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Evaluation of the highest measured Psoriasis Area and Severity Index (PeakPASI) as an additional score in the care of psoriasis patients

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Abstract

Psoriasis is a chronic inflammatory skin disease that commonly presents as red, scaly plaques on the extremities, scalp, and trunk, and often affects nails and joints as well (A. W. Armstrong and Read, 2020). It is an autoimmune condition with a genetic predisposition (Weigle and McBane, 2013) that imposes a significant psychological burden on patients (Schuster et al., 2022). Beyond skin symptoms, psoriasis is, among others, linked to cardiovascular, metabolic, and psychological comorbidities (Rendon and Schäkel, 2019). To assess skin symptoms, clinical tools such as the Psoriasis Area and Severity Index (PASI) are used, while the Dermatological Life Quality Index (DLQI) measures patients' quality of life (Carretero et al., 2018). Treatments for psoriasis include topical therapy, phototherapy, and systemic therapy (Nast et al., 2021). As the PASI only offers a snapshot of disease severity, it may not fully reflect the mental burden experienced by patients. Therefore, the highest observed PASI score of a patient (PeakPASI), could be a valuable addition (Tizek et al., 2021). This study aims to assess whether the PeakPASI could be integrated as an additional score by comparing it to the PASI, and examining its relationship to the number of therapies and comorbidities.

Psoriasis patients who visited the Technical University of Munich's university hospital between January 2019 and July 2020 were recruited to complete a questionnaire on leisure behavior (including addiction), social well-being, stigmatization, and happiness. Additionally, the medical records of these individuals were reviewed to document skin symptoms, clinical scores, comorbidities, and psoriasis treatments. Patients were classified according to psoriasis severity using three cut-off values for the PASI and PeakPASI (10, 11.4, and 13.6). Patients with PeakPASI$\geq$10, PeakPASI$\geq$11.4, and PeakPASI$\geq$13.6 underwent more phototherapy compared to patients with PeakPASI<10, PeakPASI<11.4, PeakPASI<13.6. Greater disease severity (PeakPASI$\geq$10 and PeakPASI$\geq$13.6) was more common in men than women. Smoking and diabetes mellitus were more prevalent among patients with PeakPASI$\geq$10. These patients also had one additional comorbidity and frequented the hospital more often. They required more topical and systemic therapies than their counterparts. Moreover, patients with PeakPASI$\geq$13.6 had higher DLQI scores.

During the correlation analysis conducted, a low to moderate positive correlation was observed between PeakPASI and the number of hospital visits (ρ=0.186, p=0.001), as well as with number of systemic therapies (ρ=0.296, p<0.001). A moderate positive correlation was found with the number of topical therapies (ρ=0.367, p<0.001), while a low positive correlation was present with the DLQI (ρ=0.179, p=0.006) and the number of comorbidities (ρ=0.147, p=0.010). Poisson regression models were constructed for the number of systemic therapies, comparing PASI and PeakPASI as predictors. The number of visits emerged as a positive predictor in both models, while the PASI itself was a negative predictor. In contrast, PeakPASI did not impact the

number of systemic therapies. For comorbidities, age and the number of topical therapies were positive predictors in both models.

Overall, the PeakPASI demonstrated similar relationships to the examined clinical variables as the PASI, and it may be useful to assess the disease burden placed on psoriasis patients. Possibilities to implement it as a prospective score include identifying the PeakPASI during flare-ups of patients and using it as a reference value in future flare-ups. Its inclusion as a complementary measure could enhance future assessments and therapeutic strategies.

Zusammenfassung

Psoriasis ist eine chronisch-entzündliche Hauterkrankung, die sich häufig als rote, schuppende Plaques an den Extremitäten, der Kopfhaut und dem Rumpf zeigt und oft auch die Nägel und Gelenke betrifft (A. W. Armstrong und Read, 2020). Es handelt sich um eine Autoimmunerkrankung mit genetischer Veranlagung (Weigle und McBane, 2013), die für die Patienten eine erhebliche psychische Belastung darstellt (Schuster et al., 2022). Neben den Hautsymptomen ist Psoriasis unter anderem mit kardiovaskulären, metabolischen und psychologischen Komorbiditäten verbunden (Rendon und Schäkel, 2019). Zur Bewertung der Hautsymptome werden klinische Instrumente wie der Psoriasis Area and Severity Index (PASI) verwendet, während der Dermatological Life Quality Index (DLQI) die Lebensqualität der Patient misst (Carretero et al., 2018). Zu den Behandlungen der Psoriasis gehören die topische Therapie, die Phototherapie und die systemische Therapie (Nast et al., 2021). Da der PASI nur eine Momentaufnahme des Krankheitsschweregrads darstellt, spiegelt er die psychische Belastung der Patienten möglicherweise nicht vollständig wider. Daher könnte der PeakPASI, der den höchsten beobachteten PASI-Wert eines Patienten erfasst, eine wertvolle Ergänzung sein (Tizek et al., 2021). Ziel dieser Studie ist es zu beurteilen, ob der PeakPASI als zusätzlicher Score integriert werden könnte, indem er mit dem PASI verglichen und seine Beziehung zur Anzahl der Therapien und der Komorbiditäten untersucht wird.

Psoriasis-Patienten, die zwischen Januar 2019 und Juli 2020 das Universitätsklinikum der Technischen Universität München besuchten, wurden rekrutiert, um einen Fragebogen zu Freizeitverhalten, sozialem Wohlbefinden, Stigmatisierung und Zufriedenheit auszufüllen. Zusätzlich wurden die Krankenakten dieser Personen überprüft, um Hautsymptome, klinische Scores, Komorbiditäten und Psoriasis-Behandlungen zu dokumentieren. Die Patient wurden nach dem Schweregrad der Psoriasis anhand von drei Grenzwerten für den PASI und den PeakPASI (10, 11,4 und 13,6) stratifiziert. Patienten mit einem PeakPASI-Wert von $\geq$10, $\geq$11,4 und $\geq$13,6 erhielten im Vergleich zu Patienten mit niedrigeren Werten häufiger eine Phototherapie. Ein höherer Schweregrad der Erkrankung (PeakPASI$\geq$10 und $\geq$13,6) trat häufiger bei Männern auf, während Rauchen und Diabetes mellitus bei Patienten mit PeakPASI$\geq$10 häufiger vorkamen. Diese Patient hatten auch eine zusätzliche Komorbidität und benötigten mehr topische und systemische Therapien. Darüber hinaus wiesen Patienten mit einem PeakPASI$\geq$13,6 höhere DLQI-Werte auf und besuchten häufiger das Krankenhaus.

Eine geringe bis mäßige positive Korrelation wurde zwischen dem PeakPASI und der Anzahl der Besuche (ρ=0,186, p=0,001) sowie der Anzahl der systemischen Therapien (ρ=0,296, p<0,001) festgestellt. Eine mäßige positive Korrelation wurde mit der Anzahl der topischen Therapien (ρ=0,367, p<0,001) festgestellt, während eine geringe positive Korrelation mit dem DLQI (ρ=0,179, p=0,006) und der Anzahl der Komorbiditäten (ρ=0,147, p=0,010) vorlag. Für

die Anzahl der systemischen Therapien wurden Poisson-Regressionsmodelle erstellt, die PASI und PeakPASI als Prädiktoren verglichen. Die Anzahl der Besuche erwies sich in beiden Modellen als positiver Prädiktor, während der PASI selbst ein negativer Prädiktor war. Im Gegensatz dazu hatte der PeakPASI keinen Einfluss auf die Anzahl der systemischen Therapien. Bei den Komorbiditäten waren das Alter und die Anzahl der topischen Therapien in beiden Modellen positive Prädiktoren.

Insgesamt zeigte der PeakPASI ähnliche Beziehungen zu den untersuchten klinischen Variablen wie der PASI. Er könnte nützlich sein, um die Krankheitslast von Psoriasis-Patient zu beurteilen. Möglichkeiten, ihn als prospektiven Score zu implementieren, umfassen die Identifizierung des PeakPASI während Schüben und dessen Verwendung als Referenzwert bei zukünftigen Schubsituationen. Die Einbeziehung des PeakPASI als ergänzendes Maß könnte künftige Bewertungen und therapeutische Strategien verbessern.

Abbreviations

BSA: Body Surface Area
CI: Confidence interval
CIUS: Compulsive Internet Use Scale
CHD: Coronary heart disease
CVI: Chronic venous insufficiency
CAGE: Cut, Annoyed, Guilt, Eye-opener
DAST: Drug Abuse Screening Test
DLQI: Dermatology Life Quality Index
HLA: Human leukocyte antigens
ICD-10-GM: International Classification of Diseases (10th revision), German modification
IQR: Interquartile range
NAPSI: Nail Psoriasis Severity Index
PASI: Psoriasis Area and Severity Index
PGA: Physician Global Assessment
PINTA: Prävalenz der Internetabhängigkeit
PSQ: Perceived Stigmatization Questionnaire
SCQ: Social Comfort Questionnaire
REDcap: Research Electronic Data Capture
RMSE: Root-Mean-Square Error
UV: Ultraviolet

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1 Introduction

1.1 Psoriasis

1.1.1 Epidemiology

Psoriasis is a chronic, autoimmune skin disease that impacts between 0.27% to 11.4% of adults worldwide (Parisi et al., 2020) and 1.7% to 2.5% adults in Germany (Hagenström et al., 2024). This common illness is considered a "major health problem" (Boehncke and Schön, 2015) that typically affects both genders equally (Guillet et al., 2022). The disease is characterized through scaly patches due to epidermal hyperproliferation. It occurs partly because of genetic predisposition and partly due to inflammatory processes caused by auto(immune) aspects (A. W. Armstrong and Read, 2020).

While psoriasis can begin at any age, it has a "bimodal distribution", in which the first peak of manifestation is during the second and third decade of life, and the second peak occurs during the fifth and sixth decade (Raharja et al., 2021).
Psoriasis can be classified into two types:

- Type I (early onset): This type typically manifests before the 40th birthday, has a stronger familial association and a higher prevalence with specific human leukocyte antigens (HLA). These patients show a worse progression. (Langley et al., 2005)
- Type II (late onset): Type II usually begins after the 40th birthday and there is less of a genetic component involved (Langley et al., 2005).

1.1.2 Etiology and pathogenesis

Psoriasis consists of a complex cutaneous dysregulation that includes many cell types and mediator systems of the skin (Chhabra et al., 2022). The full pathogenesis is still unclear, but research has shown that a T-lymphocyte dominated inflammatory response most likely takes place, accompanied by epidermal hyperproliferation and a differentiation disorder of the keratinocytes (Chhabra et al., 2022). This means that changes in keratinocytes and in the immune system are responsible for the 'outbreak' of the psoriasis in individuals who are already vulnerable (Chhabra et al., 2022).
An epidermal hyperproliferation occurs because the homeostasis of the epidermis is disturbed due to processes occurring within the cells (Chhabra et al., 2022). Ki-67, which is a proliferation marker that increases in tumor cells (Sun and Kaufman, 2018), also rises in skin affected by psoriasis compared to psoriasis-free skin (Borade et al., 2020).
Through this extreme proliferation of keratinocytes, a thickening (acanthosis (Hookerman, 2013)) and distortion (papillomatosis (Hookerman, 2015)) of the epidermis occurs, along with an accelerated epidermal turnover (X. Zhou et al., 2022).

In combination with the epidermal hyperproliferation, there is also a dysfunctional differentiation of the keratinocytes, for example in the form of parakeratosis (X. Zhou et al., 2022, Rendon and Schäkel, 2019).

1.1.3 Role of the immune system

Psoriasis is an immune-mediated disease in which both the adaptive and congenital immune system play a role. Until now, no specific immunogen has been identified for psoriasis, but it is presumed that there are multiple genes involved that go through a kind of molecular mimicry, meaning that exogenic antigens cause an immune reaction similar to that of certain structures of the body (Valdimarsson et al., 2009, Weigle and McBane, 2013). Biological therapies have started to be developed targeting the cytokines, dendritic cells, and T-lymphocytes in the lesions (Weigle and McBane, 2013).

1.1.4 Hereditary aspects

Along with the role that the immune system plays, there is also a genetic predisposition associated with psoriasis. It is a polygenetic disease with multiple affected alleles (such as HLA-Cw6, HLADQ*02:01, CCHCR1, CYP1A1) that increase the risk of development of this illness (A. W. Armstrong and Read, 2020). Families where one parent suffers from psoriasis show an approximately 14% risk of development for the child, and if both parents are affected, this risk increases to around 40% (A. W. Armstrong and Read, 2020).
It is not only the polygenetic inheritance, but also other factors such as the environment, skin trauma, (streptococcal) infections, stress, and certain medication that can lead to the manifestation of psoriasis in individuals who are already more genetically susceptible (A. W. Armstrong and Read, 2020).

1.1.5 Progression and course

Psoriasis is a chronic disease that comes in phases/flare-ups and can take several different forms (Langley et al., 2005). The most common form, which occurs in 90% of cases, is chronic plaque psoriasis (psoriasis vulgaris) (A. W. Armstrong and Read, 2020). The illness can start and progress gradually, for example as chronic plaques in predilection areas (extensor sides of the extremities (knees, elbows), sacral area, capillitium), or show up suddenly as a relapse – in worst case in the form of an acute exanthemic flare-up (Raharja et al., 2021).
This form of acute, exanthemic flare-up is known as guttate psoriasis (Raharja et al., 2021). The name comes from the disseminated, teardrop-shaped lesions that increase through peripheral growth, and can later on disappear or convert into the more stable chronic plaque form, which happens in 40% of cases (Saleh and Tanner, 2023).

The number of times one patient has a flare-up, as well as the length and intensity of flare-ups

is all unique, which makes it difficult to predict the course, characteristics, and severity of the psoriasis for one individual (Langley et al., 2005). Generally, psoriasis can go into remission at any stage, but a total remission is usually an exception (Farber and Nall, 1974, Langley et al., 2005).

Exogenic stimuli can lead to an exacerbation of the psoriasis, which is known as the Koebner phenomenon (Hookerman, 2014). Various skin lesions or minimal mechanical traumas such as scratches, exanthema, sunburn, scars, tattoos, and irritative local therapy can cause plaques to appear (Boehncke and Schön, 2015, A. W. Armstrong and Read, 2020). The Koebner phenomen also explains why the predilection areas of psoriasis are what they are, as the 'trauma' that is placed on the knees or elbows is for example higher than that on other parts of the body (Sarac et al., 2016).

Psoriasis can also be affected by the seasons, as there seems to be an improvement of the skin in the summer, which is likely due to the presence of more ultraviolet (UV) rays (Boehncke and Schön, 2015). This shows how the endogenous and exogenous factors work together. Although UV rays generally improve the skin condition, and are therefore used as a therapy module for treatment, a UV sensitive psoriasis also exists, in which the condition is exacerbated on account of UV radiation (Wolf et al., 2016).

Another reason for the induction or exacerbation of psoriasis is a human immunodeficiency virus (HIV) infection or the intake of various medication (such as beta blockers, lithium, chloroquine, interferone) (A. W. Armstrong and Read, 2020). Other infections, such as ones with streptococcae, can also trigger a flare-up due to the activation of the immune system through superantigens (Valdimarsson et al., 2009). The triggering of the first manifestation of a psoriasis (mostly in its guttate form), or the provocation of a flare-up directly after a streptococcal infection (for example in the tonsils) is a typical reaction (Valdimarsson et al., 2009). Even bacterial infections in the teeth and jaws, such as periodontitis, can act as a trigger for psoriasis (Han et al., 2022). The risk is increased if the person also smokes (11% for "non-smokers with periodontitis" and 26.5% for smokers with periodontitis, both when compared to non-smokers without periodontitis) (Han et al., 2022).

1.1.6 Clinical manifestations

The psoriatic lesion is a round, red plaque with a sharp limitation, some infiltration, and a characteristic lamellar scaling (silver-white, large, and coarse) (Boehncke and Schön, 2015, Oji and Luger, 2015). The plaques are loosely attached to the skin and can be gently scraped off (like how one would remove candle wax, which is why this is also known as the wax spot phenomenon) (B.-X. Yan et al., 2021). It is because of the "parakeratosis and hyperkeratosis of the

epidermis" that the plaques can be scraped off in this manner (B.-X. Yan et al., 2021).
Through the removal of many plaques, a smooth layer shows itself, known as the "last membrane phenomenon" (B.-X. Yan et al., 2021). After this, a small pinpoint-like bleeding can appear, which is known as the "Auspitz sign" (B.-X. Yan et al., 2021).

The psoriatic lesions are small at the time of development and become larger as the illness progresses (Bhagwat and Madke, 2023. They can turn into extensive plaques with sharp borders that can consolidate and cover more skin (Bhagwat and Madke, 2023). The chronic, stable form of psoriasis consists of persistent plaques in the above-mentioned predilection areas of the extremities, scalp, and trunk (Bhagwat and Madke, 2023). A complete or nearly complete affliction of the integument is known as erythrodermic psoriasis (A. W. Armstrong and Read, 2020). As the psoriatic lesions start to heal, a hypopigmented ring forms around the plaque, also known as the Woronoff ring (Prinz, 2020). The pathomechanism behind this is the suppression of melanocytes through specific cytokines, which causes a hypopigmentation around the central plaque (Prinz, 2020).
Along with the skin manifestations, patients can also suffer from pruritus, or itchiness, due to the inflammation of the skin (Komiya et al., 2020). Trigger factors that can increase the pruritus are stress, dry skin, hot water, sweating, increased room temperature, exercise, and bad mood (Komiya et al., 2020). Scratching can often lead to an aggravation of the psoriasis (Komiya et al., 2020).

1.1.7 Skin appendages and other affected areas

Other affected areas of the body are, for example, the scalp, with plaques and scales manifesting on the scalp and nearby areas (such as the nape of the neck, ears or forehead) (Ghafoor et al., 2022). While the hair itself is often normal, patients can suffer from intense dandruff and itching (Ghafoor et al., 2022). In extreme cases it can also lead to alopecia, with or without scarring (Ghafoor et al., 2022).

Along with the scalp, more than half of all psoriasis patients report nail deformities (Rendon and Schäkel, 2019). These can affect the nail matrix, nail bed, or both areas (Haneke, 2017). Changes in the nail matrix include:

- Pitted nails: Many small dents form in the nail bed (Canal-García et al., 2022). This is characteristic for psoriasis, and more commonly affects fingernails than toenails (Haneke, 2017, Canal-García et al., 2022).
- Leukonychia: White discoloration of the nail plate (Canal-García et al., 2022), due to parakeratotic cells in the mid to distal matrix of the nail plate (Haneke, 2017).
- Red spots in the lunula (Canal-García et al., 2022)

- Crumbling of the nail plate: It is brittle and disintegrates, and can lead to a complete nail plate dystrophy (Canal-García et al., 2022).

The nail bed changes consist of:

- Oil drop discoloration: This is a very common change that occurs due to psoriatic plaques in the distal matrix and in the nail bed. It looks like an oil drop has fallen on a piece of paper (Haneke, 2017). In the most severe cases, a total detachment of the nail (onycholysis) can take place, more commonly in toenails than in fingernails (Haneke, 2017, Canal-García et al., 2022).
- Subungual hyperkeratosis: An accumulation of white-grey keratin masses form below the nail bed, more common in toenails (Canal-García et al., 2022).
- Splinter hemorrhages: Similar to the Auspitz phenomenon of the skin, the dilated capillaries in the nail bed cause either a hemorrhage, or the formation of blood clots in the longitudinally arranged small blood vessels (Haneke, 2017).

Nail psoriasis can look similar to onychomycosis, which is a fungal infection of the nail, but while nail psoriasis can be treated using systemic therapy, the risk for onychomycosis increases through the systemic immunosuppressive medication given for psoriasis (A. Gupta et al., 2020, Kyriakou et al., 2022). This is why it is important to diagnose correctly (patients can also have both) and treat each sufficiently (Kyriakou et al., 2022).

Psoriatic arthritis often also occurs at the same time as nail psoriasis, with around 80% of psoriatic arthritis patients additionally suffering from nail symptoms (Rendon and Schäkel, 2019). If the psoriatic arthritis affects specific finger joints, the nail psoriasis also occurs on those afflicted fingers (McGonagle et al., 2009, Kaeley et al., 2021). The cause of this is probably the inflammation of the ligaments and tendons (enthesitis) that occurs through the psoriatic arthritis (McGonagle et al., 2009, Kaeley et al., 2021). This inflammation goes from the bone of the end phalanges to the nail bed and hyponychium (skin under the fingernail) (McGonagle et al., 2009, Kaeley et al., 2021).
Along with involvement of the nails, involvement of the scalp and anal fold, and a positive family history are also important predictors for psoriatic arthritis (Azevedo and Buiar, 2013). This is a condition that affects about 34% of patients with psoriasis (Jensen and Skov, 2017).

1.1.8 Typical clinical variations

There are several clinical variations of psoriasis:

- Psoriasis of the guttate type (eruptive psoriasis): This acute, exacerbated form has small papules with fine scaling that are mostly located on the torso or upper extremities (Weigle and McBane, 2013, W. Wu et al., 2014). It is often associated with focal infections (such as streptococcal pharyngitis) (Weigle and McBane, 2013).
- Plaque-type psoriasis (psoriasis vulgaris): This is the most common form and is also known as the chronic, stable psoriasis (A. W. Armstrong and Read, 2020). The typical appearance is a limited number of symmetrical lesions that can occur anywhere on the body, especially on the predilection areas (A. W. Armstrong and Read, 2020).
- Palmoplantar psoriasis: The palmar regions of the hands and plantar regions of the feet are affected by a pronounced hyperkeratosis and scaling (Sarac et al., 2016).
- Generalized pustular psoriasis (GPP): This is a not-so-uncommon complication of psoriasis vulgaris in which there are pustules filled with non-infectious pus (Boehncke and Schön, 2015). Psoriasis pustulosa (or palmoplantar pustulosis – PPP) is a localised form which affects the palms, and the soles of the feet (Boehncke and Schön, 2015). Trigger factors that cause a psoriasis vulgaris to change into a generalized pustular psoriasis can, for example, be infections, pregnancy, cortisone withdrawal, or hypocalcemia (A. W. Armstrong and Read, 2020).
- Psoriasis intertriginosa: Also known as inverse psoriasis, this form primarily affects the intertriginous areas in the folds of the skin (axillary, inframammary, and genital areas) (A. W. Armstrong and Read, 2020). It can be difficult to correctly diagnose because the typical desquamation of the skin is missing due to the damp mileau of the intriginous areas, and can therefore also be misdiagnosed as a fungal infection (A. W. Armstrong and Read, 2020).
- Erythrodermic psoriasis: This is a rare form where the whole integument is affected by an uncontrollable rash (Raharja et al., 2021). It is a life-threatening illness that can lead to severe complications such as infections, hypothermia, kidney injuries, and cardiac failure (Raharja et al., 2021). The psoriatic erythrodermia occurs either through the confluence of existing, chronic psoriatic plaques, or as a primary manifestation of an unstable psoriasis, triggered by an infection, drugs, or the withdrawal from corticosteroids (Langley et al., 2005).

1.2 Clinical scores

There are several clinical tools used to assess the severity of the psoriasis and measure treatment response. One of them is the Psoriasis Area and Severity Index (PASI), which is the “most useful

and reliable tool for assessing psoriasis severity in patients with moderate-to-severe disease" (Carretero et al., 2018).
Here, the body is divided into head, torso, upper extremities, and lower extremities, and the skin involvement is measured according to the following numerical scale:

- 0 = no skin affected
- 1 = <10% skin affected
- 2 = 10-29% skin affected
- 3 = 30-49% skin affected
- 4 = 50-69% skin affected
- 5 = 70-89% skin affected
- 6 = 90-100% skin affected

(Walsh et al., 2018)

The erythema level, level of infiltration, and level of desquamation are assessed on a scale of 0-4, and added together for each area of the body (Walsh et al., 2018). Each area of the body is given a certain weighting, with the head having a weighting of 0.1, the torso of 0.3, the upper extremity 0.2, and the lower extremity 0.4 (Feldman and Krueger, 2005, Walsh et al., 2018). This is then multiplied with the skin involvement and the sum of the skin symptoms (erythema level, level of infiltration, and level of desquamation) (Walsh et al., 2018). The maximum number of possible points for the PASI is 72 (Walsh et al., 2018), and a PASI of 10 or above indicates a moderate-to-severe psoriasis (von Kiedrowski et al., 2016, B.-X. Yan et al., 2021). This score is the "gold standard of disease activity measure" and should ideally be determined at each visit to the physician (Carretero et al., 2018). It is also applied while examining the efficacy of psoriasis therapies, where an improvement of the PASI score through the study medication by 75% (or more/less) in comparison to the start value (baseline) is the goal endpoint to be reached (PASI 75) (Feldman and Krueger, 2005).
Not only the PASI, but also further scores such as the Dermatological Life Quality Index (DLQI), Body Surface Area (BSA), and Physician Global Assessment (PGA) should be collected each time the patient visits a physician (Carretero et al., 2018).

The DLQI is the score that is most widely used to measure the quality of life in psoriasis (and generally dermatological) patients (Feldman and Krueger, 2005), making the DLQI and the PASI the "most relevant scores for therapeutic decision-making" according to the Delphi consensus study (Carretero et al., 2018). This is a self-assessment questionnaire with ten items and a maximum of 30 points (Herédi et al., 2014). The goal is to quantify how much the quality of

life of psoriasis patients is impaired through their dermatological disease. The higher the score, the lower their quality of life. The questions cover topics such as current symptoms, effects of treatment, daily activities, relationships, and leisure activities (Herédi et al., 2014). Answers are on a 4-point Likert scale (Herédi et al., 2014). Here too, a DLQI$\geq$10 represents a moderate-to-severe psoriasis (von Kiedrowski et al., 2016). Therefore, while the PASI is an instrument used for the "objective measurement" of the psoriasis, the DLQI is used for "patient-reported outcomes" (Kirsten et al., 2021).

The BSA, which represents the percentage of affected body surface, is another common score (Ashcroft et al., 1999). A BSA of more than 10% is also classified as a moderate-to-severe psoriasis (von Kiedrowski et al., 2016, Llamas-Velasco et al., 2017,). Involvement of 3-5% of the body surface is classified as a mild psoriasis (A. W. Armstrong and Read, 2020). Typically, a closed hand is used to estimate how much of the skin is affected, where one closed hand represents 1% of the total body surface (Ashcroft et al., 1999, Walsh et al., 2018). The rule of nines is another method that is implemented, in which the total body is divided into several parts: 9% for the head, 9% for the anterior upper trunk, 9% for the anterior lower trunk, 9% for the posterior upper trunk, 9% for the posterior lower trunk, 9% for the anterior leg, 9% for the posterior leg, 9% for each arm, and 1% for genitalia (Ramsay and Lawrence, 1991, Ashcroft et al., 1999). However, this method is not so reliable because there seems to be a lot of variability between different observers (Ramsay and Lawrence, 1991, Ashcroft et al., 1999).

As Llamas-Velasco et al., 2017 has suggested, the PASI, DLQI, and BSA are all necessary parameters for the correct classification of psoriasis. Both the PASI and the DLQI are very important and should be considered equal while determining the severity of the psoriasis because they provide an objective measure (by the dermatologist) and also a subjective measure (from the patient themselves) (Llamas-Velasco et al., 2017). Considering the subjective measure is necessary because patients have complained that their doctors underestimate the psychosocial burden of individuals suffering from skin disease (A. B. Kimball et al., 2005).

Another clinical score used is the PGA, which can be used to evaluate "extensive disease as well as localised plaques" (Feldman and Krueger, 2005). This is a score that assesses skin lesions based on erythema, scaling, and induration with a maximum of 5 points, where 0 represents clear skin and 5 represents a severe psoriasis (Robinson et al., 2012, Walsh et al., 2018). There are two forms: one is the static version, which showcases the PGA score at one specific point in time and one is the dynamic version, in which the change in PGA from the baseline is measured (Feldman and Krueger, 2005, Robinson et al., 2012, Cappelleri et al., 2013). This is a standard measure often used in clinical trials to evaluate the success of a therapy where success is defined as "PGA clear or almost clear" (Pascoe et al., 2015). As the PGA only measures the level of erythema, scale, and induration of the plaques, it is possible that the PGA does not decrease

after response to treatment like the PASI or BSA would, because the PGA does not take into account how much body area is affected (Robinson et al., 2012). This means that if the number of plaques decrease, but the few remaining plaques are the same in terms of erythema, scale and induration, the PGA would be identical (Robinson et al., 2012).

If nail involvement is present, collecting the Nail Psoriasis Severity Index (NAPSI) should also be a standard practice. The NAPSI is a validated tool to measure the extent of psoriasis on the nails (Cassell et al., 2007, Canal-García et al., 2022). The nail is divided into four quadrants, and each quadrant is further divided into nail bed and nail matrix. In the nail matrix, clinicians look out for nail pitting, leukonychia, red spotting in the lunula, crumbling of the nail, and in the nail bed the symptoms of disease include onycholysis, oildrop discoloration, splinter hemorrhage, hyperkeratosis (Rich and Scher, 2003, Cassell et al., 2007). Symptoms in one quadrant are given 1 point, and one nail can have a score from 0-8 (because both the nail matrix and nail bed can each have an individual score from 0-4) (Rich and Scher, 2003, Cassell et al., 2007). This is then repeated for all nails, making a maximum score of 80 possible (Rich and Scher, 2003, Cassell et al., 2007). If the specific symptoms are regarded for each quadrant of a specific nail (nail pitting, leukonychia, red spotting, crumbling, onycholysis, oil drop discoloration, splinter hemorrhage, and hyperkeratosis), a total of 32 points are possible for that nail (Rich and Scher, 2003, Cassell et al., 2007).

1.3 Comorbidities

Psoriasis is not only a disease of the skin, but also a systemic illness in which patients have a higher risk of developing further chronic comorbidities, ranging from cardiovascular, metabolic, psychological (such as anxiety, depression) to arthritis (Boehncke and Schön, 2015, Rendon and Schäkel, 2019). An association has been found between psoriasis and multiple internal disorders such as obesity, arterial hypertension, diabetes mellitus, lipid metabolism disorders, and metabolic syndrome (Boehncke and Schön, 2015, Rendon and Schäkel, 2019).

1.3.1 Metabolic syndrome and obesity

Individuals with metabolic syndrome and/or obesity carry more visceral fat. This fat shows a high metabolic activity and releases a row of inflammatory mediators that can worsen the psoriasis (as well as other autoimmune diseases like systemic lupus erythematosus or rheumatoid arthritis) (Jensen and Skov, 2017). If these same individuals additionally have a genetic predisposition for diseases associated with inflammation, as psoriasis does, the risk of manifestation of the disease may be greater (Polic et al., 2018). The relationship between psoriasis and metabolic syndrome goes both ways. The pro-inflammatory mediators, which are overpro-

duced in patients with psoriasis, can induce resistance to insulin, which is a part of metabolic syndrome (Gisondi et al., 2018).

Generally, patients with psoriasis seem to suffer more from metabolic syndrome and cardiovascular diseases (Gisondi et al., 2018), and the more severe the psoriasis is, the greater the risk and most likely also the severity of the metabolic syndrome (Daniel, 2020). Studies have shown that patients with moderate-to-severe psoriasis have an increased prevalence of metabolic syndrome (Gisondi et al., 2018). Metabolic syndrome is also connected to obesity and insulin resistance, and patients additionally have a higher risk for cardiovascular diseases, as do patients with psoriasis (Gisondi et al., 2018). A connection has been found between hyperlipidemia and psoriasis as well (Al-Mutairi et al., 2010).

Furthermore, it has been established that the severity of psoriasis correlates with levels of resistin, which is a peptide produced by fat cells that contributes to insulin resistance (Słuczanowska-Głabowska et al., 2023). This peptide has been known to increase inflammation, which may exacerbate the symptoms of the psoriasis (Słuczanowska-Głabowska et al., 2023).

In regards to the therapy, a link has been found between obesity and a lower response to systemic and biological treatment in psoriasis patients (Jensen and Skov, 2017). Extremely overweight psoriasis patients may therefore respond less to therapy, indicating that a controlled weight reduction could be beneficial for the treatment and management of the psoriasis (Jensen and Skov, 2017, Gisondi et al., 2018). Although the exact benefits of weight reduction on psoriasis severity are not known, weight loss does seem to help reduce side effects of medication, increase the efficacy of biologicals, and decrease treatment costs (because higher body weight means a higher dosage of medication is required) (Jensen and Skov, 2017). Along with that, reducing weight can increase the responsiveness to systemic therapy such as cyclosporine and biologics in patients who are obese (Gisondi et al., 2018). It should therefore be considered a therapy goal (Jensen and Skov, 2017). Moreover, weight reduction has a positive effect for patients with metabolic syndrome, diabetes, and cardiovascular disease too (Gisondi et al., 2018).

1.3.2 Diabetes mellitus

Studies that explore the relationship between psoriasis and diabetes mellitus have shown that patients with psoriasis have an "increased prevalence and incidence of diabetes" (A. W. Armstrong et al., 2013b). Pathophysiologically, there are immune pathways that occur in psoriasis that may show a predisposition for a diminished glucose tolerance, and therefore diabetes (A. W. Armstrong et al., 2013b).

Inflammatory cytokines have, for example, been found in psoriasis that are known to assist in

developing a resistance to insulin (Polic et al., 2018). Takeshita et al., 2015 and Wan et al., 2018 are examples of two studies that found a positive association between patients with psoriasis and the prevalence of diabetes mellitus. The diabetes study by A. W. Armstrong et al., 2013b demonstrated that patients with psoriasis have a "59% increased prevalence of diabetes" and are at a 27% increased risk of developing diabetes if they do not already have it. The more severe the psoriasis, the higher also the occurrence or risk of developing diabetes mellitus in the future (A. W. Armstrong et al., 2013b, Wan et al., 2018).

1.3.3 Cardiovascular disease and arterial hypertension

Cardiovascular diseases have likewise been linked to psoriasis (Irimie et al., 2015, Yamazaki, 2021). Several studies have shown that there is a greater prevalence of cardiovascular diseases, such as arterial hypertension, among patients with psoriasis and that this likelihood grows with increasing psoriasis severity (Takeshita et al., 2015). It has also been suggested that the risk of developing hypertension is higher among patients who already suffer from psoriasis (Takeshita et al., 2015), as is the risk of suffering from a heart attack (Al-Mutairi et al., 2010).

Many studies have reported a greater prevalence of cardiovascular diseases, such as myocardial infarction, heart disease, and atherosclerotic diseases in patients with psoriasis when compared to the general population (Kaye et al., 2008). Not only is the prevalence higher, but the risk of developing "hypertension, obesity, hyperlipidaemia, MI [Myocardial infarction], angina, atherosclerosis, peripheral vascular disease and stroke" is also greater in patients with psoriasis compared to the general population (Kaye et al., 2008).

1.3.4 Thyroid dysfunction

A connection has been found between psoriasis and thyroid diseases such as hyperthyroidism, hypothyroidism, Hashimoto thyroiditis, and Grave's disease (S.-H. Wang et al., 2019). A study by Bu et al., 2022 in Taiwan exhibited that patients with psoriasis had an increased risk for both hyperthyroidism and hypothyroidism when compared to healthy patients. The patients with thyroid dysfunction also had "significantly higher PASI scores and elevated serum C-reactive protein levels" compared to the patients who did not suffer from thyroid dysfunction, which shows that a more severe psoriasis (measured through the PASI) may play a role in thyroid dysfunction (Namiki et al., 2020, Bu et al., 2022). This hypothesis has been confirmed by multiple other studies, such as Zheng et al., 2020, where psoriasis patients had a 33% prevalence of thyroid dysfunction while the control group had a prevalence of 16%.

The reason that thyroid dysfunction is present in psoriasis patients is not entirely known yet, but it is thought that the inflammation caused by psoriasis could be a potential cause (Namiki et al., 2020, Zheng et al., 2020).

1.3.5 Psychological comorbidities

Not only can patients with psoriasis be affected by further physical ailments, but there is a large mental aspect to the illness as well (Tampa et al., 2018). Stress, for example, is one of the most common triggers of a flare-up (Tampa et al., 2018). This has been linked to the activation of cells that release neuromediators and cytokines, which leads to an exacerbation of the psoriasis (Rousset and Halioua, 2018). A study conducted in 2009 depicted that patients who worry or scratch at their skin lesions experience higher psoriasis disease severity after stressful periods in their life (Verhoeven et al., 2009, Schuster et al., 2020).

Stress leads to the release of mediators and catecholamines in the skin, which aggravates the skin and causes flare-ups of dermatological disorders (Rousset and Halioua, 2018). Patients who reported stressful events in their lives had a greater occurrence of psoriasis flare-ups after the event occurred (Rousset and Halioua, 2018, Rigas et al., 2019). The efficacy of therapies, such as a psoralen ultraviolet A (PUVA) treatment, can be affected negatively by stress (Rousset and Halioua, 2018). The link between psoriasis severity and stress severity is unclear at the moment, as some studies have not established a correlation between the two (Rousset and Halioua, 2018), while others have found one (Gaston et al., 1987, Zachariae et al., 2004, Verhoeven et al., 2009, Rigas et al., 2019).

The quality of life of individuals suffering from psoriasis is unquestionably severely impaired (Mrowietz et al., 2011). One study exhibited that the restriction on quality of life that patients with psoriasis feel is among the lowest when compared to patients with diabetes, heart disease, depression or even cancer (Choi and Koo, 2003).

Psoriasis can also present itself through the physical limitations it places on patients, such as by causing problems at the workplace, at normal everyday places (like the hairdresser), in leisure situations (such as the swimming pool), and many other areas (A. B. Kimball et al., 2005). A survey revealed that patients would be willing to pay 9-15% of their monthly salary for a cure for psoriasis (Lundberg et al., 1999). Due to the stigmatization that affects individuals with psoriasis, they exhibit an increased risk for depression, which should be screened for accordingly during patient visits (B. E. Cohen et al., 2016, Łakuta et al., 2017, Sommer et al., 2019). One study demonstrated that over 50% of patients with moderate-to-severe psoriasis reported suffering from depression (Mattei et al., 2014). Another revealed that younger patients and women with psoriasis are more susceptible to suffering from depression (Weigle and McBane, 2013, Gonzalez-Cantero et al., 2023).

Studies have shown that patients feel that the social and psychological burden psoriasis places on them is not accurately recognized by physicians and that the effect of the illness is often un-

derestimated (A. B. Kimball et al., 2005, Meneguin et al., 2020). The burden not only exists and causes quality of life changes during flare-ups, but even affects patients in phases of remission (Augustin et al., 2008). Even in today's age, when we have more knowledge about psoriasis than earlier, patients still feel frustrated, embarrassed, or helpless when it comes to their illness (Nada et al., 2023). There is a certain level of stigmatization involved with psoriasis that also affects the well-being of the patients (A. B. Kimball et al., 2005, Romiti et al., 2023). A recent survey from 31 countries revealed that 84% of psoriasis patients felt discriminated against because of their illness (A. Armstrong et al., 2018).

The subjective well-being of patients with dermatological diseases, especially ones that are chronic, is reduced (Schuster et al., 2020). In studies that examine the happiness of patients, these individuals convey lower levels of happiness compared to a control group (Schuster et al., 2022). Even in phases of remission, when current skin conditions were good, Schuster et al., 2022 found that patients still reported a low subjective well-being. This shows that even though improving the symptoms can reduce the risk for depression, it is important to consider that the mental burden of a patient may be higher than what their skin is showing at that moment – especially in more severe forms of psoriasis (i.e. the skin may be clear at the moment but the patient is still suffering mentally) (Schuster et al., 2022).

1.3.6 Addiction

Patients with psoriasis suffer from addictive diseases such as smoking, alcohol addiction, and drug addiction. Smoking, for example, not only has a negative effect on psoriasis, but has also been identified as an independent risk factor for the illness (A. Armstrong et al., 2014, H. Zhou et al., 2020). In a study conducted by Gerdes et al., 2010, 43.4% of psoriasis patients were active smokers, and the percentage increased with increasing disease severity, while age and gender did not play a role. Many studies have been conducted on psoriasis and smoking that produce similar results regarding the prevalence of smokers within the psoriasis population: there is a statistically significant, positive relationship (Al-Mutairi et al., 2010, A. Armstrong et al., 2014, Zink et al., 2017, Schielein et al., 2021). There have even been studies that depict associations between a larger number of cigarettes smoked and an increased psoriasis severity (A. Armstrong et al., 2014). This means that smokers have a greater likelihood of developing psoriasis when compared to non-smokers, and that patients with psoriasis are often former or current smokers (A. Armstrong et al., 2014).

The pathophysiology illustrates that smoking activates some of the genes and immune processes that occur during psoriasis, such as inducing the production of "proinflammatory cytokines involved in the pathogenesis of psoriasis" (Näslund-Koch et al., 2023). There is an overproduction of IL-1ß and an increase in the production of TNF-alpha and transforming growth factor-ß

when a person smokes, both of which have been positively associated with psoriasis (Ryder et al., 2002, Al-Mutairi et al., 2010,). It is likely that nicotine can lead to cellular processes that cause the acanthosis of keratinocytes and therefore the formation of the characteristic epidermal plaque psoriasis. Even the treatment outcome of psoriasis is affected by smoking, as it has been found that patients who smoke are less responsive to therapies (A. Armstrong et al., 2011).

Additionally, the percentage of alcohol addiction is greater in psoriasis patients than in the general population (Brenaut et al., 2013). This increases with the severity of the psoriasis when measured through the PASI (Gerdes et al., 2010, Zink et al., 2017), and alcohol has also been established as a risk factor for psoriasis (Brenaut et al., 2013).

Zink et al., 2017 examined the addictive tendencies of psoriasis patients and found a significant association between the severity of the psoriasis (measured through the PASI) and drug abuse (Zink et al., 2017). Though not many studies have been conducted on addictions other than smoking and alcohol, psoriasis patients do seem to have increased addictive tendencies compared to the general population. Schielein et al., 2021 displayed that drug abuse was almost double as high for psoriasis patients (3.2% in the control group and 6.0% in the psoriasis group) and that 15.0% of the individuals "displayed at least a low level of abusive behaviour regarding drugs". Along with this, internet addiction was also higher in patients with psoriasis, especially in the younger individuals (Schielein et al., 2021). Patients with psoriasis even had a greater likelihood for pathological gambling (0.2% in the control group and 1.2% in the psoriasis group) (Schielein et al., 2021).

1.4 Therapy

There is a spectrum of therapy modalities available for psoriasis patients based on their symptoms and preferences. For each patient and each situation, all factors should be considered before choosing the most fitting therapy (A. W. Armstrong et al., 2024). The aim is not only to decrease disease activity and minimize symptoms (Meneguin et al., 2020), but also to provide an improvement in the quality of life for the patient (A. B. Kimball et al., 2005, Nada et al., 2023).

Through an effective therapy, comorbidities may also be decreased. For example, studies have shown that for patients who suffer from moderate-to-severe psoriasis, the risk of cardiovascular mortality, which is increased in patients with psoriasis (Gisondi et al., 2018), can be reduced through an effective systemic therapy in the form of phototherapy, immunosuppressive substances, and biologicals (Hu and Lan, 2017). Earlier studies have confirmed that methotrexate

(MTX) is effective in decreasing the cardiovascular risk of psoriasis patients (Hu and Lan, 2017)

In Germany, the therapy scheme for psoriasis patients is based on an algorithm created by the Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaft – AWMF) (Nast et al., 2021). In this algorithm, a mild psoriasis (<10% body surface affected) should be treated with a local/topical therapy. If necessary, phototherapy can additionally be implemented. If 10% or more of the body surface is affected, a systemic therapy should be initiated. To start with, patients receive the conventional first-line systemic therapy with a substance such as MTX, and then, if that fails or if there are contraindications for the first-line therapy, a second-line therapy with biologicals or apremilast is indicated (von Kiedrowski et al., 2016). Depending on the situation, a combinational therapy consisting of topical, photo, and systemic therapy can also be carried out (von Kiedrowski et al., 2016).

If certain "upgrade criteria", as coined by Mrowietz and Augustin, 2022, are present, the psoriasis is classified as moderate-to-severe even if the PASI is <10. These include the skin involvement of visible areas (such as the face or hands), the genitoanal area, the palms of the hands/soles of the feet, the capillitium, onycholysis or onychodystrophy of at least two fingernails, and/or pronounced pruritus (Mrowietz and Augustin, 2022).These symptoms indicate that a systemic therapy can be initiated even without the necessary clinical scores (Mrowietz and Augustin, 2022). There are also guidelines in place to help decide if a therapy should be continued or adjusted (and at what point the therapy should be adjusted).

A failure in treatment is defined as such if at least a 50% reduction in the baseline PASI (PASI 50) compared to the skin's condition prior to the initiation of the treatment is not achieved (Nast et al., 2020). Treatment success is achieving at least a 75% improvement in the baseline PASI (PASI 75) (Feldman and Krueger, 2005, Nast et al., 2020). Nowadays, due to the newer therapy options, even a 90% improvement in the PASI (PASI 90) is strived for (Nast et al., 2020). Therefore, it is the skin condition, measured using the clinical scores such as the BSA and the PASI, as well as the quality of life, measured through the DLQI, which are both employed as criteria to establish if a treatment is a success or failure (Finlay and Khan, 1994, Feldman and Krueger, 2005).

As psoriasis is a chronic, relapsing condition, it is necessary to educate the affected individuals well. It should be pointed out that even if the predisposition of skin lesions cannot be influenced and recurrences cannot be prevented, psoriatic lesions are generally well treatable (Bubak et al., 2019, Chhabra et al., 2022). As of now, patients report "low complete satisfaction with current treatments" with regards to topical treatment, phototherapy, and systemic therapy (Florek et al., 2018). This taken into consideration, patients who receive biologicals have the

highest satisfaction (Florek et al., 2018). One reason for the low patient satisfaction could be the undertreatment of psoriasis patients. Florek et al., 2018 determined that 30% of patients with moderate psoriasis and 20% with severe psoriasis were treated only with a topical therapy and did not receive any kind of systemic treatment. There were various reasons for not being prescribed systemic therapy, such as "disease severity not serious enough for other kinds of treatment" (Florek et al., 2018). If the cumulative, or life-long, burden that psoriasis places on patients is considered, it is understandable that patients may feel unsatisfied. This could call for the earlier implementation of treatment strategies (Mrowietz et al., 2011).

1.4.1 General therapy

Non-specific skin care measures, such as oils, brine baths, emollients, and keratolytics do not necessarily have a healing effect by themselves, but are, nevertheless, a good additive measure in combination with other therapies (Luger et al., 2014, Sawicka et al., 2021). They can help decrease inflammation, redness, and dryness of the skin, as well as remove desquamation and reduce scaling (Luger et al., 2014). With all forms of psoriasis, there is also an indication to search for and treat any focal infections, as these can worsen the condition (Brzewski et al., 2013).

Climate therapy (through the sea and sun) can additionally be beneficial, as patients have reported an improvement in symptoms after spending time in warm and dry climates (Stephan et al., 2021). An improvement of skin symptoms of various dermatological illnesses has been reported in summer compared to winter, due to the increased exposure to the sun (Balato et al., 2013). Climate therapy at the dead sea, for example, has resulted in a decrease in the PASI score (A. D. Cohen et al., 2005, Kazandjieva et al., 2008). Due to the unique environment, with lower UV radiation levels and a high salt concentration, an improvement in psoriasis symptoms and plaque clearance is possible (A. D. Cohen et al., 2005, Kazandjieva et al., 2008). As a result of the high percentage of salt in the water, the sea itself leads to a thorough exfoliation of the skin and longer radiation is possible without the fear of a sunburn because the ultraviolet B (UV-B) part of the sunrays is lower (Kazandjieva et al., 2008).

1.4.2 Topical therapy

In terms of topical therapy, it is the location or type of psoriasis that decides what local therapy should be applied when (Boehncke and Schön, 2015). Topical calcineurin inhibitors, for example, can be used for locations that are difficult to treat, like the intertriginous regions (Boehncke and Schön, 2015).

Some substances that are commonly employed are corticosteroids, substances that contain Vitamin D3 or are analogue to Vitamin D3, calcineurin inhibitors, and keratolytics (A. W. Arm-

strong and Read, 2020). How often to apply each topical agent during the day is decided on an individual basis, as is the length of application (continuous or only occasionally) (Torsekar and Gautam, 2017, Ahmed et al., 2023). It is important to consider the concentration of the drugs as well as possible side effects. Topical keratolytics, such as salicylic acid for example, can help treat scaling, but could also cause irritation if applied in excess (A. W. Armstrong and Read, 2020). Medication that is given continuously should be associated with a low risk for long-term issues. As soon as there is a local or systemic reaction to the drug, it should be discontinued (Torsekar and Gautam, 2017, Ahmed et al., 2023).

The type of substance that is applied varies depending on the body area. On the scalp, for example, the application of a shampoo, solution or foam may be considered while thick plaques could require ointments. Less susceptible areas may need something less greasy, like a cream. Other than that, there are also gels, sprays, and lotions that can be implemented (Ahmed et al., 2023).

1.4.3 Phototherapy

Phototherapy is another treatment option, and can be used in combination with topical or systemic therapy, depending on the severity of the psoriasis (Zhang and Wu, 2018). The phototherapy treatment triggers several pathways to reduce inflammation and work against epidermal proliferation (von Kiedrowski et al., 2016), and UV-B rays are helpful for both the superficial, and the moderately extensive forms of psoriasis (Zhang and Wu, 2018). Narrowband UV-B with a main wavelength of 311nm has particularly favourable effects, although treatment can also be carried out with broadband UV-B (290-320nm) lamps if necessary (Zhang and Wu, 2018). A monotherapy of UV-B rays can cause a subtotal to total remission with many plaques that heal completely within 6-10 weeks and 3-5 expositions/week (Kurz et al., 2023). Often, phototherapy is used in combination with different local therapies (Asztalos et al., 2013). Topical substances containing emollients filter the UV-B rays, meaning that they should not be applied directly prior to the phototherapy as they can affect the penetration negatively (Asztalos et al., 2013, Kurz et al., 2023).

Apart from phototherapy, there is also photochemotherapy, which is a combination of the photosensitizer psoralen plus ultraviolet A radiation (PUVA) (Kurz et al., 2023). There is a systemic form (oral or via injection), or a topical form (bath or cream) (Zhang and Wu, 2018, Kurz et al., 2023). The indication for PUVA therapy is a more severe psoriasis, and this treatment should not be applied on a too long-term basis or too frequently as it can be harmful (Zhang and Wu, 2018, Kurz et al., 2023). There are, however, several meta-analyses which have shown that PUVA is the “gold standard of photochemotherapy modalities”, and that PUVA and UVB are both effective psoriasis therapies (Zhang and Wu, 2018). PUVA therapy has been shown to decrease

the PASI (Nada et al., 2023). The main requirements for an effective therapy are knowledge and experience of the physician – if an accurate dosage of PUVA is not given, it may not work correctly (Nast et al., 2015).

1.4.4 Systemic therapy

The next level of treatment is the systemic therapy. Some common substances used in first-line systemic therapy are acitretin, MTX, ciclosporine, and fumaric acid esters (Nast et al., 2021). Generally, the efficacy of oral treatments seems to be lower than that of biologicals for psoriasis, but they are still helpful for patients who do not want injections or for whom biologicals are not as easily accessible or are too expensive (A. W. Armstrong and Read, 2020).

Biologicals have been a breakthrough in the treatment of psoriasis (as well as in the treatment of atopic dermatitis and chronic urticaria) (Weiss et al., 2021). These are substances that block immune associated cytokines or superficial molecules and are associated with higher therapy costs (Weiss et al., 2021). Either monoclonal antibodies (with the ending "-mab") or fusion proteins are used. It is easy to recognize where the proteins came from based on the letters in the word:

- Chimeric monoclonal antibodies: end with "-ximab"
- Humanised monoclonal antibodies: end with "-zumab"
- Fully human monoclonal antibodies: end with "-umab"

(Guimaraes Koch et al., 2022)

There are several categories of biologicals:

- TNF-Inhibitors (infliximab, etanercept, adalimumab)
- IL-12 and IL-23-Inhibitors (ustekinumab, guselkumab, risankizumab, tildrakizumab)
- IL-17-Inhibitors (secukinumab, ixekizumab, brodalumab)
- Small molecules: as they are small, they can wander into cells and influence the signal transduction pathways (apremilast)

(Lee and Kim, 2023)

1.5 PASI and PeakPASI

Though the PASI is the "gold standard of disease activity measure" for psoriasis (Carretero et al., 2018), it is still only a snapshot of the skin on one specific day (Tizek et al., 2021). Additionally considering the highest measured PASI of a patient, the PeakPASI (Schielein, Tizek, Schuster, Ziehfreund, and Biedermann, 2020), could turn this short-term score into a long-term tool that can be implemented to "address the individual overall disease severity" (Zink et al., 2017).

Zink et al., 2017 first introduced the concept of the PeakPASI in a study on addiction in psoriasis patients, and Tizek et al., 2021 explored this further in a pilot study where the feasibility of this new score was tested. Two patients could both show a PASI<1 after receiving a form of treatment but one may only have had a mild form of psoriasis with PASI<5 values to begin with, while the other might have had multiple PASI>10 values in the past. The PeakPASI would be able to aid in differentiating between these two patients (Zink et al., 2017). The aim is to examine if the PeakPASI can be turned into a prospective tool to initiate treatment quicker and reduce the long-term burden of psoriasis patients (Zink et al., 2017).

As seen above in the comorbidities section, a higher PASI has been linked to multiple comorbidities: metabolic syndrome (Daniel, 2020), hyperlipidemia (Al-Mutairi et al., 2010), diabetes (A. W. Armstrong et al., 2013b), cardiovascular diseases (Irimie et al., 2015, Yamazaki, 2021), arterial hypertension (Takeshita et al., 2015), heart attack (Al-Mutairi et al., 2010), thyroid disfunction (Bu et al., 2022, Namiki et al., 2020, Zheng et al., 2020), stress (Rousset and Halioua, 2018, Rigas et al., 2019), depression (B. E. Cohen et al., 2016, Sommer et al., 2019, Łakuta et al., 2017, Mattei et al., 2014), smoking (A. Armstrong et al., 2014, Gerdes et al., 2010, Zink et al., 2017, Al-Mutairi et al., 2010, Ryder et al., 2002), alcohol addiction (Brenaut et al., 2013, Gerdes et al., 2010, Zink et al., 2017), drug addiction (Zink et al., 2017).

If the PeakPASI is additionally considered and a therapy is administered earlier than it would be if only the PASI is considered, it is possible that the onset of these comorbidities could be prevented (Zink et al., 2017).

A higher PASI has also been linked to a greater number of systemic therapies. Patients with a higher PASI might not respond well to the first systemic medication they are given and could therefore require a substitute (Özkur et al., 2021, Shin et al., 2023). Studies have shown that switching to a different biological therapy could result in a greater PASI reduction (Honda et al., 2017, Özkur et al., 2021) and a connection has been found between patients requiring a greater number of systemic therapies and a high baseline PASI (Honda et al., 2017). If the PeakPASI is taken into consideration, a therapy could be initiated earlier and it may be possible to reduce the number of times the therapy needs to be altered.

1.6 Aims of this study

The aim of this dissertation is to build on the findings of the Tizek et al., 2021 pilot study, which concluded that the PeakPASI may have potential as an additional clinical tool in the treatment of psoriasis, and that further exploration is advisable.

Even though improving the symptoms of psoriasis can, for example, reduce the risk of depression, it is important to consider that the mental burden of a patient may be greater than what their skin is showing at that moment – especially in the more severe forms of the disease (Schuster et al., 2022). In this case, the PASI alone is not enough to capture the burden, as it is only a short-term score. Patients with a low PASI can still report high DLQI values, and therefore suffer from a low quality of life, which indicates that the PASI does not accurately depict the burden placed on a patient with psoriasis (N. Golbari et al., 2021). Implementing the PeakPASI in a way that is similar to the cumulative life course impairment scale (CLCI) (Romiti et al., 2023) and including it as a long-term score in the journey of psoriasis patients could be beneficial to help reduce this burden.

For this, a two-part mixed-method study, with questionnaires that were sent to a collective of patients and a retrospective analysis of patient records, was conducted. In the past, a connection has been found between the PASI and comorbidities of psoriasis patients, depicting that a higher PASI correlates to more comorbidities and to a greater occurrence of specific comorbidities (Augustin et al., 2010). Along with this, a higher PASI has also been linked to a greater number of therapies (Honda et al., 2017). Building on this, our goal was to compare the PeakPASI with the PASI and evaluate its functionality by addressing the following questions:

- Does the PeakPASI of psoriasis patients correlate with the number of comorbidities patients have?
- Does the PeakPASI correlate with the number of systemic therapies that patients receive?

Through these questions, our aim was to investigate if the PeakPASI can be implemented as a predictive tool during the course of the psoriasis, in order to help decrease the disease burden of the patient, provide them with relief by initiating therapy earlier, and shorten the duration of their psoriasis flare-ups.

2 Materials and Methods

2.1 Study population

In this mixed-method study with two components (prospective questionnaires and retrospective collection of information from patient records), psoriasis patients who had been treated at the department of dermatology and allergy at the medical faculty of the Technical University of Munich between January 2019 and July 2020, were recruited. This list consisted of both inpatients and outpatients. The recruitment criteria included that the patient was over the age of 18, able to speak German, had had psoriasis diagnosed by a dermatologist at some point in their history (regardless of the severity), and had been a patient at the department of dermatology and allergy during the above-mentioned time frame. Exlusion criteria was a language barrier or the inability to complete a German questionnaire (Table 1).

Table 1: Inclusion and exclusion criteria to be contacted for participation in the study that involves questionnaires and patient records of individuals with psoriasis

Inclusion Criteria	**Exclusion Criteria**
Written informed consent	Language barriers/unable to complete a German questionnaire
Above 18 years of age with full legal capacity	
Psoriasis diagnosed by a dermatologist	
Patient at the department of dermatology and allergy between January 2019 and July 2020	

The computer system of the university hospital categorizes patients according to their diagnoses, which are listed using the 10th revision of the German modification of the International Statistical Classification of Diseases and Related Health Problems(ICD-10 GM) ("Deutsches Institut für Medizinische Dokumentation und Information", 2020). The code "L40. - Psoriasis", with possible subgroups from L40.0 to L40.9 of the different psoriasis subtypes were taken into consideration ("Deutsches Institut für Medizinische Dokumentation und Information", 2020). This categorization was implemented to identify the psoriasis patients who visited the hospital in the given time frame and randomly assign them a continuous numerical patient ID, which was later on utilized to pseudonymize the questionnaires and patient records. Identification of the questionnaire/patient record was simplified this way.

Each of the patients was sent a questionnaire to fill out and return. Records of all the patients who completed a questionnaire, plus additional inpatients who were on the list but had not sent back a questionnaire, were studied. These additional inpatients were taken into account on the basis that inpatients frequented the hospital more often or for longer periods of time, and therefore have more medical data to analyze.

This study was conducted in accordance with the principles of the Declaration of Helsinki, and was reviewed and approved by the local ethical committee at the Medical Faculty of the Technical University of Munich (reference number 436/19 S-SR).

2.2 Data collection

2.2.1 Questionnaire

A paper-based questionnaire, consisting of validated and non-validated measuring tools, was developed and compiled to be used in the study. Patients were sent an envelope containing the compiled questionnaire, a consent form on data processing and data protection, patient information about the study, and a prepaid return envelope. Along with collecting general patient data (such as age and gender), the questionnaire also intended to assess the psychosocial burden that patients with psoriasis face through the use of standardized tools regarding, for example, addiction and stigmatization, and therefore allowing the exploration of the effects of psoriasis on the social life of a patient.

Leisure behavior:

The first part of the questionnaire assessed leisure behavior, including addictive tendencies of patients, and the ability to enjoy certain activities while suffering from psoriasis, starting with the following open-answer questions:

- "Does your psoriasis prevent you from participating in certain leisure activities? (e.g. going to the swimming pool, sunbathing, sports, etc.)"
- "During the participation of which leisure activity do you feel most restricted?"

These questions are not validated but have been used in a previous study (Schielein, Tizek, Schuster, Ziehfreund, Liebram, et al., 2020).

After this came standardized questionnaires to explore addiction to nicotine, alcohol, computer games and internet, and drugs and illegal substances. For nicotine consumption, patients were

asked how often and how many cigarettes they smoke. The seven answer possibilities ranged from “never” to “more than 2 packets per day”, with one packet containing 20 cigarettes. Additionally, patients were also asked, if applicable, how many years they have been smoking. This was used to then calculate the number of pack years. (Schielein et al., 2021)

Alcohol addiction was evaluated through the CAGE-Test, which is a validated questionnaire for alcohol addiction that consists of four yes or no questions covering the topics of “Cutting down”, “Annoyance by criticism”, “Guilty feeling”, and “Eye openers”, hence the acronym CAGE (Ewing, 1984). Each answer of yes is awarded one point, and two or more total points are equivalent to an alcohol addiction (Ewing, 1984, Dhalla and Kopec, 2007). This test has a high test-retest reliability of 0.80-0.95, and sensitivity of 0.71, while specificity is 0.90 (Dhalla and Kopec, 2007). The German version is also well established (Schielein, Tizek, Schuster, Ziehfreund, Liebram, et al., 2020).
Along with that, participants were asked how often they drink, with five possible answers ranging from “never” to “2-4x per month” to “4x per week” and how many glasses of alcohol they consume, with six possible answers from “1-2 glasses” to “10 or more glasses”. One glass was quantified as one bottle of beer, a quarter bottle of wine, or one shot of liquor (Burger et al., 2004).

Drug abuse was assessed using the validated “Drug abuse screening test 10 (DAST-10)” (Cronbach’s α = 0.86-0.94 (Cocco and Carey, 1998, Carey et al., 2003)), a condensed version of the 28-item “Drug abuse screening test (DAST)” from Skinner, 1982. It consists of ten items to be answered with “yes” or “no” and is used to describe the degree of drug-related problems. A score of three or more indicates drug abuse (Shirinbayan et al., 2020).

Addiction to computer games and the internet was tested through the “Compulsive Internet Use Scale (CIUS)” (Meerkerk et al., 2009), which is a questionnaire that has been validated in German (Cronbach’s α = 0.93), and has, for example, also been used in the “Prävention von Internetabhängigkeit” (PINTA) study (Rumpf et al., 2011). The questionnaire has a total of 14 items about internet usage, such as if partners have complained about excessive usage and feelings towards the internet. An example of a question is “How often do you find it difficult to stop using the Internet when you are online?”. Answers are on a 5-point-scale, ranging from “(0) never” to “(4) very often”, with a total of 56 points, and a cut-off of 28 points indicating an addiction (Meerkerk et al., 2009). A general question on computer/internet usage, “How many hours do you usually spend on the Internet in a day (for private purposes)?” with eight answer possibilities ranging from “Less than one hour” to “7 hours or more” was also developed for this study, to gauge how many hours patients spent on the internet.

Social well-being:

Social well-being, which is an important indicator for the mental health of patients, was assessed using the standardized "Social Comfort Questionnaire" (SCQ), where a validated version exists for German burn victims (Cronbach $\alpha = 0.85$) (Müller et al., 2016). This questionnaire consists of eight items about how the participant feels or thinks in certain situations, such as "I feel like I fit in with most groups" or "I like meeting new people". Answers are on a 5-point scale, ranging from "(1) Never" to "(5) Always" (Lawrence et al., 2006).

Stigmatization:

Stigmatization was covered in the third part of the questionnaire through the use of the "Perceived Stigmatization Questionnaire (PSQ)", a standardized test with 20 items to measure externally perceived stigmatization. Here too, a validated version exists for German burn patients (Cronbach $\alpha = 0.86$) (Müller et al., 2016). Examples of items include "People are friendly with me" and "People seem embarrassed by my looks". Answers are on a scale from "(1) Never" to "(5) Always" (Lawrence et al., 2006).

Happiness:

Happiness of study participants was assessed as an indicator of well-being. For this, a theoretical approach in which happiness is defined as subjective well-being was chosen. According to Diener, 1984, subjective well-being consists of the following three components: Life satisfaction, presence of positive emotions, and absence of negative emotions. These three components are measured using the following items, which are validated in german:

- Satisfaction with Life Scale (SWLS) (Cronbach's $\alpha = 0.89$) (Diener et al., 1985, Hinz et al., 2018).
- Schedule of Positive and Negative Experience, subscale for positive affect and subscale for negative affect (SPANE) (Diener et al., 2010) (SPANE-P Cronbach's $\alpha = 0.88$, SPANE-N Cronbach's $\alpha = 0.82$, Rahm et al., 2017).

In addition to this theoretical approach, happiness can also be measured in a heuristic manner. For this purpose, the questionnaire contains a question taken from the European Social Survey: "All in all, how happy would you say you are?", with an answer scale ranging from "0" to "10" (Hanzlová, 2022).

2.2.2 Patient medical record

The records of the patients, which were partially paper-based and partially computerized, consisted of different document types that were catalogued into each patient file. The following document types were identified during the research:

- Anamnesis/diagnosis of the skin (‘Anamnese/Hautbefund’)
- Physician’s letter (‘Arztbrief’)
- Report of the phototherapy (‘Photodermatologischer Befund’)
- Emergency report (‘Notfall Bericht’)
- Telephone call (‘Telefonat’; this occurred during the Covid-19 pandemic)
- Other, such as surgical report or radiology report

Description of the variables:

Using these documents, each hospital visit of the patient was entered into the ‘Research Electronic Data Capture (REDCap)’ computer system as a separate record with its own ’Record ID’. This means that one patient ID could have ten different record IDs, indicating that this patient had visited the hospital ten times. During each visit, the following same items (if and when available) were documented:

- Age and gender of the patient
- Date of the hospital visit
- Type of document (as mentioned above)
- If this particular visit of the patient was classified as an inpatient, outpatient, or partially outpatient visit (‘teilstationär’)
- The official diagnosis of the patient for that specific visit, such as psoriasis vulgaris (if any diagnosis was given)
- Reason for this specific visit (if there was any)/if the patient presented with any specific symptoms at that moment (‘Grund/Anamnese’)
- Comorbidities of the patient, divided into the following groups:
  - Psychological comorbidities (such as smoking or alcohol addiction)
  - Asthma (because this is a common comorbidity that affects patients with psoriasis) (J. Wang et al., 2018)
  - Other (all comorbidities that did not fall into the first two categories)
- PASI value recorded at the start of the visit (if this was an inpatient visit over multiple days)
- PASI value at the end of the visit (if this was an inpatient visit over multiple days)

- Other scores (if these were recorded by the physician):
  - NAPSI
  - DLQI
  - PGA
  - BSA
- Diagnosis of the skin at the present moment, including the following:
  - Scalp involvement
  - Desquamation
  - Dryness of skin
  - Papules on skin
  - Itchiness
  - Involvement of the nails
  - Involvement of the joints
- Family history
- Allergies (in particular also allergic rhinoconjunctivitis (RCA), due to its association with psoriasis) (Han et al., 2021)
- Systemic psoriasis medication that the patient is receiving at the moment: this consisted of either one medication by itself, such as Secukinumab, or a combination of two medications, such as Secukinumab and MTX
- Topical psoriasis therapy, with the following subquestions:
  - Which topical therapy was given?
  - How many different substances were used in one visit?
  - How many substances were given to take home and continue using?
  - How many substances were used in total?
  - If topical therapy was given at any point during the course of treatment: yes/no
- Phototherapy, with several subquestions:
  - Which kind of phototherapy was given? (such as PUVA, UVB)
  - How long did the patient receive phototherapy?

  - Did they ever receive phototherapy in the past? (any patient who had received phototherapy at least once in their psoriasis medical history was grouped in the "yes" category)

- Medication taken for other illnesses, such as the comorbidities
- Side effects of the psoriasis medication (if the patient complained of any): this was to distinguish if a switch in therapy may also have been due to the side effects of one of the medications

From the PASI values that were collected during each hospital visit it was then possible to distinguish the highest PASI of each patient, i.e., the PeakPASI, to implement alongside the PASI for the statistical analysis. The other clinical scores that were included in the original research from patient records (NAPSI, PGA, BSA), could not be used for further analysis due to multiple missing values, as these scores were not recorded consistently during the hospital visits. To measure the quality of life, the DLQI was also recorded.

2.3 Data management and statistical analyses

2.3.1 PASI and PeakPASI

The statistical analysis was conducted using two approaches. In the first approach, exact PASI and PeakPASI values were used to analyze the data. Here, the most recently recorded (or latest) PASI value was compared to the PeakPASI. The most recent PASI was chosen as a comparison because this is the value that is assessed when a patient comes to the hospital, and this is the value that helps decide how to move further with the therapy.

In the second approach, patients were divided into groups according to their PASI and PeakPASI values. Three cut-off values were used, which led to a total of three PASI and three PeakPASI groups. The PASI value of 10 can, for example, be used to distinguish between a mild (PASI<10), and moderate-to-severe psoriasis (PASI≥ 10) (Tizek et al., 2021). This thought process was then applied to the PeakPASI too, with a group of PeakPASI<10 and a group of PeakPASI≥ 10. The other two cut-off values were introduced based on two separate median splits of the PeakPASI. One according to Tizek et al., 2021 at 13.6, with PASI<13.6 and PASI≥ 13.6 as well as PeakPASI<13.6 and PeakPASI≥ 13.6. The second median split was at 11.4, according to the data of this study, with PASI<11.4 and PASI≥ 11.4 as well as PeakPASI<11.4 and PeakPASI≥ 11.4.

For the DLQI data, which had 24% missing values, an imputed version using the mean was

created (DLQI imputed). The complete statistical analysis was conducted using the imputed DLQI, and any further mention of the DLQI refers to the imputed DLQI.

2.3.2 Statistical analysis

Descriptive statistics of the data were conducted. The mean (standard deviation (SD)) and median [interquartile range (IQR)] were generated, and due to the non-normal distribution of the data, which was determined with the Shapiro-Wilk test, further research was conducted using the median [IQR] (J. Wei, 2022).

Additional analyses were conducted to compare several patient groups. The patients were divided into groups according to the severity of their psoriasis, their gender, and their age (split at 52, which was the median age of patients in this study). The severity of the psoriasis was divided into groups according to the cut-off PASI and PeakPASI values of 10, 11.4, and 13.6. The patient groups (listed below) were the independent variables used for the group comparisons:

- Gender (women, men)
- Age<52, Age≥52
- PASI<10, PASI≥10
- PeakPASI<10, PeakPASI≥10
- The median split of this study at 11.4: PASI<11.4, PASI≥11.4
- The median split of this study at 11.4: PeakPASI<11.4, PeakPASI≥11.4
- The median split of Tizek et al. at 13.6: PASI<13.6, PASI≥13.6
- The median split of Tizek et al. at 13.6: PeakPASI<13.6, PeakPASI≥13.6

The dependent variables were either categorical (yes/no), for which a Chi-Squared-Test was performed, or continuous, for which the Mann-Whitney-U-Test was conducted to identify group differences. The following are the dependent, categorical variables examined with the Chi-Squared-Test:

- Gender
- Phototherapy
- Smoking
- Diabetes mellitus

- Alcohol addiction
- Hypothyroidism
- Depression
- Hypertension
- Drug addiction
- Age
- PASI split at 10
- PeakPASI split at 10
- PASI median split at 11.4
- PeakPASI median split at 11.4
- PASI median split at 13.6
- PeakPASI median split at 13.6

Only the six most common comorbidities (and drug addiction as an additional psychological comorbidity) were examined, as the sample sizes of the other comorbidities were not large enough to conduct a statistical analysis with.

The dependent, continuous variables examined using the Mann-Whitney-U-Test were as follows:

- Total number of visits to the hospital per patient
- Age of the patient (taken at the time of the PeakPASI)
- Most recent PASI of the patient
- PeakPASI of patient
- Imputed DLQI
- Number of comorbidities per patient
- Number of different systemic therapies the patient received during their psoriasis treatment
- Maximum number of topical therapies the patient received during one visit

Due to the non-normal distribution of the data, the Spearman's Rank Test was used to investigate the relationship between metric variables. The following variables were examined in a correlation with the PASI value, and then with the PeakPASI value:

- Total number of visits to the hospital per patient
- Number of different systemic therapies the patient received during their psoriasis treatment
- Maximum number of topical therapies the patient received in one hospital visit
- Number of comorbidities per patient
- Imputed DLQI
- Age of the patient at the time of the PeakPASI

Along with this, a Spearman's Rank correlation was also conducted between the PASI and PeakPASI.

For the next part of the analysis, regression models were created. Two separate dependent variables were chosen:

- Number of different systemic therapies the patient received during their psoriasis treatment
- Number of comorbidities per patient

As both these variables fall under count data, meaning that these are non-negative integers (Green, 2021), the choice of regression models lay between two generalized linear models: Poisson regression and Negative binomial distribution models. After checking the assumptions of the models, it was clear that both dependent variables fulfilled the criteria for Poisson regression models (such as that the mean is equal to the variance (Green, 2021)). A total of four multivariate models were created, two with the 'number of systemic therapies' as the dependent variable (one for the PASI and one for the PeakPASI) and two with the 'number of comorbidities' as the dependent variable (also one each with PASI and PeakPASI). The independent variables (which included either the PASI or the PeakPASI for each model) were first chosen according to best fit, and then kept constant to facilitate an easier comparison between the models. These independent variables were also divided into factors (categorical variables, such as gender) and covariates (continuous variables, such as age). The following tables 2 to 5 explain which variables were chosen for each model.

Table 2: Generalized Poisson regression model with the number of systemic therapies per patient as the dependent variable and the PASI (among others) as the independent variables to test the effect of the independent variables on this dependent variable

Dependent variable		Number of systemic therapies
Independent variables	Factors	Phototherapy, gender
	Covariates	PASI, number of visits, number of comorbidities, age, DLQI, number of topical therapies

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Table 3: Generalized Poisson regression model with the number of systemic therapies per patient as the dependent variable and the PeakPASI (among others) as the independent variables to test the effect of the independent variables on this dependent variable

Dependent variable		Number of systemic therapies
Independent variables	Factors	Phototherapy, gender
	Covariates	PeakPASI, number of visits, number of comorbidities, age, DLQI, number of topical therapies

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Table 4: Generalized Poisson regression model with the number of comorbidities per patient as the dependent variable and the PASI (among others) as the independent variables to test the effect of the independent variables on this dependent variable

Dependent variable		Number of comorbidities
Independent variables	Factors	Phototherapy, gender
	Covariates	PASI, number of visits, number of systemic therapies, age, DLQI, number of topical therapies

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Table 5: Generalized Poisson regression model with the number of comorbidities per patient as the dependent variable and the PeakPASI (among others) as the independent variables to test the effect of the independent variables on this dependent variable

Dependent variable		Number of comorbidities
Independent variables	Factors	Phototherapy, gender
	Covariates	PeakPASI, number of visits, number of systemic therapies, age, DLQI, number of topical therapies

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

After creating the regression models for the PASI and PeakPASI, a cross-validation of each model was conducted by dividing the dataset into a test and training set. Root-mean-square-deviation (RMSE) values were compared to identify if the model with the PASI or the model with the PeakPASI is the best fit for the dataset. This comparison was done twice, once for the number of systemic therapies (comparing the PASI and PeakPASI model) and once for the number of comorbidities (again comparing the PASI and PeakPASI model).

2.3.3 Software

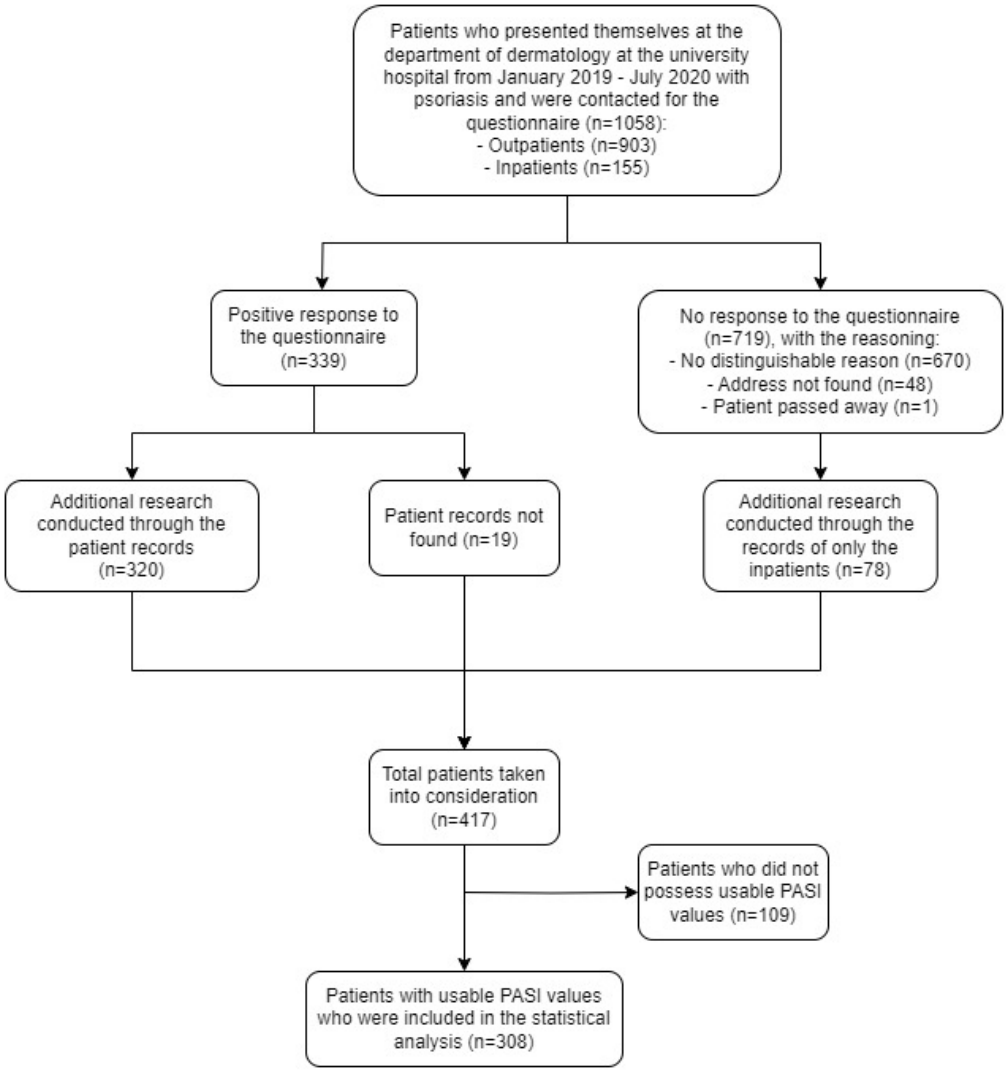
For the digitalization of the questionnaires and the patient files, the software Research Electronic Data Capture (REDCap) was implemented (Harris et al., 2009). Each questionnaire was digitalized twice, and discrepancies were noted and removed. The patient files were digitalized once. Data preparation was performed using Microsoft Excel, and the statistical analysis that followed was conducted using Jamovi Version 2.3 (The jamovi project, 2023) and R Statistical Software, version 2023.12.1 (R Core Team, 2023) with the package ‘corrplot’ (T. Wei and Simko, 2021). The alpha value was set at 0.05, and the confidence interval (CI) at 95%.

3 Results

3.1 Study population

Of the total 1058 patients who were recruited, 903 were outpatients and 155 were inpatients. Three hundred thirty-nine responded positively to the questionnaire (32.0%) and a total of 417 files were studied in detail (from the patients who sent back a questionnaire and additional inpatients). Of those 417 patients, 308 had usable PASI values (and therefore also a valid PeakPASI value). The PASI value was considered usable when a specific integer (such as PASI=2), and not a range of values (for example PASI=3-5), was recorded by the physician during one hospital visit. These were the patients included in the statistical analysis (Figure 1).

Figure 1: Flowchart to explain how patients were chosen for the statistical analysis from the original list of patients who were recruited from the department of dermatology and allergy of the university hospital of the Technical University of Munich



Abbreviations: PASI: Psoriasis Area and Severity Index

The 308 patients had a median age of 52.0 [41.0; 64.0] and 40.3% (n=124) were women. The median latest documented PASI was 2.0 [1.0; 5.1], the median PeakPASI 11.4 [5.9; 17.0], and the median imputed DLQI 12.7 [8.0; 17.0]. Forty-one of the patients (13.3%) had a latest PASI of 10 or above, while almost five times as many patients had a PeakPASI≥10 (n=193, 62.7%). Thirty-two patients (10.4%) had a PASI≥11.4, 155 patients (50.3%) had a PeakPASI≥11.4, 23 (7.5%) had a PASI≥13.6, and 124 (40.3%) had a PeakPASI≥13.6. Each patient visited the hospital a median of 12.0 [5.0; 33.0] times (Table 6).

Table 6: General attributes of the study participants, also divided by gender

	Total (n=308)	Women (n=124)	Men (n=184)
Age (years)			
Median	52.0	54.0	51.0
IQR	41.0; 64.0	42.0; 66.0	40.0; 63.0
Missing	0	0	0
Number of visits			
Median	12.0	10.0	14.5
IQR	5.0; 30.0	4.0; 28.3	6.0; 30.3
Missing	0	0	0
PASI			
Median	2.0	2.1	1.8
IQR	1.0; 5.1	1.0; 5.4	1.0; 4.9
Missing	0	0	0
PeakPASI			
Median	11.4	10.5	12.0
IQR	5.9; 17.0	4.6; 15.0	7.0; 19.6
Missing	0	0	0
DLQI			
Median	12.7	12.7	12.7
IQR	8.0; 17.0	12.0; 16.3	6.8; 17.0
Missing	0	0	0
PASI split			
PASI<10, n (%)	267 (86.7)	107 (86.3)	160 (87.0)
PASI≥10, n (%)	41 (13.3)	17 (13.7)	24 (13.0)
Missing/invalid	0	0	0
PeakPASI split			
PeakPASI<10, n (%)	115 (37.3)	55 (44.4)	60 (32.6)
PeakPASI≥10, n (%)	193 (62.7)	69 (55.6)	124 (67.4)
Missing/invalid	0	0	0
PASI median split 11.4			
PASI<11.4, n (%)	276 (89.6)	111 (89.5)	165 (89.7)
PASI≥11.4, n (%)	32 (10.4)	13 (10.5)	19 (10.3)
Missing/invalid	0	0	0
PeakPASI median split 11.4			
PeakPASI<11.4, n (%)	153 (49.7)	68 (54.8)	85 (46.2)
PeakPASI≥11.4, n (%)	155 (50.3)	56 (45.2)	99 (53.8)
Missing/invalid	0	0	0
PASI median split 13.6			
PASI<13.6, n (%)	285 (92.5)	117 (94.4)	168 (91.3)
PASI≥13.6, n (%)	23 (7.5)	7 (0.06)	16 (8.7)
Missing/invalid	0	0	0
PeakPASI median split 13.6			
PeakPASI<13.6, n (%)	184 (59.7)	84 (67.7)	100 (54.3)
PeakPASI≥13.6, n (%)	124 (40.3)	40 (32.3)	84 (45.7)
Missing/invalid	0	0	0

Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

The median number of comorbidities per patient was 2.0 [1.0; 3.0], with a total of 21 possible comorbidities recorded from the patient files: adipositas, arterial hypertension, coronary heart disease (CHD), heart attack, heart failure, heart arrthymia, metabolic syndrom, diabetes mellitus type 2, lipid metabolism disorders, asthma, arthritis, crohn's disease, ulcerative colitis, alcohol addiction, smoking, drug addiction, depression, chronic venous insufficiency (CVI), urinary tract infection, hypothyroidism, other (such as osteoporosis, gastritis and further comorbidities that were not recurring).

The six most common comorbidities were as follows (listed from most to least common):

- Smoking (n=85, 27.6%)
- Arterial hypertension (n=79, 25.6%)
- Alcohol addiction (n=47, 15.3%)
- Diabetes mellitus type 2 (n=39, 12.7%)
- Depression (n=27, 8.8%)
- Hypothyroidism (n=22, 7.1%)

Nearly all patients (n=300, 97.4%) received a topical therapy, with a median number of 6.0 [3.0; 11.0] topical therapies per hospital visit. The majority (n=252, 81.8%) required at least one systemic therapy (with a median of 1.0 different systemic therapies per patient [1.0; 2.0]), either as a standalone or in combination. For a combinational therapy, MTX or Alretinoin were used as the additional substance.
The six most common systemic therapies were:

- Secukinumab (n=74)
- Brodalumab and Altretinoin (n=73)
- Ustekinumab (n=58)
- Adalimumab (n=54)
- Dimethyl fumarate (n=50)
- MTX (n=49)

More than half of the patients (n=176, 57.1%) received at least one cycle of phototherapy during their entire psoriasis journey. Table 7 below divides the comorbidities and therapies according to the severity of the psoriasis (PASI<10, PASI≥10, PeakPASI<10, PeakPASI≥10).

Table 7: Comorbidites and therapies sorted according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 10)

	PASI<10 (n=267)	**PASI≥10 (n=41)**	**PeakPASI<10 (n=115)**	**PeakPASI≥10 (n=193)**
Number of comorbidities				
Median	2.0	2.0	1.0	2.0
IQR	1.0; 3.0	1.0; 3.0	0; 2.5	1.0; 3.0
Missing	0	0	0	0
Smoking				
No, n (%)	195 (73.0)	28 (68.3)	92 (80.0)	131 (67.9)
Yes, n (%)	72 (27.0)	13 (31.7)	23 (20.0)	62 (32.1)
Missing	0	0	0	0
Arterial hypertension				
No, n (%)	199 (74.5)	30 (73.2)	90 (78.3)	139 (72.0)
Yes, n (%)	68 (25.5)	11 (26.8)	25 (21.7)	54 (28.0)
Missing	0	0	0	0
Alcohol addiction				
No, n (%)	230 (86.1)	31 (75.6)	100 (87.0)	161 (83.4)
Yes, n (%)	37 (13.9)	10 (24.4)	15 (13.0)	32 (16.6)
Missing	0	0	0	0
Diabetes mellitus				
No, n (%)	236 (88.4)	33 (80.5)	107 (93.0)	162 (83.9)
Yes, n (%)	31 (11.6)	8 (19.5)	8 (7.0)	31 (16.1)
Missing	0	0	0	0
Depression				
No, n (%)	243 (91.0)	38 (92.3)	104 (90.4)	177 (91.7)
Yes, n (%)	24 (9.0)	3 (7.3)	11 (9.6)	16 (8.3)
Missing	0	0	0	0
Hypothyroidism				
No, n (%)	250 (93.6)	36 (87.8)	110 (95.7)	176 (91.2)
Yes, n (%)	17 (6.4)	5 (12.2)	5 (4.3)	17 (8.8)
Missing	0	0	0	0
Drug addiction				
No, n (%)	266 (99.6)	40 (97.6)	115 (100)	191 (99.0)
Yes, n (%)	1 (0.4)	1 (2.4)	0 (0)	2 (1.0)
Missing	0	0	0	0
Number of systemic therapies				
Median	2.0	1.0	1.0	2.0
IQR	1.0; 3.0	1.0; 1.0	0; 2.0	1.0; 3.0
Missing	0	0	0	0
Number of topical therapies				
Median	5.0	10.0	4.0	8.0
IQR	3.0; 10.0	6.0; 14.0	3.0; 7.5	4.0; 12.0
Missing	0	0	0	0
Phototherapy				
No, n (%)	122 (45.7)	10 (24.4)	67 (58.3)	65 (33.7)
Yes, n (%)	145 (54.3)	31 (75.6)	48 (41.7)	128 (66.3)
Missing	0	0	0	0

Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index

3.2 Comparison of patient groups

3.2.1 Gender

A difference was observed between gender and two of the most common comorbidities: alcohol addiction and hypothyroidism. More men than women suffered from an addiction to alcohol (20.7% vs 7.3%, p=0.001), and a greater number of women were diagnosed with hypothyroidism than men (11.3% vs 4.3%, p=0.020). No differences were noted between gender and the other comorbidities (smoking, arterial hypertension, diabetes, depression, drug addiction), with age (<52 and ≥52), or with phototherapy (Table 8).

Men had a higher PeakPASI than women (median(men)=12.0 [7.0; 19.6] vs median(women) =10.5 [4.6; 15.0], p=0.017), while the PASI did not differ between the genders. No disparities were observed for the visits, DLQI, comorbidities, systemic therapies, topical therapies, or the age (Table 9).

Table 8: Chi-Squared results to analyze group differences according to the gender of the patients

	Gender	
	Women (n=124)	Men (n=184)
Smoking		
No, n (%)	93 (75.0)	130 (70.7)
Yes, n (%)	31 (25.0)	54 (29.3)
p value	0.403	
Arterial hypertension		
No, n (%)	92 (74.2)	137 (74.5)
Yes, n (%)	32 (25.8)	47 (25.5)
p value	0.959	
Alcohol addiction		
No, n (%)	115 (92.7)	146 (79.3)
Yes, n (%)	9 (7.3)	38 (20.7)
p value	0.001	
Diabetes mellitus		
No, n (%)	109 (88.0)	160 (87.0)
Yes, n (%)	15 (12.0)	24 (13.0)
p value	0.806	
Depression		
No, n (%)	110 (88.7)	171 (92.9)
Yes, n (%)	14 (11.3)	13 (7.1)
p value	0.198	
Hypothyroidism		
No, n (%)	110 (88.7)	176 (95.6)
Yes, n (%)	14 (11.3)	8 (4.3)
p value	0.020	
Drug addiction		
No, n (%)	122 (98.4)	184 (100)
Yes, n (%)	2 (1.6)	0 (0)
p value	0.084	
Age		
<52, n (%)	57 (46.0)	96 (52.2)
≥52, n (%)	67 (54.0)	88 (47.8)
p value	0.285	
Phototherapy		
No, n (%)	51 (41.1)	81 (44.0)
Yes, n (%)	73 (58.9)	103 (56.0)
p value	0.615	

Table 9: Mann-Whitney-U results to analyze group differences according to the gender of the patients

		Gender	
		Women (n=124)	Men (n=184)
Number of visits	Median	10.0	14.5
	IQR	4.0; 28.3	6.0; 30.3
	p value	0.053	
PASI	Median	2.1	1.8
	IQR	1.0; 5.4	1.0; 4.9
	p value	0.707	
PeakPASI	Median	10.5	12.0
	IQR	4.6; 15.0	7.0; 19.6
	p value	0.017	
DLQI	Median	12.7	12.7
	IQR	12.0; 16.3	6.8; 17.0
	p value	0.094	
Number of comorbities	Median	2.0	2.0
	IQR	1.0; 3.0	1.0; 3.0
	p value	0.880	
Number of systemic therapies	Median	1.0	1.0
	IQR	1.0; 2.0	1.0; 2.0
	p value	0.698	
Number of topical therapies	Median	6.0	5.5
	IQR	3.0; 11.0	3.0; 11.0
	p value	0.611	
Age (years)	Median	54.0	51.0
	IQR	42.0; 66.0	40.0; 63.0
	p value	0.196	

Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

3.2.2 Age

Smoking had a higher prevalence in patients under 52 years than older patients (34.6% vs 20.6%, p=0.006), while both diabetes mellitus and arterial hypertension showed a greater prevalence in the patients who were above the age of 52 (diabetes: 17.4% vs 7.8%, p=0.012; hypertension: 39.4% vs 11.8%, p<0.001). The prevalence of the remaining comorbidities (alcohol addiction, depression, hypothyroidism, and drug addiction) did not differ according to age, similar to phototherapy (Table 10).

The number of comorbidities was higher in the patients who were older than 52 (median≥52 =2.0 [1.0; 3.0] vs median<52=1.0 [1.0; 2.0], p<0.001), just like the number of topical therapies was also greater in those above the age of 52 (median≥52=7.0 [3.0; 11.0] vs median<52=5.0 [3.0; 10.0], p=0.042). The number of visits, PASI, PeakPASI, DLQI and the number of systemic therapies showed no difference according to the age (Table 11).

Table 10: Chi-Squared results to analyze group differences according to the age of patients (<52, ≥52)

	Age	
	<52 (n=153)	≥52 (n=155)
Smoking		
No, n (%)	100 (65.4)	123 (79.4)
Yes, n (%)	53 (34.6)	32 (20.6)
p value	0.006	
Arterial hypertension		
No, n (%)	135 (88.2)	94 (60.6)
Yes, n (%)	18 (11.8)	61 (39.4)
p value	<0.001	
Alcohol addiction		
No, n (%)	128 (83.7)	133 (85.8)
Yes, n (%)	25 (16.3)	22 (14.2)
p value	0.600	
Diabetes mellitus		
No, n (%)	141 (92.2)	128 (82.6)
Yes, n (%)	12 (7.8)	27 (17.4)
p value	0.012	
Depression		
No, n (%)	141 (92.2)	140 (90.3)
Yes, n (%)	12 (7.8)	15 (9.7)
p value	0.569	
Hypothyroidism		
No, n (%)	146 (95.4)	140 (90.3)
Yes, n (%)	7 (4.6)	15 (9.7)
p value	0.082	
Drug addiction		
No, n (%)	151 (98.7)	155 (100)
Yes, n (%)	2 (1.3)	0 (0)
p value	0.153	
Phototherapy		
No, n (%)	74 (48.4)	58 (37.4)
Yes, n (%)	79 (51.6)	97 (62.6)
p value	0.052	

Table 11: Mann-Whitney-U results to analyze group differences according to the age of patients (<52, ≥52)

		Age	
		<52 (n=153)	≥52 (n=155)
Number of visits	Median	12.0	12.0
	IQR	5.0; 27.0	6.0; 32.0
	p value	0.618	
PASI	Median	1.6	2.1
	IQR	1.0; 4.5	1.0; 5.3
	p value	0.175	
PeakPASI	Median	11.5	11.3
	IQR	6.6; 17.0	5.7; 17.0
	p value	0.603	
DLQI	Median	12.7	12.7
	IQR	10.0; 19.0	7.0; 15.0
	p value	0.019	
Number of comorbities	Median	1.0	2.0
	IQR	1.0; 2.0	1.0; 3.0
	p value	<0.001	
Number of systemic therapies	Median	1.0	2.0
	IQR	1.0; 2.0	1.0; 3.0
	p value	0.312	
Number of topical therapies	Median	5.0	7.0
	IQR	3.0; 10.0	3.0; 11.0
	p value	0.042	

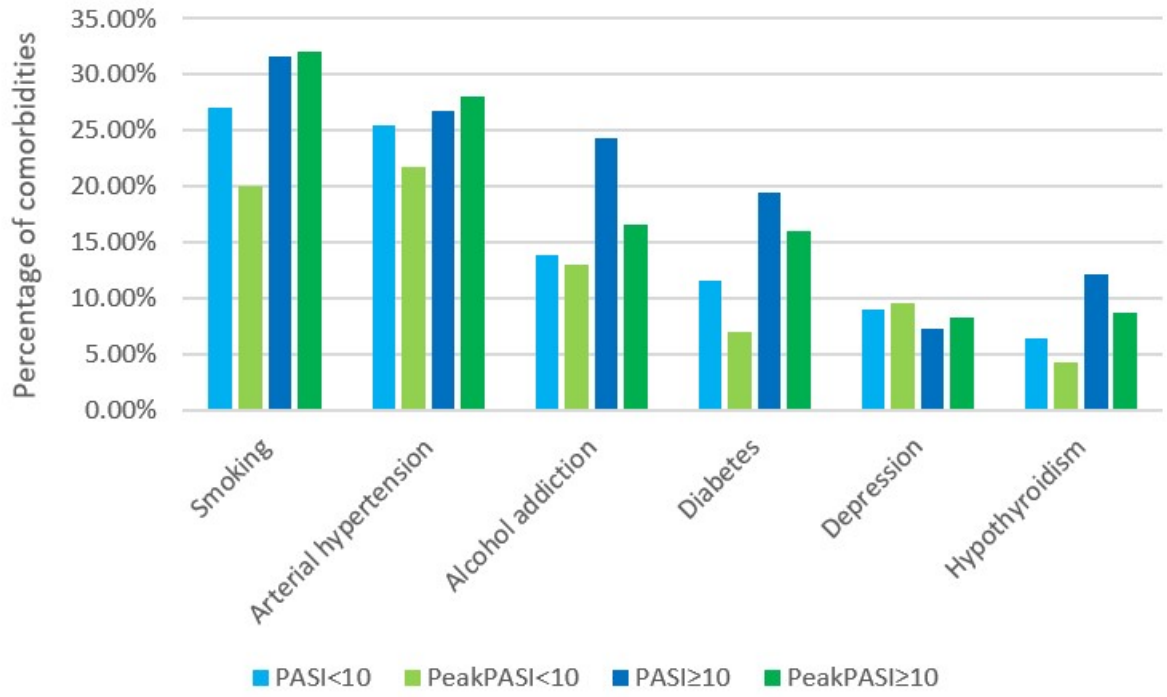
Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

3.2.3 PASI and PeakPASI 10

Both the patients with PASI≥10 and the ones with PeakPASI≥10 required more phototherapy than their counterparts. While 75% of patients (n=31/41) with PASI≥10 received at least one session of phototherapy in the past or present, only 54% of patients (n=145/267) with PASI<10 received one (p=0.010). More patients with PeakPASI≥10 (66.3%) received phototherapy than patients with PeakPASI<10 (41.7%, p<0.001). Men suffered more from a moderate-to-severe psoriasis based on the PeakPASI (40.3% vs 22.4%, p=0.037), while no such gender differences were observed for the PASI. Smoking (32.1% vs 20.0%, p=0.021) and diabetes mellitus (16.1% vs 7.0%, p=0.020) both occurred more frequently for patients with PeakPASI≥10 than patients with PeakPASI<10, but this was not observed for either comorbidity in regards to the PASI. Differences between the PASI or the PeakPASI groups were not noted for the remaining comorbidities (alcohol addiction, arterial hypertension, depression, hypothyroidism; Figure 2) or for age (Table 12).

Patients with a PASI<10 visited the hospital more frequently (median<10=14.0 [7.0; 33.0]) vs median≥10=3.0 [2.0; 8.0], p<0.001) and received one additional systemic therapy compared to patients with PASI≥10 (median<10=2.0 [1.0; 3.0] vs median≥10=1.0 [1.0; 1.0], p=0.009; Figure 3). This was inverse for the PeakPASI, where patients with PeakPASI≥10 were the ones who frequented the hospital more often (median≥10=16.0 [6.0; 33.0] vs median<10=9.0 [5; 21.5], p=0.007) and required a greater number of both systemic (median≥10=2.0 [1.0; 3.0] vs median<10=1.0 [0; 2.0], p<0.001; Figure 3) and topical therapies (median≥10=8.0 [4.0; 12.0] vs median<10=4.0 [3.0; 7.5], p<0.001). Even patients with a PASI≥10 received double the number of topical therapies compared to their counterparts (median≥10=10.0 [6.0; 14.0] vs median<10=5.0 [3.0; 10.0], p<0.001). A difference was not found for the number of overall comorbidities for the PASI, while the patients with PeakPASI≥10 suffered from one additional comorbidity (median≥10=2.0, [1.0; 3.0] vs median<10=1.0 [0; 2.5], p=0.014) compared to patients with PeakPASI<10 (Figure 4). The DLQI was equal in all groups (PASI: median<10=12.7 [7.0; 16.5] vs median≥10=12.7 [12.7; 20.0], p=0.041; PeakPASI: median<10=12.7 [9.0; 12.8] vs median≥10=12.7 [8.0; 18.0], p=0.033) and no difference in any group was found with regards to the age of patients (Table 13).

Figure 2: The prevalence of the most common comorbidities according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 10)



Abbreviations: PASI: Psoriasis Area and Severity Index

Table 12: Chi-Squared results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 10)

	PASI<10 (n=267)	**PASI≥10 (n=41)**	**PeakPASI<10 (n=115)**	**PeakPASI≥10 (n=193)**
Gender				
Men, n (%)	160 (59.9)	24 (58.5)	60 (52.2)	124 (64.2)
Women, n (%)	107 (40.1)	17 (41.5)	55 (47.8)	69 (35.8)
p value	0.866		0.037	
Age				
<52, n (%)	134 (50.2)	19 (46.3)	54 (47.0)	99 (51.3)
≥52, n (%)	133 (49.8)	22 (53.7)	61 (53.0)	94 (48.7)
p value	0.647		0.461	
Smoking				
No, n (%)	195 (73.0)	28 (68.3)	92 (80.0)	131 (67.9)
Yes, n (%)	72 (27.0)	13 (31.7)	23 (20.0)	62 (32.1)
p value	0.527		0.021	
Arterial hypertension				
No, n (%)	199 (74.5)	30 (7.3)	90 (78.3)	139 (72.0)
Yes, n (%)	68 (25.5)	11 (26.8)	25 (21.7)	54 (28.0)
p value	0.853		0.225	
Alcohol addiction				
No, n (%)	230 (86.1)	31 (75.6)	100 (87.0)	161 (83.4)
Yes, n (%)	37 (13.9)	10 (24.4)	15 (13.0)	32 (16.6)
p value	0.081		0.404	
Diabetes mellitus				
No, n (%)	236 (88.4)	33 (80.5)	107 (93.0)	162 (83.9)
Yes, n (%)	31 (11.6)	8 (19.5)	8 (7.0)	31 (16.1)
p value	0.157		0.020	
Depression				
No, n (%)	243 (91.0)	38 (92.7)	104 (90.4)	177 (91.7)
Yes, n (%)	24 (9.0)	3 (7.3)	11 (9.6)	16 (8.3)
p value	0.725		0.702	
Hypothyroidism				
No, n (%)	250 (93.6)	36 (87.8)	110 (95.7)	176 (91.2)
Yes, n (%)	17 (6.4)	5 (12.2)	5 (4.3)	17 (8.8)
p value	0.177		0.141	
Drug addiction				
No, n (%)	266 (99.6)	40 (97.6)	115 (100)	191 (99.0)
Yes, n (%)	1 (0.4)	1 (2.4)	0 (0)	2 (1.0)
p value	0.125		0.273	
Phototherapy				
No, n (%)	122 (45.7)	10 (24.4)	67 (58.3)	65 (33.7)
Yes, n (%)	145 (54.3)	31 (75.6)	48 (41.7)	128 (66.3)
p value	0.010		<0.001	

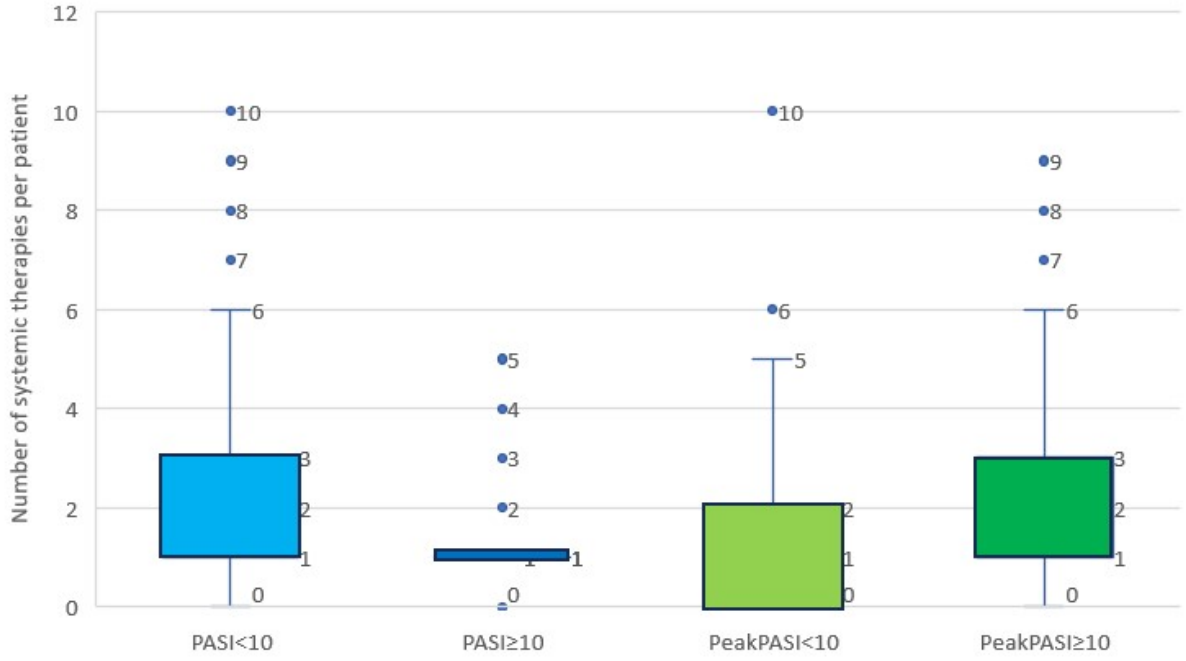
Abbreviations: PASI: Psoriasis Area and Severity Index

Table 13: Mann-Whitney-U results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 10)

		PASI<10 (n=267)	**PASI≥10 (n=41)**	**PeakPASI<10 (n=115)**	**PeakPASI≥10 (n=193)**
Age (years)	Median	51.0	53.0	53.0	51.0
	IQR	41.0; 63.5	41.0; 67.0	40.5; 63.5	41.0; 64.0
	p value	0.402		0.714	
Number of visits	Median	14.0	3.0	9.0	16.0
	IQR	7.0; 33.0	2.0; 8.0	5.0; 21.5	6.0; 33.0
	p value	<0.001		0.007	
PASI	Median	1.2	14.9	2.0	1.8
	IQR	1.0; 3.4	11.4; 19.8	1.0; 4.0	1.0; 6.1
	p value	<0.001		0.376	
PeakPASI	Median	10.5	15.9	4.7	15.0
	IQR	5.1; 15.4	12.3; 23.7	2.3; 7.1	11.7; 22.0
	p value	<0.001		<0.001	
DLQI	Median	12.7	12.7	12.7	12.7
	IQR	7.0; 16.5	12.7; 20.0	9.0; 12.8	8.0; 18.0
	p value	0.041		0.033	
Number of comorbities	Median	2.0	2.0	1.0	2.0
	IQR	1.0; 3.0	1.0; 3.0	0, 2.5	1.0; 3.0
	p value	0.169		0.014	
Number of systemic therapies	Median	2.0	1.0	1.0	2.0
	IQR	1.0; 3.0	1.0; 1.0	0; 2.0	1.0; 3.0
	p value	0.009		<0.001	
Number of topical therapies	Median	5.0	10.0	4.0	8.0
	IQR	3.0; 10.0	6.0; 14.0	3.0; 7.5	4.0; 12.0
	p value	<0.001		<0.001	

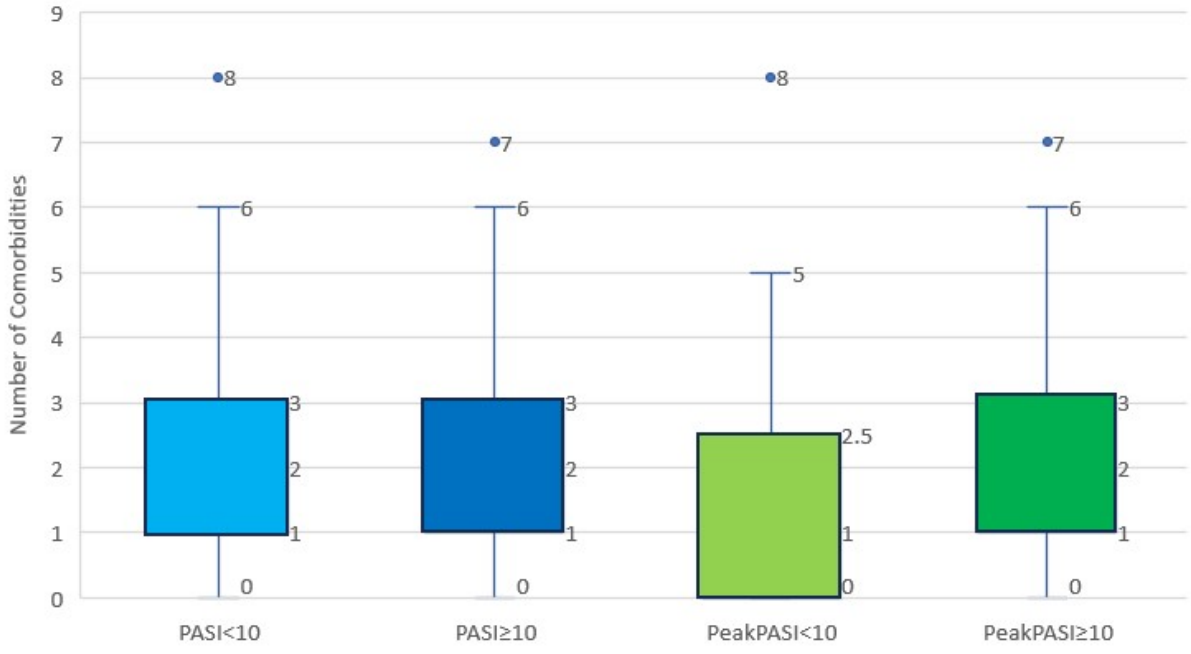
Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Figure 3: Box and whisker plot to showcase the median number of different systemic therapies that patients with a PASI and PeakPASI cut-off of 10 required



Abbreviations: PASI: Psoriasis Area and Severity Index

Figure 4: Box and whisker plot to showcase the median number of comorbidities present in the patients with a PASI and PeakPASI cut-off of 10



Abbreviations: PASI: Psoriasis Area and Severity Index

3.2.4 PASI and PeakPASI 11.4

As with the earlier cut-off of 10, both patients with PASI≥11.4 (75.0%) and patients with PeakPASI≥11.4 (47.1%) were more likely to have received phototherapy at some point in their psoriasis history compared to patients with PASI<11.4 (55.1%, p=0.031) and PeakPASI<11.4 (47.1%, p<0.001). No differences were observed for the PASI or the PeakPASI with gender, age, or any of the comorbidities (Table 14).

Similar to the psoriasis severity cut-off of 10, patients who had a PASI<11.4 visited the hospital a higher number of times (median<11.4=13.0 [7.0; 32.5] vs median≥11.4=3.0 [2.0; 6.5], p<0.001) and received a greater number of systemic therapies per patient (median<11.4=2.0 [1.0; 3.0] vs median≥11.4=1.0 [1.0; 1.0], p=0.007) than patients with PASI≥11.4 (Figure 5). This was again inverse for the PeakPASI, where patients with PeakPASI≥11.4 had a greater number of visits (median≥11.4=14.0 [6.0; 36.5] vs median<11.4=11.0 [5.0; 22.0], p=0.032) and a larger number of systemic therapies (median≥ 11.4=2.0 [1.0; 3.0] vs median<11.4=1.0 [0; 2.0], p<0.001) compared to their counterparts (Figure 5). Patients with PASI≥11.4 (median≥11.4 =11.0 [7.0; 15.0] vs median<11.4=5.0 [3.0; 10.0], p<0.001) and PeakPASI≥11.4 (median≥11.4= 8.0 [4.0; 12.0] vs median<11.4= 4.0 [3.0; 8.0], p<0.001) both required a greater number of topical therapies. While there was no difference in the number of comorbidities when the patients were split according to their PASI, the patients with PeakPASI≥11.4 had one additional comorbidity compared to their counterparts with less severe psoriasis (median≥11.4=2.0 [1.0; 3.0] vs median<11.4=1.0 [1.0; 3.0], p=0.039; Figure 6). The DLQI was identical in the PASI groups, as well as in the PeakPASI groups (median<11.4=12.7 [9.0; 13.0] vs median≥11.4=12.7 [7.5; 19.0], p=0.031). While the patients with PASI≥11.4 were 8.5 years older than the patients with PASI<11.4 (median≥11.4=59.5 [46.3; 69.3] vs median<11.4=51.0 [40.5; 63.0], p=0.048), no such difference was observed for patients stratified according to the PeakPASI (Table 15).

Table 14: Chi-Squared results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 11.4)

	PASI<11.4 (n=276)	**PASI≥11.4 (n=32)**	**PeakPASI<11.4 (n=153)**	**PeakPASI≥11.4 (n=155)**
Gender				
Men, n (%)	165 (59.8)	19 (59.4)	85 (55.6)	99 (63.9)
Women, n (%)	111 (40.2)	13 (40.6)	68 (44.4)	56 (36.1)
p value	0.965		0.137	
Age (years)				
<52, n (%)	142 (51.4)	11 (34.3)	75 (49.0)	78 (50.3)
≥52, n (%)	134 (48.6)	21 (65.6)	78 (51.0)	77 (49.7)
p value	0.067		0.819	
Smoking				
No, n (%)	201 (72.8)	22 (68.8)	118 (77.1)	105 (67.7)
Yes, n (%)	75 (27.2)	10 (31.2)	35 (22.9)	50 (32.3)
p value	0.625		0.066	
Arterial hypertension				
No, n (%)	209 (75.7)	20 (62.3)	121 (79.0)	108 (69.7)
Yes, n (%)	67 (24.3)	12 (37.5)	32 (21.0)	47 (30.3)
p value	0.105		0.059	
Alcohol addiction				
No, n (%)	235 (85.1)	26 (81.3)	131 (85.6)	130 (83.9)
Yes, n (%)	41 (14.9)	6 (18.8)	22 (14.4)	25 (16.1)
p value	0.562		0.669	
Diabetes mellitus				
No, n (%)	244 (88.4)	25 (78.1)	138 (90.2)	131 (84.5)
Yes, n (%)	32 (11.6)	7 (21.9)	15 (9.8)	24 (15.5)
p value	0.098		0.134	
Depression				
No, n (%)	252 (91.3)	29 (90.6)	139 (90.8)	142 (91.6)
Yes, n (%)	24 (8.7)	3 (9.4)	14 (9.2)	13 (8.4)
p value	0.898		0.813	
Hypothyroidism				
No, n (%)	258 (93.5)	28 (87.5)	145 (94.8)	141 (91.0)
Yes, n (%)	18 (6.5)	4 (12.5)	8 (5.2)	14 (9.0)
p value	0.214		0.195	
Drug addiction				
No, n (%)	275 (99.6)	31 (96.9)	153 (100)	153 (98.7)
Yes, n (%)	1 (0.4)	1 (3.1)	0 (0)	2 (1.3)
p value	0.065		0.159	
Phototherapy				
No, n (%)	124 (44.9)	8 (25.0)	81 (52.9)	51 (32.9)
Yes, n (%)	152 (55.1)	24 (75.0)	72 (47.1)	104 (67.1)
p value	0.031		<0.001	

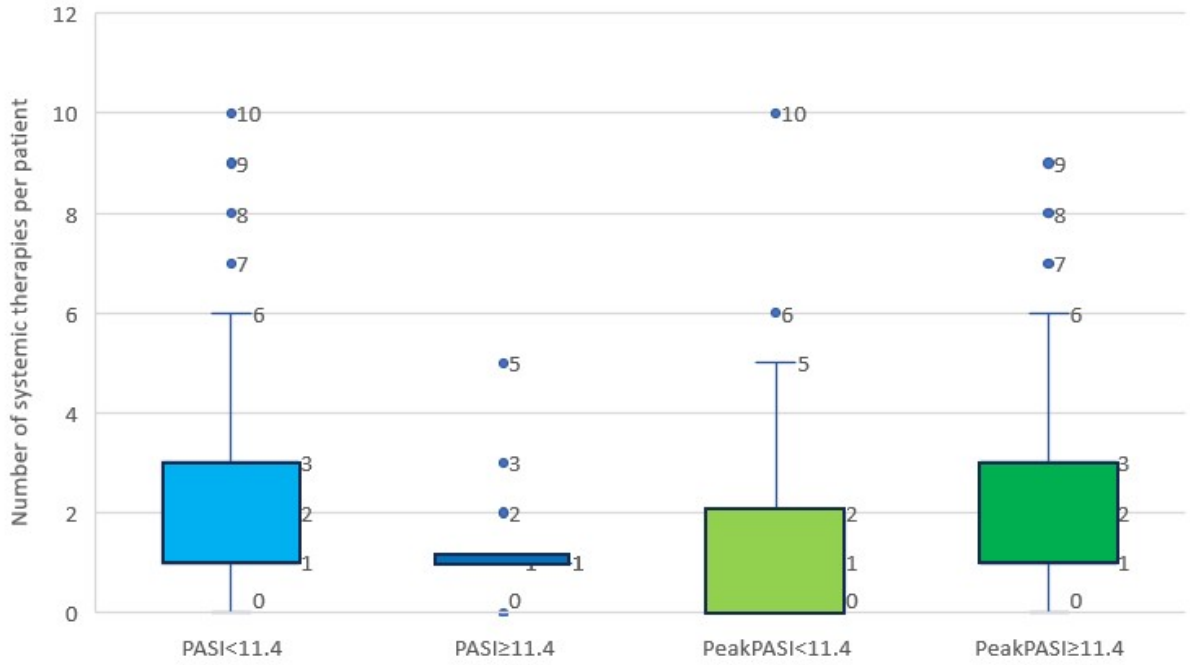
Abbreviations: PASI: Psoriasis Area and Severity Index

Table 15: Mann-Whitney-U results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 11.4)

		PASI<11.4 (n=276)	**PASI≥11.4 (n=32)**	**PeakPASI<11.4 (n=153)**	**PeakPASI≥11.4 (n=155)**
Age (years)	Median	51.0	59.5	53.0	51.0
	IQR	40.5; 63.0	46.3; 69.3	40.0; 63.0	41.0; 64.5
	p value	0.048		0.794	
Number of visits	Median	13.0	3.0	11.0	14.0
	IQR	7.0; 32.5	2.0; 6.5	5.0; 22.0	6.0; 36.5
	p value	<0.001		0.032	
PASI	Median	1.5	16.7	2.0	2.0
	IQR	1.0; 3.82	12.4; 22.1	1.0; 4.1	1.0; 6.3
	p value	<0.001		0.305	
PeakPASI	Median	10.7	17.6	5.9	17.0
	IQR	5.2; 15.2	12.4; 24.7	3.1; 9.5	14.0; 23.9
	p value	<0.001		<0.001	
DLQI	Median	12.7	12.7	12.7	12.7
	IQR	7.0; 16.0	12.7; 20.0	9.0; 13.0	7.5; 19.0
	p value	0.054		0.031	
Number of comorbities	Median	2.0	2.0	1.0	2.0
	IQR	1.0; 3.0	1.0; 3.0	1.0; 3.0	1.0; 3.0
	p value	0.111		0.039	
Number of systemic therapies	Median	2.0	1.0	1.0	2.0
	IQR	1.0; 3.0	1.0; 1.0	0; 2.0	1.0; 3.0
	p value	0.007		<0.001	
Number of topical therapies	Median	5.0	11.0	4.0	8.0
	IQR	3.0; 10.0	7.0; 15.0	3.0; 8.0	4.0; 12.0
	p value	<0.001		<0.001	

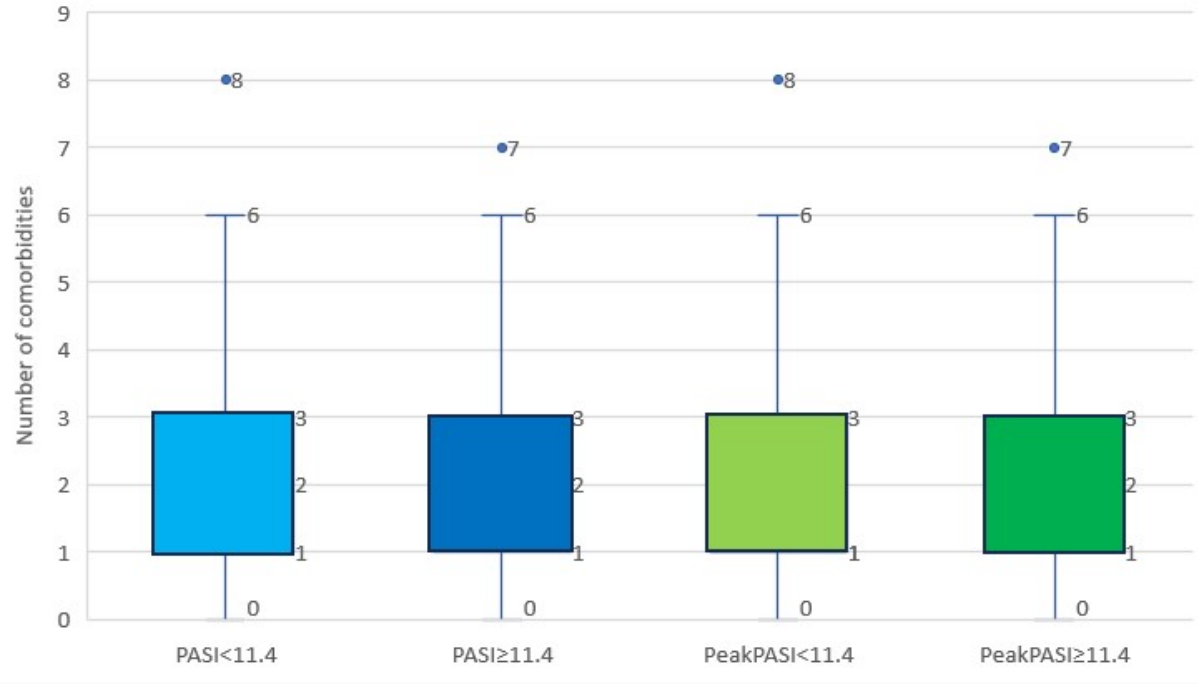
Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Figure 5: Box and whisker plot to showcase the median number of different systemic therapies that patients with a PASI and PeakPASI cut-off of 11.4 required



Abbreviations: PASI: Psoriasis Area and Severity Index

Figure 6: Box and whisker plot to showcase the median number of comorbidities present in the patients with a PASI and PeakPASI cut-off of 11.4



Abbreviations: PASI: Psoriasis Area and Severity Index

3.2.5 PASI and PeakPASI 13.6

Similar to the cut-offs of 10 and 11.4, patients with a PASI≥13.6 (87.0% vs 54.7%, p=0.003) and patients with a PeakPASI≥13.6 (69.4% vs 48.9%, p<0.001) both received phototherapy more often than patients with less severe psoriasis. While no differences were observed for the PASI and the other variables (gender, age, most common comorbidities), a difference could be observed for the PeakPASI and gender. More men than women suffered from a worse psoriasis and had a PeakPASI≥13.6 (67.7% vs 32.3%, p=0.019). There were no differences for the PeakPASI and the remaining variables (age, most common comorbidities) (Table 16).

The number of visits per patient were higher in the PASI<13.6 group than the PASI≥13.6 group (median<13.6=13.0 [6.0; 32.0] vs median≥13.6=3.0 [2.0; 7.0], p<0.001), while the number of systemic therapies was identical (median<13.6=1.0 [1.0; 2.0] vs median≥13.6= 1.0 [1.0; 1.0], p=0.031; Figure 7). Here too, patients with a PeakPASI≥13.6 frequented the hospital more often (median≥13.6=16.5 [6.0; 33.8] vs median<13.6=11.0 [5.0; 24.0], p=0.025) and required additional systemic therapy (median≥13.6=2.0 [1.0; 3.0] vs median<13.6=1.0 [0; 2.0], p<0.001; Figure 7). The number of topical therapies was greater for the patients with the more severe psoriasis, regardless of whether the PASI or the PeakPASI was taken into account (PASI: median≥13.6=11.0 [7.5; 15.0] vs median<13.6=5.0 [3.0; 10.0], p<0.001 and PeakPASI: median ≥13.6=9.0 [4.8; 12.0] vs median<13.6=4.0 [3.0; 9.0], p<0.001). No differences were observed for the number of comorbidities when patients were divided according to their PASI or their PeakPASI (Figure 8). While the DLQI was identical for both PASI groups, patients with a PeakPASI≥13.6 had a higher DLQI (median≥13.6=14.0 [8.0; 19.3] vs median<13.6=12.7 [8.0; 14.0], p=0.006) than patients with a PeakPASI<13.6. No differences were observed for age in any of the groups (Table 17).

Table 16: Chi-Squared results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 13.6)

	PASI<13.6 (n=285)	**PASI≥13.6 (n=23)**	**PeakPASI<13.6 (n=184)**	**PeakPASI≥13.6 (n=124)**
Gender				
Men, n (%)	168 (58.9)	16 (69.6)	100 (54.3)	84 (67.7)
Women, n (%)	117 (41.1)	7 (30.4)	84 (45.7)	40 (32.3)
p value	0.318		0.019	
Age				
<52, n (%)	145 (50.9)	8 (34.8)	85 (46.2)	68 (54.8)
≥52, n (%)	140 (49.1)	15 (65.2)	99 (53.8)	56 (45.2)
p value	0.138		0.137	
Smoking				
No, n (%)	208 (73.0)	15 (65.2)	139 (75.5)	84 (67.7)
Yes, n (%)	77 (27.0)	8 (34.8)	45 (24.5)	40 (32.3)
p value	0.423		0.133	
Arterial hypertension				
No, n (%)	214 (75.1)	15 (65.2)	142 (77.2)	87 (70.2)
Yes, n (%)	71 (24.9)	8 (34.8)	42 (22.8)	37 (29.8)
p value	0.297		0.167	
Alcohol addiction				
No, n (%)	243 (85.3)	18 (78.3)	159 (86.4)	102 (82.3)
Yes, n (%)	42 (14.7)	5 (21.7)	25 (13.6)	22 (17.7)
p value	0.369		0.32	
Diabetes mellitus				
No, n (%)	249 (87.4)	20 (87.0)	163 (88.6)	106 (85.5)
Yes, n (%)	36 (12.6)	3 (12.0)	21 (11.4)	18 (14.5)
p value	0.954		0.422	
Depression				
No, n (%)	261 (91.6)	20 (87.0)	168 (91.3)	113 (91.1)
Yes, n (%)	24 (8.4)	3 (13.0)	16 (8.7)	11 (8.9)
p value	0.451		0.957	
Hypothyroidism				
No, n (%)	264 (92.6)	22 (95.7)	171 (92.9)	115 (92.7)
Yes, n (%)	21 (7.4)	1 (4.3)	13 (7.1)	9 (7.3)
p value	0.588		0.949	
Drug addiction				
No, n (%)	284 (99.6)	22 (95.7)	183 (99.5)	123 (99.2)
Yes, n (%)	1 (0.4)	1 (4.3)	1 (0.5)	1 (0.8)
p value	0.022		0.778	
Phototherapy				
No, n (%)	129 (45.3)	3 (13.0)	94 (51.1)	38 (30.6)
Yes, n (%)	156 (54.7)	20 (87.0)	90 (48.9)	86 (69.4)
p value	0.003		<0.001	

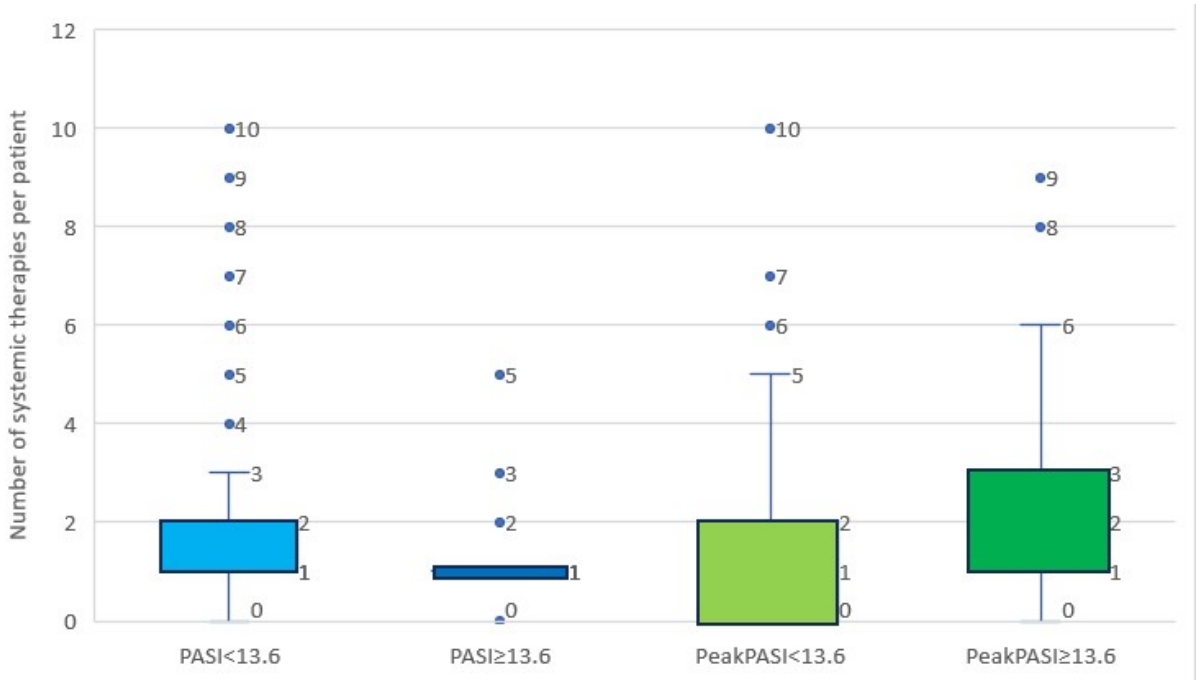
Abbreviations: PASI: Psoriasis Area and Severity Index

Table 17: Mann-Whitney-U results to analyze group differences according to the severity of the psoriasis (measured through the PASI and PeakPASI cut-off value of 13.6)

		PASI<13.6 (n=285)	**PASI≥13.6 (n=23)**	**PeakPASI<13.6 (n=184)**	**PeakPASI≥13.6 (n=124)**
Age (years)	Median	51.0	60.0	53.5	50.0
	IQR	41.0; 63.0	49.5; 68.0	41.0; 65.0	41.0; 63.0
	p value	0.093		0.292	
Number of visits	Median	13.0	3.0	11.0	16.5
	IQR	6.0; 32.0	2.0; 7.0	5.0; 24.0	6.0; 33.8
	p value	<0.001		0.025	
PASI	Median	1.7	18.8	2.1	1.6
	IQR	1.0; 4.0	16.5; 23.8	1.0; 5.1	1.0; 5.0
	p value	<0.001		0.917	
PeakPASI	Median	11	22.4	7.5	19.9
	IQR	5.2; 17.0	15.0; 24.9	3.5; 10.7	15.0; 25.0
	p value	<0.001		<0.001	
DLQI	Median	12.7	12.7	12.7	14.0
	IQR	7.0; 16.0	12.7; 20.0	8.0; 14.0	8.0; 19.3
	p value	0.096		0.006	
Number of comorbities	Median	2.0	2.0	1.0	2.0
	IQR	1.0; 3.0	1.0; 3.0	1.0; 3.0	1.0; 3.0
	p value	0.342		0.196	
Number of systemic therapies	Median	1.0	1.0	1.0	2.0
	IQR	1.0; 2.0	1.0; 1.0	0; 2.0	1.0; 3.0
	p value	0.031		<0.001	
Number of topical therapies	Median	5.0	11.0	4.0	9.0
	IQR	3.0; 10.0	75.0; 15.0	3.0; 9.0	4.8; 12.0
	p value	<0.001		<0.001	

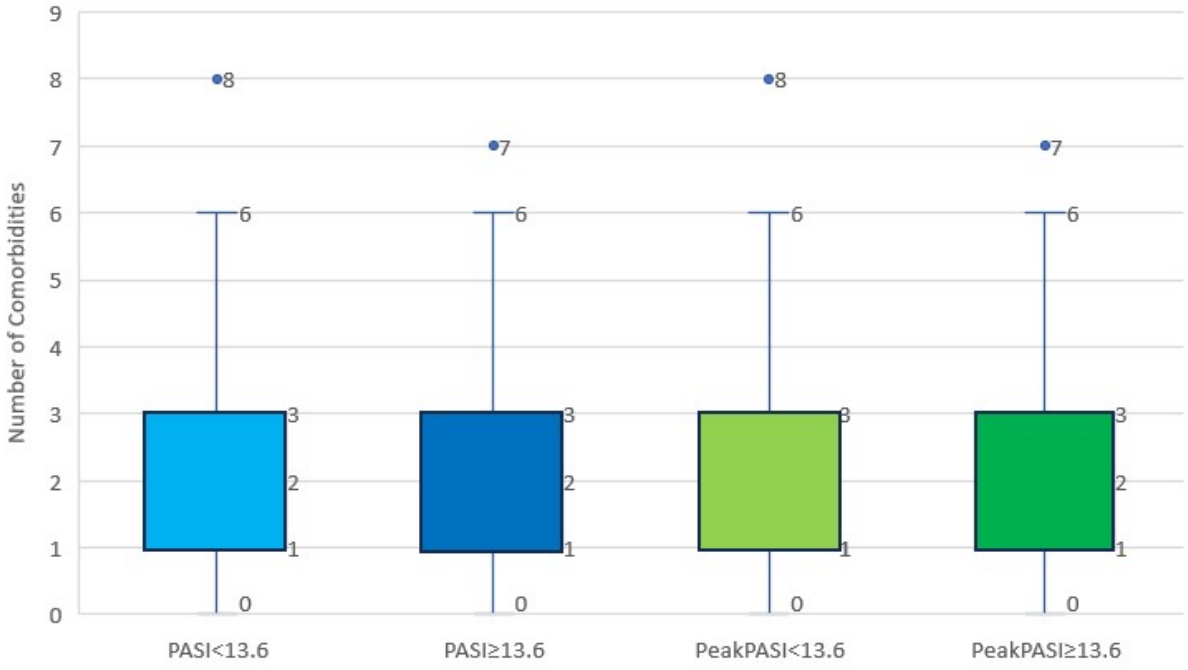
Abbreviations: IQR: Interquartile range, PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Figure 7: Box and whisker plot to showcase the median number of different systemic therapies that patients with a PASI and PeakPASI cut-off of 13.6 required



Abbreviations: PASI: Psoriasis Area and Severity Index

Figure 8: Box and whisker plot to showcase the median number of comorbidities present in the patients with a PASI and PeakPASI cut-off of 13.6



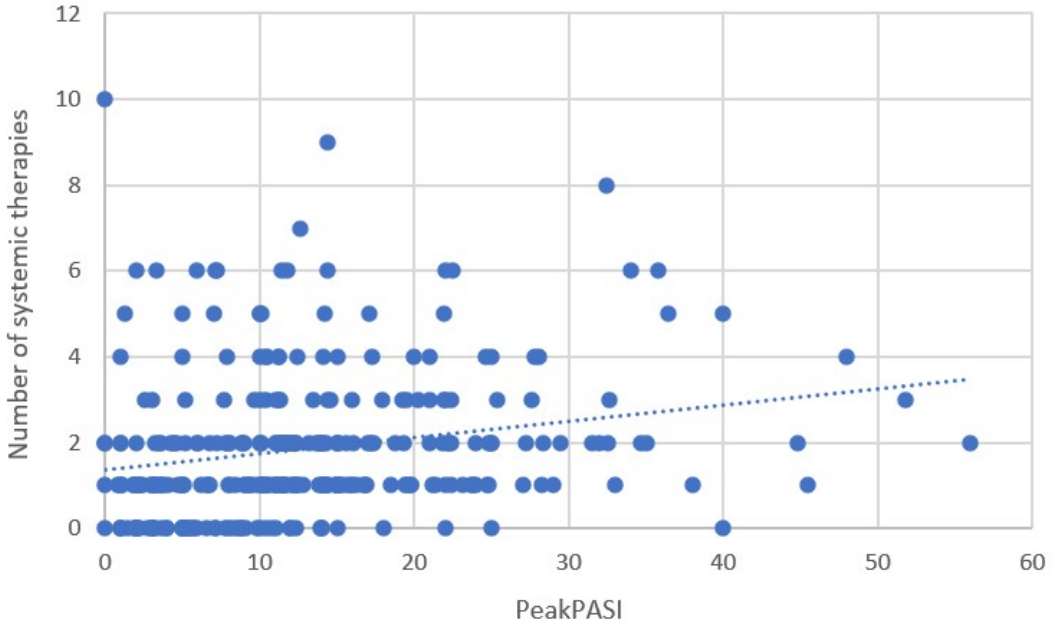
Abbreviations: PASI: Psoriasis Area and Severity Index

3.3 PASI and PeakPASI

3.3.1 Correlations

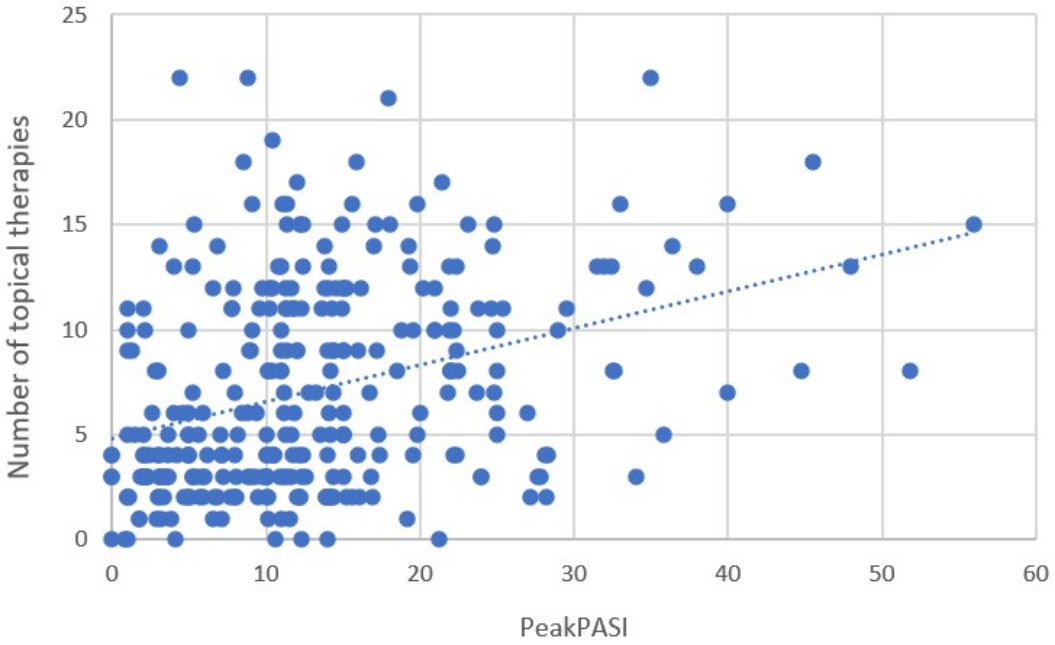
A moderate negative correlation was observed between the PASI and the number of visits (ρ=-0.430, p<0.001), as well as with the number of systemic therapies (ρ=-0.334, p<0.001). A low to moderate positive correlation was noted between the PeakPASI and the number of visits (ρ=0.186, p=0.001), and additionally with the number of systemic therapies (ρ=0.296, p<0.001) too (Figure 9). With the number of topical therapies, a low positive correlation was present with the PASI (ρ=0.202, p<0.001), while the PeakPASI exhibited a moderate positive correlation (ρ=0.367, p<0.001) (Figure 10). A negligible correlation was present between the PASI and the DLQI (ρ=0.176, p=0.007), and even the PeakPASI only had a low positive correlation with the DLQI (ρ=0.179, p=0.006). While no significant correlation was observed between the PASI and the number of comorbidities, a low positive one was noted with the PeakPASI (ρ=0.147, p=0.010). The PASI and PeakPASI both did not depict a correlation with the age of the patient. A correlation was not present between the PASI and the PeakPASI (Table 18, Figure 11).

Figure 9: Scatter plot to depict the relationship between the number of systemic therapies per patient and the PeakPASI



Abbreviations: PASI: Psoriasis Area and Severity Index

Figure 10: Scatter plot to depict the relationship between the number of topical therapies per patient and the PeakPASI



Abbreviations: PASI: Psoriasis Area and Severity Index

Table 18: Results of the Spearman's Rank correlation between the PASI/PeakPASI and the continuous variables

	PASI	PeakPASI
Number of visits		
Correlation coefficient	-0.430	0.186
p value	<0.001	0.001
Number of systemic therapies		
Correlation coefficient	-0.334	0.296
p value	<0.001	<0.001
Number of topical therapies		
Correlation coefficient	0.202	0.367
p value	<0.001	<0.001
DLQI		
Correlation coefficient	0.134	0.155
p value	0.019	0.006
Number of comorbidities		
Correlation coefficient	0.108	0.147
p value	0.059	0.010
Age		
Correlation coefficient	0.065	-0.001
p value	0.255	0.988
PASI		
Correlation coefficient	-	0.100
p value	-	0.079

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

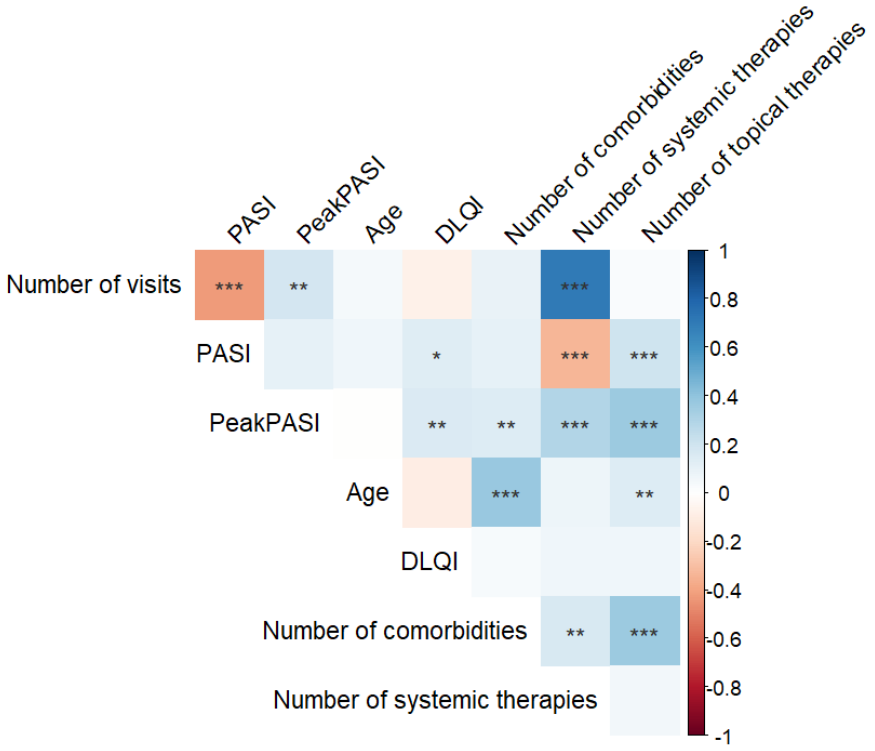


Figure 11: Correlation matrix depicting the correlation between the number of hospital visits per patient, the latest PASI, the PeakPASI, the age of the patient, the imputed DLQI, the number of comorbidities per patient, the number of unique systemic therapies per patient, and the maximum number of topical therapies per patient. An increase in blue color is an indication for a strong positive correlation, while the increasingly coral/red color indicates a negative correlation. The squares that are empty do not show a significant correlation.
(Significance levels: *** p<0.001, ** p<0.010, * p<0.050)
Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

3.3.2 Regressions

Number of systemic therapies:

In the Poisson regression model with the number of systemic therapies as the dependent variable and the PASI as one of the independent variables, there is one positive predictor: the number of hospital visits per patient. This means that if the number of visits is increased by one unit, and all other variables are held constant, then the expected number of systemic therapies will increase by the factor of exp(0.021)=1.021, (95% CI 0.018-0.025). The PASI is a negative predictor, suggesting that increasing the PASI by one unit, and holding all other variables constant, decreases the expected number of systemic therapies by the factor of exp(0.022)=1.022, (95% CI -0.043-(-0.002)). Changes in the other variables (number of comorbidities, age, DLQI, number of topical therapies, gender, and phototherapy) are not associated with any changes in the response variable (number of systemic therapies) (Table 19).

The model for the number of systemic therapies and the PeakPASI has the number of visits as a positive predictor. If the number of visits is increased by one unit, and all other variables are held constant, then the expected number of systemic therapies will increase by the factor of exp(0.022)=1.022, (95% CI 0.019-0.025). Changing the PeakPASI or any of the other variables in this model does not have an effect on the number of systemic therapies (Table 20). The cross validation depicted 1.986 as the RMSE for the PASI model and 1.999 for the PeakPASI model.

Table 19: Results of the Poisson regression model with the number of systemic therapies per patient as the dependent variable and the PASI as the main independent variable

	Estimate	95% Confidence Interval	*p* value
Intercept	0.483	0.388 – 0.576	<0.001
PASI	-0.022	-0.043 – -0.002	0.038
Number of visits	0.021	0.018 – 0.025	<0.001
Number of comorbidities	0.055	-0.008 – 0.116	0.084
Age	0.002	-0.005 – 0.008	0.644
DLQI	0.009	-0.003 – 0.021	0.134
Number of topical therapies	0.005	-0.014 – 0.025	0.586
Gender (man-woman)	-0.057	-0.228 – 0.116	0.513
Occurrence of phototherapy (yes-no)	-0.081	-0.260 – 0.099	0.377

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Table 20: Results of the Poisson regression model with the number of systemic therapies per patient as the dependent variable and the PeakPASI as the main independent variable

	Estimate	95% Confidence Interval	*p* value
Intercept	0.495	0.400 – 0.586	<0.001
PeakPASI	0.006	-0.002 – 0.015	0.130
Number of visits	0.022	0.019 – 0.025	<0.001
Number of comorbidities	0.053	-0.010 – 0.114	0.091
Age	0.002	-0.005 – 0.008	0.579
DLQI	0.006	-0.005 – 0.019	0.290
Number of topical therapies	-0.002	-0.023 – 0.019	0.860
Gender (man-woman)	-0.091	-0.265 – 0.085	0.307
Occurence of phototherapy (yes-no)	-0.104	-0.283 – 0.076	0.254

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Number of comorbidities:

In the Poisson regression model for the number of comorbidities and the PASI, the age of the patient and the number of topical therapies were observed as positive predictors. Increasing the age of the patient by one unit, while holding all other variables constant, increases the expected number of comorbidities by the factor of exp(0.017)=1.017, (95% CI 0.011-0.022). Increasing the number of topical therapies by one unit, while holding all other variables constant, increases the expected number of comorbidities by the factor of exp(0.040)=1.041, (95% CI 0.023-0.058). Changes in the other variables (including the PASI) do not lead to any changes in the dependent variable of the number of comorbidities (Table 21).

In the Poisson regression model for the number of comorbidities and the PeakPASI, the same two variables, age and the number of topical therapies, are once again positive predictors. If the age of the patient is increased by one unit, and all other variables are held constant, then the expected number of comorbidities will increase by the factor of exp(0.017)=1.017, (95% CI 0.012-0.023). Increasing the number of topical therapies by one unit while keeping all other variables constant will increase the expected number of comorbidities by a factor of exp(0.043)=1.043, (95% CI 0.025-0.060). Any changes in the PeakPASI or the other independent variables do not contribute to changes in the number of comorbidities in this model (Table 22). Here the RMSE for the PASI model is 1.847, while for the PeakPASI model it is at 1.846.

Table 21: Results of the Poisson regression model with the number of comorbidities per patient as the dependent variable and the PASI as the main independent variable

	Estimate	95% Confidence Interval	*p* value
Intercept	0.554	0.463 – 0.643	<0.001
PASI	0.009	-0.005 – 0.023	0.186
Number of visits	-3.26E-04	-0.006 – 0.005	0.905
Number of systemic therapies	0.047	-0.014 – 0.105	0.125
DLQI	0.007	-0.005 – 0.019	0.281
Age	0.017	0.011 – 0.022	<0.001
Number of topical therapies	0.040	0.023 – 0.058	<0.001
Occurrence of phototherapy (yes-no)	0.024	-0.159 – 0.210	0.796
Gender (man-woman)	-0.008	-0.181 – 0.167	0.931

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

Table 22: Results of the Poisson regression model with the number of comorbidities per patient as the dependent variable and the PeakPASI as the main independent variable

	Estimate	95% Confidence Interval	*p* value
Intercept	0.553	0.462 – 0.642	<0.001
PeakPASI	-0.001	-0.011 – 0.008	0.762
Number of visits	-0.001	-0.007 – 0.004	0.671
Number of systemic therapies	0.046	-0.015 – 0.105	0.131
DLQI	0.008	-0.004 – 0.020	0.207
Age	0.017	0.012 – 0.023	<0.001
Number of topical therapies	0.043	0.025 – 0.060	<0.001
Occurrence of phototherapy (yes-no)	0.043	-0.141 – 0.230	0.651
Gender (man-woman)	0.004	-0.172 – 0.182	0.961

Abbreviations: PASI: Psoriasis Area and Severity Index, DLQI: Dermatological Life Quality Index

4 Discussion

As of now, not much research has been conducted yet on the PeakPASI. The pilot study carried out by Tizek et al., 2021 instigated the exploration of the usefulness of this additional clinical score and this study aimed to build on that previous research. Using the PeakPASI alongside the PASI may be helpful to document the long-term disease burden of a psoriasis patient. Just like the cumulative life course impairment scale (CLCI) is used to longitudinally assess the quality of life of dermatological patients and the impact their disease has had on them (compared to quality of life indices such as the DLQI that only do this in the short-term) (A. Kimball et al., 2010, Romiti et al., 2023), the PeakPASI could be used in a similar manner to help more correctly assess the long-term severity of the psoriasis.

This mixed-method study with prospective questionnaires and retrospective analysis of patient records aimed to demonstrate if the use of the PeakPASI brings any additional value to patients in their psoriasis journey. For this, a comparison to the PASI was created, for which a relationship with the number of systemic therapies (Honda et al., 2017) and the number of comorbidities (Augustin et al., 2010, Alajmi et al., 2021) has been established. This study assessed if a similar relationship was also present between the PeakPASI and the number of systemic therapies, as well as between the PeakPASI and the number of comorbidities.

A greater number of patients were categorized with a higher PeakPASI than with a higher PASI, which shows that if only the PASI is regarded, there is a risk that the severity of the psoriasis of a patient could be underclassified. A relationship was established between the PeakPASI and therapies, depicting that patients with a higher PeakPASI required a greater number of therapies (phototherapy, systemic, and topical). Patients with a greater PeakPASI also had more comorbidities.

4.1 Comparison of patient groups

4.1.1 Gender

In this study, no differences were observed between the PASI groups and the gender of the patient, regardless of the cut-off of the PASI (10, 11.4 or 13.6). Differences were present in the PeakPASI cut-off 10 group, where almost double as many men suffered from PeakPASI$\geq$10 compared to women (40.3% vs 22.4%) and also in the PeakPASI 13.6 group, with more than double as many men than women having a PeakPASI$\geq$13.6 (67.7% vs 32.3%). A higher PeakPASI was also observed for men. There have been mixed results regarding the severity of psoriasis and gender in the present literature. Some studies have shown that disease sever-

ity differentiates between the genders, with men suffering more (Hägg et al., 2013, Hägg et al., 2017). M. A. Gupta and Gupta, 1995 and Łakuta et al., 2017, on the other hand, did not find any difference in psoriasis severity between men and women. Hägg et al., 2013 showed that while the prevalence of psoriasis was equal between the two genders, men had higher extreme PASI values and also higher PASI baseline values than women, along with a higher median PASI. One reason for this could be that psoriasis severity seems to be affected by estrogen levels and increased estrogen results in a lower disease severity, which could explain why women suffer from less severe psoriasis (Guillet et al., 2022). The trend fits to our study and explains why there were more men in the PeakPASI≥10/13.6 group, and also why men had a higher PeakPASI in general. Another study displayed that women have a less severe psoriasis, measured through lower median PASI values of patients (5.4 for women and 7.5 for men) and maybe therefore received systemic treatment less often (Hägg et al., 2017). A study by Fernández-Armenteros et al., 2019 depicted that men had a higher prevalence of psoriasis, and that gender was a factor associated with the risk of psoriasis. Results of gender distribution are conflicting and it is still unclear why there are gender disparities in the prevalence of psoriasis, or what the exact role of gender is in this illness (Guillet et al., 2022).

This study indicated that men accumulated a greater number of hospital visits compared to women, which meets expectations because if men suffer from a more severe form of psoriasis, then it would be necessary for them to visit the hospital more often. Studies have depicted that men receive systemic therapy more often than women due to a higher disease severity (White et al., 2011, Hägg et al., 2017, Guillet et al., 2022,). A study showed that men were more likely to receive phototherapy and also systemic therapy in the hospital, while women with the same disease severity were more likely to only be given topical treatments (Guillet et al., 2022). One reason for this could be that the safety of therapies was a greater concern during the treatment of women because women experienced more unfavorable effects, and they therefore received therapies with less adverse side-effects (Guillet et al., 2022). Our study was not able to confirm this trend between the therapies and genders, which could be because the group sizes of men and women affected by psoriasis were unequal and rather small (n<200), so it was difficult to facilitate a proper comparison.

Though our study did not illustrate any differences in the number of comorbidities divided by gender, the specific comorbidities did depict gender discrepancies. Almost three times as many men suffered from alcohol addiction, and almost three times as many women were affected by hypothyroidism. Previous studies have shown this same trend: that men with psoriasis have more alcohol addiction than women (Wolk et al., 2009, White et al., 2011, Brenaut et al., 2013, Guillet et al., 2022). Gerdes et al., 2010 also displayed that women with a more psoriasis (measured through the PASI) had an increased alcohol consumption compared to the women with a mild psoriasis, and that this was not the case for men. Our study was not able to confirm

this result, as no differences were found for women with more severe psoriasis compared to ones with mild psoriasis, which is again probably due to the small sample size of women that were present in this study.

Hypothyroidism affected almost three times as many women as men in this study, which is congruent with existing literature. A study in Taiwan exhibited that psoriasis patients who suffer from thyroid dysfunction have higher PASI scores and elevated serum C-reactive protein levels compared to those without thyroid dysfunction (Bu et al., 2022). Along with this, women with psoriasis especially had a high prevalence of Hashimoto thyroiditis (Bu et al., 2022). Other studies have confirmed that women with psoriasis seem to have higher cases of hypothyroidism or hyperthyroidism compared to men (Meng et al., 2015, Valduga et al., 2021, Cira et al., 2023).

There were no gender differences observed for the DLQI in our data, but literature has shown that women with psoriasis often have a lower quality of life compared to men (measured through a higher DLQI) and are more likely to suffer from depression (Guillet et al., 2022, Gonzalez-Cantero et al., 2023). One reason for this could be the strict beauty norms that women are confronted with daily, even without the presence of dermatological illnesses, which are then exacerbated through skin conditions like psoriasis. As our gender groups were not large enough, we were unable to observe this effect in our study.

4.1.2 Age

Age was another variable that showed only minimaldifferences when the severity of psoriasis was considered. The only group that had a difference was the PASI 11.4 group, where patients with PASI$\geq$11.4 were older than patients with PASI<11.4. The literature has not yet found a relationship between age and the severity of psoriasis, so it is unclear if this age difference is valid (Fernandez-Torres et al., 2012). One possible reason for older patients having greater disease severity could be that they may suffer from additional comorbidities, especially ones that also increase inflammation, which could then exacerbate the condition of the psoriasis.

Our study could not identify any information on the number of hospital visits due to psoriasis increasing with age. Existing literature was also difficult to find on this topic.

The literature has not found any differences between the systemic treatment that psoriasis patients receive and their age, which was confirmed in our study as well. This means that a higher age did not show an association with a specific treatment type or even with an increased number of necessary therapies (Fernandez-Torres et al., 2012). However, older psoriasis patients do more frequently receive therapies for other comorbidities, so it is important to pay attention to their additional therapies to prevent any adverse effects due to mixing of the drugs (Fernandez-

Torres et al., 2012). Patients over the age of 52 in this study required a greater number of topical therapies than their younger peers, which has been confirmed in other studies (Petersen et al., 2022). This could be due to systemic agents being administered less due to fear of side effects, while the safety of topical agents is greater so they are administered more readily (Petersen et al., 2022).

The older patients of this study also required more phototherapy than the younger ones. This has not yet been confirmed in the literature, as studies have not demonstrated a connection between the age of patients and phototherapy (Fernandez-Torres et al., 2012). It is possible that the reasoning for more phototherapy is similar to the topical therapy, as phototherapy has less side effects than systemic therapy (Zhang and Wu, 2018).

It was observed that the older patients in this study had one additional comorbidity compared to their younger counterparts, which meets the expectation that the number of comorbidities increases with increasing age. Multimorbidity is to be expected with higher age, as older individuals are more likely to be diagnosed with chronic illnesses (Divo et al., 2014). One study showed that most patients under 50 years old had no comorbidities, while patients above the age of 50 had two or more comorbidities (Alajmi et al., 2021). Multiple studies have also confirmed this (Augustin et al., 2010, Fernandez-Torres et al., 2012). Hypothyroidism (Meng et al., 2015), diabetes (Z. Yan et al., 2023), and arterial hypertension (Kearney et al., 2005, J. Wu et al., 2023) are just some examples of the comorbidities that older patients can suffer from. Patients in this study over the age of 52 did suffer more from diabetes and arterial hypertension. The prevalence of diabetes, and the likelihood of developing complications, is greater in those above the age of 50, especially those aged 60-69 (Z. Yan et al., 2023). It increases from 11.1% for patients aged 40-49 to double that at 23.9% in those aged 60-69 (Z. Yan et al., 2023). This is the same for arterial hypertension, which has a greater prevalence at a higher age and an increasing prevalence as age increases (Kearney et al., 2005, J. Wu et al., 2023). The comparison of the age groups of patients under 52 and over 52 also exhibited that younger patients smoked 1.6 times more than older patients. This was associated with a greater disease severity (meaning that greater disease severity was therefore associated with more smoking) and is congruent with existing literature. Fernandez-Torres et al., 2012 depicted that while 15.7% of old patients smoked, this number was more than double that (39.2%) for young people.

There was no difference observed in the imputed DLQI according to age in this study, which is contradictory to existing literature. Studies have shown that the DLQI decreases with increasing age, meaning that older patients seem to have a higher quality of life than younger patients (Fernandez-Torres et al., 2012, Altunay et al., 2014). One explanation for this could be that older patients have learned how to handle their psoriasis, as they have dealt with it for a longer time. They may also generally be less self-conscious and more settled, due to having experienced

more in life. This study did not confirm this view, which may be due to the fact that an imputed version of the DLQI was implemented because of too many missing values, which could have affected the results. Developing a study with non missing DLQI items would be an option to examine if this is actually a trend.

4.1.3 Severity of psoriasis (PASI and PeakPASI cut-offs)

An inverse relationship was established between the number of hospital visits and the psoriasis severity measured through the PASI. Patients who were in the PASI<10, PASI<11.4, and PASI<13.6 group visited the hospital more often than patients in the groups with more severe psoriasis. For the PeakPASI, this relationship was the other way around: patients suffering from more severe psoriasis (PeakPASI$\geq$10, $\geq$11.4 or $\geq$13.6) frequented the hospital 3-7 times more often than their peers with less severe psoriasis. This seems logical, as patients who are in worse condition will most likely require more serious treatment and a greater number of visits to the doctor. Past studies have also confirmed that patients with more severe psoriasis require more time in the hospital (Augustin et al., 2008). Not only that, but the patients in the PASI<10, PASI<11.4, PASI<13.6 groups also received one additional systemic therapy compared to their counterparts, while this was the opposite when the PeakPASI was considered. Patients with a greater disease severity (PeakPASI$\geq$10, PeakPASI$\geq$11.4 or PeakPASI$\geq$13.6) received one more systemic therapy. The literature depicts that patients with more severe psoriasis require a greater number of systemic therapies (Shin et al., 2023), showing that the relationship is similar to that of the PeakPASI, and not the PASI.

One reason for this could be that this study took the latest PASI of a patient into account, which was often a low number (0 or 1). This means that while the patient visited the hospital continuously and received their systemic therapy to combat the high starting disease severity (and therefore high PASI), by the end of the treatment cycle the disease severity (and therefore also the PASI) was low, as the patient was in recovery. This latest PASI was the one taken into account, and therefore a negative relationship was established with the number of hospital visits and systemic therapies. This mean that a lower PASI correlated with a greater number of hospital visits and systemic therapies. Regarding both the number of visits and the number of systemic therapies, the latest PASI does not provide an accurate depiction of how these variables change as the PASI increases. If only the PASI was taken into account here without the PeakPASI, it may depict an incorrect tendency. It is possible that this relationship between the variables would differ if the PASI is taken at a specific, predetermined point in time that is constant for all patients, which could be interesting to study further.

Patients with the more severe psoriasis measured through the PASI did require more topical therapies though, which was identical for the PeakPASI. Patients with both PASI$\geq$10 and

PeakPASI≥10 required double the number of topical therapies compared to their peers with mild psoriasis, which was consistent with the 11.4 and 13.6 cut-off groups as well. Numerous studies have confirmed that patients with moderate-to-severe psoriasis require a greater number of topical therapies than patients with mild psoriasis, as topical therapy plays an important role in the treatment of psoriasis (Bagel and Gold, 2017, Ahmed et al., 2023, Pinter and van de Kerkhof, 2023). Considering that it is still the latest PASI value that was used here, it is possible that the positive tendency could be even stronger, with patients requiring even more topical therapies as their severity of psoriasis increases.

Both the analysis with the PASI and with the PeakPASI illustrated that there were a greater number of patients in the more severe psoriasis group who had received at least one phototherapy treatment in their past when compared to patients with mild psoriasis. This was the same for all of the cut-offs, 10, 11.4, and 13.6. Each higher severity PASI group (PASI≥10, 11.4, and 13.6) and each higher severity PeakPASI group (PeakPASI≥10, 11.4, and 13.6) had more patients with phototherapy in their history than their counterparts. This is consistent with the guideline-based recommendation of phototherapy for patients with moderate-to-severe psoriasis (N. M. Golbari et al., 2018), which has been associated with a decrease in the PASI score afterwards (Nada et al., 2023). Nada et al., 2023, for example, demonstrated that a PUVA treatment decreased the mean PASI score of patients significantly from "28.94±11.02 to 22.51±11.66".

No difference was observed with the number of comorbidities of patients in any of the PASI groups, as they each had two comorbidities. However, the patients with a more severe psoriasis measured through the PeakPASI for the cut-offs of 10 and 11.4 each had one additional comorbidity compared to the individuals with the less severe psoriasis. There was no difference observed for the PeakPASI 13.6 cut-off. One reason for this could be insufficient sample size, as the PeakPASI≥13.6 group was smaller than the PeakPASI≥11.4 or PeakPASI≥10 groups. Existing literature shows that patients suffering from a more severe psoriasis do seem to have more comorbidities than patients with a mild psoriasis, which would make sense due to the pathophysiology behind psoriasis and the overlapping pathways that can be active in other comorbidities too (Yeung et al., 2013).

None of the PASI cut-offs exhibited a difference with any of the specific comorbidities that were tested in this study, but the PeakPASI 10 group did exhibit one for smoking and diabetes mellitus. This has been confirmed in the existing literature, as past studies have established a relationship between smoking and psoriasis. Smokers suffer from psoriasis more often and "heavy smokers are more likely to have severe disease" (Al-Mutairi et al., 2010). Psoriasis patients who smoke indicate significantly higher PASI scores compared to patients who are non-smokers (A. Armstrong et al., 2014, Emre et al., 2013), which depicts that smoking may increase the severity of psoriasis and also lower the response to treatment (leading to a higher

PASI that is difficult to decrease) (Emre et al., 2013). It is therefore understandable that this study observed a relationship with the PeakPASI and smoking, because the PeakPASI is higher than the PASI.

For diabetes, the more body surface that was affected by the psoriasis, the significantly higher the increased incidence of diabetes was (A. W. Armstrong et al., 2013b, Abramczyk et al., 2020). Individuals with a greater BSA (especially those with a BSA>10% (Łakuta et al., 2017)) were at a greater risk for developing diabetes mellitus compared to individuals without psoriasis (Wan et al., 2018). This study illustrated that slightly over double the number of patients with PeakPASI$\geq$10 suffered from diabetes mellitus compared to those with PeakPASI<10.

In past and recent literature, a relationship has been found between the severity of psoriasis and the other most common comorbidities that were also investigated in this study: depression, arterial hypertension, and alcohol addiction. This study, however, could not determine if patients with a higher PASI or PeakPASI suffer more from depression, arterial hypertension or alcohol addiction.

Depression is a comorbidity that has received mixed responses in existing literature. Łakuta et al., 2017 reported that the severity of the psoriasis did not seem to correlate with depressive symptoms of the patients (Łakuta et al., 2017), while Sahi et al., 2020 established contrasting results. The patients with severe psoriasis showed an increased risk for depression compared to those with just mild psoriasis (adjusted hazard ratio (HR) 1.72 vs HR 1.38) (Sahi et al., 2020, Olivier et al., 2010). Another study in China displayed that their patients with psoriasis had a 1.3 times higher risk for depression than the control group, but that there was no significant correlation observed between depression and patients with mild psoriasis compared to depression and patients with moderate-to-severe psoriasis (Jing et al., 2021). In this study too, no relationship could be established between the severity of the psoriasis and the prevalence of depression, which could also be due to the sample size. Only 8.8% of the patient collective of this study were diagnosed with depression, and it is likely that these are too few patients to test out this hypothesis.

Literature is also inconsistent regarding psoriasis and arterial hypertension. A positive association has been found between hypertension and psoriasis in one study (Yamazaki, 2021), in which psoriasis patients have a greater incidence and prevalence of hypertension in comparison to the general population (A. W. Armstrong et al., 2013a). Along with that, it has also been observed that patients with more severe psoriasis have greater odds of hypertension compared to patients with mild psoriasis (A. W. Armstrong et al., 2013a). A study in 2015 found a positive correlation between the severity of psoriasis (measured through the PASI of the patient) and high blood pressure (diagnosed by a doctor of internal medicine) (Salihbegovic et al., 2015).

On the other hand, there have been studies that depict no difference in the prevalence of hypertension for patients with mild psoriasis compared to patients with moderate-to-severe psoriasis (psoriasis classified through the PASI and hypertension diagnosed by the physician) (Ku et al., 2016), which shows that results are mixed. In our study as well, the results for hypertension with regards to severity of psoriasis were inconclusive, which again could be related to the smaller size of the subgroup. It is therefore not possible for us to make an accurate statement regarding the severity of psoriasis and arterial hypertension.

Multiple studies have reported an association between the severity of psoriasis and alcohol (Gerdes et al., 2010, Brenaut et al., 2013, Zink et al., 2017). Zink et al., 2017 observed that the disease severity (measured through the PASI) and alcohol addiction (measured through the CAGE questionnaire) were linked. An excessive alcohol consumption, meaning more than 1 drink per day on a regular basis, was found to be more common in individuals with psoriasis than the general population (Gerdes et al., 2010, Brenaut et al., 2013). Due to the small sample size in this study, a difference was not noted between the alcohol addiction and the severity of psoriasis patients. Though there were more patients with greater disease severity who had an alcohol addiction, the result was not significant because the examined patient group was too small. Perhaps further investigation of this could be beneficial.

The imputed DLQI was another variable for which no differences were observed between the different groups. Each PASI and PeakPASI cut-off, except for the PeakPASI 13.6 cut-off, had an identical DLQI. Only the patients with a PeakPASI$\geq$13.6 had a higher imputed DLQI (14.0) compared to patients with PeakPASI<13.6 who had a DLQI of 12.7. This is contradictory to existing data, as a higher PASI generally results in a higher DLQI too, showing that quality of life is reduced when disease severity is higher (Gerdes et al., 2010, Milidrag et al., 2023). This study did not reflect this trend, which may be related to the multiple missing values of the DLQI for which an imputation was performed. Conducting a trial with valid DLQI values could be useful.

Usefulness of the PeakPASI in relation to the above-mentioned variables:

Number of hospital visits: Regardless of the cut-off value, the relationship with the number of hospital visits was opposite for the PASI and PeakPASI groups. While the patients in the groups with PASI<10, PASI<11.4, and PASI<13.6 (therefore the lower disease severity) all visited the hospital more frequently, it was the patients with PeakPASI$\geq$10, PeakPASI$\geq$11.4, or PeakPASI$\geq$13.6 (therefore those with higher disease severity) that accumulated a greater number of hospital visits. The latter is the trend that is present in the literature (Shin et al., 2023),

which shows that the PeakPASI provides additional value here.

Number of systemic therapies: There was a similar relationship with the number of different systemic therapies as with the number of hospital visits. While the patients with PASI<10 and PASI<11.4 had more systemic therapies than their counterparts, the PASI 13.6 analysis did not show a difference between the two groups. With the PeakPASI, the number of systemic therapies was higher in the groups with the more severe psoriasis, which was patients with PeakPASI≥10, PeakPASI≥11.4, and PeakPASI≥13.6.

With both the number of hospital visits and the number of systemic therapies, taking the PeakPASI into account in addition to the latest PASI of a patient seems to add value. The existing literature also confirms that the relationship between these variables goes in a positive direction (a more severe psoriasis results in a greater number of hospital visits and/or systemic therapies), showing that only observing the PASI here would not accurately depict the relationship (Augustin et al., 2008, Shin et al., 2023).

Number of topical therapies: For the number of topical therapies, the relationship is positive, regardless of which PASI or PeakPASI cut-off is observed. The number of topical therapies is greater in each group with patients suffering from more severe psoriasis (i.e. the patients with a higher PASI or PeakPASI). This fits to the existing literature, as patients with a more severe form of psoriasis may require a greater number of topical therapies compared to patients with a mild psoriasis (Ahmed et al., 2023, Pinter and van de Kerkhof, 2023, Bagel and Gold, 2017). Here, both the PASI and the PeakPASI depict similar results.

Phototherapy: When comparing the severity groups amongst each other, the relationship with the occurrence of phototherapy stayed identical. In each of the six groups, more patients with the higher PASI or PeakPASI received phototherapy compared to the patients with the less severe psoriasis. This is fitting to the literature, which shows that patients with a more severe psoriasis require phototherapy more often than patients with a mild psoriasis (as phototherapy is also a recommended treatment modality for patients with a moderate-to-severe psoriasis) (N. M. Golbari et al., 2018). Once again, the analyses with the PASI and PeakPASI provide comparable results.

Number of comorbidities: The number of comorbidities in the PASI groups were identical across all groups. On the other hand, if the PeakPASI was considered, then both the PeakPASI≥10 and the PeakPASI≥11.4 group had one comorbidity more than the other group. There have been studies that describe that a more severe psoriasis correlates with a greater number of comorbidites (Yeung et al., 2013), so this would fit to the existing literature. The PeakPASI is a good addition in this case.

Specific comorbidities (smoking, alcohol, diabetes, hypertension, depression): No differences were observed between the severity of the psoriasis and the specific comorbidities that were investigated in this study, apart from in the PeakPASI 10 group. More patients with PeakPASI≥10 were smokers, and there were also a greater number of patients who suffered from diabetes mellitus compared to their counterparts. Though results for the other comorbidities are rather inconclusive due to small sample sizes, the PeakPASI does seem to provide additional value, at least regarding smoking and diabetes.

Imputed DLQI: For the DLQI, there was no difference between the groups except for the PeakPASI 13.6 group, where the patients with a more severe psoriasis, so PeakPASI≥13.6, had a higher DLQI than the patients with a mild psoriasis. In the available literature, the relationship that exists generally seems to be that as the severity of the psoriasis increases (for example measured through the PASI), the quality of life of the patient decreases (therefore leading to an increase in the DLQI) (Milidrag et al., 2023). In this case too, the PeakPASI seems to provide further value.

In regards to the examined variables, the PeakPASI did provide additional value than if only the PASI had been considered, which shows that further, larger, studies regarding this can be conducted.

Which PeakPASI cut-off is the most beneficial?

Each PeakPASI cut-off (10, 11.4, 13.6) that was explored in this study displayed usefulness. Patients in each of the three cut-off groups visited the hospital more frequently and received a greater number of systemic and topical therapies, as well as phototherapy. Patients with the cut-offs of 10 and 11.4 had additional comorbidities, while this was not observed for the PeakPASI 13.6. Only two of the specific comorbidities showed a group difference, and that too only those with a the cut-off of 10 (not with 11.4 or 13.6). A difference was observed in the DLQI based on the PeakPASI 13.6, but not with the other cut-offs. As the number of patients in each of the groups was rather low in this study, it would be beneficial to conduct a larger investigation to examine if the cut-off of 11.4 or 13.6 is favourable to the cut-off of 10. However, even just the PeakPASI cut-off of 10 was more advantageous than the PASI cut-off of 10, which shows that the PeakPASI could be an acceptable addition in the psoriasis journey of patients.

4.2 PASI and PeakPASI

4.2.1 Correlations

In the literature, the PASI has shown a positive correlation with the number of visits and the number of systemic therapies. However, the data from this study showed a moderate negative correlation between the PASI and these two variables. The literature shows a positive correlation because patients who receive systemic therapy generally suffer from a more severe psoriasis, which requires more frequent hospital visits (Syversen, Goll, et al., 2021. These patients visit the hospital in timed intervals (for example every 12 weeks for certain biologicals (Syversen, Jørgensen, et al., 2021)) and continue to receive the medication (such as biologicals) even once the condition of their psoriasis has been brought back under control. By the end of the successful treatment cycle, the patients will have a low latest or most recent PASI. As this is the PASI value that was analysed in this study, the correlation turned out to be negative, because patients had a low PASI value but still had a high number of visits and a high number of systemic therapies.

The PeakPASI however, displayed a weak positive correlation with the number of hospital visits and a weak-to-moderate positive correlation with the number of systemic therapies. This fits to the existing literature. Studies have shown that a high PASI makes it more likely that patients will require a switch in their systemic therapy, as it is possible that when the psoriasis is more severe, the response to biologicals is not as good and several therapies are test before finding a good fit (Shin et al., 2023). Tizek et al., 2021 observed that patients with a higher PeakPASI were more likely to receive a greater number of systemic therapies, which may be due to these patients requiring changes of treatment due to unsuccessful results.
In this case, relying on the PeakPASI as an additional score would make sense, as this is the correlation that fits to the existing literature, while only taking the latest PASI into account may result in an alternate interpretation of the correlation.

For the number of topical therapies, the PASI displayed a weak positive correlation, while the PeakPASI showed a moderate positive correlation. In the literature, it has been observed that patients with more severe psoriasis require more topical therapy. This makes sense because topical therapies play a big role in the treatment of skin and have been shown to have positive effects (Pinter and van de Kerkhof, 2023). Topical therapies are used alone or alongside systemic therapies because they are beneficial not only for the mild form of psoriasis but also for the more severe forms, and therefore patients generally receive numerous topical therapies (Ahmed et al., 2023, Pinter and van de Kerkhof, 2023, Bagel and Gold, 2017).

No correlation was observed between the PASI and the number of comorbidities, while only a weak positive one was present with the PeakPASI. More severe psoriasis, objectively measured through the BSA, has been shown to have higher odds of at least one major comorbidity com-

pared to patients without psoriasis (Yeung et al., 2013). Another study depicted that patients with psoriasis had increased prevalence rates for comorbidities compared to patients without psoriasis (Augustin et al., 2010). Yet a further study displayed that some patients with psoriatic arthritis had at least two or more comorbidities and all patients with erythrodermic arthritis had two or more comorbidities (Alajmi et al., 2021). As psoriasis is a disease that is linked to multiple other illnesses, especially the inflammatory ones, it would make sense that a more severe psoriasis results in a great number of comorbidities (Irimie et al., 2015, Daniel, 2020).

A weak positive correlation was observed for both the PASI and the PeakPASI with the imputed DLQI. Studies have shown mixed responses for the relationship that is present between the PASI and the DLQI. While some have noted a strong positive correlation between the PASI and the DLQI, because when one is reduced, the other also decreases (Mattei et al., 2014, Milidrag et al., 2023), others only showed weak-to-moderate positive correlations between the two (Griffiths et al., 2015, Gerdes et al., 2020) or even no correlation at all (Silva et al., 2013). It stands to reason that a correlation does exist between the two, because if the psoriasis is more severe, measured with the PASI, and there are additional symptoms, it is understandable that the patient's subjective well-being and quality of life is reduced (and therefore the DLQI is increased) (Milidrag et al., 2023).

Neither the PASI nor the PeakPASI displayed a correlation with the age of the patient, showing that older or younger patients do not necessarily have a more severe psoriasis. Studies have also depicted similar results, as an association between severity of psoriasis and age has not yet been found (M. A. Gupta and Gupta, 1995, Fernandez-Torres et al., 2012).

In this study, no correlation was found between the PASI and PeakPASI, unlike the findings of Tizek et al., 2021, who reported a strong correlation between the two ($r=0.505$, $p<0.001$). One possible explanation for this difference is that Tizek et al., 2021 conducted their analysis using mean values, which were generally higher than those in this study (mean PASI of Tizek et al., 2021 was 7.3 ± 7.7 and mean PeakPASI was 15.4 ± 9.2). In contrast, this study used the median values of each patient's latest PASI, which were lower (PASI 2.0 [1.0; 5.1] and PeakPASI 11.4 [5.9; 17.0]). Since the latest PASI often reflected improved skin conditions after treatment, an increase in this score does not necessarily correspond to an increase in the PeakPASI. Therefore, the PeakPASI appeared to be independent of the latest PASI.

4.2.2 Regressions

The regression models with the PASI and number of systemic therapies showcased that the PASI was a negative predictor. This means that if the PASI was increased, the number of systemic therapies would decrease, which is similar to what was observed in the correlations and does not fit to the existing literature (Shin et al., 2023). As stated above, this was most likely due to the use of the latest PASI for the statistical analysis. The number of visits was a positive predictor, so increasing that led to an increase in the number of systemic therapies. This is to be expected because a greater number of visits may mean a worse psoriasis and therefore a greater number of systemic therapies which are necessary to help the patient.

The model for the PeakPASI and number of systemic therapies displayed the same relationship as the previous model with the PASI. Increasing the number of visits, and holding all other variables constant, also increased the expected number of systemic therapies. Once again, this fits expectations because a more severe psoriasis requires a higher number of hospital visits to combat the psoriasis, and therefore also requires a greater number of systemic therapies. However, in this model the PeakPASI did not affect the number of systemic therapies. This is not what we would have expected and does not fit to the earlier correlations conducted or to the existing literature, because it would be plausible that a greater disease severity could mean a greater number of systemic therapies. One reason for the regression not showing what we expect could be that because we kept the variables constant in both models (to facilitate an easier comparison between the two), it skewed the results, as multiple variables were now affecting the number of systemic therapies - compared to the correlation analysis where only one variable at a time (such as the PeakPASI) had an affect on the number of systemic therapies.
While conducting the cross-validation of the models through the RMSE, the PASI model had a lower score (1.986 while the PeakPASI model had 1.999), which is more advantageous. However, both values are so similar that it is difficult to interpret which model is more favorable.

The regression model for the number of comorbidities and the PASI exhibited that increasing the age, as well as increasing the number of topical therapies, both increased the expected number of comorbidities. This same effect was also present in the PeakPASI model. In general, this makes sense because the older a patient, the more vulnerable they are to suffering from multiple comorbidities (Alajmi et al., 2021, Augustin et al., 2010, Fernandez-Torres et al., 2012), which is mirrored in both models. In this case though, it is also plausible that age could be an independent factor that affects the number of comorbidities, but is perhaps unrelated to the psoriasis itself.

Increasing the number of topical therapies increases the number of comorbidities too, which is unexpected as there is not much literature on this connection. It is presumable that patients with

a higher number of topical therapies require these because their psoriasis is worse. These patients with a more severe psoriasis could then possibly have a greater number of comorbidities. However, it was difficult to find literature that confirms this theory. In both models, the PASI or the PeakPASI did not seem to affect the number of comorbidities at all, which once again does not fit to the results of the previous statistical analyses, in which the PeakPASI did display a relationship with the number of comorbidities, whereas the PASI did not. It is therefore possible that when all of the other independent variables were added into the regression model, the affect of the PASI or the PeakPASI was altered. Existing literature does show that patients with more severe psoriasis have more comorbidities, so that part of the explanation is plausible (Yeung et al., 2013).
Here too, for the cross-validation, the RMSE values of both models were essentially identical, which shows that distinguishing which model fits the dataset better is challenging (RMSE for the PASI was 1.847, while for the PeakPASI it was 1.846).

4.3 The PeakPASI as a prospective score

One approach to implementing the PeakPASI as a prospective score could be to identify it during a specific flare-up phase of a patient, in which a patient has more frequent hospital visits over a shorter period. This value could then serve as a reference point for future flare-ups. It may be possible to initiate the necessary treatment earlier during the next flare-up, even if the guideline of PASI$\geq$10 is not yet met (Nast et al., 2021). It is also helpful if the successful therapy is documented. The physician can then react faster with the targeted therapy because it is already known that the patient has a history of higher PASI and PeakPASI values, and therefore more severe psoriasis. In this way, the PeakPASI could be hindered from becoming so high again, and the mental burden of the patient may be reduced. There are already certain "upgrade criterias" that have been established by Mrowietz and Augustin, 2022), to which the PeakPASI could even be included as one.

A further option could be to calculate the PeakPASI at a predetermined point in time, such as after the fifth, tenth or fifteenth visit of a patient. If the PeakPASI differs in the first ten visits compared to in the first five, then the value of the PeakPASI can be adjusted accordingly with time, and the latest PeakPASI can always be kept in mind while discussing therapy options and treatment of the patient. Reacting earlier with the necessary therapy could help prevent the onset of comorbidities that are linked to severe psoriasis.

Another similar method could be to categorize the psoriasis as severe, as soon as the PeakPASI crosses a predetermined cut-off value (for example of 11.4). Once the patient has been classified

like this, the severity can be kept in mind even if the patient presents with low PASI values in the future. Naturally, it's important to consider how long ago the PeakPASI was recorded. For instance, if a patient had a PeakPASI of 20 ten years ago, but more recent scores have consistently been below 10, the PeakPASI should be updated.

4.4 Limitations

As with every study, this one also had its limitations. Not every patient had a recorded PASI value, which led to the exclusion of those patients in the statistical analysis. This could be, for example, if it was not necessary to record the PASI value on a regular basis for the clinical routine. The same issue occurred with the DLQI. As patients did not fill out a DLQI questionnaire each time they visited the hospital, there were several missing DLQI values. This led to having to calculate an imputed DLQI, using the mean, for the statistical analysis.

Another limitation is that if the patient consults multiple doctors along their psoriasis journey, then each doctor will only have the information and clinical scores (such as PASI and DLQI values) from certain periods in time. For example, if a patient with severe symptoms presents themselves at the hospital once, then later continues their treatment at a dermatological practice near them, information is lost in the process, which the digitalization of patient data could help correct.

As this research was conducted at a university hospital, patients who presented themselves for treatment may generally have had a more severe psoriasis. This could have led to an overestimation bias, as these patients with the more severe psoriasis would automatically have a higher PASI (and therefore also PeakPASI) than patients who may not have such a severe psoriasis and therefore only be receiving treatment at a dermatological practice. Along with that, there was a selection bias present, as the patients who were included in the analysis were the ones who were motivated to take part in the study and sent back the questionnaire.

The latest PASI was utilized in the statistical analysis, but a specific endpoint was not defined for it. While some patients visited the hospital 40 times for their therapy, and their last PASI was taken at the end of a therapy cycle (meaning that it was very low), other patients came maybe 10 times and had a most recent PASI that was higher because they were still in the middle of their treatment. A standardized point in time was not set to collect the latest PASI as this was a retrospective study, making this value slightly difficult to compare. The reason that we still decided to work with the latest PASI was because this is the PASI that the physician refers to when the patient comes to the practice or hospital. That is the value utilized most in the clinical

day-to-day, and helps decide if a treatment plan is working or if a patient requires a change in the treatment.

Another limitation is that the case numbers in the specific groups were not equal, and partly also very small (such as the individual comorbidities).

4.5 Conclusion

Overall, this study demonstrates that the PeakPASI can be implemented as an additional score in the treatment of psoriasis patients. Using only the PASI is perhaps not an accurate representation of the overall condition of the patient, as this score shows how the skin looks at one moment in time. Taking the PeakPASI into account could help depict the long-term impact more correctly. As a relationship was observed between the PeakPASI and the number of systemic therapies, where patients with a higher PeakPASI required more systemic therapies, and also with the number of comorbidities, it depicts that the PeakPASI is capable of indicating what the PASI already does too. This means it is possible to consider implementing the PeakPASI additionally.

Further studies with larger patient groups should be conducted to continuing testing this. A clinical trial where the PASI is recorded at each visit could be performed to study the importance of the PeakPASI in a more controlled environment, with a better comparison to the PASI. If this is a long-term study executed over many years, then the start point of comorbidities can also be recorded, as well as the instance when each specific systemic therapy is initiated. The study could also be taken further by observing the first manifestation of the psoriasis (for example by following individuals who have a history of psoriasis in their family), and recording the onset of specific comorbidities in relation to the disease severity and point in therapy. A connection between the PeakPASI and specific comorbidities, as well as with the different systemic therapies that are currently used in psoriasis treatment, could be found in this manner. If the patient also fills out a DLQI questionnaire each time they visit the hospital, it may be possible to observe an appropriate relationship between the PeakPASI and DLQI without the missing values.

As mentioned above, using the PeakPASI as a prospective tool could aid physicians in reacting earlier to patients with a history of a higher PeakPASI and greater disease severity. Perhaps these patients can receive a systemic therapy more promptly, to proactively hinder the current PASI from becoming the PeakPASI. Using the cut-off values of 11.4 or 13.6 for the PeakPASI is also a feasible option. All three PeakPASI groups (10, 11.4, 13.6) had more systemic therapies in the group with the higher PeakPASI, and both the 10 and 11.4 group had more comorbidities in that group too. Only the specific comorbidities did not show a relationship with the 11.4 or

13.6 group, and also only two (smoking and diabetes) showed one with PeakPASI 10. Even just keeping the cut-off of 10 of the PeakPASI may be preferable compared to the PASI cut-off of 10 because more patients would be taken into consideration with the PeakPASI.

All of this indicates that implementing the PeakPASI as an additional tool in the clinical day-to-day to help more correctly assess the psoriasis and cumulative burden of a patient is a good option that should be explored further. If it is possible to indeed implement the PeakPASI as a prospective tool, the hope would be that it can change the lives of psoriasis patients for the better.

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Appendix

4.6 Patient information

Klinik und Poliklinik
für Dermatologie und Allergologie am Biederstein
des Klinikums rechts der Isar
der Technischen Universität München
Anstalt des öffentlichen Rechts
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Probandeninformation

PeakPASI Predict
„Analyse des klinischen Schweregrades der Psoriasis gemessen mit dem PeakPASI als Prädiktor für das Therapieansprechen und patientenspezifische Komorbiditäten, sowie einer daraus resultierenden psychosozialen Belastung“

Sehr geehrte Damen, sehr geehrte Herren,

wir möchten Sie fragen, ob Sie bereit sind, an der nachfolgend beschriebenen Studie teilzunehmen. Die Studie wurde von der zuständigen Ethikkommission zustimmend bewertet und wird von der Hautklinik der Technischen Universität München (TUM) veranlasst, organisiert und durchgeführt. Ihre Teilnahme an dieser Studie ist **freiwillig**. Sie werden in die Studie also nur dann einbezogen, wenn Sie dazu schriftlich Ihre Einwilligung erklären. Bei einer Teilnahme entstehen für Sie **keine** zusätzlichen Kosten.

1. Warum wird diese Studie durchgeführt?
Schuppenflechte (Psoriasis) zählt zu den häufigsten Hauterkrankungen in Deutschland und etwa 2-4 % der Bevölkerung in Deutschland leiden daran. Auch wenn die typischen Hautveränderungen heute durch verschiedene neue Medikamente gut behandelt werden können, wird der Einfluss von Begleitkrankheiten und anderer sozialer Faktoren immer spürbarer. Bisher gab es zahlreiche Studien zu Begleiterkrankungen von Psoriasis, wie z.B. Übergewicht und das Metabolische Syndrom oder kardiovaskuläre Erkrankungen. Gleichzeitig lassen erste Studien vermuten, dass Menschen mit Psoriasis auch häufiger an psychischen Erkrankungen, wie Suchterkrankungen, leiden. Insbesondere erhöhter Nikotin- und Alkoholkonsum gilt so z.B. bereits als Risikoerkrankung bei Psoriasis.
Um das Risiko für Suchterkrankungen bei Menschen mit Psoriasis zu untersuchen und psychosoziale Belastungsfaktoren, wie eine mögliche vorliegende Stigmatisierung zu ermitteln, untersucht die vorliegende Studie das Auftreten von Suchterkrankungen und den psychosozialen Einfluss bei knapp über 1000 Menschen, die an Psoriasis erkrankt sind.

2. Wie ist der Ablauf der Studie und was muss ich bei Teilnahme beachten?
Für eine Studienteilnahme werden Sie gebeten einen kurzen Fragebogen (ca. 5-10 Minuten) auszufüllen und die Einwilligungserklärung (auf der ersten Seite des Fragebogens) mit „ja“ zu bestätigen, wenn Sie mit der Studienteilnahme einverstanden sind.

3. Welchen persönlichen Nutzen habe ich von der Teilnahme an der Studie und gibt es Risiken?
Durch ihre Teilnahme helfen Sie uns, das Risiko von Suchterkrankungen und psychosozialen Belastungen für Menschen mit Psoriasis zu untersuchen. So soll langfristig die Basis für eine bessere „ganzheitliche“ Behandlung geschaffen werden, die neben den Hautveränderungen auch andere medizinische Probleme wie Suchterkrankungen oder eine mögliche Stigmatisierung berücksichtigt. Sollte durch diese Studie eine Suchterkrankung nahegelegt werden, bieten wir gerne beigefügtes Infomaterial mit Kontakten oder Internetlinks als Betreuungskonzept an. Dieses Material ist freiwillig für jeden Patienten. **Es bestehen keinerlei gesundheitlichen Risiken für Sie bei einer Teilnahme.**

4. Erhalte ich eine Aufwandsentschädigung?
Es ist KEINE finanzielle Aufwandsentschädigung vorgesehen.

5. Was geschieht mit meinen Daten?

Ihr Fragebogen und die Dokumentation Ihrer Daten werden im Studienzentrum unter Beachtung des gesetzlichen Datenschutzes aufbewahrt und die Daten **pseudonymisiert** gespeichert und spezifisch, ohne Einbezug Ihrer personenbezogenen Daten, für die vorliegende Studie ausgewertet.
Pseudonymisiert bedeutet, dass der Fragebogen nicht mit Ihrem Namen und/oder Geburtsdatum, sondern mit einem Code, gespeichert und ausgewertet werden. Die Zuordnung von Code und Namen kann nur durch einen sonst unbeteiligten Treuhänder erfolgen. Dieser ist am sonstigen Studienablauf nicht beteiligt und hat keinen Zugriff zu den Fragebogenergebnissen. Alle erhobenen Daten werden unter strenger Beachtung des gesetzlichen Datenschutzes aufbewahrt und sind gegen unbefugten Zugriff gesichert.

In dieser Studie ist die Fakultät für Medizin der Technischen Universität München, Ismaninger Str. 22, 81675 München, für die Datenverarbeitung verantwortlich. Die Verarbeitung Ihrer Daten setzt Ihre Einwilligung voraus (Rechtsgrundlage).

Ihre Daten werden ausschließlich im Rahmen dieser Studie verwendet. Dazu gehören personenidentifizierende Daten wie Name, Anschrift und sensible personenbezogene Gesundheitsdaten. Alle unmittelbar auf dem Fragebogen identifizierende Daten wie Name, Geburtsdatum und Anschrift werden durch einen Identifizierungscode ersetzt (pseudonymisiert). Dies schließt eine Identifizierung Ihrer Person durch Unbefugte weitgehend aus. Ihre Daten werden in der Poliklinik für Dermatologie und Allergologie der Technischen Universität München gespeichert. Sie werden nach Ablauf der gesetzlichen Löschfristen gelöscht. Die Einwilligung zur Verarbeitung Ihrer Daten ist freiwillig, Sie können jederzeit die Einwilligung ohne Angabe von Gründen und ohne Nachteile für Sie widerrufen. Sie haben das Recht, Auskunft über die Sie betreffenden Daten zu erhalten, auch in Form einer unentgeltlichen Kopie. Darüber hinaus können Sie die Berichtigung oder Löschung Ihrer Daten verlangen.

Wenden Sie sich in diesen Fällen an:

<table>
<tr><th><u>Verantwortliche für die Datenverarbeitung:</u></th><th><u>Im Falle einer Beschwerde wenden Sie sich an:</u></th></tr>
<tr><td rowspan="3">Fakultät für Medizin der Technischen Universität München
vertreten durch den Dekan Prof. Dr. Peter Henningsen
Ismaninger Str. 22 81675 München
E-Mail:dekanat.medizin@tum.de
Oder an:

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Klinik und Poliklinik für Dermatologie und Allergologie
Technischer Universität München
Biedersteiner Str. 29 80802 München.</td><td>Behördlicher Datenschutzbeauftragter
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Postanschrift: Postfach 22 12 19, 80502 München
Hausanschrift: Wagmüllerstr. 1, 80538 München
Email: poststelle@datenschutz-bayern.de</td></tr>
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E-Mail: beauftragter@datenschutz.tum.de
Technische Universität München
Arcisstr. 21 80333 München</td></tr>
</table>

6. An wen wende ich mich bei weiteren Fragen?
Bei weiteren oder später auftretenden Fragen können Sie sich jederzeit an das Studienteam wenden.

Ihr Ansprechpartner:

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4.7 Questionnaire

Klinik und Poliklinik
für Dermatologie und Allergologie am Biederstein
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PeakPASI Predict

„Analyse des klinischen Schweregrades der Psoriasis gemessen mit dem PeakPASI als Prädiktor für das Therapieansprechen und patientenspezifische Komorbiditäten, sowie einer daraus resultierenden psychosozialen Belastung“

Wir haben diesen Fragebogen im Rahmen einer Studie an der Technischen Universität München entworfen, um mehr über die psychosoziale Belastung von Menschen mit Psoriasis in Erfahrung zu bringen. Ihre Daten werden selbstverständlich vertraulich behandelt und dienen ausschließlich Forschungszwecken. Das Ausfüllen des Fragebogens wird ca. 5-10 Minuten in Anspruch nehmen, wofür wir uns sehr herzlich bei Ihnen bedanken möchten! **Die Teilnahme ist freiwillig.**

Vielen Dank für Ihre Mithilfe!
PD Dr. Dr. med. Alexander Zink

Einwilligungserklärung Ich habe den Text der Patienteninformation gelesen und hatte ausreichend Zeit, mich zu entscheiden. Ich bin damit einverstanden, dass ich jederzeit aus dieser Studie ausscheiden kann, ohne dass mir persönliche Nachteile entstehen und dass meine Daten in **pseudonymisierter** Form unter strenger Einhaltung des Datenschutzes erhoben, gespeichert und verarbeitet werden. Ich habe keine weiteren Fragen mehr **Ich erkläre mich bereit, freiwillig an dieser Studie teilzunehmen**.	☐Ja ☐Nein

Alter in Jahren:	___ Jahre		
Geschlecht:	☐weiblich	☐männlich	☐divers

Fragebogen 1: Freizeitverhalten

Kreuzen Sie bitte jeweils 1 Antwortmöglichkeit an

Hindert Sie Ihre Psoriasis daran, bestimmte Freizeitaktivitäten auszuüben? (z.B. Schwimmbad-Besuch, Sonnenbaden, Sport usw.)	o nie o selten o ab und zu o häufig o ständig
Bei welcher Freizeitaktivität fühlen Sie sich am stärksten eingeschränkt? _____	

Zigaretten	
Wie oft rauchen Sie? **Und wieviel?**	○ nie ○ selten ○ täglich, aber weniger als 1 Schachtel/Tag ○ ca. 1 Schachtel/Tag ○ ca. 1,5 Schachteln/Tag ○ ca. 2 Schachteln/Tag ○ mehr als 2 Schachteln/Tag **(1 Schachtel = 20 Zigaretten)** **Falls zutreffend:** Seit wann rauchen Sie? _____ Jahre

Alkohol		
Wie oft und wie viele Gläser pro Mal trinken Sie Alkohol? *[1 Glas = 1 Flasche Bier/Most = 1/4 Wein/Sekt = 1 Schnaps (2 cl.)]*	o nie o 2 x pro Monat oder seltener o 2 – 4 x pro Monat o 2 – 3 x pro Woche o 4 x pro Woche oder mehr	Nur zu beantworten, wenn Sie Alkohol trinken o 2 – 4 x pro Monat o 1 – 2 Gläser o 3 – 4 Gläser o 5 – 6 Gläser o 7 – 9 Gläser o 10 oder mehr
Hatten Sie jemals das Gefühl, Sie sollten Ihren Alkoholkonsum einschränken?		o Ja o Nein
Wurden Sie jemals wegen Ihres Alkoholkonsums kritisiert und ärgerten sich darüber?		o Ja o Nein
Fühlten Sie sich jemals schuldig wegen Ihres Alkoholkonsums?		o Ja o Nein
Haben Sie jemals als erstes am Morgen Alkohol getrunken, um Ihre Nerven zu beruhigen oder um einen Kater loszuwerden?		o Ja o Nein
Medikamenten-/ Drogenkonsum		
Haben Sie Medikamente/Drogen aus anderen als medizinischen Gründen eingenommen?		o Ja o Nein
Haben Sie mehr als ein Medikament/eine Droge auf einmal missbraucht?		o Ja o Nein
Können Sie jederzeit mit der Einnahme von Arzneimitteln/Drogen aufhören?		o Ja o Nein
Hatten Sie schon mal einen „Blackout“ oder „Flashback“ als Folge von Arzneimittel/Drogenkonsum?		o Ja o Nein
Fühlten Sie sich jemals schlecht oder schuldig wegen Ihres Arzneimittels /Drogenkonsums?		o Ja o Nein
Haben sich Ihr Partner/Ihre Partnerin oder Ihre Eltern jemals über Ihren Kontakt mit Arzneimitteln/ Drogen beklagt?		o Ja o Nein
Haben Sie Ihre Familie aufgrund des Arzneimittel-/ Drogenkonsums vernachlässigt?		o Ja o Nein
Haben Sie sich auf illegale Machenschaften eingelassen, um an Arzneimittel/Drogen zu gelangen?		o Ja o Nein
Haben Sie jemals an Entzugserscheinungen gelitten, wenn Sie den Konsum einstellten?		o Ja o Nein
Hatten Sie als Folge Ihres Arzneimittel-/Drogenkonsums gesundheitliche Probleme wie z.B. Gedächtnisverlust, Hepatitis, Krämpfe, Blutungen etc.?		o Ja o Nein
Internetkonsum		
An wie vielen Tagen pro Woche nutzen Sie aus privaten Gründen das Internet?	o <1x pro Woche o ____ Tage pro Woche	

Wie viele Stunden sind Sie üblicherweise an einem Tag (privat) im Internet?					
o weniger als 1 Stunde o 1 Stunde o 2 Stunden o 3 Stunden o 4 Stunden o 5 Stunden o 6 Sunden o 7 Stunden oder mehr					
Wie oft...	**nie**	**selten**	**manch-mal**	**häufig**	**sehr häufig**
... fällt es Ihnen schwer, die Internetsitzung zu beenden, wenn Sie online sind?	o	o	o	o	o
... setzen Sie Ihre Internetsitzung fort, obwohl Sie eigentlich gerade offline gehen wollten?	o	o	o	o	o
... sagen Ihnen Andere (z.B. Partner, Freunde, Familie), Sie sollten das Internet weniger häufig nutzen?	o	o	o	o	o
... denken Sie darüber nach, das Internet weniger häufig zu nutzen?	o	o	o	o	o
... haben Sie erfolglos versucht, weniger Zeit im Internet zu verbringen?	o	o	o	o	o
... vernachlässigen Sie Ihre täglichen Verpflichtungen (Studium, Arbeit, Freunde), weil Sie lieber online gehen?	o	o	o	o	o
... sind Sie wegen Ihrer Internetnutzung unausgeschlafen?	o	o	o	o	o
... denken Sie an das Internet, obwohl Sie nicht online sind?	o	o	o	o	o
... nutzen Sie lieber das Internet anstatt mit Anderen (z.B. Partner, Freunde, Familie) Zeit zu verbringen?	o	o	o	o	o
... beeilen Sie sich sehr mit Ihren alltäglichen Aufgaben oder Verpflichtungen, um früher online gehen zu können?	o	o	o	o	o
... sehnen Sie sich nach der nächsten Internetsitzung?	o	o	o	o	o
... fühlen Sie sich ruhelos, frustriert, oder gereizt, weil Sie das Internet nicht nutzen können?	o	o	o	o	o
... gehen Sie online, wenn Sie sich bedrückt fühlen?	o	o	o	o	o
... nutzen Sie das Internet, um Ihren Sorgen zu entfliehen oder sich von negativen Gefühlen zu befreien?	o	o	o	o	o

Fragebogen 2: Sozialbefinden

Kreuzen Sie bitte jeweils 1 Antwortmöglichkeit an

	nie	**Fast nie**	**manch-mal**	**oft**	**immer**
Ich habe das Gefühl, dass ich in die meisten Gruppen gut hineinpasse.	o	o	o	o	o
Niemand versteht mich.	o	o	o	o	o
Ich wäre lieber allein als mit anderen Leuten zusammen	o	o	o	o	o
Ich treffe gerne neue Leute.	o	o	o	o	o

Es fällt mir leicht, mich mit anderen Gleichaltrigen zu unterhalten	o	o	o	o	o
In einer Menschenmenge fühle ich mich wohl.	o	o	o	o	o
Ich habe das Gefühl, dass ich nicht zu anderen Leuten passe.	o	o	o	o	o
Es fällt mir leicht, mich mit anderen Menschen zu vertragen.	o	o	o	o	o

Fragebogen 3: Stigmatisierung

Kreuzen Sie bitte jeweils 1 Antwortmöglichkeit an

Schätzen Sie ein, wie andere Menschen Sie **über das letzte Jahr hinweg** behandelt haben	**nie**	**Fast nie**	**manch-mal**	**oft**	**immer**
Andere Menschen sind freundlich zu mir	o	o	o	o	o
Andere Menschen beleidigen mich mit Worten.	o	o	o	o	o
Andere Menschen vermeiden es, mich anzuschauen.	o	o	o	o	o
Leute, die ich nicht kenne, reagieren überrascht oder erschrocken, wenn sie mich sehen.	o	o	o	o	o
Andere Menschen sind nett zu mir.	o	o	o	o	o
Andere Menschen wissen nicht, was sie zu mir sagen sollen.	o	o	o	o	o
Leute, die ich nicht kenne, grüßen mich.	o	o	o	o	o
Andere Menschen lachen mich aus.	o	o	o	o	o
Andere Menschen sind in meiner Gegenwart entspannt.	o	o	o	o	o
Andere Menschen haben Mitleid mit mir.	o	o	o	o	o
Andere Menschen hänseln mich.	o	o	o	o	o
Leute, die ich nicht kenne, lächeln mir freundlich zu.	o	o	o	o	o
Andere Menschen wissen nicht, wie sie sich in meiner Gegenwart verhalten sollen.	o	o	o	o	o
Andere Menschen schauen mich zweimal an oder drehen sich nach mir um.	o	o	o	o	o
Andere Menschen sind lieb zu mir.	o	o	o	o	o
Andere Menschen plagen mich.	o	o	o	o	o
Fremde Leute sind höflich zu mir.	o	o	o	o	o
Andere Menschen machen sich lustig über mich.	o	o	o	o	o
Leute, die ich nicht kenne, starren mich an.	o	o	o	o	o
Andere Menschen behandeln mich mit Respekt.	o	o	o	o	o
Leute scheinen durch mein Aussehen in Verlegenheit zu geraten.	o	o	o	o	o

Fragebogen 4: Happiness/Subjektives Wohlbefinden

Kreuzen Sie bitte jeweils 1 Antwortmöglichkeit an

Alles in allem, was würden Sie sagen, wie glücklich sind Sie?

äußerst unglücklich									äußerst glücklich	
0	1	2	3	4	5	6	7	8	9	10
o	o	o	o	o	o	o	o	o	o	o

Es folgen fünf Aussagen, denen Sie zustimmen bzw. die Sie ablehnen können. Bitte benutzen Sie die folgende Skala von 1-7, um Ihre Zustimmung bzw. Ablehnung zu jeder Aussage zum Ausdruck zu bringen.

	Starke Ablehnung 1	Ablehnung 2	Leichte Ablehnung 3	Weder noch 4	Leichte Zustimmung 5	Zustimmung 6	Starke Zustimmung 7
1. In den meisten Punkten ist mein Leben meinem Ideal nahe.	o	o	o	o	o	o	o
2. Meine Lebensbedingungen sind hervorragend.	o	o	o	o	o	o	o
3. In bin zufrieden mit meinem Leben.	o	o	o	o	o	o	o
4. Ich habe bisher die wichtigen Dinge, die ich mir vom Leben wünsche, auch bekommen.	o	o	o	o	o	o	o
5. Wenn ich mein Leben noch einmal leben könnte, würde ich fast nichts ändern.	o	o	o	o	o	o	o

Bitte geben Sie an, wie oft Sie sich **in den vergangenen zwei Wochen** entsprechend der unten aufgeführten Begriffe gefühlt haben.

Wie oft fühlten Sie sich…	Sehr selten oder nie				Sehr oft oder immer
…positiv?	o	o	o	o	o
…gut?	o	o	o	o	o
…angenehm?	o	o	o	o	o
…glücklich?	o	o	o	o	o
…von Freude erfüllt?	o	o	o	o	o
…zufrieden?	o	o	o	o	o
…negativ?	o	o	o	o	o
…schlecht?	o	o	o	o	o
…unangenehm?	o	o	o	o	o
…traurig?	o	o	o	o	o
…ängstlich?	o	o	o	o	o
…wütend?	o	o	o	o	o

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