	***29.1*** *	***29.0*** *	8.315	**0.032**(2)
Do you do any sports or do you have a hobby?	Yes	95	27.1	26.0	8.139	>0.05
	No	27	28.3	30.0	9.272	

Table 37: Median Helplessness scores in several subgroups of the patient population
Significances were measured with a 2-sided Independent Sample T-test (1) and a Mann-Whitney-U-test(2).

Anxious-depressive mood **Subgroups**		N	Mean	Median	SD	p values
Language of questionnaire	German	94	20.4	20.0	6.368	>0.05
	English	69	19.6	18.0	7.993	
Treatment status	New patient	163	***21.3****	***20.5****	7.001	**0.009**(1)
	Enrolled with IFPD	259	***19.5****	***19.0****	6.279	**0.023**(2)
Gender	Male	136	***18.2*****	***16.5*****	6.286	**<0.001**
	Female	286	***21.2*****	***21.0*****	6.560	
Age groups	< 35 years	107	20.9	20.0	6.924	>0.05
	> 35 years	315	20.0	20.0	6.511	
Skin phototypes groups	I-III	353	20.2	20.0	6.505	>0.05
	IV-VI	69	20.2	20.0	7.229	
Family history	Yes	108	20.3	20.0	6.268	>0.05
	No	176	20.5	20.5	7.217	
Psychological stress influential	Yes	211	***21.4*****	***21.0*****	5.948	**<0.001**(1)(2)
	No	81	***17.5*****	***17.0*****	6.103	
Vitiligo caused by injuries	Yes	60	20.3	20.0	5.565	>0.05
	No	97	19.3	20.0	6.610	
Vitiligo caused by other diseases	Yes	24	21.4	22.0	7.672	>0.05
	No	111	19.0	19.0	6.062	
Disease severity (self-assessed) Face	Little	258	20.6	20.0	6.422	>0.05
	Severe	101	20.0	19.0	6.231	
Neck	Little	142	20.4	21.0	6.544	>0.05
	Severe	146	21.2	20.0	6.483	
Hands	Little	88	20.6	20.0	7.047	>0.05
	Severe	281	20.5	20.0	6.376	
Arms	Little	169	***19.0*****	***19.0*****	6.006	**<0.001**(1)(2)
	Severe	167	***21.9*****	***22.0*****	6.645	
Trunk	Little	172	***19.1*****	***19.0*****	6.250	**<0.001**(1)(2)
	Severe	162	***21.7*****	***22.0*****	6.333	
Legs	Little	203	20.0	20.0	6.357	>0.05
	Severe	142	21.2	21.0	6.940	
Do you do any sports or do you have a hobby?	Yes	95	19.9	19.0	6.851	>0.05
	No	27	20.6	20.0	7.313	

Table 38: Median *Anxious-depressive Mood* scores in several subgroups of the patient population
Significances were measured with a 2-sided Independent Sample T-test (1) and a Mann-Whitney-U-test(2).

6.4 Beck Depression Inventory (BDI)

6.4.1 Comparison of patients and healthy controls

Since there is no agreement in the literature about the role of depression in vitiligo, it was our interest to find out, how depressive our patients are compared to healthy controls.

A direct comparison of both groups' scores yielded that the median BDI score of the patients (5.0, n=123) was higher than in the control group (3.0, n=51, *p=0.02, Mann-Whitney-U-test). However, comparison of the means (6.8 vs. 5.1) showed no significant difference (p>0.05, Independent Sample T-test, **Table 39**).

Since the skewness coefficient is 1.114, there is no normal distribution of our patients' BDI scores.

Taken together, we can conclude that our patients are generally more depressed than healthy controls.

Groups	N	Mean	Median	SD	p value
Patients	123	6.8	***5.0****	6.689	>0.05(1)
Healthy controls	51	5.1	***3.0****	7.242	**0.02**(2)

Table 39: BDI scores in patients with vitiligo and healthy controls
Significances were measured with 2-sided Independent Sample T-test(1) and Mann-Whitney-U-test(2).

A more detailed assessment of whether patients are more depressed is based on the distribution of cases throughout the BDI categories (not depressed, moderately depressed, etc). The results of this analysis are presented in **Table 40** showing that less patients than controls are in the *no depression* category (72.4% / n=89 vs. 82.4% / n=42) and more patients than controls are *mild-moderately depressed* (21.1% / n=26 vs. 13.7% / n=7) and *moderately-severely depressed* (5.7% / n=7 vs. 2.0% / n=1). However, these differences are not statistically significant as measured with the Pearson Chi-Square test ($p>0.05$, **Table 40**).

Taken together, patients with vitiligo are more depressed compared to healthy controls. However, the difference is statistically weak and cannot be confirmed by distribution analysis of cases in the BDI categories.

BDI categories		Patients	Healthy controls
No depression	N	89	42
	%	72.4	82.4
Mild-moderate depression	N	26	7
	%	21.1	13.7
Moderate-severe depression	N	7	1
	%	5.7	2.0
Severe depression	N	1	1
	%	0.8	2.0
	Total N	**123**	**51**

Table 40: Frequencies of cases in BDI categories in patients and healthy controls

6.4.2 BDI scores in several subgroups of the patient population

Next we loked at differences between demographic or other subgroups of our patient group.

The results are listed in **Table 41** and show that most of the characteristics were not influential on levels of depression, i.e. age group, skin colour, presence / absence of a family history of vitiligo, Koebner phenomenon and disease severity on most of the body parts (all $p>0.05$, Mann-Whitney-U-test).

However, we found a median score of 7.0 of our female patients (n=77), which was much higher than the median score of our male patients (2.5, n=46). This difference is highly significant (**$p=0.001$, Mann-Whitney-U-test).

Since there was a strong effect of perceived psychological stress on DLQI and ACS scores, we were interested whether this was also the case in the BDI. The results further supported that there is indeed a strong effect, because patients, who believed that psychological stress is influential (n=44), scored much higher in the BDI compared to those patients who did not think so (n=24). The difference between the median scores (8.0 vs. 2.5) is highly significant as measured with a Mann-Whitney-U-test (***$p<0.001$, **Table 41**).

As mentioned above, disease severity on different body parts proved not to be influential, apart from the trunk. Patients with extended vitiligo on their trunk (n=36) were much more depressed compared to patients with only minor vitiligo (n=50) based on their median BDI scores (7.0 vs. 3.0, *$p=0.008$, Mann-Whitney-U-test).

Interestingly, patients who used the German-language questionnaire (n=72) scored higher in the BDI than those who filled out the English version (n=49, medians 7.0 vs. 3.0, *$p=0.013$, Mann-Whitney-U-test). This difference was not observed in the other questionnaires.

Beck Depression Inventory **Subgroups**		N	Mean	Median	SD	p values
Language of questionnaire	German	72	7.7	***7.0****	6.552	>0.05(1)
	English	49	5.6	***3.0****	6.849	**0.013**(2)
Treatment status	New patient	74	7.7	6.5	7.374	0.06
	Enrolled with IFPD	49	5.4	3.0	5.267	
Gender	Male	46	***4.5****	***2.5****	5.913	**0.003**(1)
	Female	77	***8.2****	***7.0****	6.782	**0.001**(2)
Age groups	< 35 years	37	6.1	4.0	6.464	>0.05
	> 35 years	86	7.1	5.5	6.802	
Skin phototypes	I-III	100	6.8	5.0	6.272	>0.05
	IV-VI	21	7.0	2.0	8.746	
Family history	Yes	37	5.7	4.0	5.851	>0.05
	No	81	7.3	5.0	6.871	
Psychological stress influential	Yes	44	***9.1****	***8.0****	6.703	**<0.001**(1)(2)
	No	24	***3.4****	***2.5****	3.437	
Vitiligo caused by injuries	Yes	30	6.4	5.0	5.957	>0.05
	No	36	6.5	5.0	5.710	
Vitiligo caused by other diseases	Yes	9	6.8	5.0	7.085	>0.05
	No	44	6.6	5.0	5.955	
Disease severity (self-assessed) – Face	Little	76	6.5	4.0	6.865	>0.05
	Severe	32	7.7	7.0	6.855	
Disease severity (self-assessed) – Neck	Little	38	7.4	5.0	6.533	>0.05
	Severe	35	6.5	5.0	7.640	
Disease severity (self-assessed) – Hands	Little	26	7.0	6.0	6.155	>0.05
	Severe	78	6.8	4.5	6.688	
Disease severity (self-assessed) – Arms	Little	48	6.1	4.0	5.904	>0.05
	Severe	43	7.3	6.0	7.210	
Disease severity (self-assessed) – Trunk	Little	50	***4.6****	***3.0****	5.126	**0.007**(1)
	Severe	36	***8.3****	***7.0****	7.162	**0.008**(1)
Disease severity (self-assessed) – Legs	Little	53	6.5	4.0	6.447	>0.05
	Severe	38	7.5	5.5	7.240	
Do you do any sports or do you have a hobby?	Yes	86	7.0	5.0	7.069	>0.05
	No	22	6.4	5.0	5.473	

Table 41: BDI scores in several subgroups of the patient population
Significances were measured with a 2-sided Independent Sample T-test (1) and a Mann-Whitney-U-test(2).

6.4.3 Influence of gender

As already shown in **Table 41**, female patients showed significantly increased BDI scores compared to males. Therefore, we wanted to know how female and male patients are distributed throughout the BDI categories. We performed crosstabulation (**Table 42**), which revealed that many more women than men are *mild-moderately depressed* (29.9% / n= 23 vs. 6.5% / n=3) and more men than women are *not depressed* (87.0% / n=40 vs. 63.9% / n=49). There are no differences regarding *moderate-severe depression* and *severe depression*. The differences in all categories between women and men are significant as measured with the Pearson Chi-Square test (*p=0.016).

Based on the median scores and the distribution of cases in the BDI categories, we can conclude that women with vitiligo are generally more depressed compared to male patients.

BDI categories		Gender	
		Male	Female
Not depressed	N	**40**	**49**
	%	87.0	63.6
Mild-moderate depression	N	**3**	**23**
	%	6.5	29.9
Moderate-severe depression	N	**3**	**4**
	%	6.5	5.2
Severe depression	N	**0**	**1**
	%	0.0	1.3
Total N		**46**	**77**

Table 42: Distribution of females and males in BDI categories

6.4.4 Influence of age on BDI scores

Our next aim was to find out whether levels of depression of patients with vitiligo depended on their age.

Pearson correlation analysis between age in years and the BDI scores yielded a correlation coefficient of 0.089 (n=123) indicating that there is neither a negative nor positive correlation between BDI scores and age ($p>0.05$).

Next we looked at single *age groups* to test whether the members of any age group are more depressed (**Table 43**). We found indeed a significant difference between the age groups analysed (*$p<0.05$, Kruskal-Wallis-test). However, there is no clear tendency. The lowest BDI score was found in the youngest patients (n=4, <20 years old, median 1.0) followed by the middle-aged patients (30-39 years, n=34, median 4.0 and 40-49 years old, n=42, median 3.0). Interestingly, patients between 20 and 29 years as well as between 60 and 70 years scored highest in the BDI (median 8.5 / n=16 and 9.0 / n=10, respectively).

Taken together, levels of depression do not automatically increase or decrease with age. Teenagers and middle-aged patients were least depressed.

Age groups (years)	N	Mean	Median	SD	p value
<20	4	***1.3***	***1.0***	1.500	
20-29	16	***10.4***	***8.5***	7.126	
30-39	34	***5.7***	***4.0***	5.572	**0.03**[(1)] **0.023**[(2)]
40-49	42	***5.5***	***3.0***	5.899	
50-59	17	***8.0***	***7.0***	7.778	
60-70	10	***10.1***	***9.0***	8.825	

Table 43: BDI scores in different age groups
Significances were measured with a one-way ANOVA test[(1)] (means) and Kruskal-Wallis-test[(2)]

6.4.5 Influence of age of disease onset on BDI scores

It has also been of interest whether age at *disease onset* had any influence on depression. In order to assess this, we performed Pearson correlation analysis, which yielded a correlation coefficient of 0.071 (n=122) again indicating that there is neither a positive nor a negative correlation between BDI scores and age of disease onset ($p>0.05$).

Although there is no linear correlation, it might still be possible that certain age at disease onset *groups* are more prone to depression. Therefore, we examined the BDI scores of each group in more detail. There are apparent differences between patients with a disease onset in their teenage years (12-19 years, n=30, median BDI score 3.5) and patients with an onset after their 40th birthday (40-59 years, n=15, median 7.0, **Table 44**). However, these differences are not significant as measured by a Kruskal-Wallis-test.

Taken together, age at disease onset does not influence levels of depression, because there is neither a linear correlation nor are there any groups of age at disease onset more depressed than others.

Age at onset (years)	N	Mean	Median	SD	p value
0-11	19	6.4	5.0	5.910	
12-19	30	6.2	3.5	6.727	
20-39	57	7.4	5.0	7.114	>0.05
40-59	15	6.7	7.0	6.519	
>60	1	0.00	0.0	--	

Table 44: BDI scores in different groups of age at disease onset
Significances measured with a one-way ANOVA (means) and Kruskal-Wallis-test.

6.4.6 Influence of duration of disease

Next we asked the question whether *duration* of vitiligo has any influence on levels of depression. For this purpose we performed Pearson correlation analysis and calculated a correlation coefficient of 0.011 (n=122) which implied that there is neither a positive nor a negative significant correlation between levels of depression and duration of the disease ($p>0.05$).

6.4.7 BDI and avoidant behaviour

Since there was a strong association between avoidant behaviour, especially hiding white spots, and both the other questionnaires' scores, we wanted to know whether this also applied to the Beck Depression Inventory.

Hiding of white spots correlates with depression

A comparison of median BDI scores depending on frequencies of hiding vitiligo (**Figure 36**) revealed that the more often patients hide their white spots in front of other people the more depressed these patients are. Patients, who had done this *very often,* scored highest in the BDI (median 8.5, n=32), followed by the *quite often* group (median 5.5, n=38) and the *very rarely* group (median 3.0, n=26). The lowest score was found in patients, who had *never* hidden their white spots (median 1.0, n=13). The difference between the scores is highly significant as measured with a Kruskal-Wallis-test (***$p<0.001$).

To further substantiate this finding, we analysed the distribution of patients with different frequencies of hiding vitiligo throughout the BDI categories (**Table 45**). The

results revealed that the more often vitiligo was hidden, the more likely these patients can be found in *mild-moderate-severe depression* categories and less likely in the *not depressed* category. These differences are significant (Pearson Chi-Square test, *p=0.016) (**Table 45**).

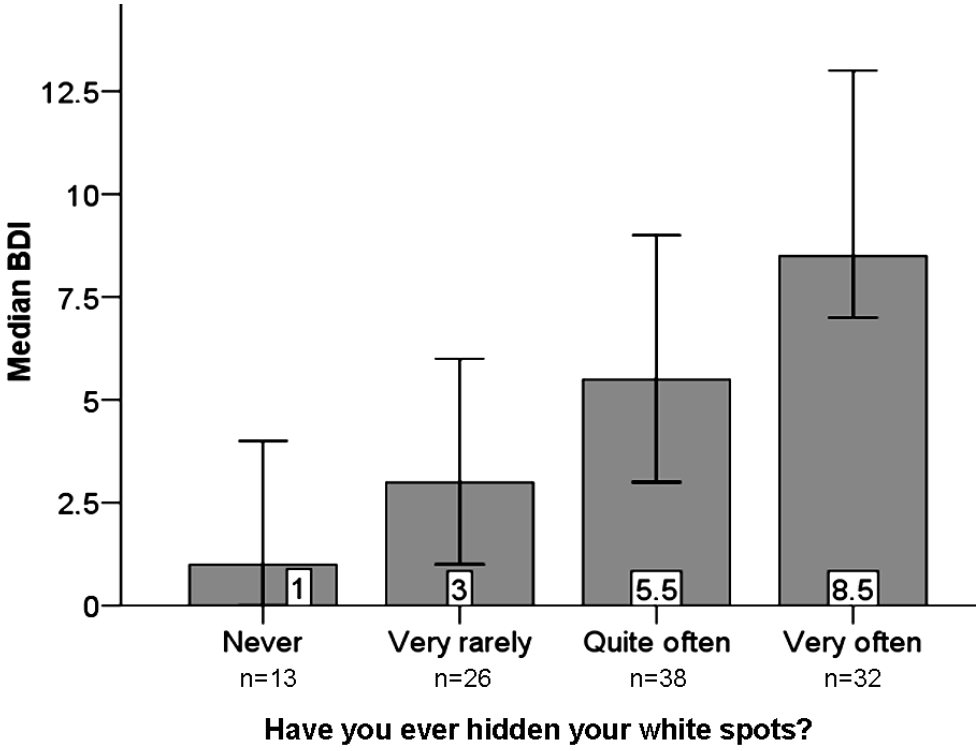


Figure 36: Influence of hiding the disease on median BDI scores

BDI categories		Have you ever hidden your white spots?			
		Never	Very rarely	Quite often	Very often
Not depressed	N	13	24	26	17
	%	100.0	92.3	68.4	53.1
Mild-moderate depression	N	0	2	10	9
	%	0.0	7.7	26.3	28.1
Moderate-severe depression	N	0	0	2	5
	%	0.0	0.0	5.3	15.6
Severe depression	N	0	0	0	1
	%	0.0	0.0	0.0	3.1
Total	**N**	**13**	**26**	**38**	**32**
	%	**100.0**	**100.0**	**100.0**	**100.0**

Table 45: Distribution of patients in BDI categories according to frequency of hiding vitiligo

The second indicator of avoidant behaviour in this thesis is, whether patients had avoided *situations* because of their vitiligo. In order to find out whether such behaviour could influence depression levels, we compared the median BDI scores of patients who had avoided situations (5.5, n=70) to those who had never done this (3.0, n=35). The difference between both scores was significant (*p<0.05, Mann Whitney-U-test). There is no significantly different distribution of both groups in the BDI categories (data not shown, p>0.05, Pearson Chi-Square test).

It can be concluded that patients with vitiligo, who tend to avoid situations because of their disease, are more depressed.

Subgroups		N	Mean BDI	Median	SD	p value
Have you ever avoided certain situations because of your vitiligo?	Yes	70	***7.7******	***5.5****	7.158	<0.001(1)
	Never	35	***4.7******	***3.0****	4.892	<0.034(2)

Table 46: BDI and avoidant behaviour
Significances were measured with a 2-sided Independent sample T-test (1) and a Mann-Whitney-U-test(2).

6.5 The outcome of our study

Finally, we wanted to know whether the results from the three adult questionnaires utilised in this thesis were supporting one another. In order to achieve this aim, we employed Pearson correlation analysis for each questionnaire against the two other questionnaires.

The results are shown in **Table 47**. We found a positive correlation for all items of interest (**p<0.005).

Taken together, patients with vitiligo had an impaired *quality of life* along with increased levels of *social anxiety / avoidance, helplessness, anxious-depressive mood* and *depression*. This result indicates that patients are most likely affected in multiple ways.

	DLQI	Social Anxiety / Avoidance	Helplessness	Anxious-depressive mood	BDI
DLQI	--				
Social Anxiety / Avoidance	**0.768**** (n=164)	--			
Helplessness	**0.676**** (n=164)	**0.840**** (n=422)	--		
Anxious-depressive mood	**0.565**** (n=164)	**0.659**** (n=422)	**0.615**** (n=422)	--	
BDI	**0.527**** (n=122)	**0.517**** (n=122)	**0.475**** (n=122)	**0.661**** (n=122)	--

Table 47: Correlations of all questionnaires with one another (Pearson correlation coefficients)

6.6 Children patient population and control group

6.6.1 Controls

Eighteen children without vitiligo or other skin diseases served as controls. 13 were girls and 5 were boys. They were enrolled with a private paediatric practice and were treated for diseases not affecting the skin. The mean age of the control group was 9.3 years, median 9 years ranging from 6 to 13 years. All controls were German-speaking and had fair skin phototypes II or III (Fitzpatrick classification).

The control group was *sex*-matched to our patient group ($p>0.05$, Chi-Square test), but different regarding

- *age* (slightly younger, $p=0.022$, Independent Sample T-Test; $p=0.026$, Mann-Whitney-U-test),
- *language* ($p<0.001$, Chi-Square test) and
- *skin phototypes* ($p=0.003$, Chi-Square test).

6.6.2 Children / adolescents of the patient group

A total of 103 children and adolescents, aged from 5 to 17 years (mean age 11.1, median 11.0 years, SD 3.226) took part in this project. Fourty were boys (38.8 %) and 63 were girls (61.2 %).

The majority of participants (n=79, 76.7%) was not enrolled with the Institute for Pigmentary Disorders. The remaining 24 children (23.3%) were already enrolled and

undergoing treatment for vitiligo using narrow-band UVB activated pseudocatalase PC-KUS.

The German-language questionnaire was used by 61 participants (59.2%), whereas the remaining 42 children used the English-language questionnaire (40.8%).

The majority of participating children had fair skin phototypes I-III (69.3%, n=70/101). About one third (n=31, 31%) had the darker skin phototypes IV to V (**Figure 37**).

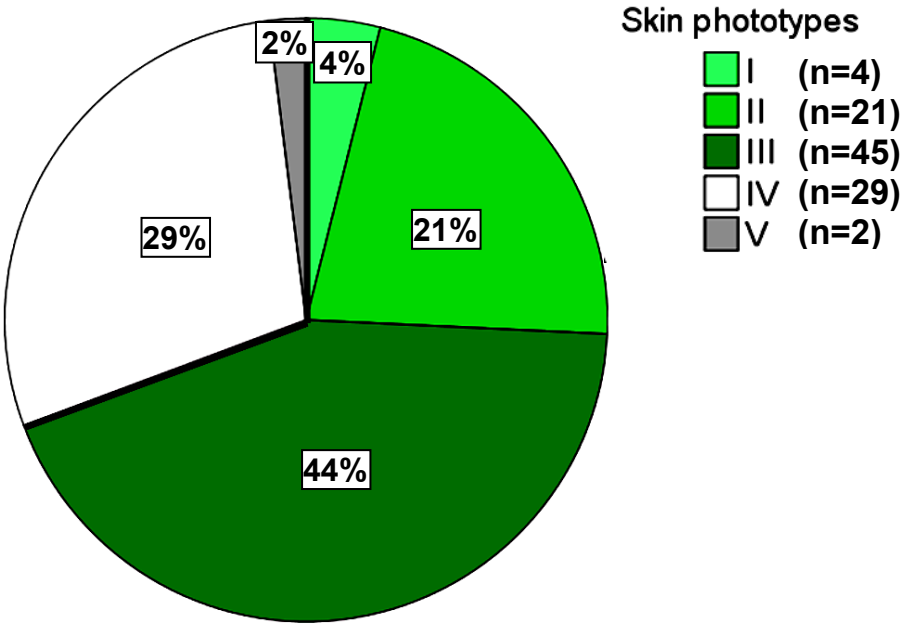


Figure 37: Distribution of skin phototypes in the patient population (n=101, n=2 missing)

6.6.3 Disease severity

Disease severity was assessed by the parents. The results revealed that the *legs* were most often mentioned as *severely* affected, followed by *trunk* and *hands*. Least often mentioned were *face* and *arms* (**Table 48**).

Body parts affected		N	%
Face	1	58	72.5
	2	22	27.5
	Total	**80**	**100.0**
Not affected or missing		23	
Total		103	
Neck	1	29	59.2
	2	20	40.8
	Total	**49**	**100.0**
Not affected or missing		54	
Total		103	
Hands	1	26	45.6
	2	31	54.4
	Total	**57**	**100.0**
Not affected or missing		46	
Total		103	
Arms	1	38	59.4
	2	26	40.6
	Total	**64**	**100.0**
Not affected or missing		39	
Total		103	
Trunk	1	36	45.0
	2	44	55.0
	Total	**80**	**100.0**
Not affected or missing		23	
Total		103	
Legs	1	27	32.5
	2	56	67.5
	Total	**83**	**100.0**
Not affected or missing		20	
Total		103	

Table 48: Disease severity in children as assessed by their parents

1- Slightly affected, 2- Severely affected

6.6.4 Disease onset in children

Similar to the adults, we wanted to find out where the first spot appeared on the affected child. It was our special interest whether this was also predominantly on exposed parts as it was documented in the adult population. The location most often mentioned by the parents was the *trunk* (20.3%, n=12), followed by the *legs* (15.3%, n=9) and equally *knees* and *head* (10.2%, n=6 each). Least often mentioned as single body parts were *hands* and *feet* (**Table 49**).

In conclusion, the most common sites of disease onset in children were not the exposed parts as in the adult group.

Body parts	N	%
Trunk	12	20.3
Legs	9	15.3
Knees	6	10.1
Head	6	10.1
Back	5	8.5
Arms	3	5.1
Genitals	3	5.1
Neck	3	5.1
Feet	2	3.4
Trunk + face	2	3.4
Legs + anogenital area	2	3.4
Neck + genitals	1	1.7
Back + grey hair	1	1.7
Knees + grey hair	1	1.7
Legs + back	1	1.7
Trunk + genitals	1	1.7
Hands	1	1.7
Total	**59**	**100.0**
Missing	44	
Total	103	

Table 49: Sites of disease onset in the children population

6.6.5 Leisure time activities

Besides typical demographic data we also wanted to know more about children's leisure time. The main aim was to identify possible coping resources, for instance number of friends or active / passive leisure time activities.

Leisure time is strongly connected to friendships. The question how many *best friends* the children had, was answered by only one child with *'none'* (1%), 35 said they had *'a few'* (32%) and about two thirds of the children had *'many'* (n=67, 65%). There was no significant difference to the group of healthy children (p>0.05, Chi-Square test, **Figure 38**), where 33% (n=6) had *a few* friends and 61% (n=11) had *many* friends. One child of the control group also had no friend (6%).

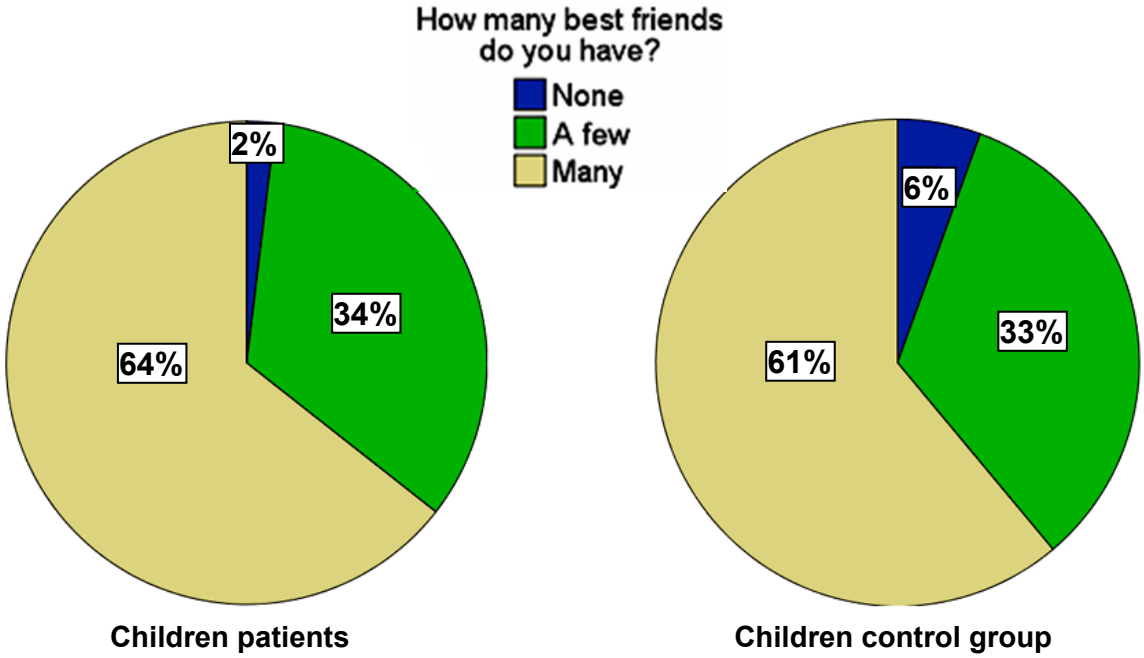


Figure 38: Numbers of best friends of patients (n=103) and healthy controls (n=18)

The vast majority (n=90/101, 89.3%) of our children confirmed that they had *a hobby* or that they did *sports* in their leisure time. Only 11 children (10.7%) denied this. There was no difference between girls and boys (n=35/40, 87.5% vs. n=55/61, 89.1%, respectively, p>0.05, Pearson Chi-Square test) (**Figure 39**).

Importantly, our young patients did not do significantly less sport / hobbies compared to healthy controls (89.1%, n=90/101 vs. 100%, n=18, p>0.05, Pearson Chi-Square test, **Figure 39**).

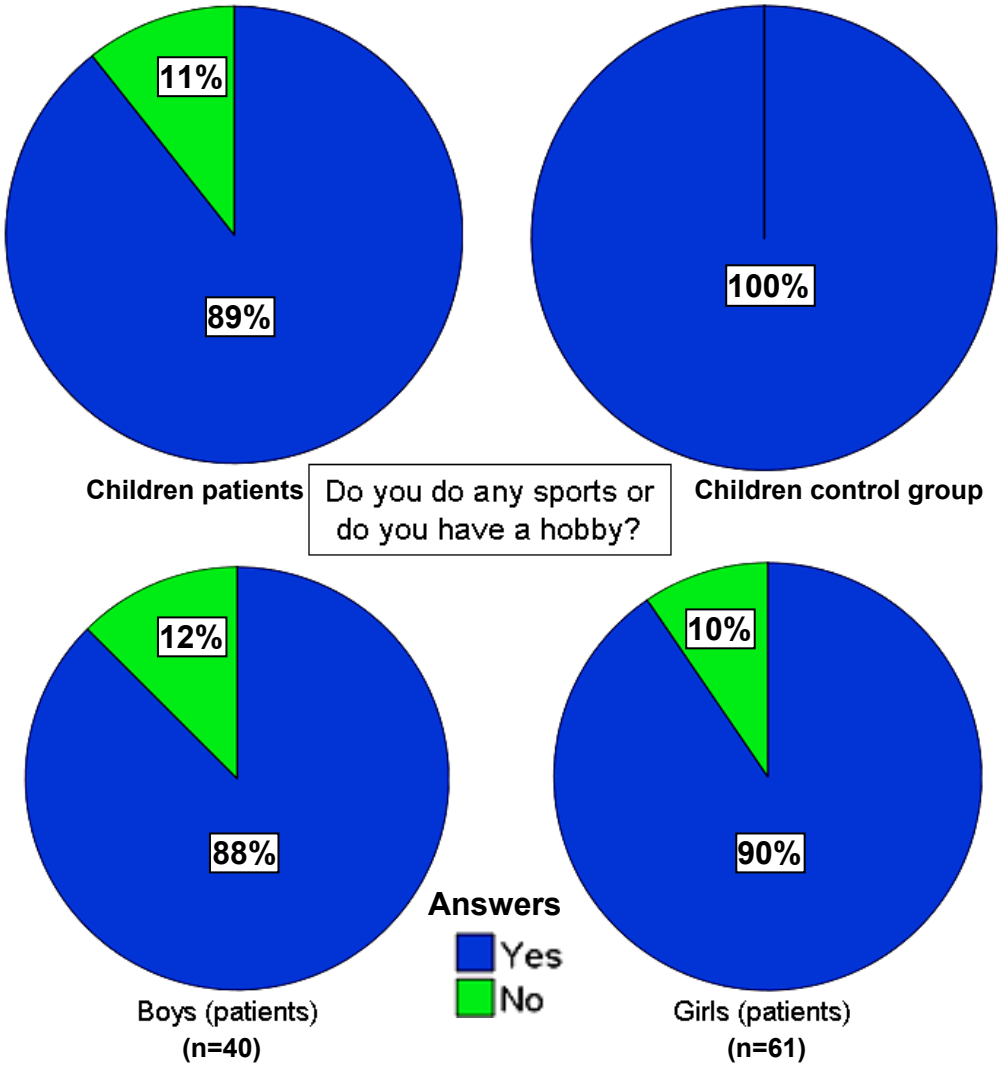


Figure 39: Sports / hobbies in boys and girls of the patient group (n=101) and healthy controls (n=18)

We then looked at how many different hobbies / sports our children were involved in our children's lives. Data were available from 66/90 children with an actively spent leisure time. 24 participants neither stated what they did nor how many hobbies they had. About half of the former group had *one* hobby / preferred sport (n=36/66, 54.5%). More than one quarter (n=19/66, 28.9%) had two hobbies. Only a few children were very active as indicated by claiming 4 or more hobbies or sports (n=3/66, 4.5%, **Table 50**).

Numbers of hobbies	N	%
1	36	54.5
2	19	28.9
3	8	12.1
4	1	1.5
6	2	3.0
Total	**66**	**100.0**

Table 50: Frequencies of how many hobbies children stated

Next we wanted to know what exactly our children did in their leisure time. The results are listed in **Table 51** and indicate that there is a striking diversity of activities. Importantly, sportive activities, where vitiligo patches might be revealed to others, were on the top of the list, i.e. *football* (7.6%, n=5), *gymnastics* (6%, n=4), *martial arts* and *dancing* (each n=4, 6%).

Hobbies or sports mentioned	N	%
Football	5	7.6
Gymnastics	4	6.1
Martial art	4	6.1
Dancing	4	6.1
Dancing + making music	3	4.5
Handball	3	4.5
Football, gymnastics	2	3.0
Ballet	2	3.0
Swimming	2	3.0
Fitness, tennis	2	3.0
Football, tennis	2	3.0
Hip hop, dancing	1	1.5
Swimming, gymnastics	1	1.5
Swimming, riding, trampoline, equestrian vaulting, reading, playing	1	1.5
Judo, football	1	1.5
Riding, dancing, animals and plants	1	1.5
Basketball, singing, dancing	1	1.5
Riding, judo	1	1.5
Playing the clarinet, judo	1	1.5
Tennis	1	1.5
Chess	1	1.5
Riding	1	1.5
Hockey	1	1.5
Tennis, cycling, snowboarding	1	1.5
Dancing, riding	1	1.5
Reading	1	1.5
Inline-skating	1	1.5
Kart racing, martial art	1	1.5
Gymnastics, cycling, playing the violin	1	1.5
Scouting + badmington + dance	1	1.5
Basketball, football, fishing, rugby, swimming, watching TV	1	1.5
Tennis + playing the piano	1	1.5
Karate	1	1.5
Surfing, tennis, snowboarding	1	1.5
Basketball	1	1.5
Playing the piano, organ, writing	1	1.5
Fishing	1	1.5
Swimming, horse riding	1	1.5
“Bosseln” (unique east Frisian road sport)	1	1.5
Athletics	1	1.5
Dancing, badmington	1	1.5
Socialising	1	1.5
Football, tennis, cricket, rugby	1	1.5
Running	1	1.5
Total	**66**	**100.0**

Table 51: Distribution of hobbies and sportive activities in our children group

We then analysed which season of the year the children liked best. We hoped to get a hint, whether they particularly liked or disliked those seasons (spring, summer) when short clothes might reveal their vitiligo to others (**Figure 40**). A comparison of both groups yielded a significant difference between patients and healthy children with, unexpectedly, *patients* preferring summer and spring (n=80/99, 80.8% vs. n=9/18, 50.0%). There were no differences regarding autumn and winter. Overall, the differences between patients and controls are highly significant (***p<0.001, Pearson Chi-Square test).

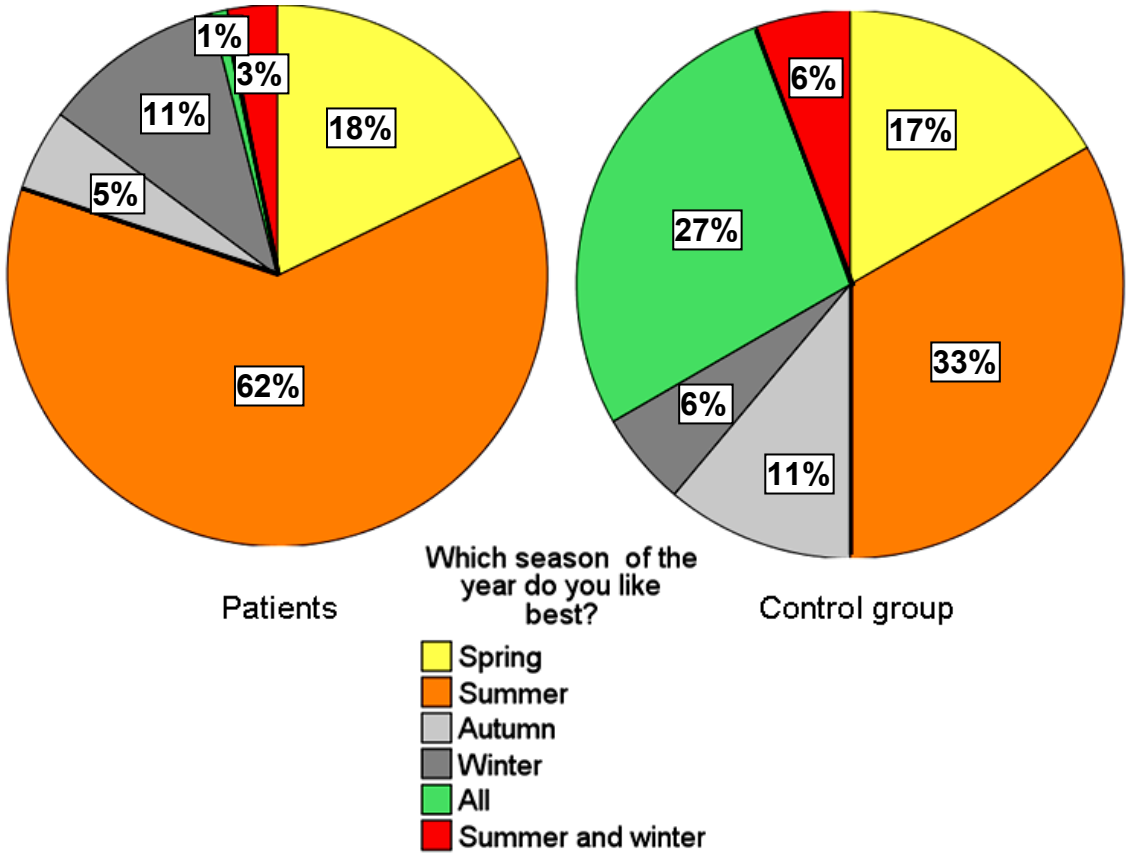


Figure 40: Analysis of the preferred seasons of the year in children patients (n=99) and healthy controls (n=18)

However, interpretation of these results need to be done with caution, since our control group were children who had other diseases at the time of our investigation. This could lead to a false difference, especially with regards to their attitudes to the seasons.

6.6.6 Family history and affected relatives

To establish how many participants had somebody else in the family with vitiligo is important when searching for possible (e.g. genetical) causes for the disease. We found a positive family history of vitiligo in **33%** (n=34) of participating children. Similar to the adult group, *mothers* and *fathers* were mentioned most often (20.6% / n=7 and 14.9% / n=5). **Table** 52 shows a breakdown who else in the families had vitiligo.

	N	%
Mother	7	20.6
Father	5	14.9
Sister / brother	4	11.8
Grandfather	4	11.8
Aunt	3	8.8
Grandmother	2	5.9
Father & sibling	2	5.9
Father and aunt	1	2.9
Grand aunt	1	2.9
Mother + father	1	2.9
Uncle	1	2.9
Mother + grandmother	1	2.9
Cousin + grandfather	1	2.9
Mother + sibling	1	2.9
Total	**34**	**100.0**

Table 52: List of family members who also had vitiligo

6.6.7 Earlier treatments for vitiligo

At the time when the participants filled out the questionnaires, only 8.7% (n=9) of all children had not been to a doctor because of their vitiligo. Of those 94 children who went to a doctor, 81% (n=76) had received some kind of treatment for vitiligo. When asked about which treatment modality was tried, a broad range of more or less successful treatment modalities was mentioned by the children (**Table 53**).

This variety of treatment modalities reflects the current situation for patients with vitiligo. Many methods are attached to one of the hypotheses which try to explain vitiligo. As long as there is no scientific agreement on what exactly causes vitiligo, many treatments will remain available on the market.

Treatment modalities	N	%
'Cream'	10	13.6
Steroids	6	8.1
Radiation	6	8.1
UVB light	3	4.1
Elidel	3	4.1
Protopic	3	4.1
Homoeopathy	3	4.1
Dermavate	2	2.7
Cream and light	2	2.7
Dr. Shimshoni (Germany)	2	2.7
Protopic, UVB light, Dr. Matschurat (Germany)	2	2.7
Vitamins, steroids, radiation	2	2.7
UVB, Dead Sea	2	2.7
Protopic + Elidel	2	2.7
'Unanni' /Indian treatment	2	2.7
Homoeopathy / calcium	1	1.4
Radiation, oxygen, special diet, cream	1	1.4
Vitamins + amino acids	1	1.4
PUVA + Protopic	1	1.4
Tablets	1	1.4
UVB, Protopic, Advantan	1	1.4
Saltwater bath + light therapy	1	1.4
Vitix, Protopic, light	1	1.4
Vitix + light	1	1.4
Elidel + UVB light	1	1.4
UVB, tablets and cream	1	1.4
Folic acid + vitamin B12	1	1.4
Laser	1	1.4
UVB, pseudocatalase, vitamins, supplements	1	1.4
Aloe vera	1	1.4
Vitamins, enzymes, radiation	1	1.4
Laser + cream	1	1.4
Vitix + Elidel + Protopic	1	1.4
Dead Sea	1	1.4
Protopic + Elidel + steroids	1	1.4
Protopic + Tazara	1	1.4
Protopic + Elidel + steroids + UVB light	1	1.4
Others	1	1.4
Total	**73**	**100.0**

Table 53: Treatments received earlier by participating children

6.6.8 Attitudes towards vitiligo

An important part of this project was to find out what the children think about their disease. Besides the Children's Dermatology Life Quality Index, we included some direct questions about their thoughts.

The first question was whether our children felt *bothered* by their disease. The answers showed that 29% of the children were *not* bothered by vitiligo (n=30/103). One quarter of the group was indeed *bothered* (25%, n=26), whereas 46% (n=47) felt this *sometimes* (**Figure 41**). If the two latter groups are taken together, then we found that 70% (n=73) felt at least sometimes bothered by their vitiligo.

There was no significant difference between boys and girls ($p>0.05$, Chi-Square test, **Figure 42**).

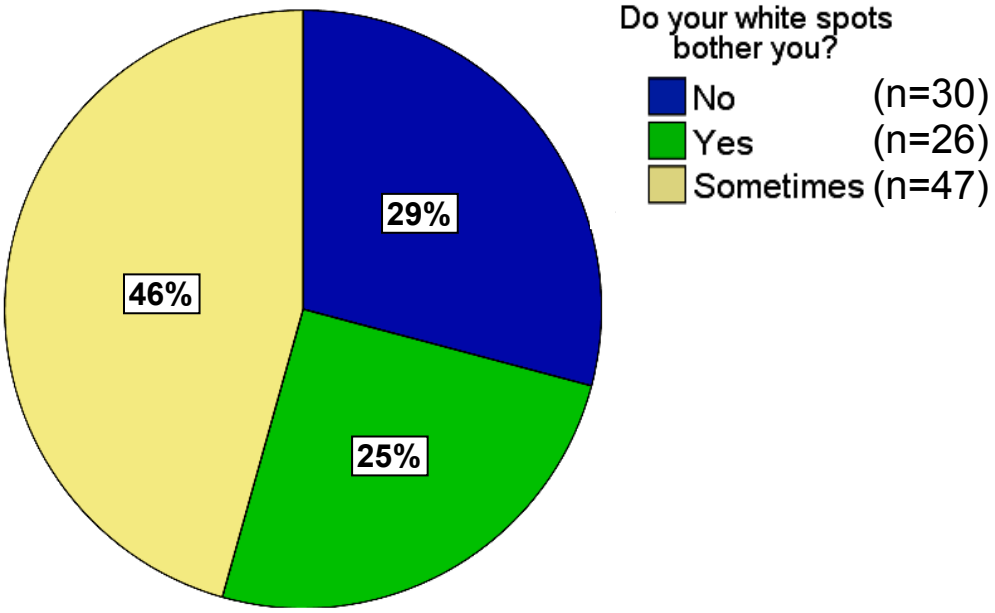


Figure 41: Levels of disturbance in children with vitiligo

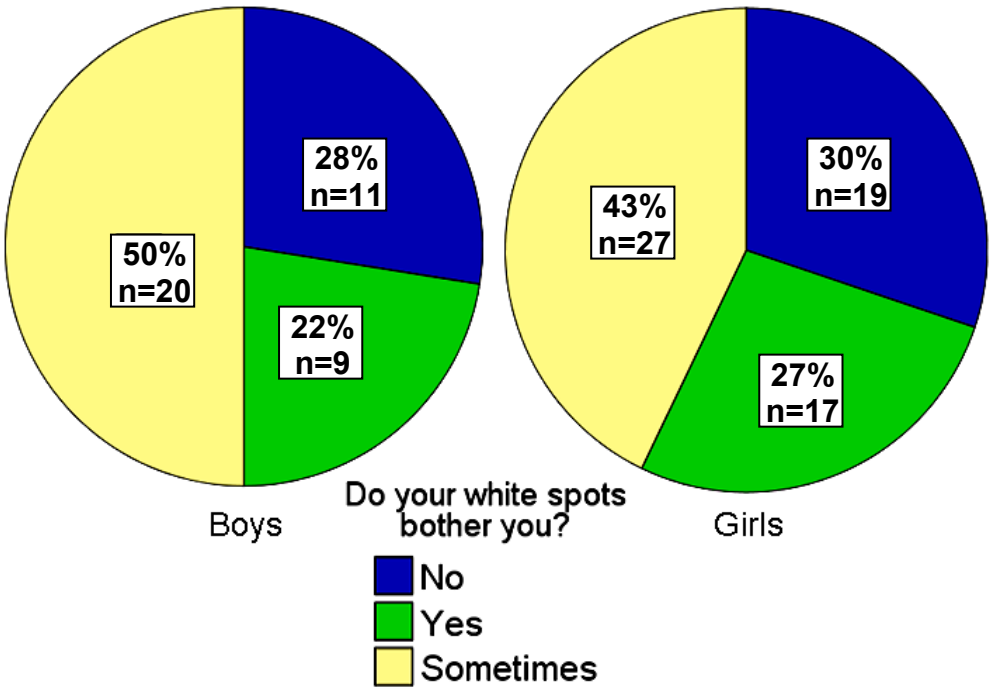


Figure 42: Levels of disturbance in boys (n=40) and girls (n=63) with vitiligo

A rather indirect question was about which spots the children preferred to disappear first. We postulated that the difference between spots *visible to others* and *all spots* might give a hint about the importance of the disease in children's relations to other people (**Table 54**). Three quarters of children (73.5%, n=72/99) wished that *all* of their spots would disappear, only a minority would chose only those visible to others (16.3%, n=16/99). A few children preferred specific spots to disappear, for example *legs* and *trunk+arms* (each 2% / n=2).

Taken together, our results indicate that for the children vitiligo is important as a disease, but it has no strong impact on their inter-personal relationships.

Question	Answers	N	%
If you could have a wish which spots should disappear first?	***All spots***	***72***	***73.5***
	Those visible to other people	***16***	***16.3***
	Others, such as…	***10***	***10.2***
	Legs	*2*	*2.04*
	Trunk + arms	*2*	*2.04*
	Elbows and knees	*2*	*2.04*
	Knees, feet and elbows	*1*	*1.02*
	Knees, lower abdomen	*1*	*1.02*
	Legs, genitals, trunk, hands	*1*	*1.02*
	Genitals	*1*	*1.02*
	Total	**98**	**100.0**
	Missing	**5**	

Table 54: Preferences of children on which spots should disappear first

Finally, we asked how important it was to the children that their white spots disappeared *one day*. Here we hoped to get an impression about basic thoughts about the disease (**Figure 43**). The vast majority of children wished that their white spots would disappear one day (79%, n=79/100, 3 missing). However, 17 children neither wished that nor did they care about it (17%). There was no significant difference between girls and boys as measured with a Pearson Chi-Square test ($p>0.05$**, Figure 43**).

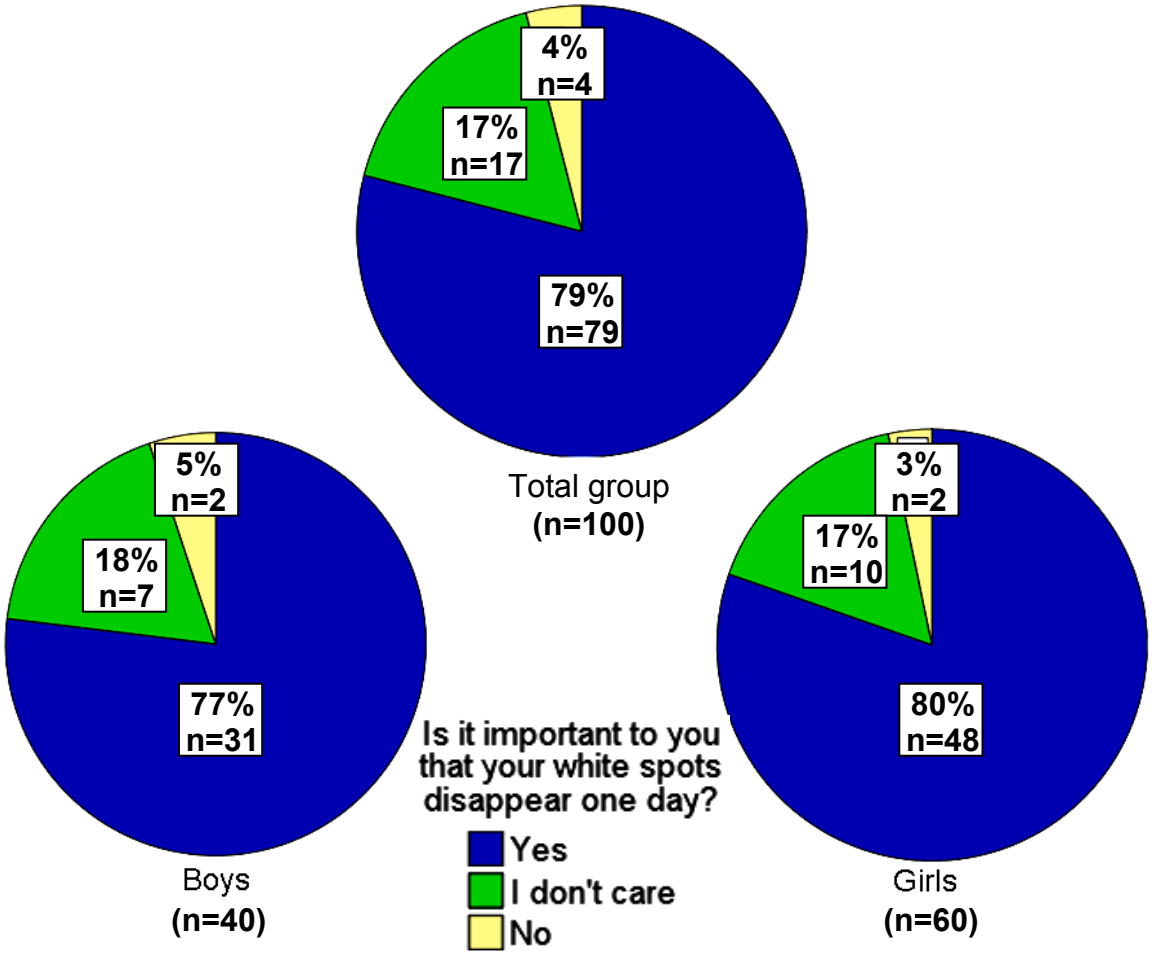


Figure 43: Importance to children (n=100) that the white spots should disappear one day

6.6.9 Children's behaviour and experiences

This part includes questions about *avoidant behaviour* (as indicator if and how much children's life is limited), and *stigmatisation* (questions by others, nasty comments, bullying, physical violence), because these factors have been shown to be highly influential on quality of life measurements.

In our group there is a clear majority of children who had *never* avoided any situations because of their vitiligo (70.4%, n=69/98, n=5 missing). There are differences between the genders with girls being more likely to avoid situations (38%, n=23/60) compared to boys (16%, n=6/38; *p=0.014, Pearson Chi-Square test) (**Figure 44**).

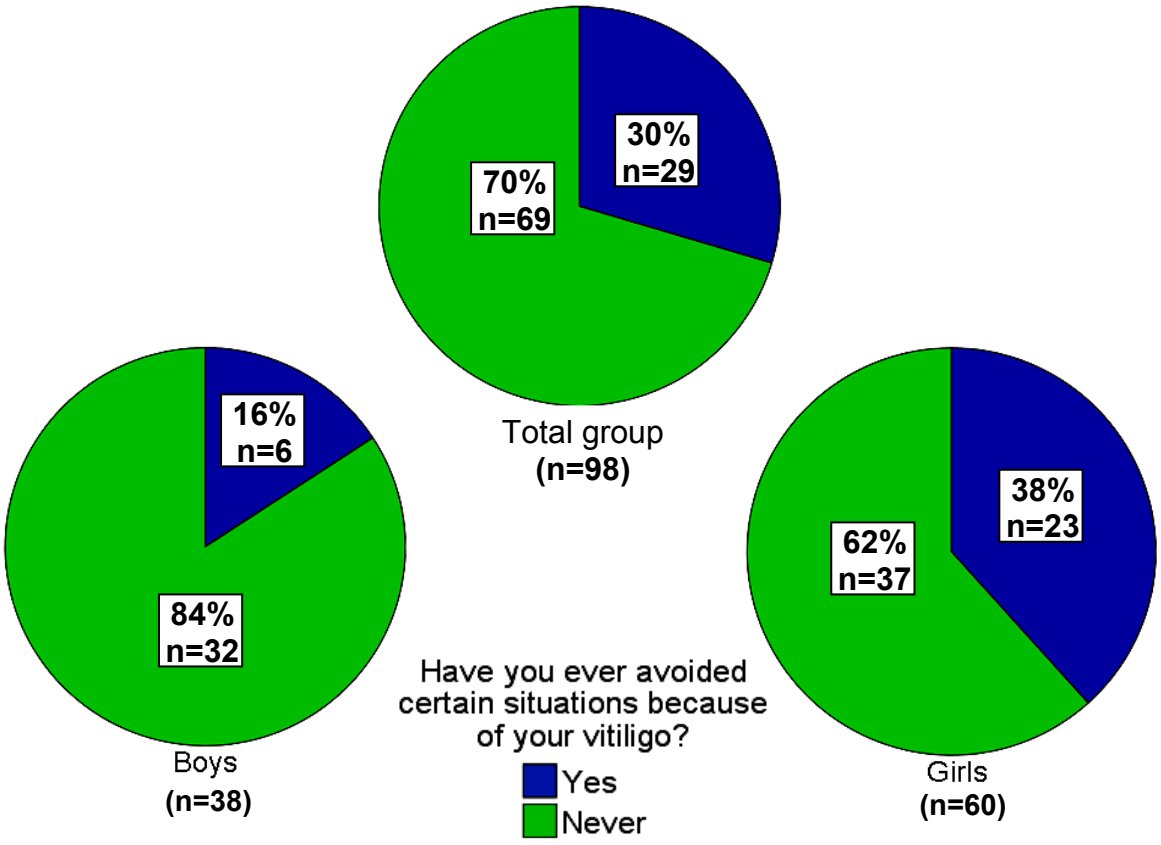


Figure 44: Avoidant behaviour in children with vitiligo (n=98)

Furthermore, we wanted to know which situations exactly were avoided by the children, because this has rarely been reported in the literature.

The children of our group particularly avoided *swimming / bathing* (44.8%, n=13/29), followed by *undressing in changing rooms* (13.8%, n=4/29) and *talking to other people* (7%, n=2/29). Some children stated two or more different situations (**Table 55**).

Question	Answers	N	%
Have you ever avoided certain situations because of your vitiligo?	Swimming / bathing	13	44.8
	Undressing in changing rooms	4	13.8
	Talking to other people	2	7.0
	Swimming / bathing + sports	2	7.0
	Swimming / bathing + undressing in changing rooms	2	7.0
	Doing sports	1	3.4
	Shaking hands	1	3.4
	Avoiding sun in summer	1	3.4
	Swimming / bathing + sports + talking to other people + wearing shorts in summer	1	3.4
	Swimming / bathing + sports + talking to other people + undressing in changing rooms	1	3.4
	Swimming / bathing + shaking hands + undressing in changing rooms	1	3.4
	Total	**29**	**100.0**

Table 55: Frequencies of avoided situations
Multiple answers were possible.

We then looked at possible reasons for avoidant behaviour. Consequently, we set avoidant behaviour in relation to socio-demographic and disease-related characteristics (skin colour, gender, new patients / enrolled with the IFPD etc). There were no differences regarding any of the subgroups (all $p>0.05$, Pearson Chi-Square test) with two exceptions:

Children who felt *bothered* by their vitiligo reported more often to have avoided situations (62.5%, n=15/24) compared to those who did not care about the disease (24.1%, n=7/29). This difference was highly significant (***$p<0.001$, Pearson Chi-Square test, **Table 56**). This result indicates that the question about being bothered has been answered honestly.

			Do your white spots bother you?		
			No	**Yes**	**Sometimes**
Have you ever avoided certain situations because of your vitiligo?	Yes	N	7	15	7
		%	24.1	62.5	15.6
	Never	N	22	9	38
		%	75.9	37.5	84.4
		Total N	**29**	**24**	**45**

Table 56: Avoidant behaviour depending on levels of disturbance by vitiligo

Moreover, we also tested whether avoidant behaviour depended on stigmatising experiences. While there was no relation to *approaches / questions* ($p>0.05$, Pearson Chi-Square test), the picture regarding *nasty comments* is different. The results showed that the more often our children had experienced that they were *picked on*, the more likely they were to avoid situations because of their vitiligo (**Table 57**). Almost two thirds of all children who had been picked on stated that they had avoided situations

(62.5%, n=5/8), whereas this was 17.3% only in the group who were never subjects to nasty comments (n=9/52). This difference was significant as measured with a Pearson Chi-Square test (*p=0.008).

			Have you ever been picked on because of your vitiligo?		
			Yes, very often	**Yes, sometimes**	**No**
Have you ever avoided certain situations because of your vitiligo?	Yes	N	5	15	9
		%	62.5	39.5	17.3
	Never	N	3	23	43
		%	37.5	60.5	82.7
		Total N	**8**	**38**	**52**

Table 57: Avoidant behaviour depending on stigmatising experiences

Although stigmatisation has been shown to be influential on children with vitiligo (Linthorst Homan et al. 2008), this phenomenon has hardly been investigated so far in children with this disease. Therefore, we included questions about how often and what kind of stigmatisation was experienced by our children group.

Importantly, we found that only 6% of participating children (n=6/99) had not experienced that other people *made comments about the white spots* and / or *asked questions* about their disease. A considerable proportion had experienced this even *very often* (41%, n=41/99, **Figure 45**). Girls were more frequently asked questions *very often* compared to boys (46% / n=28/61 vs. 34% / n=13/38), but this difference was not significant (p>0.05, Pearson Chi-Square test).

Taken together, stigmatisation on a low level is a very common experience of boys and girls with vitiligo.

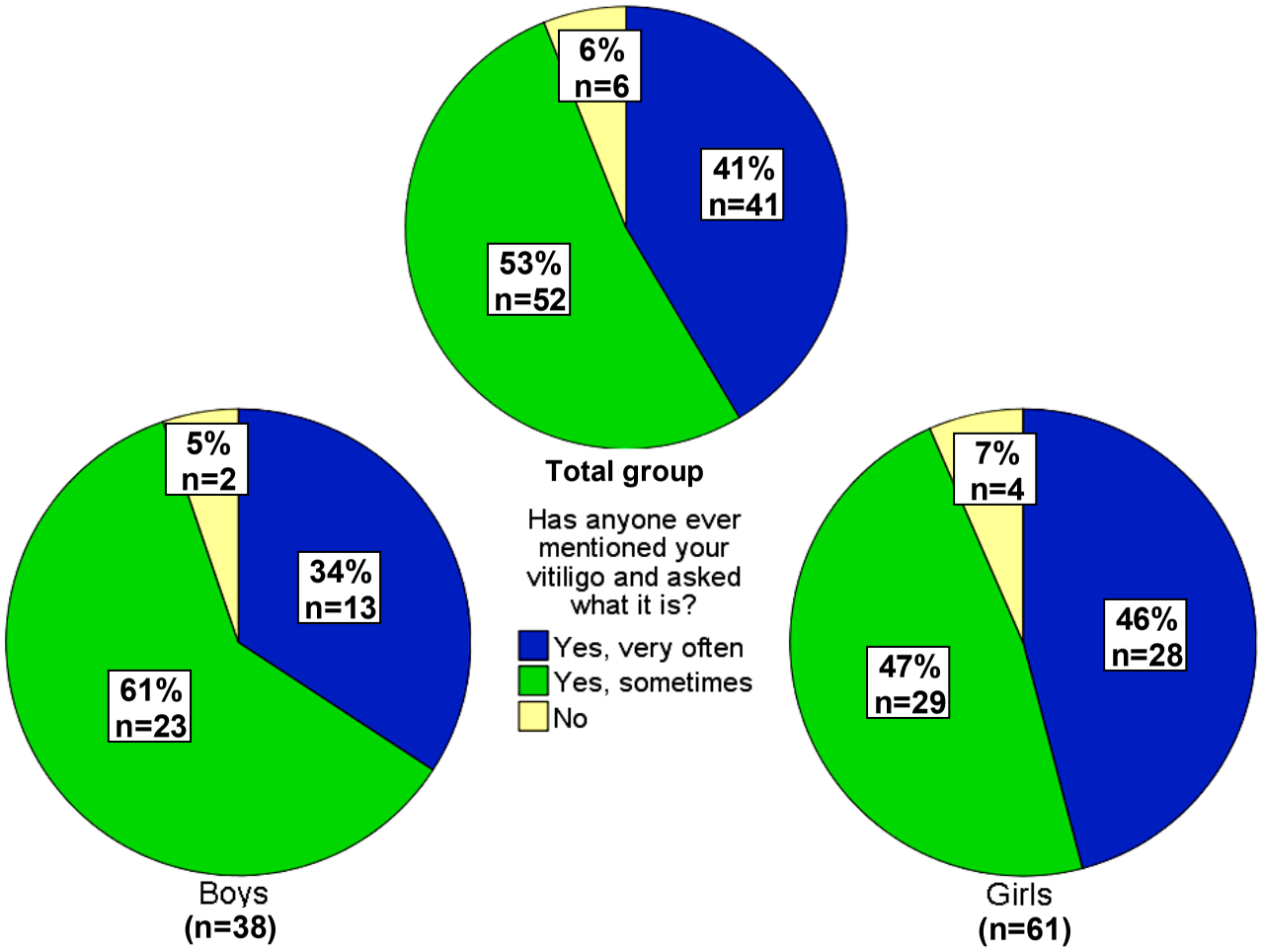


Figure 45: Frequencies of stigmatising experiences (approaches / questions) (n=99)

Experiences of *nasty comments* or that our children were *picked on* were not as frequent as *questions / approaches* by other people. We found that about half of our children group had experienced nasty comments (8% / n=8/99 *very often* and 39% / n=39/99 *sometimes*). Girls (n=61) seemed to have experienced this more frequently (52% / n=32/61 *very often* + *sometimes*) compared to the 38 boys (40%, n=15/38). However, the difference is not significant ($p>0.05$, Pearson Chi-Square test, **Figure 46**).

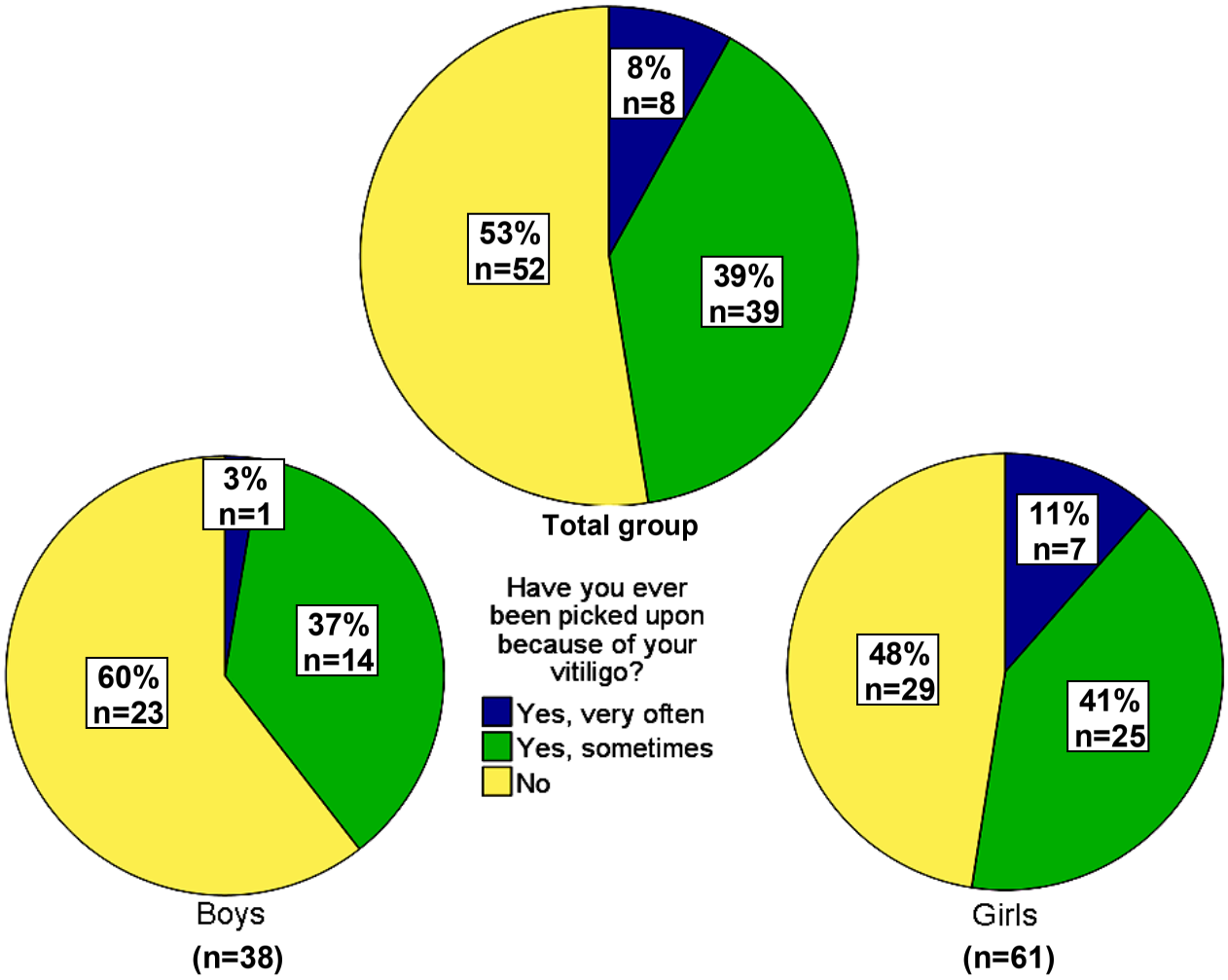


Figure 46: Nasty comments / picking on experienced by children with vitiligo (n=99)

A third indicator of stigmatisation concerns *bullying*. The vast majority of our children had not been bullied because of their vitiligo (81%, n=34/42, **Figure 47**[14]). However, 14% reported that they had been bullied *quite often* (n=6/42) and another 5% said that this happened even *very often* (n=2/42). Nobody of the boys was bullied *very often*, whereas 12% had experienced this *quite often* (n=2/17). The numbers are higher for the girls (8% / n=2/25 *very often* and 16% / n=4/25 *quite often*). Nevertheless, the difference between boys and girls is not significant (p>0.05, Pearson Chi-Square test) (**Figure 47**).

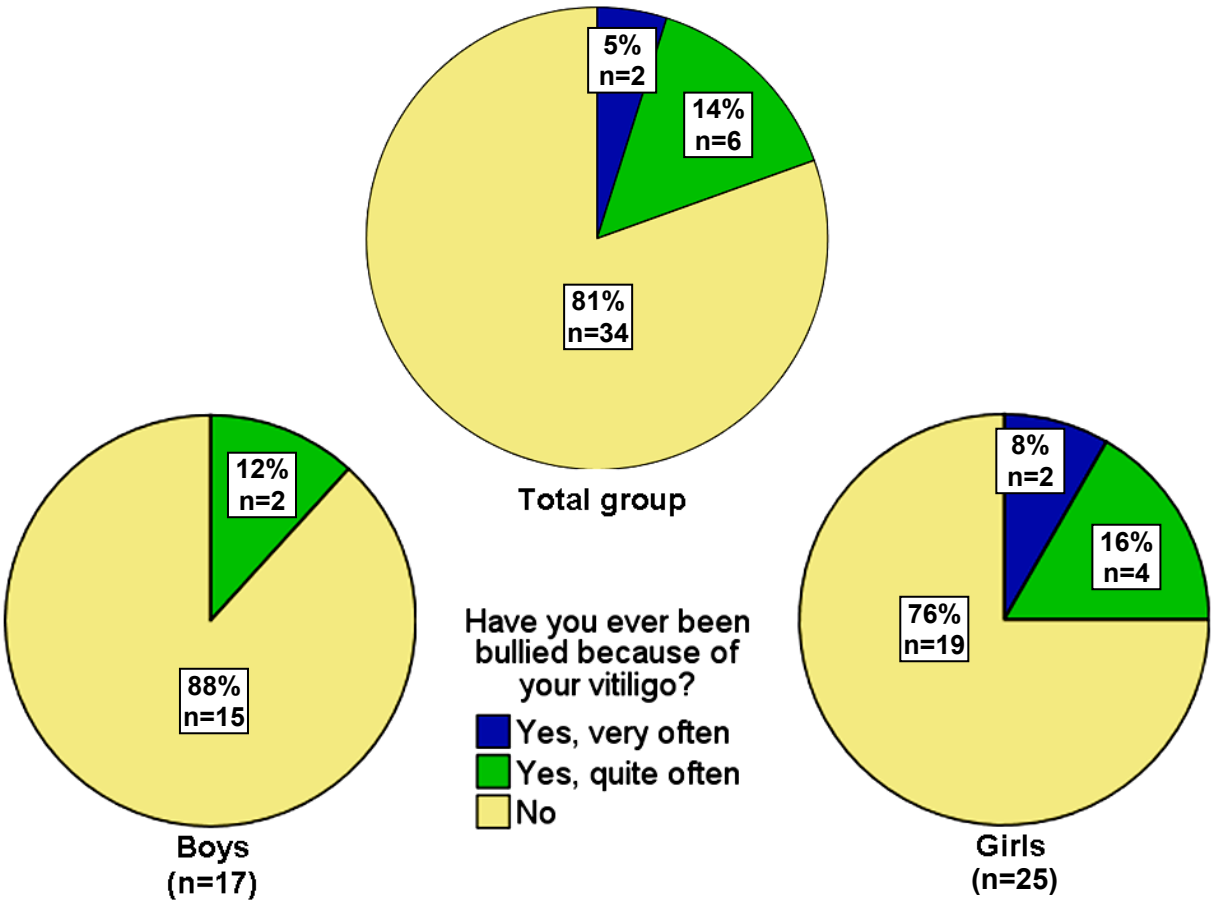


Figure 47: Frequencies of bullying because of vitiligo

[14] This question was part of the English-language questionnaire only

Almost no child had ever experienced *physical violence* because of its vitiligo. One child out of the 56 German children, who were exclusively asked this question, reported to have been beaten once. Taken together, physical violence because of vitiligo among children is extremely rare.

6.6.10 Support

We had not only the intention to obtain data on (negative) experiences, but also on levels of support our children received. Support by other people seems to be important, for example to prevent situations from escalating or to prevent or limit any long-term effects on a child's emotions.

We therefore asked our children, who exactly supported them in those situations when they were being bullied, picked on or otherwise subject to stigmatisation. **Table 58** shows who mostly came to help the children. The results revealed that about one third of children with vitiligo had *never* experienced support in critical situations (30.8%, n=24/78). Secondly, if support was given by somebody, *friends* and *members of the family* were the most important sources of help in those situations (first three ranks n=47/54, 87%, **Table 58**). Occasionally, other persons were mentioned, for example *teachers* (n=3), *strangers* or a *clerk in a department store* (each n=1).

		N	%
Have you ever received help in those situations of being picked upon or being bullied?	***No***	***24***	***30.8***
	Yes, by friends + members of family	18	23.1
	Yes, by friends	17	21.8
	Yes, by members of family	12	15.4
	Yes, by friends + members of family + teachers	3	3.7
	Yes, by others	1	1.3
	Yes, by friends + members of family + strangers	1	1.3
	Yes, by members of family + teachers	1	1.3
	Yes, by members of my family + by a clerk in a department store	1	1.3
	Total	**78**	**100.0**
	Missing	25	
	Total	**103**	

Table 58: List of supporting persons in critical situations

We focussed not only on persons who actually helped children with vitiligo, we also wanted to know who were the preferred contacts in the case of a problem with somebody because of the disease. The majority of our children group would seek support from their *mothers* or their *parents* in general (46.3%, n= 25/54 and 16.7%, n=9/54, respectively). Other sources such as *fathers, teachers* (n=2 each) and *sisters* (n=1) were mentioned less often (**Table 59**).

Only 3 children (5.6%) said that they would not contact anybody when they just had a problem with somebody else because of their vitiligo.

Question	Answer	N	%
Which person would you contact first when you just had a problem with another person because of your vitiligo?	Mother	25	46.3%
	Parents	9	16.7%
	My best friend(s)	5	9.3%
	Mother and best friend	3	5.5%
	I would never tell anybody	3	5.5%
	Family	2	3.6%
	Father	2	3.6%
	Sister	1	1.9%
	Family + school friends	1	1.9%
	Mother + teacher	1	1.9%
	Parents + teachers	1	1.9%
	Best friend + sister	1	1.9%
	Total	**54**	**100.0%**
	Missing	49	
	Total	103	

Table 59: Contacts of first choice for children after critical situations

6.7 Children's Dermatology Life Quality Index scores

6.7.1 CDLQI main score

The Children's Dermatology Life Quality Index has been filled out by 103 children. The mean score for this population was **2.7** (SD 3.504), the median **1.0**. These scores are significantly higher than the ones of the 18 members of the control group (mean **0.6** and median **0.0**, **p=0.004, Mann-Whitney-U-test and *p=0.014, Independent Sample T-test). The patients' scores also showed a wider range (**Figure 48**).

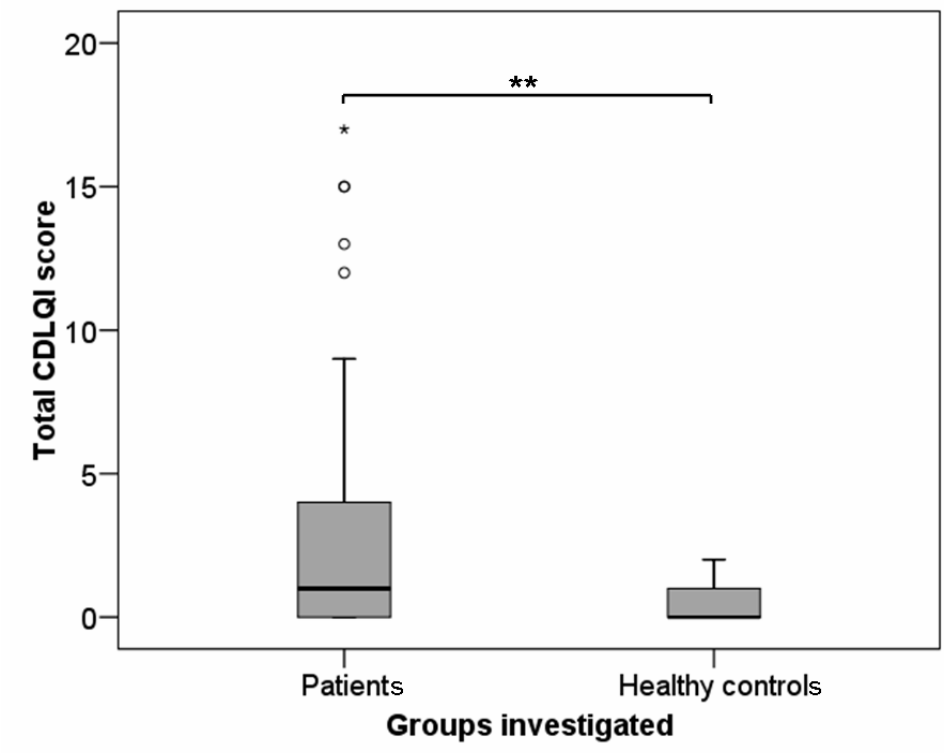


Figure 48: CDLQI scores from children with vitiligo (n=103) and healthy controls (n=18)

We then applied distribution and skewness analysis to obtain more details about the disease-related quality of life of the young patients and controls. **Figure 49** and **Figure 50** show that the scores are clearly positively skewed, which is confirmed by the calculated skewness coefficient of 2.109 for the patients.

This result indicates that there were much more scores below the mean of 2.7 than above. Consequently, the median of 1.0 is the more appropriate number to reflect the central tendency of quality of life in our patient group.

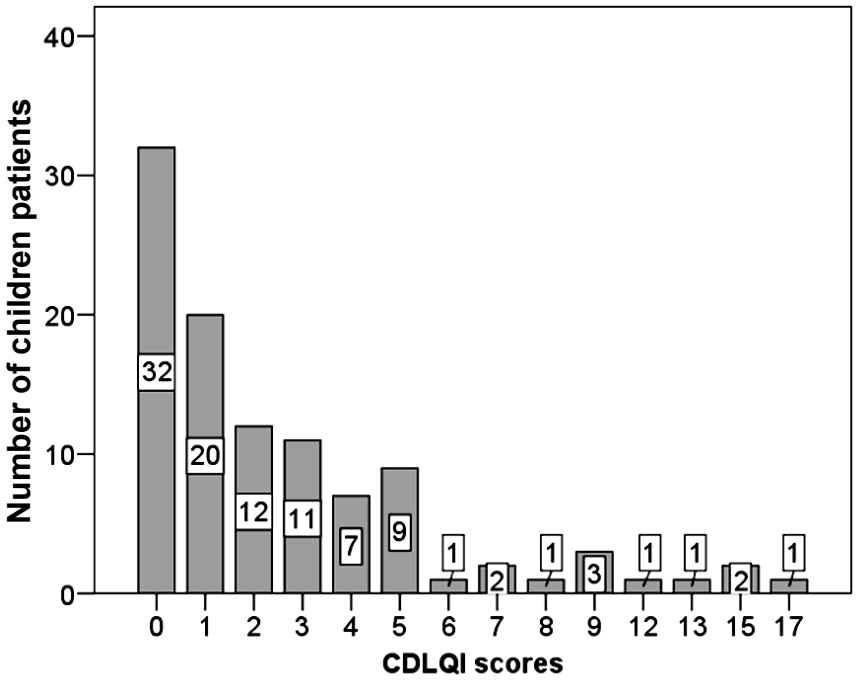


Figure 49: Distribution analysis of CDLQI scores of children with vitiligo (n=103)

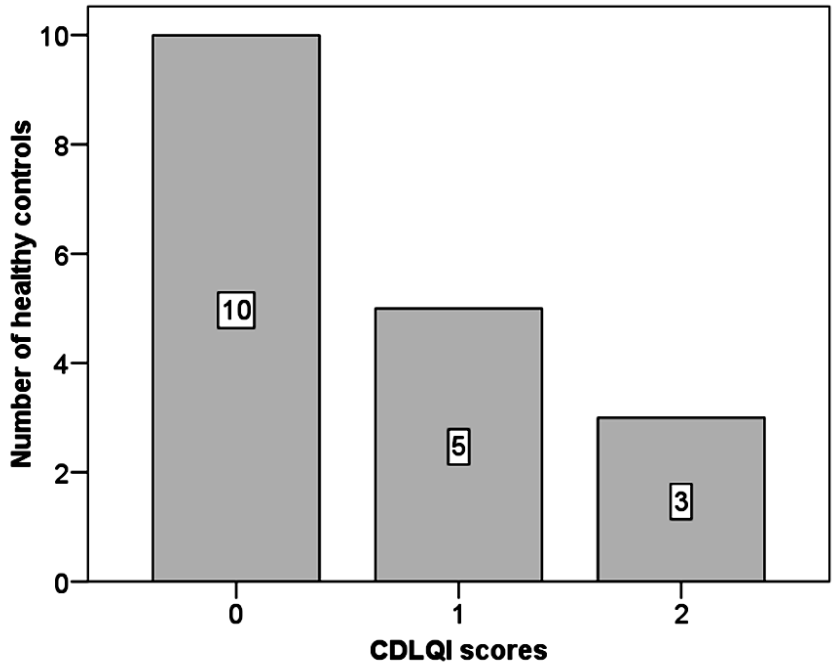


Figure 50: Distribution analysis of CDLQI scores of healthy controls (n=18)

Similar to our adult population, we grouped the children according to their CDLQI scores (**Table 60**). The results revealed that about 88% of our children group are hardly affected in their quality of life (50.5%, n=52 *not affected* and 37.9%, n=39 *minor impairement*). Seven children had a *moderately* impaired quality of life (6.8%), whereas there were only 5 children (4.9%) whose quality of life was *severely affected* by vitiligo (**Table 60**).

CDLQI scores	Impact on quality of life	N	%
0-1	None	52	50.5
2-5	Minor	39	37.9
6-10	Moderate	7	6.8
11-20	Severe	5	4.9
21-30	Extreme	0	0.0

Table 60: CDLQI scores in our patient group (n=103) according to Gajur's grouping order (Gajur 2008)

6.7.2 Single item analysis of the CDLQI for several subgroups of children population

Single item analysis of the CDLQI can provide much more detailed information than the main score alone as each of the 10 questions can be linked to a essential part of children's daily life (friendships, school, going out / playing, wearing of clothes etc). Therefore, all 10 single items were investigated regarding demographic and other factors.

Single item analysis revealed no influence of the following charcteristics on quality of life:

- whether children went to a doctor before,
- whether or not they were enrolled with the Institute for Pigmentary Disorders,
- gender and skin colour,
- how many best friends the children had,
- how important it was to the children that their white spots would disappear one day

(data not shown, all $p>0.05$, Mann-Whitney-U-test and Independent sample T-test).

A comparison of all 103 patients' scores yielded that vitiligo had the strongest effect on *emotional reactions, i.e.* embarrassment, sadness, upset (mean 0.5), followed by *outdoor activities* (0.4 in *swimming / other sports*, 0.3 in *going out / hobbies* and *wearing clothes / shoes*). The least influenced parts were *friendships* (0.0) and *sleep* (0.1). Surprisingly, there was a high score in *physical symptoms* (0.4), even though vitiligo normally does not cause any physical sensations, apart from occasional itching in actively spreading vitiligo (**Figure 51**).

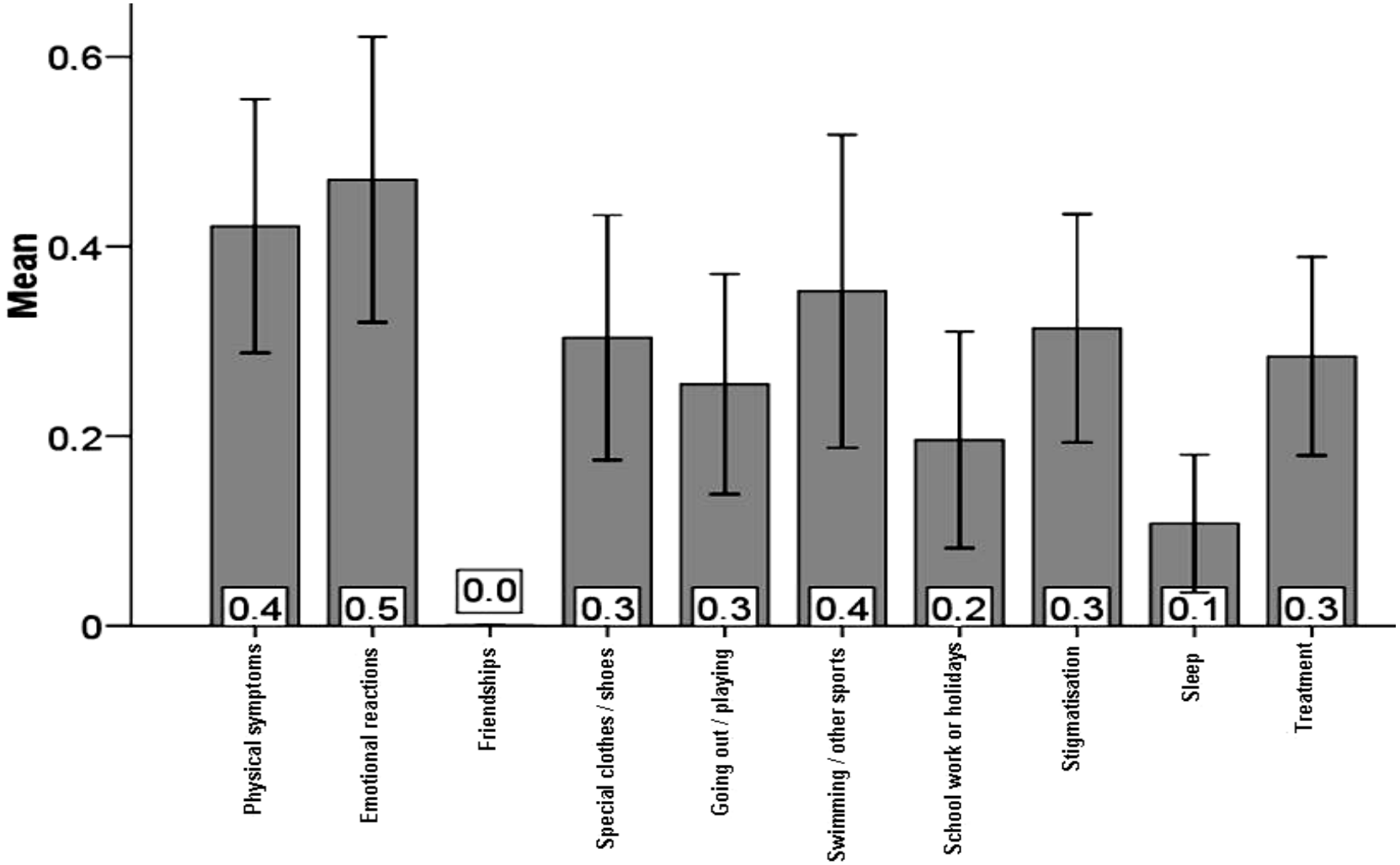


Figure 51: Mean scores in single items of the CDLQI questionnaire (n=103)

Interestingly, when analysing for differences between German and English-speaking children, we found some between both language groups. *Swimming / sport* and *wearing of clothes* were less impaired in German-speaking patients (mean 0.2 each, n=61) compared to their English-speaking counterparts (means 0.6 and 0.5, respectively, n=42). Both differences were significant when measured with a Mann-Whitney-U-test (*p<0.05). There were no other significant differences in any of the other single items and regarding the total CDLQI scores (**Table 61**).

CDLQI items	Language	N	Mean	SD	p value
Question 1	1	61	0.5	.676	>0.05
Physical symptoms	2	42	0.4	.692	
Question 2	1	61	0.6	.851	>0.05
Emotional reactions	2	42	0.3	.612	
Question 3	1	61	0.0	.000	>0.05
Friendships	2	42	0.0	.000	
Question 4	1	61	***0.2****	.537	**0.026**(1)
Clothes / shoes	2	42	***0.5****	.773	**0.013**(2)
Question 5	1	61	0.2	.490	>0.05
Going out / playing	2	42	0.3	.715	
Question 6	1	61	***0.2****	.632	**0.027**(1)
Swimming / other sports	2	42	***0.6****	1.039	**0.025**(2)
Question 7	1	61	0.2	.666	>0.05
School works or holidays	2	42	0.2	.437	
Question 8	1	61	0.3	.541	>0.05
Stigmatisation	2	42	0.4	.701	
Question 9	1	61	0.1	.415	>0.05
Sleep	2	42	0.1	.297	
Question 10	1	61	0.2	.490	>0.05
Treatment	2	42	0.4	.582	
Total CDLQI index	**1**	61	**2.5**	**3.218**	>0.05
	2	42	**3.1**	**3.900**	

Table 61: Analysis of CDLQI regarding language of questionnaire
Significances measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2)
1 – German, 2 - English

We then looked at the influence of an actively spent leisure time on quality of life of our children group. We aimed to test whether quality of life is less impaired in children who do sports or have a hobby. The results showed that the total CDLQI is not influenced. However, single items analysis revealed that children who had a hobby or were doing sports were less affected when it comes to *wearing clothes / shoes, going out / playing, swimming / other sports* and are less likely to perceive the *treatment* as something negative (only regarding means, p values range from 0.052 to *0.029, Independent Sample T-test) (**Table 62**).

Doing sports or having hobbies?		N	Mean	SD	p value
Question 1	Yes	92	0.4	.698	>0.05
Physical symptoms	No	10	0.5	.527	
Question 2	Yes	92	0.5	.762	>0.05
Emotional reactions	No	10	0.5	.850	
Question 3	Yes	92	0.0	.000	>0.05
Friendships	No	10	0.0	.000	
Question 4	Yes	92	***0.3****	.591	**0.044**(1)
Clothes / shoes	No	10	***0.7****	.059	0.158(2)
Question 5	Yes	92	***0.2***	.531	**0.052**(1)
Going out / playing	No	10	***0.6***	.966	0.124(2)
Question 6	Yes	92	***0.3****	.764	**0.029**(1)
Swimming / other sports	No	10	***0.9****	1.287	0.084(2)
Question 7	Yes	92	0.2	.597	>0.05
School works or holidays	No	10	0.2	.422	
Question 8	Yes	92	0.3	.584	>0.05
Stigmatisation	No	10	0.5	.850	
Question 9	Yes	92	0.1	.365	>0.05
Sleep	No	10	0.2	.422	
Question 10	Yes	92	***0.3****	.483	**0.048**(1)
Treatment	No	10	***0.6****	.843	0.149(2)
Total CDLQI index	**Yes**	**92**	**2.5**	**3.164**	>0.05
	No	**10**	**4.7**	**5.677**	

Table 62: Influence of an actively spent leisure time on CDLQI
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

An interesting question was whether children would have a less impaired quality of life if they had somebody else in the family with vitiligo. The idea behind was whether other family members could act as role models and show what could possibly be achieved in life despite having vitiligo.

An analysis of the total CDLQI score and all of its single items yielded no significant differences (p>0.05, Mann-Whitney-U-test), with one exception. Children who had somebody else in the family with vitiligo (n=34) were much less likely to perceive the *treatment as a burden* compared to children with negative family history (n=68, means 0.1 vs. 0.4, *p<0.05, Mann-Whitney-U-test) (**Table 63**).

Positive family history?		N	Mean	SD	p value
Question 1 ***Physical symptoms***	No	68	0.4	.674	>0.05
	Yes	34	0.4	.705	
Question 2 ***Emotional reactions***	No	68	0.5	.743	>0.05
	Yes	34	0.4	.824	
Question 3 ***Friendships***	No	68	0.0	.000	>0.05
	Yes	34	0.0	.000	
Question 4 ***Clothes / shoes***	No	68	0.4	.731	>0.05
	Yes	34	0.2	.459	
Question 5 ***Going out / playing***	No	68	0.3	.638	>0.05
	Yes	34	0.2	.496	
Question 6 ***Swimming / other sports***	No	68	0.5	.937	0.08
	Yes	34	0.2	.558	
Question 7 ***School works or holidays***	No	68	0.2	.497	>0.05
	Yes	34	0.3	.719	
Question 8 ***Stigmatisation***	No	68	0.3	.614	>0.05
	Yes	34	0.3	.618	
Question 9 ***Sleep***	No	68	0.1	.368	>0.05
	Yes	34	0.1	.379	
Question 10 ***Treatment***	No	68	***0.4****	.599	**0.008**(1)(2)
	Yes	34	***0.1****	.288	
Total CDLQI index	**No**	**68**	**3.0**	**3.753**	>0.05
	Yes	**34**	**2.2**	**2.952**	

Table 63: Quality of life depending on family history of vitiligo
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

The next part concerned the question whether treatment for vitiligo received earlier in life (regardless which treatment) would affect quality of life. A comparison of children who were treated in the past (n=76) and those who were not (n=25) yielded that the *treated* group was surprisingly more affected regarding *wearing clothes / shoes, swimming / other sport,* and more likely to think of the current *treatment* as something negative (*p<0.05, Mann-Whitney-U-test). However, the same group's daily life was less impaired in *school works / holiday* (also *p<0.05). In all the other single items no significant differences have been found (**Table 64**).

Ever received treatment?		N	Mean	SD	p value
Question 1	No	25	0.3	.627	>0.05
Physical symptoms	Yes	76	0.5	.700	
Question 2	No	25	0.4	.768	>0.05
Emotional reactions	Yes	76	0.5	.756	
Question 3	No	25	0.0	.000	>0.05
Friendships	Yes	76	0.0	.000	
Question 4	No	25	***0.1****	.277	**0.047**(1)
Clothes / shoes	Yes	76	***0.4****	.730	**0.041**(2)
Question 5	No	25	0.2	.473	>0.05
Going out / playing	Yes	76	0.3	.624	
Question 6	No	25	***0.0****	.000	**0.014**(1)
Swimming / other sports	Yes	76	***0.5****	.945	**0.005**(2)
Question 7	No	25	***0.4****	.764	**0.02**(1)
School works or holidays	Yes	76	***0.1****	.450	**0.005**(2)
Question 8	No	25	0.4	.700	>0.05
Stigmatisation	Yes	76	0.3	.585	
Question 9	No	25	0.2	.577	>0.05
Sleep	Yes	76	0.1	.271	
Question 10	No	25	***0.1****	.277	**0.025**(1)
Treatment	Yes	76	***0.4****	.582	**0.024**(2)
Total CDLQI index	**No**	**25**	**2.1**	**2.798**	>0.05
	Yes	**76**	**2.9**	**3.700**	

Table 64: Influence of earlier received treatment on quality of life
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

An analysis of the influence of disease severity on different body parts yielded no major influence, except for the face. Children with extensive facial vitiligo (n=22) scored significantly higher in the CDLQI and in some of its single items, i.e. *physical symptoms*, *wearing clothes / shoes* and *going out / playing*, compared to participants with only minor vitiligo (n=57, all *p<0.05, Mann-Whitney-U-test) (**Table 65**).

Face affected?		N	Mean	SD	p value
Question 1	1	57	***0.3****	.602	**0.02**(1)
Physical symptoms	2	22	***0.7****	.883	**0.025**(2)
Question 2	1	57	0.4	.704	>0.05
Emotional reactions	2	22	0.6	.902	
Question 3	1	57	0.0	.000	>0.05
Friendships	2	22	0.0	.000	
Question 4	1	57	***0.2****	.455	**0.011**(1)
Clothes / shoes	2	22	***0.6****	.858	**0.013**(2)
Question 5	1	57	***0.1****	.350	**0.001**(1)
Going out / playing	2	22	***0.6****	.854	**0.006**(2)
Question 6	1	57	0.2	.549	**0.035**(1)
Swimming / other sports	2	22	0.6	1.098	>0.05 (2)
Question 7	1	57	***0.1****	.441	**0.02**(1)
School works or holidays	2	22	***0.4****	.908	>0.05 (2)
Question 8	1	57	***0.2****	.423	**0.022**(1)
Stigmatisation	2	22	***0.6****	.959	>0.05(2)
Question 9	1	57	0.1	.426	>0.05
Sleep	2	22	0.1	.351	
Question 10	1	57	***0.2****	.464	**0.025**(1)
Treatment	2	22	***0.4****	.581	>0.05 (2)
Total CDLQI index	**1**	57	***1.9****	2.008	**0.001**(1)
	2	22	***4.6****	5.178	**0.038**(2)

Table 65: Quality of life and severity of facial vitiligo
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

1 – Minor facial vitiligo, 2 - Severe facial vitiligo

We also tested whether there were any differences between boys and girls with severe or minor facial vitiligo. The results showed that girls with severely affected faces (n=8) scored significantly higher in the CDLQI total score (*p<0.05, Mann-Whitney-U-test) and also in its single items *physical symptoms* and *going out / playing* compared to girls with only minor facial vitiligo (n=22). There was no differences in the CDLQI total scores in boys, but rather in the single items *wearing of clothes / shoes* and *stigmatisation* (*p<0.05, Independent Sample T-Test).

Face affected?		Boys					Girls			
		N	Mean	SD	p value		N	Mean	SD	p value
Question 1 ***Physical symptoms***	1	22	0.3	.550	>0.05		35	***0.3****	.639	0.018(1) 0.025(2)
	2	8	0.4	.518			14	***0.9****	.997	
Question 2 ***Emotional reactions***	1	22	0.2	.395	>0.05		35	0.5	.817	>0.05
	2	8	0.4	.744			14	0.8	.975	
Question 3 ***Friendships***	1	22	0.0	.000	>0.05		35	0.0	.000	>0.05
	2	8	0.0	.000			14	0.0	.000	
Question 4 ***Clothes / shoes***	1	22	***0.1****	.294	0.038(1) >0.05 (2)		35	0.2	.531	>0.05
	2	8	***0.5****	.756			14	0.6	.938	
Question 5 ***Going out / playing***	1	22	0.2	.395	>0.05		35	***0.1****	.323	<0.001(1) 0.001(2)
	2	8	0.4	1.061			14	***0.7****	.726	
Question 6 ***Swimming / other sports***	1	22	0.2	.664	>0.05		35	0.2	.473	>0.05
	2	8	0.5	1.069			14	0.6	1.151	
Question 7 ***School works or holidays***	1	22	0.1	.213	>0.05		35	0.2	.531	>0.05
	2	8	0.0	.000			14	0.6	1.082	
Question 8 ***Stigmatisation***	1	22	***0.2****	.395	0.035(1) >0.05(2)		35	0.3	.443	>0.05
	2	8	***0.8****	1.035			14	0.5	.941	
Question 9 ***Sleep***	1	22	0.1	.213	>0.05		35	0.2	.514	>0.05
	2	8	0.0	.000			14	0.2	.426	
Question 10 ***Treatment***	1	22	0.3	.550	>0.05		35	0.2	.406	>0.05
	2	8	0.1	.354			14	0.5	.650	
Total CDLQI index	**1**	**22**	**1.5**	**1.625**	>0.05		**35**	***2.2****	**2.184**	0.004(1) 0.048(2)
	2	**8**	**3.0**	**4.276**			**14**	***5.6****	**5.557**	

Table 66: Differences in CDLQI between girls and boys depending on disease severity in face
Significances were measured with a 2-sided Independent Sample T-test(1) and a Mann-Whitney-U-test(2).

1 - Minor facial vitiligo, 2- Extended facial vitiligo

The following parts concerned different levels of stigmatisation ranging from *approaches / questions* to *picking on / nasty comments* to *bullying*.

Children, who had experienced other people *asking questions* about the disease '*very often'* (n=41), were significantly more affected than those with '*sometimes'* (n=52) and '*no'* (n=6) regarding *school works / holiday* (*p<0.05) and *stigmatising encounters* (**p<0.005, Kruskal-Wallis-test) (**Table 67**). The fact that children, who had experienced stigmatisation, scored high in question 8 (stigmatisation) can be seen as confirmation that the CDLQI can indeed positively identify stigmatisation.

The whole '*very often'* group had a significantly more affected quality of life (median 4.0) compared to the '*sometimes*' (1.9) and '*no*' (1.0) groups (*p<0.05, Kruskal-Wallis-test) (**Table 67**).

Has anyone ever mentioned your white spots and asked what it is?		N	Mean	SD	p value
CDLQI question 1	1	41	0.5	.745	
Physical symptoms	2	52	0.4	.664	>0.05
	3	6	0.3	.516	
CDLQI question 2	1	41	0.7	.879	
Emotional reactions	2	52	0.3	.678	>0.05
	3	6	0.3	.516	
CDLQI question 3	1	41	0.0	.000	
Friendships	2	52	0.0	.000	>0.05
	3	6	0.0	.000	
CDLQI question 4	1	41	0.5	.840	
Clothes / shoes	2	52	0.2	.509	>0.05
	3	6	0.0	.000	
CDLQI question 5	1	41	***0.4****	.808	**0.026**(1)
Going out / playing	2	52	***0.1****	.345	0.058(2)
	3	6	***0.0****	.000	
CDLQI question 6	1	41	0.5	.978	
Swimming / other sports	2	52	0.3	.776	>0.05
	3	6	0.0	.000	
CDLQI question 7	1	41	***0.3****	.762	>0.05(1)
School works or holidays	2	52	***0.1****	.388	**0.033**(2)
	3	6	***0.2****	.408	
CDLQI question 8	1	41	***0.6*****	.808	**0.001**(1)
Stigmatisation	2	52	***0.1*****	.345	**0.002**(2)
	3	6	***0.0*****	.000	
CDLQI question 9	1	41	0.2	.422	
Sleep	2	52	0.1	.334	>0.05
	3	6	0.0	.000	
CDLQI question 10	1	41	0.4	.581	
Treatment	2	52	0.2	.509	>0.05
	3	6	0.2	.408	
Total CDLQI index	**1**	**41**	***4.0****	**4.517**	**0.007**(1)
	2	**52**	***1.9****	**2.378**	**0.015**(2)
	3	**6**	***1.0****	**1.265**	

Table 67: Single item analysis of CDLQI regarding whether or not the children had experienced other people asking questions about the disease
Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1- Yes, very often, 2 – Yes, sometimes, 3 - No

Another level of disease-related stigmatisation are experiences of *nasty comments*. This turned out to be a very influential factor. Children who had been picked on or who had experienced other people being nasty because of vitiligo '*very often'* (n=8) scored much higher in the total CDLQI (**p=0.001) and in a majority of its single items compared to the *sometimes* group (n=39) and the patients who had *not* made these experiences (n=52, p values ranging from **<0.005 to *<0.05, **Table 68**). This was not the case only regarding *physical symptoms, friendships, sleep* and *treatment* (all p>0.05, Kruskal-Wallis-test).

The third indicator of stigmatisation in children was *bullying*. An analysis of its influence on quality of life revealed that children who had received bullying '*very often'* (n=2) were more affected when it comes to *going out / playing* compared to children who were bullied *sometimes* (n=6) or *not* at all (n=34, *p<0.05, Kruskal-Wallis-test) (**Table 69**). There were no significant differences in any of the other single items or regarding the total CDLQI score (all p>0.05, Kruskal-Wallis-test, **Table 69**).

Have you ever been picked upon or has anyone ever been nasty to you because of your white spots?		N	Mean	SD	p value
Question 1	1	8	0.9	.835	
Physical symptoms	2	39	0.5	.756	>0.05
	3	52	0.3	.585	
Question 2	1	8	***1.1*****	.991	**0.001**(1)
Emotional reactions	2	39	***0.7*****	.927	**0.002**(2)
	3	52	***0.2*****	.469	
Question 3	1	8	0.0	.000	
Friendships	2	39	0.0	.000	>0.05
	3	52	0.0	.000	
Question 4	1	8	***1.3*****	1.282	**<0.001**(1)
Clothes / shoes	2	39	***0.3*****	.614	**0.004**(2)
	3	52	***0.2*****	.430	
Question 5	1	8	***1.5*****	1.195	
Going out / playing	2	39	***0.3*****	.442	**<0.001**(1)(2)
	3	52	***0.1*****	.235	
Question 6	1	8	***1.3*****	1.389	**0.003**(1)
Swimming / other sports	2	39	***0.4*****	.938	**0.025**(2)
	3	52	***0.2*****	.561	
Question 7	1	8	***0.9*****	1.356	**0.001**(1)
School works or holidays	2	39	***0.2*****	.522	**0.02**(2)
	3	52	***0.1*****	.334	
Question 8	1	8	***1.0*****	1.414	**<0.001**(1)
Stigmatisation	2	39	***0.4*****	.549	**0.006**(2)
	3	52	***0.1*****	.323	
Question 9	1	8	0.3	.463	
Sleep	2	39	0.1	.384	>0.05
	3	52	0.1	.334	
Question 10	1	8	0.5	.756	
Treatment	2	39	0.4	.628	>0.05
	3	52	0.2	.398	
Total CDLQI index	**1**	**8**	***8.8*****	**6.606**	**<0.001**(1)
	2	**39**	***3.2*****	**3.235**	**0.001**(2)
	3	**52**	***1.4*****	**1.685**	

Table 68: Single item analysis of CDLQI regarding whether or not the children had been picked on or subject to nasty comments
Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1- Yes, very often, 2 – Yes, sometimes, 3 - No

Have you ever received bullying because of your white spots?		N	Mean	SD	p value
Question 1	1	2	0.5	.707	
Physical symptoms	2	6	0.8	1.329	>0.05
	3	34	0.3	.579	
Question 2	1	2	0.5	.707	
Emotional reactions	2	6	0.3	.816	>0.05
	3	34	0.2	.496	
Question 3	1	2	0.0	.000	
Friendships	2	6	0.0	.000	>0.05
	3	34	0.0	.000	
Question 4	1	2	**1.5**	2.121	**0.059**(1)
Clothes / shoes	2	6	**0.7**	.816	>0.05(2)
	3	34	**0.3**	.589	
Question 5	1	2	***1.5*****	2.121	**0.002**(1)
Going out / playing	2	6	***0.8*****	1.169	**0.031**(2)
	3	34	***0.1*****	.327	
Question 6	1	2	1.0	1.414	
Swimming / other sports	2	6	0.5	1.225	>0.05
	3	34	0.5	.929	
Question 7	1	2	0.5	.707	
School works or holidays	2	6	0.0	.000	>0.05
	3	34	0.1	.409	
Question 8	1	2	1.0	1.414	
Stigmatisation	2	6	0.7	1.211	>0.05
	3	34	0.2	.431	
Question 9	1	2	0.0	.000	
Sleep	2	6	0.0	.000	>0.05
	3	34	0.1	.239	
Question 10	1	2	1.0	1.414	
Treatment	2	6	0.2	.408	>0.05
	3	34	0.3	.462	
Total CDLQI index	**1**	**2**	**7.5**	**10.607**	**0.055**(1)
	2	**6**	**4.0**	**4.690**	>0.05(2)
	3	**34**	**2.2**	**2.414**	

Table 69: Single item analysis of CDLQI regarding whether or not the children had received bullying

Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1- Yes, very often, 2 – Yes, sometimes, 3 - No

The last part of the CDLQI single item analysis was the question whether quality of life is measurably impaired in children with different levels of disturbance by their disease. Children, who felt indeed *bothered* (n=26), were significantly more affected in their quality of life than children who are *not* (n=30) or only *sometimes* (n=46) bothered by their vitiligo (CDLQI means 5.1, 2.0 and 1.9, respectively). The differences between the mean and also between the median scores are highly significant (***$p<0.001$, one-way ANOVA and Kruskal-Wallis-test) (**Table 70**).

Moreover, the influence of disturbance by vitiligo was particularly high on the single items *emotional reactions* and *going out / playing* (both ***$p<0.001$), but also on *swimming / sport* and *stigmatisation* (*$p\leq0.05$, Kruskal-Wallis-test).

Do your white spots bother you?		N	Mean	SD	p value
Question 1	1	30	0.4	.615	
Physical symptoms	2	26	0.7	.892	>0.05
	3	46	0.3	.560	
Question 2	1	30	**0.2*** **	.664	
Emotional reactions	2	26	**1.0*** **	.958	**<0.001**(1)(2)
	3	46	**0.3*** **	.519	
Question 3	1	30	0.0	.000	
Friendships	2	26	0.0	.000	>0.05
	3	46	0.0	.000	
Question 4	1	30	0.3	.691	
Clothes / shoes	2	26	0.5	.859	>0.05
	3	46	0.2	.453	
Question 5	1	30	**0.3***	.785	**0.007**(1)
Going out / playing	2	26	**0.5***	.647	**<0.001**(2)
	3	46	**0.1***	.285	
Question 6	1	30	**0.2***	.664	**0.027**(1)
Swimming / other sports	2	26	**0.7***	1.116	**0.01**(2)
	3	46	**0.2***	.705	
Question 7	1	30	0.1	.254	
School works or holidays	2	26	0.4	.898	>0.05
	3	46	0.2	.486	
Question 8	1	30	0.2	.679	>0.05(1)
Stigmatisation	2	26	0.5	.761	**0.051**(2)
	3	46	0.2	.431	
Question 9	1	30	0.1	.507	
Sleep	2	26	0.2	.368	>0.05
	3	46	0.1	.250	
Question 10	1	30	0.2	.504	
Treatment	2	26	0.5	.647	>0.05
	3	46	0.2	.467	
Total CDLQI index	**1**	**30**	***2.0**** **	**3.643**	
	2	**26**	***5.1**** **	**4.408**	**<0.001**(1)(2)
	3	**46**	***1.9**** **	**1.996**	

Table 70: Single item analysis of CDLQI regarding how the children felt bothered by their white spots

Significances were measured with a one-way ANOVA test(1) and a Kruskal-Wallis-test(2).

1 – No, 2 - Yes, 3 - Sometimes

6.7.3 Correlation of CDLQI with duration of the disease

Since there are conflicting reports in the literature about a correlation between duration of disease and adult DLQI, we wanted to know whether or not there is such correlation in the children population.

Pearson correlation analysis of CDLQI scores and duration of disease yielded a correlation coefficient -0.087 (2-tailed significance $p>0.05$), meaning that the total score of the CDLQI does not correlate with duration of vitiligo.

The single items of the CDLQI do also not correlate with duration, neither positively nor negatively (Pearson correlation coefficients ranging from -0.162 to +0.115, 2-tailed significance always $p>0.05$), except for **question 7** (*school works or holiday*) where the Pearson correlation coefficient is -0.194 (2-tailed significance $*p=0.05$), indicating that there is a weak negative correlation between duration of vitiligo and level of affected school work or holidays. The longer the children had vitiligo the less their schoolwork / holiday was affected.

6.8 Children and their parents

6.8.1 Parents' characteristics

At the same time when children filled out their questionnaire, we also asked the parents to participate.

In total, parents of 103 children took part (120 parents in total). In 21 cases both parents of a child took part, in the remaining ones (n=99) it was either the mother (71.8%, n=71) or the father (28.2%, n=28). Two questionnaires had to be excluded as they were incomplete.

The mean age of the parents was 42.1 years (SD 5.439), median age was 42.0 years. The mothers were significantly younger than the participating fathers (mean and median ages 41.0 vs 45.0 years, **p=0.001, 2-sided Independent Sample T-test; **p=0.001, Mann-Whitney-U-test).

When both parents participated, the analysis showed that more fathers (n=13, 61.9%) and less mothers (n=8, 38.1%) answered. The mean age was 42.1 years (SD 6.472, median 40.0 years) with no significant differences between mothers and fathers (42.6 vs. 43.1 years, p>0.05, 2-sided Independent Sample T-test; median 39.0 vs. 40.0 years, p>0.05, Mann-Whitney-U-test).

6.8.2 Searching for new white spots

One part of the survey concerned the question how often the parents examined their children for the presence of new white spots. We found that there is a considerable percentage of parents doing that quite often (**Table 71**). About 43% of the parents confirmed that they searched their children often for new white spots (18.6% / n=16 *quite right* – 12.8% / n=11 *mostly right* – 11.6% / n=10 *totally right*). There was no significant difference between mothers and fathers ($p>0.05$, Pearson Chi-Square test) (**Table 71**).

I search my child often for new white spots		**Parent**		**Total**
		Mother	**Father**	**Parents**
Not at all right	N	**18**	**6**	***24***
	%	27.6	28.6	***27.9***
Hardly ever right	N	**17**	**8**	***25***
	%	26.2	38.1	***29.1***
Quite right	N	**13**	**3**	***16***
	%	20.0	14.3	***18.6***
Mostly right	N	**10**	**1**	***11***
	%	15.4	4.7	***12.8***
Totally right	N	**7**	**3**	***10***
	%	10.8	14.3	***11.6***
Total N		**65**	**21**	***86***

Table 71: Frequencies of mothers and fathers searching their children for new white spots

6.8.3 Parents' coping with vitiligo of their children

By evaluating the ACS scores it is possible to get an impression how parents cope with the chronic skin disease of their children.

Direct comparison of patients' parents and control group

A direct comparison yielded that parents of children with vitiligo scored a median *social anxiety / avoidance* score of 26.0 (n=120), which is much higher compared to parents of healthy controls (15.5, n=18, ***p<0.001, Mann-Whitney-U-test). The median scores of *helplessness* were also significantly different (22.0 / n=120 vs. 10.0 / n=18, ***p<0.001, Mann-Whitney-U-test) (**Figure 52**).

Interestingly, this difference was not present in *anxious-depressive mood*. Here, the parents of children patients scored a median of 16.0 (n=120) and the parents of healthy controls a median of 14.0 (n=18). The difference is not significant (p>0.05) (**Figure 52**). In this context it is again noteworthy that *anxious-depressive mood* is the only ACS scale not specified for skin diseases.

In conclusion, parents of children with vitiligo have difficulties in coping with their children's chronic skin disease. This is particularly the case for situations where the disease might be revealed to others (*social anxiety / avoidance*) and regarding the course of vitiligo (*helplessness*).

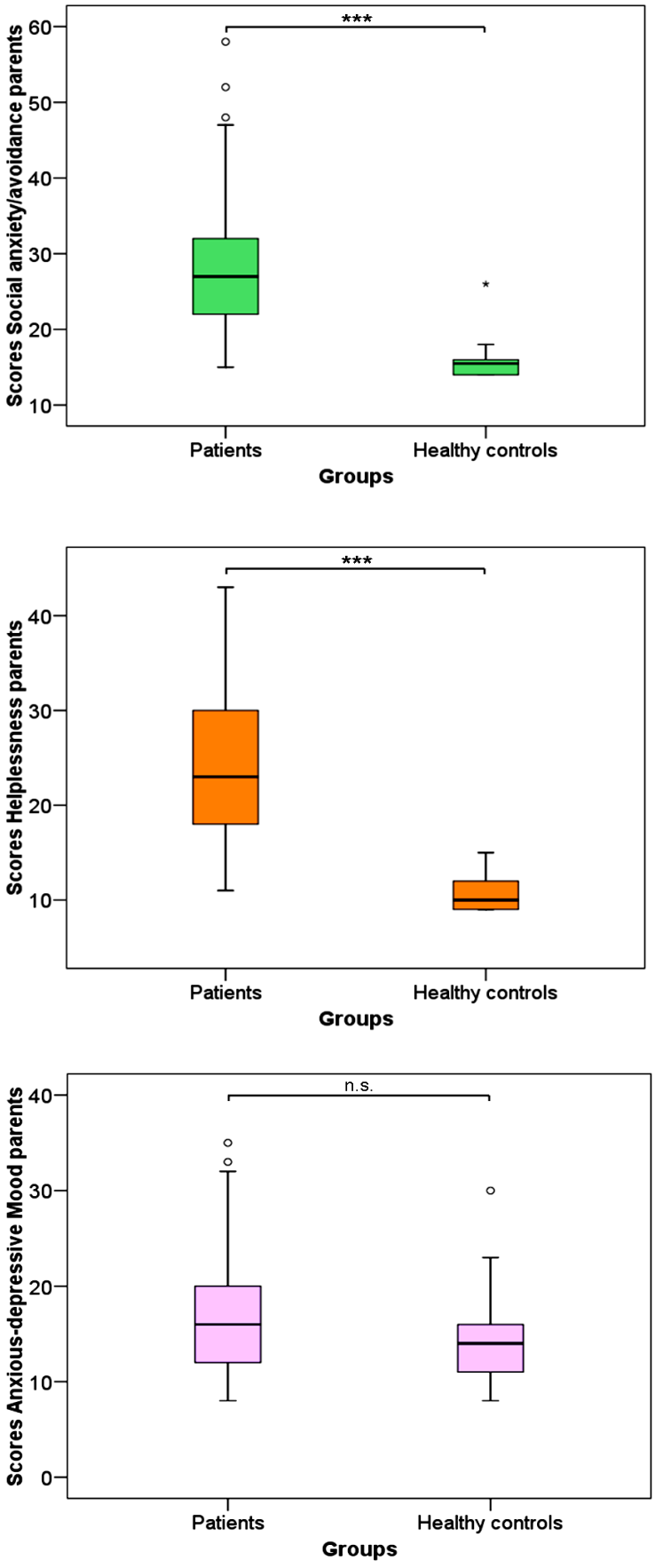
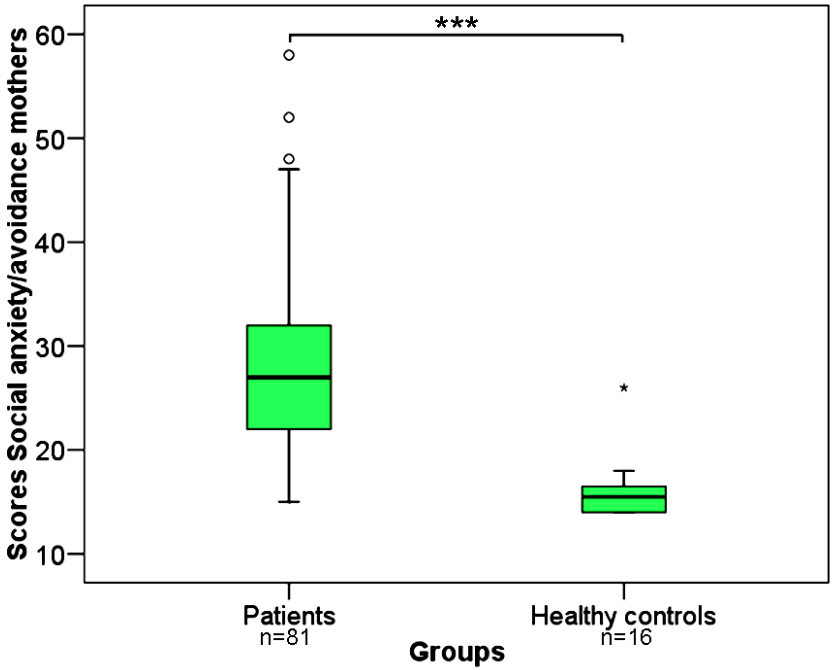


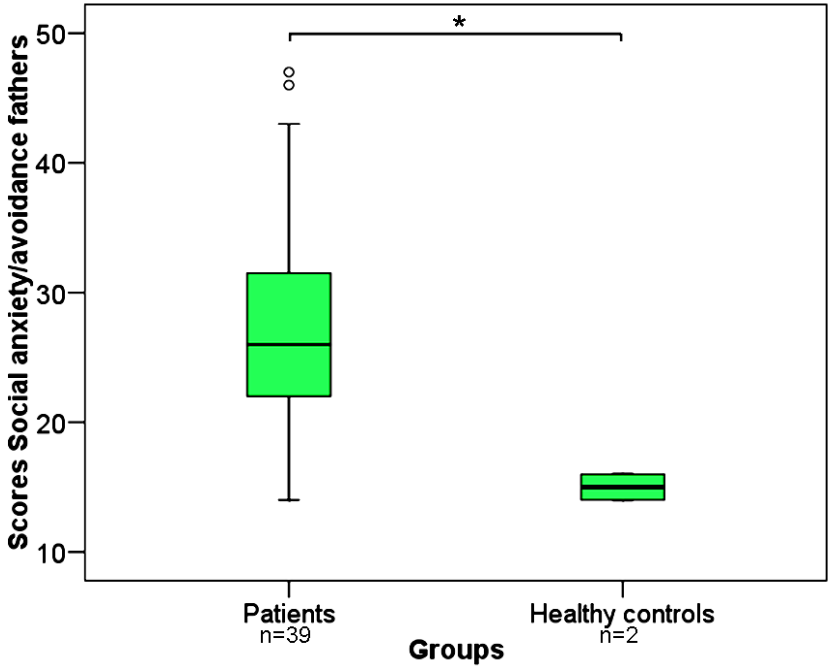
Figure 52: Median ACS scores of parents of children with vitiligo (n=120) and healthy controls (n=18)
Significances were measured with a Mann-Whitney-U-test.

Evaluation of differences between mothers and fathers of patients and controls

Next it was tempting to test for any differences in coping-related emotions between mothers of patients and controls and fathers of the patients and controls.

Consequently, we directly compared their scores in *social anxiety / avoidance* (**Figure 53**), *helplessness* (**Figure 54**) and *anxious-depressive mood* (**Figure 55**). All three tests revealed that the differences regarding *social anxiety / avoidance* and *helplessness* as shown for the total group of parents can also be found equally in mothers (***$p<0.001$) and fathers (*$p<0.05$) of patients compared to the control group. Moreover, there were no significant differences in *anxious-depressive mood*, neither in mothers nor in fathers ($p>0.05$, Mann-Whitney-U-test) (**Figure 56**).

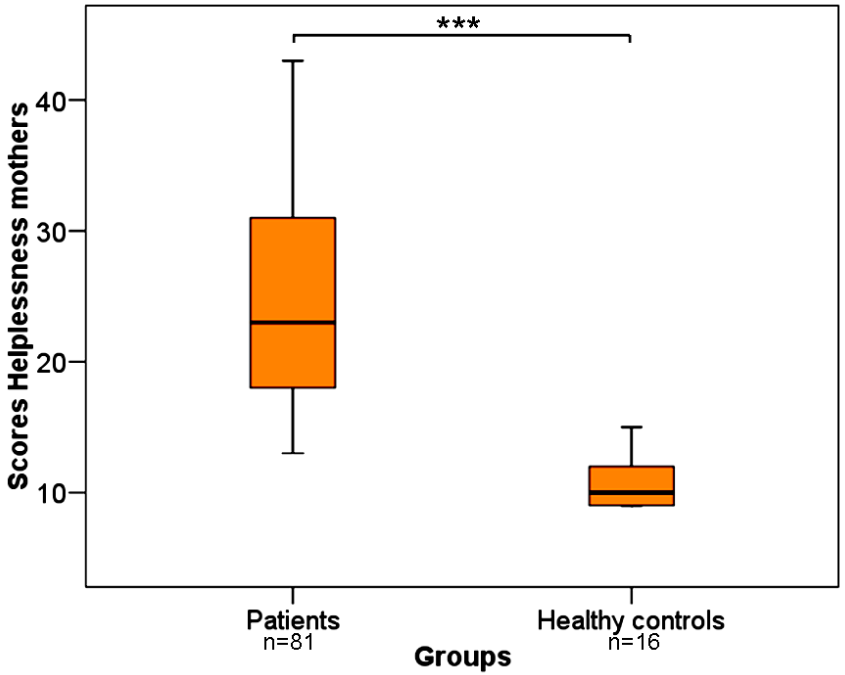


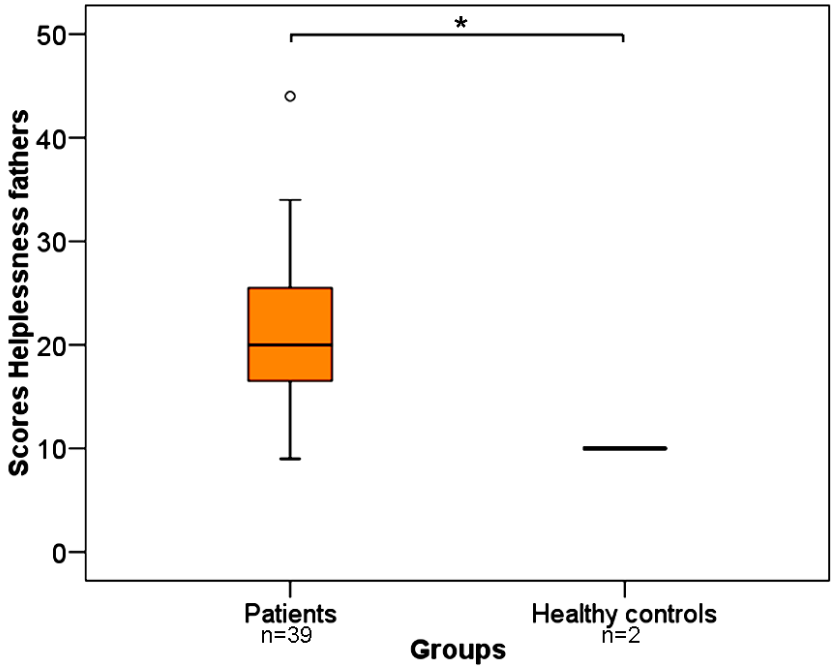


Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Mothers patients	81	15	58	***28.2******	***27.0******	9.415	**<0.001**(1)
Control mothers	16	14	26	***16.0******	***15.5******	3.033	**<0.001**(2)

Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Fathers patients	39	14	47	***26.9****	***26.0****	8.050	**0.046**(1)
Control fathers	2	14	16	***15.0****	***15.0****	1.414	**0.01**(2)

Figure 53: Social anxiety / avoidance scores of mothers and fathers of children with vitiligo compared to healthy controls
Significances were measured with an (1)Independent Sample T-Test (means) and a (2)Mann-Whitney-U-test.

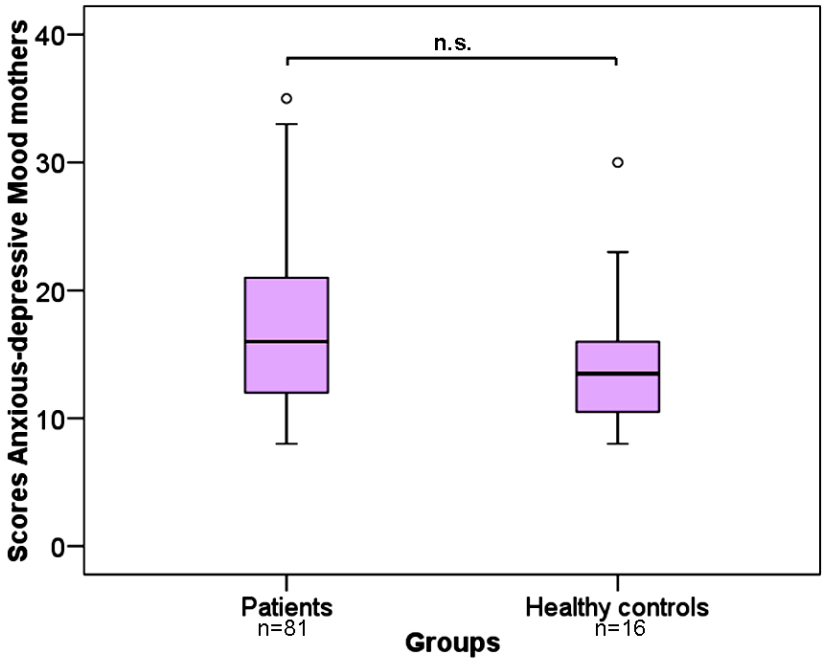


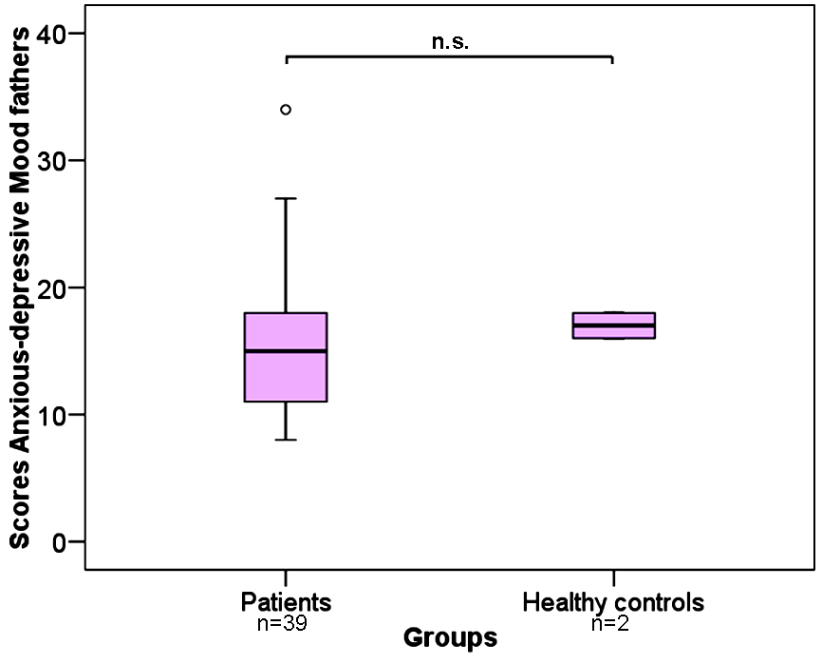


Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Mothers patients	81	13	43	*25.1***	*23.0***	8.204	<0.001(1)
Control mothers	16	9	15	*10.7***	*10.0***	1.815	<0.001(2)

Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Fathers patients	39	9	44	*21.0**	*20.0**	7.103	0.036(1)
Control fathers	2	10	10	*10.0**	*10.0**	---	0.01(2)

Figure 54: Helplessness scores of mothers and fathers of children with vitiligo compared to healthy controls
Significances were measured with an (1)Independent Sample T-Test (means) and a (2)Mann-Whitney-U-test.





Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Mothers patients	81	8	35	**17.5**	**16.0**	6.928	>0.05(1)
Control mothers	16	8	13	**14.4**	**13.5**	5.715	>0.05(2)

Social anxiety / avoidance	N	Min.	Max.	Mean	Median	SD	p values
Fathers patients	39	8	34	**15.4**	**15.0**	5.425	>0.05(1)
Control fathers	2	16	18	**17.0**	**17.0**	1.414	>0.05(2)

Figure 55: Anxious-depressive Mood scores of mothers and fathers of patients and healthy controls
Significances were measured with an (1)Independent Sample T-Test (means) and a (2)Mann-Whitney-U-test.

Coping depending on age of the parents

An interesting question was, whether age of the parents would influence coping with their children's skin disease. In order to evaluate this, we performed Pearson correlation analysis for each ACS score and age of the parents.

The correlation coefficients obtained were as follows:

- *Social anxiety / avoidance* -0.089 (mother, n=81) 0.061 (father, n=39)
- *Helplessness* -0.077 (mother, n=81) -0.145 (father, n=39)
- *Anxious-depressive mood* -0.004 (mother, n=81) 0.164 (father, n=39)

These results indicate that none of the ACS scores correlates with age of the parents ($p>0.05$). It can be concluded that coping with their children's vitiligo does not depend on the age of the parents.

Influence of disease duration

The next question we wanted to answer was, whether there was any correlation between coping of the parents and duration of their children's vitiligo. We again performed Pearson correlation analysis and obtained the following correlation coefficients:

- *Social anxiety / avoidance* -0.185 (mothers, n=81) -0.011 (fathers, n=39)
- *Helplessness* -0.192 (mothers, n=81) -0.287 (fathers, n=39)
- *Anxious-depressive mood* -0.158 (mothers, n=81) -0.139 (fathers, n=39)

These results reveal that duration of the children's skin disease does not influence coping-related emotions of their parents ($p>0.05$).

Influence of children's disease status on coping of their parents

This part concerned the question whether coping-related emotions of the parents were influenced by the disease status, i.e. whether vitiligo was currently actively spreading, remaining stable or improving. We analysed the ACS scores of mothers and fathers in relation to the mentioned states.

The results revealed that the status of vitiligo was only influential on feelings of helplessness of mothers. When their children's vitiligo was *spreading* (n=19), the score was with a median of 30.0 higher than the scores in case of *stable* disease (21.0, n=23) or *improving* vitiligo (26.0, n=9) (**Table 72**). The difference between the three scores is significant (*p<0.05, Kruskal-Wallis-test). Surprisingly, it seems to be that any change of the state (worsening or improving) made mothers more helpless compared to a stable disease, where the score was lowest.

Disease state of children		N	Mean	Median	SD	p value
Social anxiety / avoidance mother	Active	19	29.8	28.0	7.850	>0.05
	Stable	23	23.8	22.0	7.114	
	Re-pigmenting	9	26.7	27.0	10.524	
Helplessness mother	Active	19	***28.8****	***30.0****	8.310	**0.006**(1) **0.013**(2)
	Stable	23	***21.3****	***21.0****	5.138	
	Re-pigmenting	9	***24.9****	***26.0****	8.609	
Anxious-depressive mood mother	Active	19	20.4	19.0	5.994	>0.05
	Stable	23	16.5	16.0	5.053	
	Re-pigmenting	9	17.6	15.0	8.791	
Social anxiety / avoidance father	Active	6	25.7	27.5	6.314	>0.05
	Stable	14	24.1	23.0	5.196	
	Re-pigmenting	5	29.2	27.0	11.520	
Helplessness father	Active	6	22.7	23.5	4.676	>0.05
	Stable	14	17.9	16.5	5.797	
	Re-pigmenting	5	25.8	20.0	12.696	
Anxious-depressive mood father	Active	6	14.8	14.5	4.535	>0.05
	Stable	14	13.7	13.5	3.791	
	Re-pigmenting	5	19.2	15.0	10.895	

Table 72: ACS scores of parents depending on disease state of their children
Significances were measured with one-way ANOVA test (1) and Kruskal-Wallis-test(2).

Correlation of difficulties in parental coping and avoidant behaviour of the children

An important part of this project was to find out whether there were any correlations between disturbed emotions of the parents and avoidant behaviour of their children. In order to evaluate this, we compared the ACS scores of mothers and fathers depending on the frequencies their children hide their vitiligo in front of other people.

The results shown in **Table 73** revealed that parents of children who had *never* hidden their white spots, scored lowest in *social anxiety / avoidance, helplessness* (fathers only) and *anxious-depressive mood* (fathers only) (p values ranging from **<0.005 to *<0.05, Mann-Whitney-U-test).

From these numbers it remains unclear whether avoidant behaviour of the children disturbed their parents' emotions or whether this happened the other way around. Therefore, it could also be concluded that children benefit from unaffected parents by showing an normal non-hiding behaviour.

How often have you hidden your white spots?		N	Mean	Median	SD	p value
Social anxiety / avoidance mother	1	36	***24.3****	***23.0****	6.488	
	2	23	***32.0****	***31.0****	9.207	**0.005**(1)
	3	9	***30.3****	***29.0****	6.557	**0.004**(2)
	4	12	***31.7****	***30.0****	13.937	
Helplessness mother	1	36	22.5	21.0	7.177	
	2	23	27.4	26.0	7.272	>0.05
	3	9	24.1	24.0	8.358	
	4	12	28.0	29.0	9.899	
Anxious-depressive mood mother	1	36	16.4	16.0	5.857	
	2	23	17.6	15.0	7.445	>0.05
	3	9	15.7	14.0	7.297	
	4	12	20.4	20.5	7.428	
Social anxiety / avoidance father	1	18	***22.8****	***23.0****	4.870	
	2	13	***29.6****	***28.0****	7.911	**0.005**(1)
	3	6	***33.7****	***32.0****	9.416	**0.008**(2)
	4	2	***30.5****	***30.5****	2.121	
Helplessness father	1	18	17.7	***17.0****	4.800	
	2	13	2387	***21.0****	8.814	0.052(1)
	3	6	23.0	***20.5****	6.693	**0.039**(2)
	4	2	26.5	***26.5****	.707	
Anxious-depressive mood father	1	18	***12.4****	***12.5****	3.556	
	2	13	***18.2****	***17.0****	6.699	**0.037**(1)
	3	6	***17.5****	***17.0****	4.037	**0.046**(2)
	4	2	***16.5****	***16.5****	6.364	

Table 73: ACS scores of parents depending on hiding vitiligo
Significances were measured with one-way ANOVA test (1) and Kruskal-Wallis-test(2).

1 - Never, 2 – Very few times, 3 – Quite often, 4 – Very often

Coping emotions and searching for new white spots

As shown above, there were considerable parts of the parents frequently examining their children for new white spots. It was tempting to test whether those parents who search for white spots often were more affected in their coping.

The results are very clear. The stronger mothers agreed that they searched their children often for new white spots, the higher they score in all ACS sub-scales. The differences between levels of agreement are highly significant as measured with a Kruskal-Wallis-test (***$p<0.001$, **Figure 56**).

The stronger fathers agreed that they search their children often for new white spots, the higher they score in *helplessness* (*$p<0.05$) and *anxious-depressive mood* (***$p<0.001$). There was no difference in *social anxiety / avoidance* ($p>0.05$) (**Figure 57**).

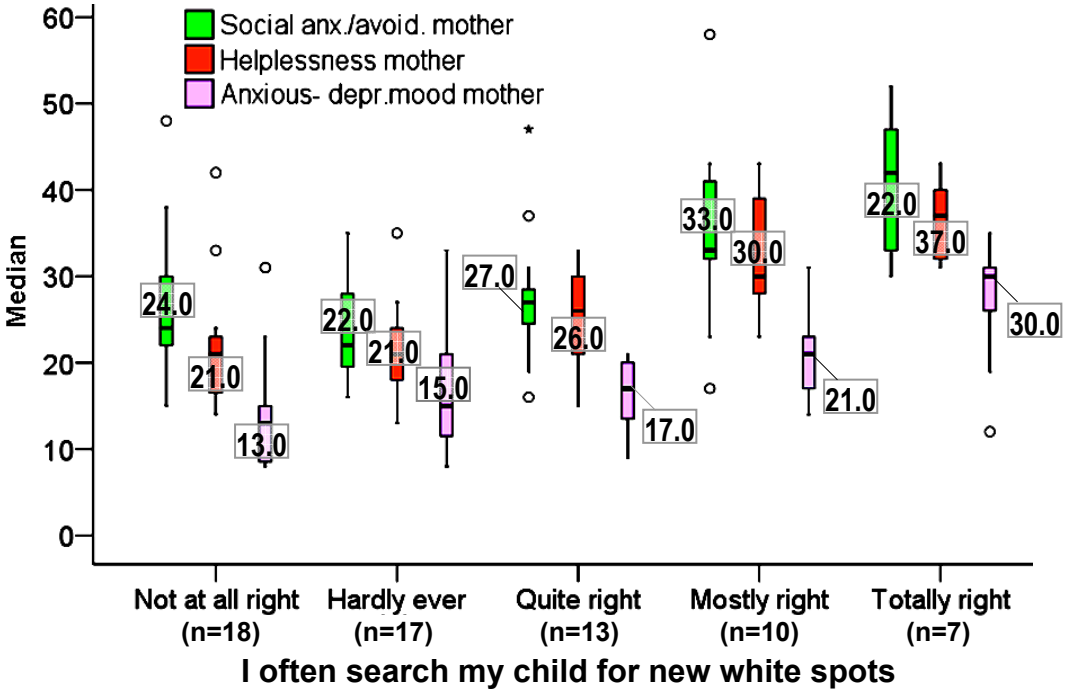


Figure 56: ACS scores of mothers depending on frequencies of searching for new white spots (n=65)

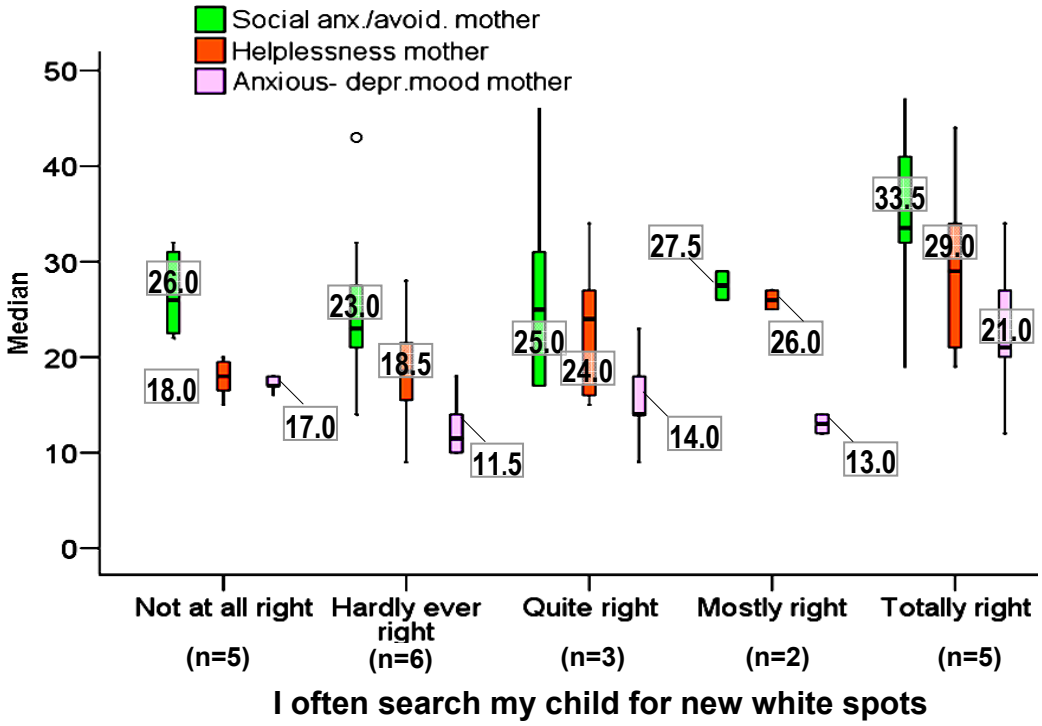


Figure 57: ACS scores of fathers depending on frequencies of searching for new white spots (n=21)

6.8.4 Parents' beliefs about what causes vitiligo

Since there are many factors suggested in the literature as either triggering or worsening vitiligo, it was our interest what parents think is influential on their children's vitiligo and whether there were any differences between the parents.

There were only a few parents thinking that *psychological stress* (41%, n=31/76), *other diseases* (22%, n=8/37) or *injuries* (23%, n=10/44*)* are involved in vitiligo (**Figure 58**). There were no significant differences between fathers and mothers (data not shown, p>0.05, Pearson Chi-Square test).

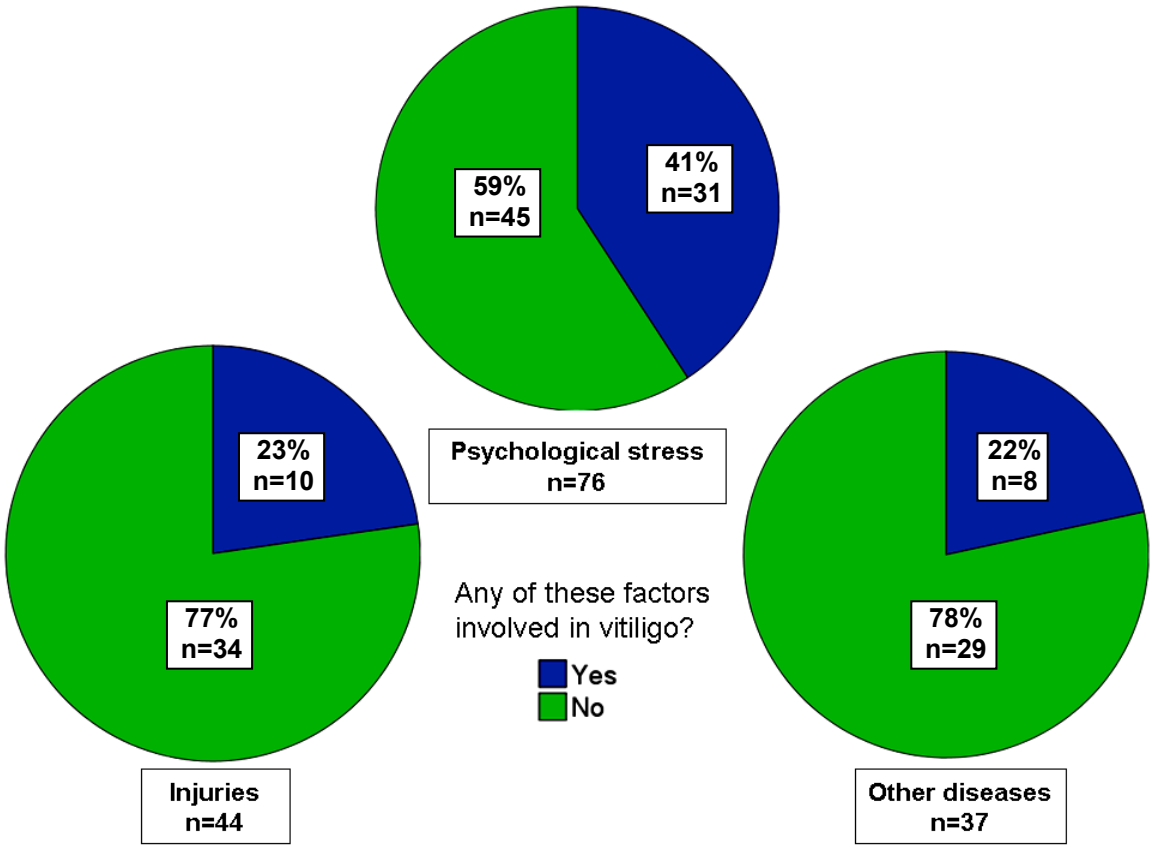


Figure 58: Beliefs of parents about trigger factors

6.8.5 Influence of parents' beliefs on their ACS scores

Next we wanted to know whether parents' beliefs regarding a possible involvement of psychological stress, other diseases and injuries in vitiligo influence their ACS scores. There was no association found regarding *injuries* ($p>0.05$, data not shown). Some correlations were found regarding *psychological stress* (**Table 74**) and *other diseases* (**Table 75**).

Mothers who think that psychological stress is influential (n=23), showed a higher mean *anxious-depressive mood* score (19.8) compared to mothers who did not think this way (n=37, mean 15.7). The difference was significant (*$p<0.05$, Independent Sample T-test). The same applied to the fathers, but even stronger in *anxious-depressive mood* and additionally regarding *social anxiety / avoidance* (*$p<0.05$, **Table 74**).

Mothers, who think that other diseases are involved showed higher *anxious-depressive mood* scores (*$p<0.05$). There were no other differences ($p>0.05$, **Table 75**).

Psychological stress influential in vitiligo?		N	Mean	Median	SD	p value
Social anxiety / avoidance mothers	Yes	23	29.1	28.0	10.207	>0.05
	No	37	25.4	24.0	6.534	
Helplessness mothers	Yes	23	25.1	22.0	9.160	>0.05
	No	37	23.9	23.0	5.629	
Anxious-depressive mood mothers	Yes	23	***19.8****	16.0	7.493	**0.012**(1)
	No	37	***15.7****	16.0	4.730	0.065(2)
Social anxiety / avoidance fathers	Yes	14	***30.1****	***30.0****	8.033	**0.011**(1)
	No	18	***23.7****	***23.0****	5.120	**0.018**(2)
Helplessness fathers	Yes	14	22.3	21.0	7.311	>0.05
	No	18	18.7	17.0	5.367	
Anxious-depressive mood fathers	Yes	14	***17.2****	***17.0****	4.228	**0.002**(1)
	No	18	***12.7****	***12.0****	3.461	**0.006**(2)

Table 74: ACS scores of parents and perceived influence of psychological stress
Significances were measured with 2-sided Independent Sample T-test(1) and Mann-Whitney-U-test(2).

Other diseases involved in vitiligo?		N	Mean	Median	SD	p value
Social anxiety / avoidance mothers	Yes	7	27.14	27.0	10.040	>0.05
	No	25	25.88	24.0	7.513	
Helplessness mothers	Yes	7	26.57	26.0	7.254	>0.05
	No	25	24.12	23.0	5.637	
Anxious-depressive mood mothers	Yes	7	***21.29****	***20.0****	5.678	**0.032**(1)
	No	25	***16.28****	***16.0****	5.062	**0.023**(2)
Social anxiety / avoidance fathers	Yes	4	30.00	27.0	12.055	>0.05
	No	12	25.42	24.5	5.435	
Helplessness fathers	Yes	4	25.75	21.5	12.606	>0.05
	No	12	20.75	20.0	5.225	
Anxious-depressive mood fathers	Yes	4	17.75	16.0	6.652	>0.05
	No	12	14.00	13.5	3.357	

Table 75: ACS scores of parents regarding belief that other diseases are involved in vitiligo
Significances were measured with 2-sided Independent Sample T-test (1) and Mann-Whitney-U-test(2).

6.8.6 ACS scores of both parents

As mentioned above, in 21 cases both parents of a child with vitiligo filled out the questionnaires. This offered the chance to compare both scores and also to test whether they correlate.

A direct comparison of both parents' ACS scores yielded that they differ in *helplessness* and *anxious-depressive mood.* Here, mothers had significantly higher median scores compared to their partners / spouses (*helplessness* 26.0 vs. 20.0 and *anxious-depressive mood* 19.0 vs. 14.0, *p<0.05, Wilcoxon signed-rank test) (**Table 76**).

This was followed by correlation analysis, which revealed that the scores of mothers and fathers positively correlated in *social anxiety / avoidance* (**p=0.001) *and helplessness* (*p=0.02), but not in *anxious-depressive mood* (p>0.05) (**Table 76**).

	Mean	**Median**	**N**	SD	p value difference	Pearson correlation coefficient	p value correlation
Social anxiety / avoidance *mother*	28.8	28.0	21	7.661	>0.05(1)(2)	***0.679***	****0.001**
Social anxiety / avoidance *father*	26.7	27.0	21	7.457			
Helplessness *mother*	***25.6****	***26.0****	21	7.580	**0.019**(1)	***0.504***	***0.02**
Helplessness *father*	***21.3****	***20.0****	21	7.716	**0.037**(2)		
Anxious-depressive mood *mother*	18.8	***19.0****	21	6.774	>0.05(1)	0.190	>0.05
Anxious-depressive mood *father*	16.0	***14.0****	21	6.233	**0.045**(2)		

Table 76: Comparison and correlation analysis of ACS scores of both parents
(1) Paired samles T-test (2)Wilcoxon signed-rank test

6.8.7 Correlations between parents' scores and CDLQI scores

Finally, it was our interest to find out whether an impaired quality of life of the children correlated to disturbed coping-related emotions of the parents, because that would indicate that both scores (and parents' and children's feelings) influence each other.

For this purpose we utilised Pearson correlation analysis, which showed that there were positive and significant correlations between mothers' scores in *social anxiety / avoidance* (n=82, ***p<0.001) and *helplessness* (*p<0.01) with the CDLQI scores of their children. There were no correlations of the CDLQI with any of the father's ACS scores and mother's *anxious-depressive mood* (p>0.05) (**Table 77**).

Parents' scores	N	*Pearson* correlation coefficient to CDLQI	p value
Social anxiety / avoidance (mother)	82	***0.440******	**<0.001**
Social anxiety / avoidance (father)	39	0.242	>0.05
Helplessness (mother)	82	***0.264****	**0.017**
Helplessness (father)	39	0.229	>0.05
Anxious-depressive mood (mother)	82	0.161	>0.05
Anxious-depressive mood (father)	38	0.111	>0.05

Table 77: Correlation analysis of parents' scores and CDLQI scores

7 Discussion

7.1 Adult patients characteristics

7.1.1 Demographical and clinical features

With regards to most of the demographic features, our adult patient population is not particularly different from others.

It is very common that more women than men participate in studies on vitiligo (Behl and Bhatia 1972; Hann and Lee 1996; Tawade et al. 1997; Al-Mutairi and Sharma 2006), although rarely there is a male predominance (Dutta and Mandal 1969; Sarin and Kumar 1977; Kar 2001). A female predominance could be explained because women are more likely to visit a doctor for their vitiligo (Ongenae et al. 2004) and since most of the studies available are in any way associated with dermatological clinics, it seems realistic that often more women took part then men. Hence, the relatively high proportion of women in our study (67.8%) is not *exceptionally* high as there are other reports with similar (Alkhateeb et al. 2003; Wu et al. 2008) or even higher proportions (Mason and Gawkrodger 2005; Hallaji et al. 2006).

The mean / median age of our patient group is high. However, this is not exceptional in the field of vitiligo (Alkhateeb et al. 2003).

Our results revealed a mean / median age of disease onset of about 24 years with a peak between 10 and 19 years. This is in agreement with other reports confirming that although vitiligo can occur at any time in life, the onset tends to be in the first third of the life span. Our finding of an earlier disease onset in male patients is in agreement with earlier reports (Das et al. 1985; Majumder et al. 1993).

A very interesting finding is that patients who think that psychological stress is influential in vitiligo have a much *higher* age of disease onset. This cannot be explained by a gender factor as there is no significant difference between female and male patients regarding beliefs that psychological stress is involved (Pearson Chi-Square test, $p>0.05$, data not shown). It is tempting to speculate that older patients link their vitiligo to certain life events and experiences.

It seems that in the case of an earlier disease onset patients avoid certain situations more often because of their vitiligo, while a later onset does not affect patients that much as many will have settled by then and physical appearance will have become less important.

The predominance of fair skin phototypes (I-III) in our study can be explained by the geographical location of the Institute for Pigmentary Disorders in Western Europe (Greifswald / Germany and Bradford / UK). Although patients from five continents are enrolled with the institute, the majority is from Germany and the UK with predominantly Caucasian populations.

To the best of our knowledge there are no studies available comparing English and German speaking patients. There are reports from South Africa where different languages and cultures are included (Jobanputra and Bachmann 2000). It is noteworthy that many of our patients filled out our questionnaires without having English or

German as first language, so that the obtained data may only be of limited value to conclude anything about the countries involved (Germany vs. UK / USA / Australia).

A positive family history of 37.8% in our patient group is in agreement with other publications with a range from 1 to 48% (Singh et al. 1985; Al-Khawajah 1997). Our finding that the *parents* of children in our group often had vitiligo themselves supports earlier reports that there is an increased risk for children to develop vitiligo when their parents also suffer from this disease (Majumder et al. 1993; Shah et al. 2008).

The state of disease (spreading, stable, re-pigmenting) is difficult to compare to other studies as this would also depend on the success rates of treatment modalities associated with the studies. A proportion of 46% having progressing vitiligo seems neither exceptional high nor low (Sarin and Kumar 1977). In the subgroup of patients enrolled with the Institute for Pigmentary Disorders there are less patients having actively spreading disease compared to those not enrolled (39% vs. 53%, p=0.059) reflecting the medical success of this modality.

The initial sites of disease onset in our population are not different from those reported in the literature as they also are predominatly on exposed parts of a patient's body (hands, face, neck). However, *hands* as most frequently mentioned site of onset has only been reported once before (Lerner 1959). When *face and neck* are counted as one part as commonly done in the literature (Kanwar et al. 1993; Handa and Kaur 1999; Al-Mutairi et al. 2005), these locations would be the most frequently mentioned part where the first vitiliginious spot appeared.

Pruritus in association with vitiligo has rarely been reported. Hence, our prevalence number of 34.3% adds another piece of information to the knowledge about vitiligo.

The prevalence of grey hair on scalp and in eyelashes / eyebrows was about 40% in the younger patients. A link to vitiligo was suggested earlier (Lerner 1959).

7.1.2 Experiences and behaviour – role of stigmatisation

As discussed earlier, stress, life events and emotional problems have often been suggested as being influential on onset and / or course of vitiligo. Our patient population is no exception with a majority thinking that psychological stress is influential on their vitiligo. Our proportion of 72% of patients is higher than reported anywhere else.
One reason could be that the term *psychological stress* is only one of several used in the literature so far; in other reports it has often been *'stress', 'emotional undertones', 'life events', 'nervouseness'* and similar, all with less patients reporting them. Another reason might be the high number of stigmatisation experiences in our group. Almost 90% have experienced that other people approached them and asked questions about their white spots. This number is higher than reported in the literature so far, where 72% was the highest (Porter et al. 1979). Since it is well established that stigmatisation leads to impaired quality of life, this could explain why many of our patients link psychological stress to vitiligo.

About 38% linked their vitiligo to injuries (Koebner phenomenon) and 18% related vitiligo to other diseases. These numbers are slightly higher compared to earlier reports (**Table** 4) (Dutta and Mandal 1969; Papadopoulos et al. 1998).

As already mentioned above there is a high prevalence of patients reporting stigmatisation experiences. Almost 90% stated that they have been approached and / or asked questions about the disease by others. Less, but still a quarter of our patients said

that they had been subject to nasty comments or that they were picked on because of the disease. This is the highest prevalence reported so far. While Porter et al found that 50% in their group had experienced rude remarks, this was 16% only in another study (Porter et al. 1979; Porter et al. 1987).

Interestingly, *female* patients and those with hands and / or legs *severely* affected are more likely to experience approaches / questions by others. The gender difference is in contradiction to other reports (Kent 1999; McLeod 2004), but one of those studies used less patients (n=45 in McLeod's study) with a probably reduced statistical sensitivity or different ways to measure stigmatisation (Kent 1999). The increased likelihood for patients with severely affected hands could be explained by a correlation between visibility of vitiligo and level of stigmatisation (Kent 1999). Since hands (and legs at least sometimes) are exposed parts, it can be expected that patients with severe vitiligo will also experience stigmatisation more often. The problem is that hands are apparently difficult to treat (Schallreuter et al. 2008b), so that there are not many medical options left to do something about it. The same applies to our finding that patients with severely affected arms are more likely to be picked on or to become subject to nasty comments.

Interestingly, when looking at groups of age at disease onset, patients with an onset in their teenage years were most often picked on or subjects to nasty comments because of their vitiligo, compared to younger and older patients. It might be the nature of adolescence / puberty (appearance becoming more important, peer pressure, mood swings) that such differences will be mentioned more often by others in the same age.
Taken together, since there are only a handful of publications available containing prevalence data on stigmatisation, our data add some more important information to this field.

7.1.3 Avoidant behaviour - hiding of the disease

63% of our patient population have quite often or very often hidden their white spots in front of other people in the past, 65% had avoided certain situations where an exposure of the disease was feared. This number is lower than the 76% reported in a comparable publication (McLeod 2004). Porter et al reported that about half of their patients *felt* forced to hide their white spots (Porter et al. 1979).

About 40% of our patients preferred a combination of multiple strategies over just one. However, hiding the white spots under clothes was most popular, followed by camouflage and using of body positions. This is in agreement with earlier reports (McLeod 2004). In our group, female patients are more likely to hide their spots *very often* and less likely to do this *never* or *very rarely,* which confirms earlier findings of a gender-difference (McLeod 2004; Ongenae et al. 2004).

Avoided situations were most often *shaking hands / undressing in changing rooms* and *swimming / bathing*. These situations have also been reported earlier as commonly avoided ones (McLeod 2004). In contrast to our findings McLeod found *undressing in changing roms* the least avoided activity in their group. We found no further differences between any subgroups in our patients population regarding frequencies of avoided situations.

7.2 Dermatology Life Quality Index

The median Dermatology Life Quality Index (DLQI) for our patients population as a whole is 4.0 (mean is 5.5), and this is significantly increased compared to healthy controls.

It is consistent that all DLQI scores of patients with vitiligo are much higher than those published for healthy controls (about 0.5) (Finlay and Khan 1994). Compared to other mean scores from the literature, this is rather in the lower part of the range. The lowest DLQI score reported so far is 3.7 and it is of a group associated with an Australian dermatologic practice (Chee et al. 2008), the highest is about 15 of a group of Saudi college students (Al Robaee 2007) and a group of patients in the beginning of a trial into the effects of cognitive-behavioural therapy in vitiligo (Papadopoulos et al. 1999). However, an exact comparison is not possible as all the groups mentioned will differ regarding state and severity of vitiligo, treatment and also cultural backgrounds.

Interestingly, about 60% of our patients did not have or had an only slightly impaired quality of life (DLQI scores from 0-5). This is more than one would expect when looking at our mean and median DLQI scores. However, 16% of the participants suffered from a severly or even extremely reduced quality of life as indicated by high DLQI scores from 11 to 30. The question remains whether all patients had filled out this questionnaire honestly. It can be expected that more than 16% suffer from limitations in essential parts of their daily lives.

There is a significant difference between patients enrolled with the Institute for Pigmentary Disorders and those not enrolled, with the latter group having higher mean scores. That confirms that the treatment modality offered by the institute (narrow-band

UVB activated pseudocatalase PC-KUS) is not only medically effective, it also improves quality of life. This association, however, is significant only when using mean DLQI scores, it is not measurable with non-parametric measurements. Single item analysis showed that patients enrolled with the institute benefit particularly regarding their daily activities, such as shopping or gardening.

According to our results there is no difference between female and male patients regarding quality of life. This is in agreement only with a minority of publications, whereas most of earlier reports emphasised such difference.

Although female patients are more likely to experience stigmatisation, i.e. approaches / questions by others, this apparently has not lead to a more impaired quality of life in our group. It might be that a certain level of stigmatisation can be compensated by support by friends, which women are more likely to receive (Porter and Beuf 1994).

It has been reported earlier that perceived stigmatisation is influential on quality of life. In our group, however, we found that those who had *never* been approached by others had the *highest* DLQI scores (in female and male patients equally, data not shown). The lowest total DLQI score and the lowest scores in the DLQI items *partners / friends / relatives* and *sexual relationships* were found in those patients who had *sometimes* experienced approaches / questions.

This result seems to be the opposite of Moss' *inverted-U*-relationship regarding severity of a general disfigurement, where patients with moderate severity suffered most when compared to those with lower and higher extreme of severity. This was explained by that in the latter cases other peoples' *reactions* are more predictable as with moderate severity where such reactions are more varied and ambigious (Rumsey and Harcourt 2004; Moss 2005).

In our group, however, moderate ('*sometimes*') and thus less predictable reactions by other people (approaches / questions) did not have such profound impact on quality of life as with no approaches at all or those happened very often. It might be that patients who had never experienced stigmatisation do *fear* such encounters and will do everything they can to prevent them from happening. This could be done for example by avoiding situations, which automatically leads to a more impaired quality of life.
Strikingly, stigma-related experiences of patients such as being picked on or being subjects to nasty comments had no influence at all on DLQI scores, in spite of being more malignant than "just" approaches / questions by others. Perhaps, there are different coping strategies attached to either kind of experience. Taken together, we could not confirm earlier findings that perceived stigma and DLQI scores correlate (Kent and Al-Abadie 1996a) and it may be that stigmatisation is not that influential, at least in some patient groups.

Severity of vitiligo on different body parts is not influential on DLQI scores, except for the trunk, where severe vitiligo goes along with higher DLQI scores compared to just slight vitiligo. This result is in agreement with earlier reports (Ongenae et al. 2005b).
Given that the trunk is the biggest of all body parts mentioned in the questionnaire, we can assume that having severe vitiligo there most often means that the total vitiligo of these patients can be judged as severe. Therefore, severity of vitiligo can be regarded as influential on DLQI scores. This correlation has been reported earlier (Kent and Al-Abadie 1996a; Ongenae et al. 2005a; Ongenae et al. 2005b; Dolatshahi et al. 2008). Overall, we can only partially confirm that disease severity on different body parts is a good predictor that DLQI scores will be increased.

Surprisingly, skin colour has no influence on the total DLQI score. This contradicts earlier reports where it was found that patients with dark skin have a more impaired

quality of life (Kent and Al-Abadie 1996a; Dolatshahi et al. 2008). As shown by McLeod's study and Porter's group, darker skin correlates with an increased frequency of stigmatisation (Porter and Beuf 1991; McLeod 2004). The fact that this has not been the case in our group (**Table 17** and **Table 18**) explains why quality of life is not more affected in our patients with skin phototypes IV-VI. However, single item analysis showed that these patients are more affected when it comes to sport activities. An increased visibility of white spots on darker skin apparently obviously prevents those patients from doing this.

Interestingly, patients who think that psychological stress influences their vitiligo had much higher DLQI scores ($p=0.002$). This could mean that those patients with an impaired quality of life are aware of this fact, and thus link this skin disease to their mindset. This is not only influential on the total score, it also affects 7 out of 10 single items, which are more than any other factor explored in this thesis.
However, since the term *psychological stress* is a very general one and since we have not asked our patients for more specific details about why they think that there is a link, the data obtained cannot provide conclusive answers.

There is a clear association between avoidant behaviour and DLQI scores. Patients who had avoided certain situations because of their vitiligo, have significantly increased DLQI scores, and they are particularly affected in *daily activities* (shopping / gardening), *wearing clothes* and also doing *sports*. Hiding white spots influenced the total DLQI score as there are higher DLQI scores with increasing frequencies of hiding.
Data on this subject are scarce in the literature. Kent and Al-Abadie found in their investigation that patients who avoided certain situation had higher scores in the General Health Questionnaire (GHQ) indicating higher levels of psychiatric morbidity (Kent and Al-Abadie 1996b). Although not really the same dimension, it is clear that

avoidant behaviour and impaired well-being correlate. Such correlation can be expected, because both avoidant behaviour and impaired quality of life can be seen as *disability* according to the WHO: *'any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being'* (Finlay 1997).

Interestingly, patients with a positive family history of vitiligo were less affected in sexual relationships according to DLQI single item analysis. This has never been reported before. It could be that growing up with somebody in the family, who, in spite of having white spots, leads a normal life in a partnership, makes patients more easy-going in sexual relationships. Otherwise, family history has not been found as being influentiual on quality of life.

Of all the single items of the DLQI, our patients were most affected in their emotional reaction to vitiligo (*embarrassment, self-consciousness,* DLQI item 2). This is in agreement with other publications (Ongenae et al. 2005a; Ongenae et al. 2005b; Al Robaee 2007). However, we could not find any differences between female and male patients as reported earlier (Ongenae et al. 2005b; Borimnejad et al. 2006; Al Robaee 2007). Our data show that those with shorter disease duration and patients who think that psychological stress influences vitiligo are very affected. This has not been reported so far in the literature.

Second-most affected area according to DLQI single item analysis was item 4 (*influence on clothes patients wear*). Our data are in agreement with earlier publications (Ongenae et al. 2005a; Ongenae et al. 2005b; Al Robaee 2007). There are no differences between male and female patients which has previously been reported (Aghaei et al. 2004), but not consistenly (Ongenae et al. 2005b; Borimnejad et al. 2006; Al Robaee 2007).

Moreover, we found that this item affects particularly patients who think that psychological stress influences their vitiligo, those who had avoided situations because of the disease and patients with severe vitiligo on arms. This has not been reported in the literature before.

Our data show that the third-most impaired parts of daily life were *social or leisure activities* and *relationships with partners, friends and relatives* (items 5 and 8). Our patients seem to be more affected compared to other patient groups (Ongenae et al. 2005a; Ongenae et al. 2005b; Borimnejad et al. 2006; Al Robaee 2007). There are no differences between male and female patients, but we found that those patients were more affected who think that psychological stress influences the disease.

The overriding factor influencing these DLQI items in our patients population is their impression that psychological stress influences their vitiligo. As shown before, it also strongly influences the total DLQI score.

The least affected part of daily life in our patient population was *doing sports / work and studying* (items 6 and 7). However, patients with darker skin phototypes IV-VI had avoided situations because of their vitiligo. Moreover, patients with severe vitiligo on face and neck were also more affected.

There have been contradicting data published so far regarding a possible correlation between DLQI scores and duration of vitiligo. Some authors detected such correlation (Gajur et al. 2007), whilst others could not confirm this (Kent and Al-Abadie 1996a; Ongenae et al. 2005b; Dolatshahi et al. 2008). Our results clearly support the latter groups with no measurable correlation between DLQI scores and time since diagnosis. It can be expected that other factors have a much greater influence on quality of life.

7.3 Adjustment to Chronic Skin Disorders Questionnaire

The Adjustment to Chronic Skin Disorders Questionnaire (ACS) has rarely been used in the English-language literature in the field of vitiligo. There are only a few reports available (Rehme 2002; Stangier et al. 2003; Cordalija 2004; Jecht 2005; Schmid-Ott et al. 2007), some of them in German and with limitations[15].

This minimises the options to compare our results to other reports. However, the obtained data will introduce some new aspects into vitiligo-related research, especially since the ACS's main scales *social anxiety / avoidance, helplessness* and *anxious-depressive mood* have not been widely investigated. A recent survey on 1023 German patients with vitiligo associated with several self-support organisations rated for example reduction of *helplessness* as one of their most important goals (Gajur et al. 2007).

7.3.1 Comparison to healthy controls and other groups

First of all, our patients feel significantly more *socially anxious / avoidant, helpless* and *anxious-depressive* compared to healthy controls, and thus patients show difficulties to cope with this chronic skin disease (***$p<0.001$). To the best of our knowledge there is only one study available which included ACS scores of healthy controls and patients with vitiligo (Cordalija 2004). The results of this study indicate a significant difference

[15] Jecht and Rehme used the same patient population as Schmid-Ott et al (all n=363 of a hospital at Castle Friedenburg in Germany); Rehme's work is an unpublished medical thesis; Cordalija used a patient group mixed of vitiligo and psoriasis patients and, unfortunately, some of the results are only stated for the whole of the group and not seperately for each disease.

between both groups[16]. Other studies on vitiligo published so far, included only comparisons to other skin disease such as psoriasis (Stangier et al. 2003).

All scores of our group are comparable to those from Schmid Ott's / Jecht's group and Stangier's report (Stangier et al. 2003; Jecht 2005; Schmid-Ott et al. 2007), except for *social anxiety / avoidance*, where our population showed slightly increased scores (mean 38.7 / median 37.0 vs. means 34.8[17] and 35.5[18]).

These scores were lower compared to other skin diseases, such as *psoriasis* (mean 40.2, n=75) (Jecht 2005) or *epidermolysis* (41.9, n=30) (Stangier et al. 2003). Even lower than the scores of the vitiligo groups were those of patients with *contact eczema* (33.0, n=42) and *acne* (31.02, n=50) (Stangier et al. 2003).

All of the cited studies have been conducted on patients of dermatology clinics. Since our group is of a mixed nature[19], it can be expected that a certain proportion of untreated sufferers in our group scored higher than treated patients. This assumption could not be confirmed since both groups (enrolled or not enrolled with the Institute for Pigmentary Disorders) do not differ regarding their scores, except for *anxious-depressive mood*.

In the latter case we could show that patients who are enrolled with the Institute for Pigmentary Disorders and are undergoing treatment for vitiligo with narrow-band UVB activated pseudocatalase PC-KUS, are less *anxious-depressive* than those not enrolled. This further supports that this treatment modality is not only effective in re-gaining skin colour, it is also beneficial regarding patients' well-being.

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[16] However, scores are only provided in diagrams; and to make it even more difficult, the control group's scores read 1.25 and 1.7 which cannot be correct as this should be at least 15, 9 or 8 depending on the scale. It can only be suspected that the point has (consistently) been put at the wrong decimal rank (Cordalija 2004).

[17] n=363 (Jecht, 2004)

[18] n=33 (Stangier et al. 2003)

[19] as shown above: patients enrolled with the IFPD and undergoing treatment, and patients not enrolled

7.3.2 Influence of gender, age, visibility and duration of the disease

There is a significant difference between male and female patients in all three ACS sub-scales with women having higher mean and median scores. This is only partially in agreement with earlier results.

Although Stangier et al reported consistently higher scores of female patients in all sub-scales, this applied to all of their participants regardless of skin disease. Unfortunately, it is not stated in the publication whether or not there was a gender difference in the vitiligo group (n=33) (Stangier et al. 2003).

Schmid-Ott's group found a significant difference only regarding *helplessness*, but not in *social anxiety / avoidance* and *anxious-depressive mood* (both p=0.11), even though this group shared some demographic features with our population, i.e. majority were women and the mean age of 43.5 years (Schmid-Ott et al. 2007).

According to an earlier study, visibility of vitiligo correlates with ACS sub-scores (Schmid-Ott et al. 2007). This is also the case in our population, at least regarding *severity* of vitiligo on visible parts such as arms (valid for all sub-scores), legs (all but anxious-depressive mood) and neck (social anxiety / avoidance only), but not face. Patients with extended vitiligo on the mentioned body parts scored significantly higher.

Earlier it has been reported that age does not correlate with ACS sub-scores (Stangier et al. 2003; Schmid-Ott et al. 2007). These results are in contradiction to our results, because we found a negative correlation. Older patients have less difficulties in coping with this chronic skin disease. This confirms Cordalija's finding that patients younger

than 32 years were more affected than those older than 32 years (Cordalija 2004). It might be that either accumulating experiences when getting older supports coping with vitiligo, or it is just that appearance becomes less important with age.

In addition to this, we also found a negative correlation between age at disease onset and *social anxiety / avoidance*, but not for the other main scales. This correlation means that the younger patients were when they developed vitiligo, the more they were affected at the time when filling out the questionnaire. There was no correlation between duration of vitiligo and any of the ACS scales.

Taken together, the older patients are, and the later their disease onset in life, the better they cope with vitiligo, independently of duration of their disease.

7.3.3 Influence of stigmatisation and avoidant behaviour

Social anxiety / avoidance, but not the other sub-scales, are influenced by frequencies of stigmatising encounters (approaches / questions by others) in a similar manner as the Dermatology Life Quality Index. Those who had *never* experienced such approaches showed the highest scores, followed by the '*very often'* group. The lowest scores showed those patients who had experienced *sometimes* approaches and questions by others. However, the significance is weak. It is only significant when using means, whereas it is only borderline significant when the Kruskal-Wallis-test is employed. Further investigations with probably a greater number of patients are needed to clarify this association.

Contrary to the DLQI evaluation, there is an influence on ACS scores after including stigmatisation experiences, such as when patients were picked on or subject to nasty comments. Patients who had indeed experienced stigmatisation scored significantly

higher in *social anxiety / avoidance* and *anxious-depressive mood*. It can be concluded that stigmatisation of that kind increases fear of situations where patients think that their vitiligo might be exposed to others.

Similar to quality of life, there is a positive correlation between all ACS sub-scales and avoidant behaviour, especially hiding of the white spots. The more often patients had hidden their vitiligo in front of other people, the more *socially anxious / avoidant, helpless* and *anxious-depressive* they feel. There is also a significant difference between patients who had avoided certain situations because of their disease and those had never done this.

This seems obvious especially for *social anxiety / avoidance* as his scale *is* about fear of situations where patients think that their skin disease might be revealed to others. Therefore, this can be seen as confirmation that the Adjustment to Chronic Skin Disorders questionnaire can indeed identify correctly those patients who are avoidant in their daily life.

Strikingly, as in our quality of life measurements there are again significant differences between patients who were thinking that psychological stress is involved in vitiligo and those who did not think so, especially regarding *anxious-depressive mood*. Patients, who think that psychological stress is involved, were found to be much more affected in all three sub-scales. It can be assumed that those patients either had experienced situations that indeed triggered or exacerbated their vitiligo, or they were just aware that their emotions are disturbed directly by the disease or indirectly via vitiligo-related experiences.

Again, the term psychological stress is a very general one, so that more focussed research is needed.

7.4 Beck Depression Inventory

Many of the results obtained with the Beck Depression Inventory are similar to those of the above mentioned questionnaires with one important difference.

It can be concluded that our patients are not much more depressed than healthy controls. When comparing means, there is no significant difference at all. When utilising the Mann-Whitney-U-test there is a weak significance[20].

A comparison of numbers of patients and controls with mild to severe depression (27.6% vs. 17.7%) does not reveal any significant difference ($p>0.05$).

Therefore, our data can contribute only little to clarify the inconsisting reports on depression in vitiligo so far. To date, there is no conclusive agreement whether patients are more depressed than healthy controls. One reason might be that all the reports that showed indeed a difference had been conducted with other tools than the BDI, for example Zung Depression Scale (Kökçam et al. 1999) or the depression subscale of the Minnesota Multiphasic Personality Inventory (Elgoweini et al. 2003). Further investigations involving a bigger number of patients and controls as well as the parallel use of the BDI and other instruments are needed to clarify this matter in more detail.

A comparison of the results from the English-speaking vs. German-speaking patients showed that the English-speaking patients were less depressed than the German group. Since we used validated translations, this result might indicate that cultural background influences the outcome.

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[20] The Mann-Whitney-U-test as a non-parametric method is the more appropriate one as our BDI scores are considerably skewed (skewing coefficient is 1.114)

We could show that female patients are more depressed than males. This was not only the case regarding mean / median scores, there were also more female patients within the BDI categories, whereas more men were in the *not depressed* category. This contradicts some of the earlier reports (Lee et al. 2000), but supports our finding in the *anxious-depressive* mood section of the ACS questionnaire.

One earlier study claimed that the longer patients had vitiligo the less depressed they became (Gieler et al. 2000)[21]. Our results cannot support this data, because longer duration of the disease does not correlate with depression. Moreover, our finding that there was no difference between patients younger and older than 35 years are not novel. The same was already reported earlier (Lee et al. 2000)[22]. We could neither find negative nor positive correlations of BDI scores with age and age of disease onset, so that it can be concluded that if patients are depressed because of their vitiligo, it happens independently of how old they are at the time of the survey, how old they were when they got vitiligo and how long they had their disease. Other factors must therefore be more important. One could be patients' perception that psychological stress is involved in the disease, which in turn could either be caused by actual experiences and observations (stress / life events followed by disease onset) or awareness that vitiligo can affect psychosocial well-being. It is not the case that this particular patient group has experienced more stigmatisation (both Chi-square tests, $p>0.05$, data not shown). In any case, perceived psychological stress is highly influential on all questionnaires and their sub-scales.

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[21] Strangely, in the abstract of Gieler's publication it says that '*depression scores tended to **increase** with the duration of illness*', but this contradicts their own finding in the text, where it reads '*there was a significant **negative** correlation between BDI scales and the duration of disease. Patients suffering longer from vitiligo showed **lower** depression scores*' (bold by this author). The latter must be correct as the correlation coefficient is -0.41 (Gieler et al. 2000).

[22] Lee used younger and older than **30** years of age

The same applies to severity of vitiligo. Patients with widely spread vitiligo on the trunk scored significantly higher in the BDI as well as in all the other questionnaires. As already mentioned above, if patients have extended vitiligo on the trunk as the biggest of all body parts mentioned in the questionnaire, then the total disease of these patients becomes severe. Therefore, it can be concluded that the more extended somebody's vitiligo is, the more are these patients at risk to become depressive. This result is surprising because one would think that especially patients with exposed vitiligo would be more affected.

Our data also show that levels of depression are linked to avoidant behaviour. There is a highly significant increase of the median BDI scores the more often patients had hidden their white spots in the past (***$p<0.001$). Moreover, none of the patients who had *never* hidden their vitiligo were depressed, whereas this was only the case in half of those who had hidden their white spots *very often*.

Furthermore, patients who avoided certain situations because of their vitiligo showed higher median BDI scores. However, there is no difference between both groups regarding distribution within BDI categories.

Taken together, we could show that increased levels of depression go along with a tendency to avoid situations because of the disease and to hide the white spots in front of other people. This result can be expected as depression normally involves episodes of retreat and loss of interest in usual activities (Gupta and Gupta 2003).

7.5 Comparison of Adults questionnaires in general

1. Correlation analysis showed that there is a positive and significant correlation between all questionnaires. That means for example that patients with an impaired quality of life are also more likely to be *socially anxious / avoidant, helpless, anxious-depressive* and *depressive*.

This can additionally be seen as confirmation that:

- Social anxiety / avoidance *is* related to quality of life. Both involve the influence of a skin disease on social situations. The ACS addresses this item in general and the DLQI regarding relationships with friends, partners, daily activities such as shopping or sport.
- Depression is indeed present when the ACS reveals increased anxious-depressive mood levels.

2. In all but one questionnaire, no significant difference has been found between the German and English-language questionnaires' scores. As mentioned before, the BDI showed that English-speaking patients were less depressed than the German-speaking ones. This difference could not be caused by translation mistakes as we used official versions of the BDI, but might indeed have been caused by cultural issues. The lack of differences in the other scores also showed that our own translation of the ACS has not lead to severe differences between the original German version and the translated English one.

3. In our study we included active leisure time (sports or hobby), because we wanted to know whether spending the leisure time actively could improve any of the questionnaires' scores. We postulated that this own activity could have a positive effect

on patients' quality of life. Unfortunately, this could not be proven. There were no significant differences between patients with an actively spent leisure time and those who did not do anything special.

7.6 Children's characteristics

7.6.1 Demographic and clinical features

The majority of our children were girls (n=63, 61.2%), but this is not uncommon in the field of vitiligo. Other studies have reported similar distributions (Jaisankar et al. 1992; Njoo et al. 2000) or even higher ones (Grimes and Billips 2000; Iacovelli et al. 2005). However, the question remains whether this is the case only within the groups seeking treatment or in all children with this disease[23]. It might be that the awareness of good appearance may be higher in girls.

While there were only 10% of adult patients with darker skin phototypes IV-VI, the proportion was higher in our children group (n=31, about 30%). Although most of the younger patients were still from around the main geographical areas where the Institute for Pigmentary Disorders is operating (Middle and Western Europe), there were a considerable number of children from ethnic minorities. Some were taking part during an annual meeting of the American Vitiligo Research Foundation (AVRF). This charity does not only raise funds for research, they also organise meetings for affected children and their parents, and many of those children were African-Americans or of other non-Caucasian origin.

[23] Strikingly, an extensive examination of 12,586 school children aged 6-14 from Northern India stated *vitiligo* and *pityriasis alba* as the only dermatologic disorders with *significant female predominance*. Since *all* children in the mentioned age group in selected schools were examined, certain issues such as gender-related awareness of appearance can be ruled out. This indicates at least for this part of the world that there might be indeed a predominance of girls within the children population with vitiligo (Dogra and Kumar, 2003).

When asked for their children's disease severity on different body parts, the parents stated that the *legs* were affected most often *severely*, followed by the trunk. This is different from our findings in the adults group, where hands were most often mentioned. If we take into account that many patients develope vitiligo on sites after an injury (Koebner phenomenon), then this could explain a good part why legs as a common site of injuries in children were mentioned so often by the parents.

The *face* was least often mentioned as being severly affected, which was the same in the adults group. This was followed equally by the neck and arms (but legs and trunk in adults).

One of the reasons that the face is less of a problem when it comes to severity of vitiligo, might be that it obviously responds better to certain treatment modalities such as narrow-band UVB activated pseudocatalase PC-KUS (Schallreuter et al. 2008b).

There are similarities to the adult population regarding positive family history and affected relatives. Both groups do not differ much with 33% of the children (n=34) and 38% of adults (n=111) claiming somebody else in the family positive for vitiligo. When asked for who exactly has got vitiligo, then children and adults name either of their parents most often (in both groups about 34%), followed mainly by their siblings and grand-parents.

Since both our groups have different median ages of disease onset, but apparently a comparable percentage of positive family history and affected relatives, we cannot confirm earlier reports that there is an extended family history in those patients with earlier disease onset (Schallreuter et al. 1993; Pajvani et al. 2006).

The vast majority of our children (>90%, n=94) had been to a doctor because of vitiligo and more than 80% (n=76) of them received treatment. These are numbers similar to

adult populations, where 98.3% of patients (n=362) had been to a doctor and had tried on average of 2-5 doctors (Uesseler 2002).

The broad range of at least 38 different treatment modalities / combinations that had been tried by our children and their parents reflects the current situation regarding medical treatment for the disease. Since to date there is no agreement about what exactly causes vitiligo, it is no surprise that there is a plethora of more or less effective treatments on the market with none of them dominating the field. Even corticosteroids or psoralens + UVA (PUVA) as popular treatments in the past were not mentioned particularly more often than others[24].

7.6.2 Attitudes, activities and experiences

Our children population can be characterised as an active group, well integrated into their social environment.

Almost 90% of participants (n=92) stated to have a hobby or that they were doing sports in their leisure time with no differences between boys and girls. Of those who confirmed that more than 83% preferred one or two hobbies / sports (n=55), the remaining did even more. This is a rather high proportion when compared to a representative sample of German children (n=1,592, aged 8-11 years) where 81% were found to actively spend their leisure time (Hurrelmann and Andresen 2007).

This particular study also stated that an actively spent leisure time is found in children of middle or upper classes rather than in those of lower classes (Hurrelmann and

[24] There is, however, 13.7% of children who stated just 'cream' as their treatment modality with no further differentiation.

Andresen 2007). Whether that means that our children are more from middle or upper class environments is difficult to assess as this was not part of our questionnaire.

A break-down of what exactly was done revealed that surprisingly few children preferred inactive or quiet ways to spend their leisure time (only 2 out of 66 stated *fishing* or *reading*), all the other ones did something actively including sport or anything in arts (music, dancing).

When we asked the children which season of the year they liked best, a majority of more than 80% (n=81) said that it was spring or summer. Since people tend to wear shorther clothes during those seasons, these answers were surprising, because there was apparently no fear with regards to their vitiligo. In our opinion this is a positive sign and this answer clearly indicates that the daily life of our children was not completely influenced by their white spots.

There are no comparable data available in the literature. Only McLeod addressed something similar by asking adult patients about the significance of the summer months. However, this was more related to sun exposure and how much patients were avoiding sun. The majority of female patients did avoid such situations, whereas this was not the case in men (McLeod 2004).

These different kind of questions makes it difficult to compare both groups. However, in general it seems that summertime is more an issue in the adult group than in children. This issue is frequently mentioned by patients attending the Institute for Pigmentary Disorders for the first time (Prof. KU Schallreuter, personal observation).

About two thirds of our children group had *many* friends, one third had just a *few* and only one child claimed not to have a single friend. In the German study mentioned above, there were less children with a few friends (15%) and more who had many

friends (Hurrelmann and Andresen 2007). However, it still seems that the vast majority of our children group is well integrated into their social environment, at least in terms of friends. This is important as friends are potential sources of support for psychosocial well-being.

Other indicators for level of integration are stigma-related experiences such as bullying or approaches / questions by others. About 94% (n=93) had experienced approaches / questions by others, almost half had been picked on or subjects to nasty comments (n=47) and about 20% reported that they had been bullied because of their vitiligo (n=8). Only one child had experienced physical violence because of vitiligo. There were no differences between girls and boys.

These numbers seem to be rather high. By comparison, only 34% of German children in a representative study (n=1,592) stated to have experienced bullying, nasty comments or physical violence within the last year (Hurrelmann and Andresen 2007). Taking this number into consideration, the proportion of bullying in our group is smaller than in the German study, but if taken together with nasty comments, it is actually increased, and it can be expected that vitiligo is one of the reasons for it.

When compared to our adult group, it can be concluded that the proportion of children that had been approached / asked questions is only slightly bigger than in our adult population (**Table 78**) where in addition women are more likely to be asked questions.

However, children are more likely to be picked on or to become subjects to nasty comments (only 24% of adults, **Table 78**). It seems to be that this kind of stigmatisation is age-related. This is also confirmed by those adults patients with disease onset in their teenage year. In all age groups there is no differences between female and male patients.

Stigmatisation experiences	Children		Adults	
	%	N	%	N
Questions / approaches by others	**94**	99	**90**	123
Picked on / nasty comments	**47**	99	**25**	123
Bullying	**19**	42	n.d.	--
Physical violence	**2**	47	n.d.	--

Table 78: Comparison of our children and adult groups regarding frequencies of stigmatisation

There are studies available on levels of support patients with vitiligo have received (Porter et al. 1979; Cordalija 2004). This has never been investigated in children, therefore our results contribute something novel to the field.

Our results revealed that in situations where children had a problem with somebody else because of their vitiligo, they were helped particularly often by friends and members of the family. Less often mentioned were teachers and others. However, about one third had not received help in such situations. Considering that this question had been asked semi-openly, we are certain that we provided the right choices to answer, because the open answer 'others' was only chosen by one participant.

The importance of friends and family as sources of support is strenghtened by the children's answers whom they would contact first when they had experienced disease-related problems. Here again, members of the family (especially the mother) and best friends were mentioned most often. The importance of the mother is more pronounced compared to the father. It seems to be that mothers either can empathise better with their children or that they are just in closer contact compared to the fathers. It can also be that the father is not as present as the mother, be it due to work commitment or complete absence, for instance after a divorce. These findings are absolutely relevant, although the possibility to answer this item was an open one.

Only 5% of the children said that they would never tell anybody when they just had a problem related to vitiligo. Seeking somebody else's support is important for coping and obviously it is not the case that the majority of children lack this source.

When asked directly for their attitudes towards vitiligo, about 70% of our children group said that they are at least sometimes bothered by their white spots. There are no differences between girls and boys.

It seems to be that the children are generally concerned about vitiligo, not just about their relationships to others, because when asked about which spots should disappear first, only 16% (n=16) said that it should be only those spots visible to others. About three quarters of our population (n=72) whished that *all* patches should go away.

A vast majority of our children (79%, n=79) said that it is important to them that their disease would eventually disappear one day, only 4% (n=4) denied that. That means that even though a considerable proportion said that they are *currently* not bothered by their vitiligo, they still wished to get rid off the disease sometime later on in life.

Taken together, in all the three questions there was a consisting majority of at least 70% of the children who showed difficulties with having white spots – they felt not only bothered and wanted that their spots should disappear one day, they also wanted *all* of them to go away.

There are 30% (n=27) of our children group that have avoided certain situations because of their vitiligo. Here, girls are more likely to do that compared to boys and so are young patients who have experienced that they had been picked on. Also, there is a strong link between avoidant behaviour and feelings of disturbance by the disease, because we found that especially those had avoided situations who felt bothered by their vitiligo. These results weaken our finding about the positive attitudes of our children toward summer and spring. It is obviously the case that children do like the warm

seasons of the year, but this has nothing to do with their actual behaviour and tendency to hide the white spots.

Most often avoided were situations where an exposure of the disease to other children was very likely, i.e. swimming / bathing and getting undressed in changing rooms. Less often mentioned were social situations such as shaking hands and talking to other people.

7.7 Children's Dermatology Life Quality Index

The Children's Dermatology Life Quality Index has rarely been used in young patients with vitiligo. Therefore, there are not many possibilities to compare our results with others.

Children with vitiligo have a more impaired quality of life compared to healthy controls. Other authors reported similar low scores for healthy controls, for example Chuh et al with a mean score of 0.6 (n=30) or Lewis-Jones and Finlay with mean scores of 0.4 and 0.7 (n= 47 and n=55) (Lewis-Jones and Finlay 1995; Chuh 2003).

To the best of our knowledge, this thesis includes the first direct comparison between children with vitiligo and healthy controls using the Children's Dermatology Life Quality Index (CDLQI). The results show that this skin disease influences essential parts of young patients' daily life, which is the same as in adult patients.

Compared to other publications, our mean score of 2.7 (median 1.0) is rather low.

Njoo reported a mean CDLQI score of 5.6 in 51 children with vitiligo prior to treatment with narrow-band UVB over one year. After the therapy this score decreased to 2.1 and was only then comparable to our group's score (Njoo et al. 2000).

Agarwal et al included 18 children with vitiligo in their study and reported median CDLQI scores of 1.0, 1.5 and 3.0 in two groups at the beginning and the end of a medical trial (Agarwal et al. 2005), the latter two are increased compared to our group.

Guttman reported that 21 children with vitiligo scored a mean of 3.8 in an unpublished study by Schwartz and Sepulveda (Guttman 2007).

Beattie and Lewis-Jones provided a score for children with *'pigmentary abnormality'* of 1.5 (n=7). It remains unclear whether any cases of vitiligo were included (Beattie and Lewis-Jones 2006). There are no other publications available for the use of the CDLQI in children with vitiligo[25].

In addition, when compared to other skin diseases including *viral warts*, *molluscum* or *psoriasis*, the CDLQI score of our group is still low (Chuh 2003; Holme et al. 2003). Higher scores have also been reported for *scabies, eczema, acne, epidermolysis bullosa* or *urticaria*. *Naevi* was the only condition where a lower CDLQI score was reported (Lewis-Jones and Finlay 1995; Chuh 2003; Holme et al. 2003; Guttman 2007).

Single item analysis showed that vitiligo had the strongest impact on *emotional reactions*, followed by *sport / swimming* and, equally, *physical symptoms*. Similar tendencies have been reported from groups of children with various skin diseases (n=107) (Lewis-Jones and Finlay 1995; Holme et al. 2003).
Surprisingly, not a single one of our children said that vitiligo had affected their friendships to other children during the week prior to answering the questionnaire. This is in sharp contrast to our adult group. Our results suggest that friendships between children are hardly influenced by physical appearance. Similar findings have been reported for children with various skin diseases (Lewis-Jones and Finlay 1995; Holme et al. 2003). In our group it remains unclear why so many of the children reported that their skin disease had caused them any kind of physical sensations (pain, soreness etc) during the last week.

[25] A search in *www.pubmed.com* using 'CDLQI' and 'vitiligo' as keywords yielded only Njoo et al's report

Interestingly, children who had somebody else with vitiligo in the family did complain less about that the treatment itself poses a problem. Since in many cases children's parents also had vitiligo, it could mean that if both parts do the treatment together in a certain way, then quality of life can be improved. At the same time, the treatment is also less annoying to the children.

Stigmatising encounters such as other people asking questions about the disease, proved more influential in young patients compared to adult patients. Children who had been approached by others and asked questions, showed significantly increased CDLQI scores. Single item analysis showed that especially daily activities such as *going out, playing* and *doing sports* were impaired.

This effect is even stronger when the children were subjects to nasty comments or when they had been picked on. Those children scored much higher in the CDLQI, and particularly in *emotional reactions,* essential *daily activities*, their *performance in school* and their *choices of clothes* to wear.

Similar to the adult population, disease severity influenced the outcome of the CDLQI scores. Girls with severely affected faces scored significantly higher in the CDLQI and particularly regarding *physical symptoms* and *going out / playing*. This was not the case in boys, who would still go out and play. Hence it can be concluded that a good appearance is more important to girls compared to boys.

Having received treatment for vitiligo earlier or being enrolled with the Institute for Pigmentary Disorders alone does not make a difference for children regarding their quality of life. However, our results indicate that children who underwent treatment are

more concerned about choice of *clothes / shoes, swimming / sports* and by the *treatment itself,* whereas their *school work* is less likely affected.

It can be concluded that severity of vitiligo or certain stigmatising experiences are much more influential on children's quality of life.

7.8 Children and their parents

To the best of our knowledge there have never been any investigations into the child-parent relationship in the field of vitiligo using questionnaires for both sides as it was done in other skin diseases, for instance atopic dermatitis (Lawson et al. 1998)[26].

Our results suggest that parents of children with vitiligo are also more *socially anxious / avoidant, helpless* and *anxious-depressive*, when it comes to views on their children's skin disease. This group scored much higher in all subscales than parents of healthy children. That means that those parents show a similar behaviour pattern as adult patients. They have in common that they fear situations where vitiligo might be exposed to other people, and they also feel helpless with regards to the disease's course.

This is confirmed by our findings that parents whose children had *never* hidden their white spots felt least *socially anxious / avoidant*. There were differences between fathers and mothers with fathers being additionally less *helpless* and *anxious-depressive.*

In general, levels of *anxious-depressive mood*, a sub-scale not directly linked to skin diseases, are increased in parents of patients compared to healthy controls.

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[26] Guttman reported that Schwartz and Sepulveda used children with vitiligo and their parents and asked each group to fill out separate questionnaires. However, this has not been published properly, only by a third person in an article based on interviews with the researchers in the Dermatology Times (Guttman 2007)

There is a correlation between mothers' and fathers' scores, meaning that if one parent is more *socially anxious / avoidant* or *helpless*, then it is very likely that the other parent is affected as well. This could be the results of inter-parental relation and interaction, especially regarding their child's disease.

There is no correlation in the *anxious-depressive mood* subscale, which, interestingly, is the only one not specified for skin diseases. That means that parents often feel (and fear) the same when it comes to their child's skin disease, but they do not have to have the same basic personality structures or problems.

Despite the mentioned correlations between mothers and fathers, only the *social anxiety / avoidance* and *helplessness* scores of the mother do correlate with the CDLQI scores of their children. It could be that mothers are more sensitive about their childrens' quality of life, but it could also mean that an increased fear of situations where vitiligo might be exposed to others leads to an impaired quality of life of the children.

Here again, there is no correlation regarding *anxious-depressive mood* and CDLQI, as this scale is not disease-related, but about a basic personality structure.

Something completely new in the field of vitiligo are our findings about parents' searching their children for new white spots. We found that more than 40% admitted to do that often with no differences between mothers and fathers. Also, higher scores in all ACS sub-scales correlate with an increased frequency that parents search their children for new white spots (except for fathers in *social anxiety / avoidance*). It might be that this habit reflects helplessness regarding and also concern about the course of the disease as if parents seek reassurance or hope that the disease has gone better.

All scores do not depend on the age of parents or duration of their child's disease. Moreover, there was no strong influence of disease status, whether the vitiligo of their children was actively spreading, stable or improving except for *helplessness* of mothers. They felt much more helpless when the disease was progressing, whereas mothers were hardly affected when the disease was stable. Obviously mothers feel more secure and less helpless when there is no change in their children's vitiligo at all, not even an improvement.

Parents differ from patients with vitiligo regarding their beliefs about possible causes for vitiligo. While patients strongly believe that psychological stress, but not other diseases or injuries, are involved in triggering or exacerbating vitiligo, this is not the case in parents. None of these factors play a role according to parents' beliefs. There were no differences between mothers and fathers. Since we did not offer the possibility of an open answer, we cannot conclude whether any other causes come ito the picture by parents.

Interestingly, those fathers who did believe that psychological stress is involved, scored significantly higher in *social anxiety / avoidance* and *anxious-depressive mood*. This could be caused by actual observations that the disease onset followed certain live events or experiences. It is puzzling why this is not the case for mothers.

8 Summary

Vitiligo is a common depigmentation disorder known for thousands of years. Only from the 20th century some progress has been made to find the cause and an appropriate treatment for this disease. However, less effort has been spent on the psychological effects of the disease. Although many aspects, such as quality of life, depression, self-consciousness or embarrassment have been covered since the 1970s, this has not been the case for social anxiety / avoidance, helplessness and anxious-depressive mood. There is even less known about the influence of vitiligo on children. Therefore we felt it was in need to close some of these gaps and to further substantiate earlier findings.

In this cross-sectional study we investigated 422 adult patients and 103 children with vitiligo for disease-related experiences, behaviours and well-being. Our results can add some more pieces to the knowledge about the psychosocial effects of this disease.

Adults

1. The adult patient group was socio-demographically not different from other groups in the literature. There was a majority of women, a median age of 43 years and a peak of disease onset between 10 and 19 years of age. However, hands as most often mentioned site of onset has only once reported before.
2. We found that this patients group had experienced a high degree of stigmatisation (90%). Women and patients with extended vitiligo on their hands and legs were more likely to get stigmatised.
3. Two thirds of our patients showed avoidant behaviour, especially hiding the white spots and avoiding situations because of vitiligo.

4. Quality of life was limited compared to healthy controls, but less impaired compared to other groups. Our patients were mostly affected regarding their emotional reactions (upset, embarrassment). Levels of quality of life were not influenced by stigmatisation, duration of the disease or skin colour, but by disease severity on trunk and presence of avoidant behaviour. 60% had an only slightly impaired quality of life, wheras this was severely or even extremely reduced in another 16% of the patients.
5. There were severe problems in coping with this chronic skin disease. Our patients were significantly more socially-anxious, helpless and anxious-depressive compared to healthy controls on a level comparable to other groups in the literature. Female patients, individuals who had been picked on or had become subjects to nasty comments as well as patients with extended disease on their trunks, arms, necks and legs had more difficulties in coping. Older patients were less affected. Impaired coping and avoidant behaviour correlate.
6. Patients with vitiligo were more depressed than healthy controls. However, there was only a weak significance of this difference as the number of patients was too small. Depression is more common in female patients. Disease severity on trunk and avoidant behaviour are influencing factors. German-speaking patients showed higher levels of depression.
7. Correlation analysis of the three questionnaires revealed that all of these limitations are very likely to occur together in one patient. Women were generally more affected. Hiding behaviour and levels of stigmatisation were highly influential on coping.
8. Three quarters of our patients believed that psychological stress is influential on the disease. This group had a later disease onset and a reduced quality of life. They were

also much more socially anxious / avoidant, helpless, anxious-depressive and depressed.

9. Treatment with narrow-band UVB activated pseudocatalase PC-KUS is medically successful. There were less patients with spreading vitiligo compared to untreated patients. The treatment also improves quality of life and eases anxious-depressive mood.

Children and their parents

1. Our group included more girls than boys which is not uncommon in this field. Earlier reports of an extended family history with earlier disease onset could not be confirmed by our results.
2. When compared to a representative sample of German children, members of our groups were slightly more active in their leisure time, but had less often many best friends.
3. Almost everybody had experienced stigmatisation (questions), half of our children had been picked on and every fifth had received bullying. However, physical violence because of vitiligo is very rare. Picking on / nasty comments and bullying were much more common compared to the general German children population.
4. Family members and friends are important sources of support in critical situations, and were most often sought as contact of first choice after such incidents. Mothers were more important than any other person mentioned.
5. More than two thirds of our children were bothered by their disease. Every third child had avoided situations because of vitiligo. Girls were more likely to do so compared to boys.
6. Quality of life was significantly more impaired in our young patients compared to healthy children. Vitiligo had the strongest effect on emotional reactions.

Surprisingly, friendships to other children were not affected at all. Influential factors were levels of stigmatisation and disease severity in the face.

7. The parents of our young patients were considerably socially anxious / avoidant and helpless in their views towards their children's skin disease. Children of parents with lowest social anxiety / avoidance scores were least likely to hide their white spots.
8. Mothers' and fathers' scores correlated in the disease-related scores of the ACS, but not in anxious-depressive mood as the only disease-independent scale.
9. Parents' ACS and children's CDLQI scores correlated only in social anxiety / avoidance and helplessness scores of the mother.
10. More than 40% of parents examine their children often for new white spots.
11. Any change in their children's vitiligo (improving or worsening) affected negatively feelings of helplessness of mothers, whereas stable vitiligo made them feeling less helpless.

Future work

Some of the results of this project as well as some of its limitations invite to more work that should be done in the future.

1. Since our results regarding depression in vitiligo could not clarify the inconsistent reports in the literature so far, the Beck Depression Inventory should be used again, but probably with more patients and together with other validated tools to measure depression levels. By doing so, it should be possible to determine whether the results obtained with the BDI are comparable to those of other depression questionnaires.

2. It should be avoided to introduce certain questionnaires later after the project has started. Our results which are based on the Adjustment to Chronic Skin Disorders questionnaire, are clearly valid for our total patient group, whereas this is less certain for the DLQI and BDI measurements, because these were not used in all patients.

3. Parents of children with vitiligo should be included more often in any future research on quality of life or coping with vitiligo. Our results clearly underlined the importance of the parents, especially as sources of support in critical situations or as role models. Despite this importance, parents of children with vitiligo have never really been used in studies undertaken so far. Therefore, there is a need for future work including the role of the parents and possible support for them by providing a better insight in the parents-children relationships.

4. The socio-economic status of the parents should be considered in any future studies on vitiligo in children. This could help to recommend different strategies of supporting the affected children if there are indeed differences between the economic classes.

9 Appendix

9.1 Adults' questionnaire

Patient

This first page is just about your life <u>OVER THE LAST WEEK</u>. Please tick one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	yes no	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

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The following questions <u>are not just only about the past week</u>.

	Not at all	hardly ever	quite	mostly	totally
1. My appearance worries me.	1	2	3	4	5
3. I am less attractive than other people because of my skin disease.	1	2	3	4	5
4. There are situations I avoid because of my skin disease.	1	2	3	4	5
5. Because of my skin I am unable to get in contact with unknown people easily.	1	2	3	4	5
6. I am nervous very often.	1	2	3	4	5
7. I am feeling blocked sexually because of my skin disease.	1	2	3	4	5
8. I cannot make many of my wishes true because of my skin disease.	1	2	3	4	5
9. I am preoccupied with why I especially got this disease.	1	2	3	4	5
10. I pay attention to other people's skin.	1	2	3	4	5
11. Because of the disease it is difficult to find a (new) partner.	1	2	3	4	5
13. I am getting upset by very little things.	1	2	3	4	5
16. I separate myself from my family / partner.	1	2	3	4	5
19. I avoid sauna or pool because other people might be repulsed.	1	2	3	4	5
21. I feel tired very often.	1	2	3	4	5
22. I would like to be as easy-going as other people.	1	2	3	4	5
23. I've got the feeling that other people stare at my skin.	1	2	3	4	5
24. My skin disease limits myself generally in my life.	1	2	3	4	5
30. I am sensitive to how other people react to my skin disease.	1	2	3	4	5
31. I am scared of being rejected by strangers.	1	2	3	4	5
32. I loose my energy.	1	2	3	4	5

	Not at all	hardly ever	quite	mostly	totally
34. When I look into a mirror I pay special attention to my skin.	1	2	3	4	5
36. I am scared that my skin disease is getting worse.	1	2	3	4	5
37. The disease takes a lot of spontaneity from me.	1	2	3	4	5
39. I am sometimes desperate because of my skin disease.	1	2	3	4	5
40. I am concerned by how other people view my skin disease.	1	2	3	4	5
41. Often I wonder what life would be like without my skin disease.	1	2	3	4	5
42. Because of my white spots I am feeling uncomfortable when other people see me naked.	1	2	3	4	5
43. Many things bother me.	1	2	3	4	5
46. I should be less stressed.	1	2	3	4	5
47. I can't often concentrate.	1	2	3	4	5
48. I pay a lot attention to my skin.	1	2	3	4	5
49. Sometimes I feel I could climb up the wall.	1	2	3	4	5

Finally, please answer the following questions

Age: _____ years Sex: ( ) male ( ) female

In which age did your disease appear? In the age of _____ years.
Except if you were a baby: In the age of _____ months.

Have the following factors influenced your disease?

- Psychological stress Yes ◯ No ◯
- Trauma to the skin (injuries, burns, sun burns...) Yes ◯ No ◯
- other diseases Yes ◯ No ◯
- Hereditary disposition (is there anybody else in your family with vitiligo?) Yes ◯ No ◯
  If yes, who:_____ (how related)

What skin type is yours?

Pale/ light, I always get sunburn ◯
Pale/light, tan slightly ◯
Pale/light, tan well ◯
Dark, tan well ◯
Very dark ◯

Do you any sports, or do you have a hobby?

Yes ◯ No ◯

If yes, what? .....

Which parts of your body are affected at present?
If affected, slightly or heavily?

	slightly	heavily
( ) face	( )	( )
( ) neck	( )	( )
( ) hands	( )	( )
( ) arms	( )	( )
( ) body	( )	( )
( ) legs	( )	( )

Is your vitiligo spreading?

◯ *Yes*

◯ *No, it's stable*

◯ *No, it's repigmenting*

Has anyone (strangers, colleagues or so) ever mentioned your white spots, or have you been asked what it is?

Yes, very often ◯ Yes, a few times ◯ Never ◯

Have you ever been picked upon or has anyone ever been nasty to you because of your white spots?

Yes, very often ◯ Yes, sometimes ◯ No ◯

How often have you tried to hide your white spots in front of other people?

Never ◯ Very rarely ◯ Quite often ◯ Very often ◯

How did you hide your white spots?

- Hiding under your clothes ◯
- Hiding by certain positions (hands in pockets, turning body away…) ◯
- By covering up ◯
- By others, like ……
- I have never hidden my white spots ◯

Have your ever avoided one or more of the following situations because of your white spots?

Swimming / bathing ---------- ◯
Sports ---------- ◯
Shaking hands ---------- ◯
Talking to other people ---------- ◯
Undressing in changing rooms ---------- ◯
Others, like ……
I have never avoided any situation because of my white spots ◯

Do you have single white hair in your scalp hair Yes ◯ No ◯

or single white hair in your eyelashes or eyebrowes Yes ◯ No ◯

Where on your body did your first white spot appear? _____

BDI

Please could you circle the number against the most appropriate statement

1
0 I do not feel sad.
1 I feel sad
2 I am sad all the time and I can't snap out of it.
3 I am so sad and unhappy that I can't stand it.

2.
0 I am not particularly discouraged about the future.
1 I feel discouraged about the future.
2 I feel I have nothing to look forward to.
3 I feel the future is hopeless and that things cannot improve.

3.
0 I do not feel like a failure.
1 I feel I have failed more than the average person.
2 As I look back on my life, all I can see is a lot of failures.
3 I feel I am a complete failure as a person.

4.
0 I get as much satisfaction out of things as I used to.
1 I don't enjoy things the way I used to.
2 I don't get real satisfaction out of anything anymore.
3 I am dissatisfied or bored with everything.

5.
0 I don't feel particularly guilty
1 I feel guilty a good part of the time.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6.
0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7.
0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

8.
0 I don't feel I am any worse than anybody else.
1 I am critical of myself for my weaknesses or mistakes.
2 I blame myself all the time for my faults.
3 I blame myself for everything bad that happens.

9.
0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10.
0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry all the time now.
3 I used to be able to cry, but now I can't cry even though I want to.

11.
0 I am no more irritated by things than I ever was.
1 I am slightly more irritated now than usual.
2 I am quite annoyed or irritated a good deal of the time.
3 I feel irritated all the time.

12.
0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.

13.
0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions more than I used to.
3 I can't make decisions at all anymore.

14.
0 I don't feel that I look any worse than I used to.
1 I am worried that I am looking old or unattractive.
2 I feel that there are permanent changes in my appearance that make me look unattractive.
3 I believe that I look ugly.

15.
0 I can work about as well as before.
1 It takes an extra effort to get started at doing something.
2 I have to push myself very hard to do anything.
3 I can't do any work at all.

16.
0 I can sleep as well as usual.
1 I don't sleep as well as I used to.
2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3 I wake up several hours earlier than I used to and cannot get back to sleep.

17.
0 I don't get more tired than usual.
1 I get tired more easily than I used to.
2 I get tired from doing almost anything.
3 I am too tired to do anything.

18.
0 My appetite is no worse than usual.
1 My appetite is not as good as it used to be.
2 My appetite is much worse now.
3 I have no appetite at all anymore.

19.
0 I haven't lost much weight, if any, lately.
1 I have lost more than five pounds.
2 I have lost more than ten pounds.
3 I have lost more than fifteen pounds.

20.
0 I am no more worried about my health than usual.
1 I am worried about physical problems such as aches and pains, or upset stomach, or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think about anything else.

21.
0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I have almost no interest in sex.
3 I have lost interest in sex completely.

9.2 Children's questionnaire

Questionnaire

To start we have some questions about you...

1. Are you

a boy ◯ or a girl ◯ ?

---

2. How old are you? …years

---

3. How many best friends do you have?

None ◯ A few ◯ Many ◯

---

4. Do you do any sports or do you have any hobbies?

Yes ◯ No ◯
if yes, which? .....

---

5. Which of the following seasons do you like most?

Spring ◯ Summer ◯ Autumn/Fall ◯ Winter ◯

---

6. What does your skin look like?

Pale/light, I always get a sunburn ◯
Pale/light, tan slightly ◯
Pale/light, tan well ◯
Dark, tan well ◯
Very dark ◯

Now we would like to ask some questions about your white spots...

7. Can you remember how long you have your white spots?

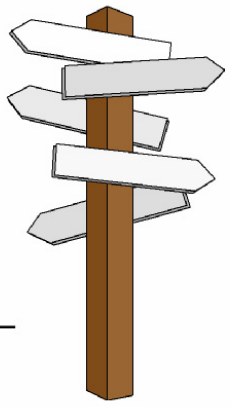
For …….years

---

8. Are there any other persons in your family with white spots?

No ◯ **Yes** ◯

If yes, who? ……..



9. Have you ever been to a doctor because of your white spots?

No ◯ **Yes** ◯

---

10. Have you ever been treated for your white spots?

No ◯ **Yes** ◯

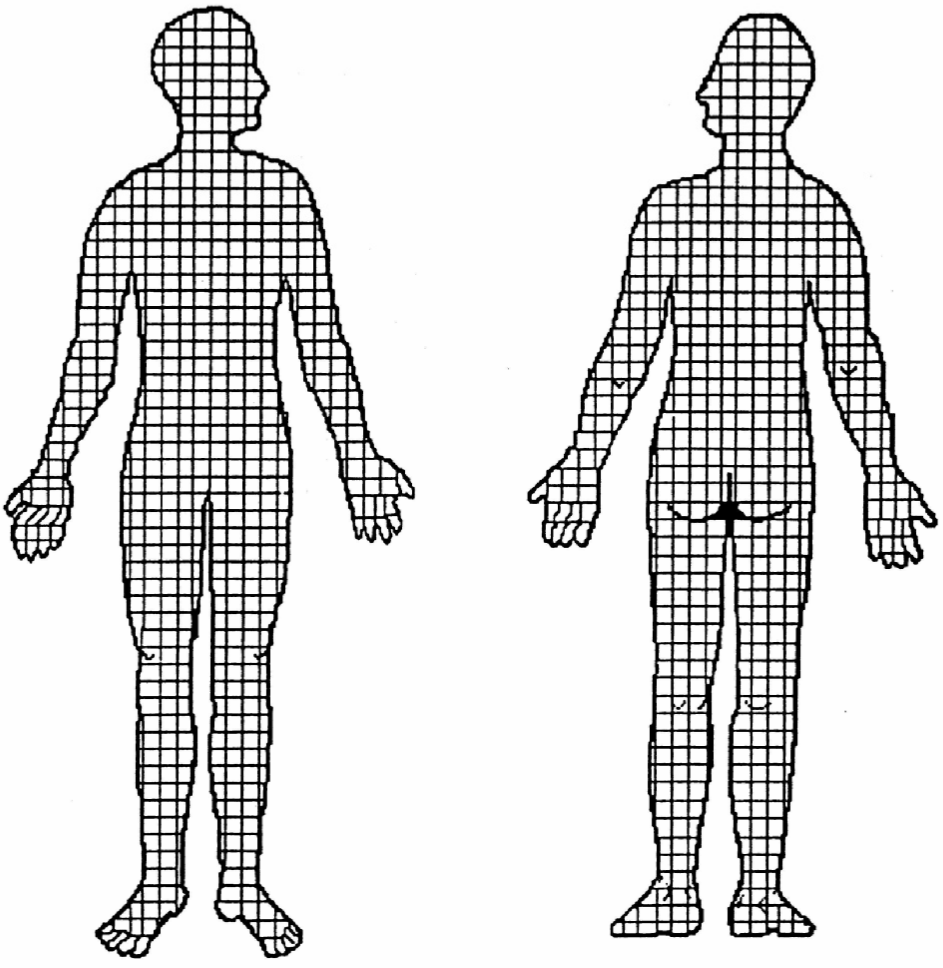
If yes, by which treatment? ……..

---

11. Here is a drawing of your body both front and back

(of course, in reality you are much more beautiful!)

We would like to know from you, where are your white spots. Please draw them into this drawing!



We have also some questions about your last week ...

The aim of this part of the questionnaire is to measure how much your skin problem has affected you OVER THE LAST WEEK. Please tick ❒ one box for each question.

12. Over the last week, how **itchy**, **"scratchy"**, **sore** or **painful** has your skin been?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒
13. Over the last week, how **embarrassed** or **self conscious**, **upset** or **sad** have you been because of your skin?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒
14. Over the last week, how much has your skin affected your **friendships**?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒
15. Over the last week, how much have you changed or worn **different** or **special clothes/shoes** because of your skin?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒
16. Over the last week, how much has your skin trouble affected **going out**, **playing**, or **doing hobbies**?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒
17. Over the last week, how much have you avoided **swimming** or **other sports** because of your skin trouble?	Very much Quite a lot Only a little Not at all	❒ ❒ ❒ ❒

18. Last week, was it ❒ **school time?**

***If school time**: Over the last week, how much did your skin affect your **school work**?*

Prevented school ❒
Very much
Quite a lot ❒
Only a little ❒
Not at all ❒

OR

was it **holiday time?**

***If holiday time**: How much over the last week, has your skin problem interfered with your enjoyment of the **holiday**?*

Very much ❒
Quite a lot ❒
Only a little ❒
Not at all ❒

---

19. Over the last week, how much trouble have you had because of your skin with other people **calling you names**, **teasing**, **bullying**, **asking questions** or **avoiding you**?

Very much ❒
Quite a lot ❒
Only a little ❒
Not at all ❒

---

20. Over the last week, how much has your **sleep** been affected by your skin problem?

Very much ❒
Quite a lot ❒
Only a little ❒
Not at all ❒

---

21. Over the last week, how much of a problem has the **treatment** for your skin been?

Very much ❒
Quite a lot ❒
Only a little ❒
Not at all ❒

Finally, how do you feel about your white spots?

22. Do your white spots bother you?

No ◯ **Yes** ◯ **Sometimes** ◯

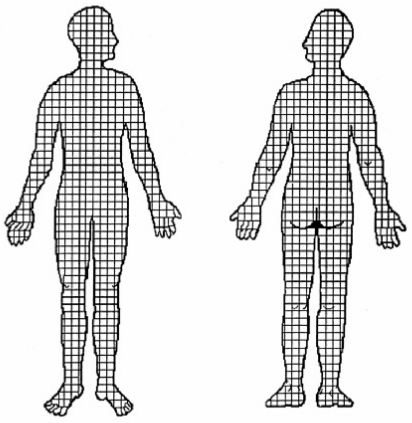
---

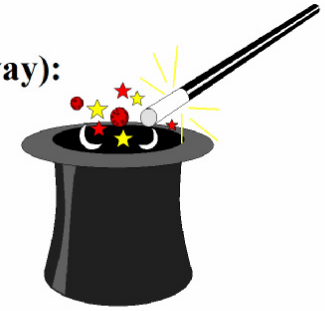
23. If you could have a wish which spot should disappear first?

The ones people can see ◯ all of your spots ◯ *or*

something else

(Please draw where you want the spots to go away):





---

24. How often did you try to hide your white spots in front of other people?

Never ◯ Very rarely ◯ Quite often ◯ Very often ◯

---

25. How did you hide your white spots?

- **Hiding under your clothes◯**
- **Hiding by certain positions (hands in pockets, turning body away…) ◯**
- **By covering up ◯**
- **By others, like ……..**
- **I have never hidden my white spots ◯**

26. Have your ever avoided one or more of the following situations because of your white spots?

Swimming / bathing ◯
Sports ◯
Shaking hands ◯
Talking to other people ◯
Undressing in changing rooms ◯
Others, like ……
I have never avoided any situation because of my white spots ◯

---

27. Has anyone ever mentioned your white spots and asked what it is?

Yes, very often ◯ **Yes, sometimes** ◯ **No** ◯

---

28. Have you ever been picked upon or has anyone ever been nasty to you because of your white spots?

Yes, very often ◯ **Yes, sometimes** ◯ **No** ◯

---

29. Have you ever received bullying because of your white spots?

Yes, very often ◯ **Yes, sometimes** ◯ **No** ◯

30. Have you ever received help in those situations of being picked upon or being bullied?

Yes, by friends ◯
Yes, by members of your family ◯
Yes, by strangers ◯
Yes, by others, like …….
No ◯

---

31. Which person would you contact first when you just had a problem with another person because of your vitiligo?

To the following person: .....
I would keep it for myself ◯

---

32. Is it important to you that your white spots disappear one day?

Yes ◯ **I don't care** ◯ **no** ◯

Now you have finished the questionnaire. Thank you very much for your help!!!

Date: |___| |___| |___|
Day / Month / Year

9.3 Parents' questionnaire

Marburg Skin Questionnaire (MHF)

-modified for parents-

On the following pages you will find many statements about several points, which might be correct for you or your child. We are interested in how much those statements are correct for your child. This questionnaire is about your own and personal opinion. There are no "right" or "wrong" answers!

Please cross out a number at every question and do not miss any question in the survey.

The meaning is

1 = not at all right
2 = hardly ever right
3 = quite right
4 = mostly right
5 = totally right

Example:

The appearance of your child hardly worries you. In this case please cross off the number:

The appearance of my child worries me. 1 ~~2~~ 3 4 5

Please read carefully the statements, but don't spend too much time at every single point. Your first answer is the best!
The claims will not apply to you or your child sometimes, but please don't miss any claim. Please choose the level, which applies *to you* mostly.

Do you know the exact diagnosis of your child's skin disease?

Diagnose: _____

	Not at all	hardly ever	quite	mostly	totally
1. The appearance of my child worries me.	1	2	3	4	5
2. I sleep badly because of my child's skin disease.	1	2	3	4	5
3. My child is less attractive than other people because of its skin disease.	1	2	3	4	5
4. There are situations I avoid because of my child's skin disease.	1	2	3	4	5
5. Because of its skin my child is unable to get in contact with unknown people easily.	1	2	3	4	5
6. I am nervous very often.	1	2	3	4	5
7. ----------					
8. I cannot make many of my wishes true because of my child's skin disease.	1	2	3	4	5
9. I am preoccupied with why my child especially got this disease.	1	2	3	4	5
10. I pay attention to other people's skin.	1	2	3	4	5
11. It will be difficult for my child in the future to find a partner.	1	2	3	4	5
12. I search my child often for new white spots.	1	2	3	4	5
13. I am getting upset by very little things.	1	2	3	4	5
14. I still need to learn a lot more how to cope with the skin disease.	1	2	3	4	5
15. I should take care of my child's skin better.	1	2	3	4	5
16. I seperate myself from my partner / my family to show consideration.	1	2	3	4	5
17. ----------					
18. I care little about my child's food.	1	2	3	4	5
19. I avoid sauna or pool for my child because other people might be repulsed.	1	2	3	4	5
20. I am feeling uncomfortable when other people see my child' white spots.	1	2	3	4	5
21. I feel tired very often.	1	2	3	4	5
22. I would like to be as easy-going as other people.	1	2	3	4	5

	Not at all	hardly ever	quite	mostly	totally
23. I have got the feeling that other people stare at my child's skin.	1	2	3	4	5
24. My child's skin disease limits myself generally in my life.	1	2	3	4	5
25. I am not as able as other people to take stress.	1	2	3	4	5
26. I should know more about my child's skin disease.	1	2	3	4	5
27. Sometimes I would like to give up regarding the disease.	1	2	3	4	5
28. Other people stare at my child because of its skin disease.	1	2	3	4	5
29. Due to my child's skin disease I have a lot of expenses.	1	2	3	4	5
30. I am sensitive to how other people react to my child's skin disease.	1	2	3	4	5
31. I am scared that my child might be rejected by strangers because of its skin disease.	1	2	3	4	5
32. I loose my energy.	1	2	3	4	5
33. My child will not be able to work in certain professions because of its skin disease.	1	2	3	4	5
34. When I look my child I pay special attention to its skin.	1	2	3	4	5
35. My family / partner is also affected by my child's skin disease.	1	2	3	4	5
36. I am scared that my child's skin disease is getting worse.	1	2	3	4	5
37. The disease takes a lot of spontaneity from me.	1	2	3	4	5
38. When I see my child's white spots I feel ill.	1	2	3	4	5
39. I am sometimes desperate because of my child's skin disease.	1	2	3	4	5
40. I am concerned by how other people view my child's skin disease.	1	2	3	4	5
41. Often I wonder what life would be like without my child's skin disease.	1	2	3	4	5
42. I feel uncomfortable when other people see my child naked with its white spots.	1	2	3	4	5

	Not at all	hardly ever	quite	mostly	totally
43. Many things bother me.	1	2	3	4	5
44. My child's white spots get on my nerves.	1	2	3	4	5
45. I've got the impression that my child is being stared at because of its white spots.	1	2	3	4	5
46. I should be less stressed.	1	2	3	4	5
47. I cannot often concentrate.	1	2	3	4	5
48. I pay a lot of attention to my child's skin.	1	2	3	4	5
49. Sometimes I feel I could climb up the wall.	1	2	3	4	5
50. My child' s vitiligo gets me down.	1	2	3	4	5
51. I feel depressed often because of my child's skin disease.	1	2	3	4	5

Finally, please answer the following questions

Your age: _____ years Sex: ( ) male ( ) female
Your child's age: _____ years Sex: ( ) male ( ) female

How hold was your child when its skin disease appeared? …… years
In case it was still an infant.... ..... months

The following factors have influenced my child's disease:

- Hereditary disposition (is there anybody else in your family with vitiligo?) Yes ◯ No ◯
  if yes, who _____ (how related to your child)
- Psychological stress Yes ◯ No ◯
- Trauma to the skin (injuries, burnings...) Yes ◯ No ◯

Which parts of your child's body are affected *at the moment*? If affected, slightly or heavily?

	slightly	heavily
( ) face	( )	( )
( ) neck	( )	( )
( ) hands	( )	( )
( ) arms	( )	( )
( ) body	( )	( )
( ) legs	( )	( )

Is your child's vitiligo spreading? Yes ◯ No, it's stable ◯ No, it's repigmenting ◯

Does your child have single grey hair within its scalp hair? Yes ◯ No ◯
or does it have single grey hair within its eyelashes or eyebrowes? Yes ◯ No ◯

Where did appear the first white spot on your child's body? _____

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