MASTER THESIS

Private and public health insurance schemes impacting liver health and shaping experiences for autoimmune hepatitis patients at University Medical Center Hamburg- Eppendorf

For the attainment of the academic degree

Master of Public Health (MPH)

Submitted: 08 March 2024

Nagham Issa

[redacted]

1. Examiner: Prof. Dr. Johanna Buchcik
2. Examiner: Dr. rer. biol. hum. Caren Ramien

In cooperation with

University Medical Center Hamburg-Eppendorf (UKE),

Hamburg

Hamburg University of Applied Sciences

Faculty of Life Sciences

Department Health Sciences

Master of Public Health

Ulmenliet 20

21033 Hamburg

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Acknowledgements

First, I would like to thank Professor Johanna Buchcik for her support, patience, and trust throughout the entire thesis writing journey. Her belief in my abilities, evident from the moment she accepted me as one of her advisees, provided me with the positivity and strength to overcome the challenges that I encountered. I am truly grateful to her for consistently appreciating and recognizing my efforts at every step.

I am very grateful to Dr. Caren Ramien for her invaluable guidance and unflagging support, which were the driving force that helped bring my thesis to completion. Dr. Ramien mentored me, cleared my confusions, challenged my thought process and most importantly steered me in the correct direction. I learned so much from her and I am immensely thankful.

A heartfelt recognition and gratitude to Professor Dr. Ansgar W. Lohse for entrusting me with the opportunity to work on this remarkable project. He supported me, trusted my abilities, and pushed me to pursue the project without hesitation. I am very appreciative of all his support and trust. To the entire ERN RARE-LIVER team, Juliane, Sabina, Laura, Hendrik and Felix, thanks for all the support and encouragement, which were a source of motivation. I am also thankful to my two favorite nurses, Finja and Katja, who, despite their workload, were so patient, supportive, and always available to answer any question and helped me with the survey and data collection. I extend my sincere appreciation to Dr. Marcial Sebode for his support and invaluable medical expertise. Despite his busy schedule, Dr. Sebode consistently made time to address my concerns and to provide me with guidance. His expertise, knowledge and support were very essential to harmonize my entire thesis.

To my dearests, Nai and Layal, I am also very thankful. Despite being miles away, they never stopped encouraging and supporting me. To Sagor and Edmond, who were my sound of reason and my companions.

To my parents and my sisters, thanks for always making me feel like a star. I know how much each one of you believed in me. Thank you for all the encouragement and support. You were very confident that I could do it, even when I sometimes self-doubted.

Finally, I want to thank my partner, Moustafa, for being my rock and number one fan. I am very grateful for all the support and motivation you provided me with.

Abbreviations

AASLD	American Association for the Study of the Liver Disease
AIH	Autoimmune Hepatitis
ALF	Acute Liver Failure
ALT	Alanine transaminase
ANA	Antinuclear antibody
AST	Aspartate transaminase
BMI	Body mass index
CPMS	Clinical patient management system
EASL	European Association for the Study of the Liver
EC	European Commission
ERN	European Reference Network
ERN RARE-LIVER	European Reference Network on Rare Hepatological Diseases
EURORDIS	European Organization for Rare Diseases
EU	European Union
FDA	Food and Drug Administration
GDPR	General Data Protection Regulation
HCP	Healthcare provider
HrQoL	Health-related quality of life
IAIHG	International Autoimmune Hepatitis Group
IgG	Gamma-immunoglobulin
IQR	Interquartile range
IRDiRC	International Rare Diseases Research Consortium
LFTs	Liver function tests
LKM	Anti-liver/kidney microsomal antibody
Mdn	Median
MOS	Medical Outcome Study
NASH	Nonalcoholic steatohepatitis
NKT	Natural killer T-cells
PBC	Primary Biliary Cholangitis

PubHI	Public health insurance
PvtHI	Private health insurance
PSQ	Patient satisfaction questionnaire
PSC	Primary Sclerosing Cholangitis
QoL	Quality of Life
RDs	Rare diseases
SF-12	Short Form health outcomes- 12 items
SF-36	Short Form health outcomes- 36 items
SD	Standard deviation
SMA	Smooth muscle antibody
SPSS	Statistical Package for the Social Sciences
UHC	Universal Health Coverage
UKE	University Medical Center Hamburg-Eppendorf
UN	United Nations
WHO	World Health Organization

Abstract

Background: Autoimmune hepatitis (AIH) is a chronic and progressive liver disease leading to inflammation and scarring of the liver. This study investigated the impact of the two health insurance schemes in Germany, public health insurance (PubHI) and private health insurance (PvtHI), on the liver health of AIH patients and assessed the difference in overall Health-related quality of life (HrQoL) and satisfaction with the healthcare services.

Methods: Data of this cross-sectional study was collected for 34 study participants (PubHI=17 and PvtHI=17). Three liver surrogates, AST, ALT, and IgG, were extracted from the R-LIVER registry at two different time points. Additionally, a survey was distributed to collect data on HrQoL and satisfaction with healthcare. Group differences between the two groups in liver health, HrQoL and satisfaction were tested.

Results: No significant differences were observed between groups in the laboratory values at baseline or at 1-year. There was a significant difference within groups after 1-year of treatment. Liver inflammation improved in both groups over time, where complete remission was achieved in PubHI (5/17) and PvtHI (10/17). There was no difference in the overall QoL between the two groups. However, a difference was found in satisfaction between the two insurance groups.

Conclusion: In this pilot study, liver health and HrQoL between groups did not differ. Satisfaction with healthcare services differed between PubHI and PvtHI.

Keywords: Autoimmune hepatitis, public health insurance, private health insurance, HrQoL, patient satisfaction, healthcare services

1. Introduction

1.1 German healthcare insurance system

Germany is considered to have one of the largest expanding economies in the European Union (EU), and among other European countries, it has one of the highest health expenditures (1). In 1883, during Otto von Bismarck's chancellorship, Germany achieved a tremendous milestone by being the first country to introduce social health insurance (2). This was a groundbreaking step towards improvement in healthcare, which in turn inspired and encouraged other nations to adapt. Health insurance is mandatory for all citizens and permanent residents in Germany, and is provided by either public health insurance (PubHI) or private health insurance (PvtHI) (1). The health system serves 83 million people, and the country's health expenses are split between public and private funding sources, with 73.5 percent being covered by public funds and 26.5 percent by private contributions (1).

PubHI in Germany is compulsory for the majority of low- and middle-income employees, pensioners, recipients of unemployment benefits, and students (2,3). Spouses and the non-earning dependents of the PubHI insured persons are insured free of charge in this scheme (2). PubHI is only voluntary for the self-employed and those with a yearly gross income above a certain threshold limit (3). The opt-out income threshold limit recorded in 2017 was 57,600 € per year (2). Therefore, anyone who has a salary exceeding this required income threshold value is free to choose between PubHI and PvtHI (1,2). Additionally, individuals in specific professional groups, such as civil servants, have the option to choose between PubHI and PvtHI (1).

The concept of solidarity is a unique feature of the PubHI system, such that the premium offered is income-dependent and unrelated to the individual's health risks (1,3). This means that there is an equally distributed premium between the poor and rich (3). Moreover, this also allows for an equivalent distribution from healthy individuals to sick individuals (3). In contrast, PvtHI premiums are risk-related and independent of the income of the insured (1,3). This means that individuals who are sick with various health problems have higher tariffs than those with lower health risks (3). Unlike PubHI, family members

of the PvtHI person must be insured separately and interestingly in the PvtHI, women are charged more than men (3).

In Germany, patients in the PvtHI and PubHI are supposed to freely choose their doctors and be provided with the same equitable healthcare services (1,3). The only difference is the physician's reimbursement schemes, where doctors receive higher tariffs from PvtHI than PubHI (1,3). This leads to the preferential selection of patients for treatment by healthcare providers (3). PubHI patients are seen by a restricted number of general physicians, whereas PvtHI patients or individuals paying out-of-pocket fees have unrestricted access to all healthcare providers, irrespective of specialty (1,3).

Germany is renowned for having one of the world's best healthcare systems, offering high-quality health services that align with the concept of Universal Health Coverage (UHC). The WHO defines UHC as the ability of people to access a wide range of health services, whenever and wherever they need them, without any financial obstacles (4). The German healthcare system is continuously evolving and aims to improve citizens' care by ensuring the provision of a vast range of healthcare services (1).

Despite its comprehensive benefits, the healthcare system in Germany still faces challenges. Some of these include fragmentation of service provision and disruption of the patient care plan due to organizational differences between inpatient and outpatient ambulatory settings (1). These challenges contradict the principle of solidarity in the German healthcare system. Services covered by the PvtHI, such as diagnostic tests or procedures, dental care, or psychotherapeutic services, are not offered free of charge to PubHI patients, and they can decide whether to pay out-of-pocket for these extra services (1,5).

It is difficult to directly establish a causal link between a country's healthcare system and individuals' health. In particular, with a very diverse package of health services being offered, as in the case of German health insurance. The goal of this thesis paper is to investigate the impact of the German healthcare system on the health status of patients with rare diseases. However, investigating the specific factors within the healthcare system that could contribute to any observed differences is beyond the scope of this study.

Thus, the topic of the German health insurance scheme is not discussed in depth. Instead, in subsection 1.2, the problem of rare liver diseases will be explored, along with the quality of life and patient satisfaction in sub-section 1.3 for patients living with rare diseases. In subsection 1.4, an in-depth overview of autoimmune hepatitis (AIH), a rare liver disease, will be highlighted in detail. The rest of the paper is organized as follows: Sections 2 and 3 discuss the objectives and methodology. The results are presented in Section 4, and discussion is presented in Section. Section 6 concludes the study.

1.2 Rare liver diseases

Rare diseases (RDs) are an emerging public health problem worldwide. In Europe, different concerted efforts have been put forward by organizations to increase the awareness of RDs. Of these organizations is the European Organization for Rare Diseases (EURORDIS), a non-profit organization. EURORDIS has been actively advocating for patients' rights to equitable healthcare and to improve the lives of over 300 million individuals and their families living with rare diseases globally (6). Presently around 7,000 various diseases are identified as rare, affecting about 400 million people worldwide (7). RDs affect approximately 3.5 to 5.9 percent of the world population, and approximately 30 million people live in Europe (8). Although many people and their families are affected by RDs worldwide, this marginalized group is still neglected by healthcare systems (9).

The global trajectory to increase awareness about RDs and to voice the unmet needs of millions of people living with RDs is the cornerstone to push policymakers to take action. EURORDIS for instance, designed a campaign titled "30 million reasons for European action on rare diseases" to raise the voices of people living with a rare condition to policymakers in Europe (8). Other organizations, such as the International Rare Diseases Research Consortium (IRDiRC), also developed a 2017-2027 ten years vision, with the main goal being to target the healthcare challenges of RDs (9). In the United Nations (UN) call for action to recognize RDs as missing pillars in the UHC, it was stated that "UHC shall never be attained nor realized if people living with RDs are left behind and their needs are left unmet" (10). This aligns with the central goal of the UN in the attainment of the Sustainable Development Goal "leave no one behind" to be achieved in the 2030 agenda (11).

There is no universal definition of RDs because of their heterogeneous nature, insufficient epidemiological data available, and the absence of structured databases (12). However, the European Commission (EC) of Public Health defined RDs as "a group of life-threatening or chronically debilitating diseases that are of such low prevalence that special combined efforts are needed to address them" (7). Point prevalence is a robust indicator to define RDs, as it quantifies disease burden per population at a given time, which helps in tailoring medical services to the patients' specific needs, improves pharma-economic treatment evaluation, and legislation given the small RDs population size (12). In Europe any disease with a prevalence less than 1/ 2,000 inhabitants is a RD (7). On the contrary, the USA considers a disease to be rare if the prevalence is less than 1/1,500 inhabitants (7). Another concept used to define the rarity of diseases is geolocalization, where certain diseases are prevalent in some geographical locations and not in others (7). This concept is used mostly for infectious diseases but is also widely applied to other rare conditions such as rare liver diseases (7).

Most RDs are genetic and progressive, with no cure available (13). The low prevalence of RDs is a big challenge, and diagnosis is often delayed owing to the scarcity of research and limited clinical knowledge (7,9). The average reported time for a patient to be correctly diagnosed with RD is approximately five years (7). These diseases are also referred to as orphans, suggesting that drug development is very limited, and most of the time, FDA approval is not secured. Orphanet, a European database, reported that 25 percent of patients with rare disorders die within five years after diagnosis, and approximately 37 percent have a reduced life expectancy (7).

The presence of liver problems is a common feature of any RD, where the liver can either be a primary factor contributing to mortality and morbidity or as a collateral manifestation in cases of multiple organ damage (7,14). Rare liver diseases of autoimmune origin occur when the body fails to distinguish self from non-self and thus attacks its own liver cells, leading to inflammation of the liver (14).

With the rising concern about RDs, the EC established 24 European Reference Networks (ERNs) for RDs in 2017 (15). The goal of ERNs is to achieve and ensure equitable access

to care for all patients with rare or low-prevalence and complex diseases across Europe (15). Their vision is to spread clinical knowledge of rare diseases in Europe and to improve care for patients with rare conditions (15). Spreading clinical knowledge and expertise will help to further educate physicians about rare diseases and also provide patients with high-quality information (15). An essential tool created by the EU for all ERNs is the online Clinical Patient Management System (CPMS), which is an interactive tool between healthcare providers to share and discuss clinical management of complex cases (15).

The European Reference Network on Rare Hepatological Diseases (ERN RARE-LIVER) is one of the ERNs established by the EC (15). It is a network of medical centers that provides clinical management for adult and pediatric patients with rare liver diseases across Europe (16,17). Patients with rare liver diseases are disadvantaged due to several factors which stem from delayed or overlooked diagnosis, insufficient expertise knowledge, poor disease understanding, and limited treatment choices (18).

The main objective of the network is to improve the care of patients living with rare liver diseases across Europe by conducting prospective registries and offering expert advice on difficult cases using CPMS (16). The ERN RARE-LIVER is affiliated with 80 expert centers throughout Europe and is continuously expanding to include more centers (17).

There are different types of rare liver diseases, the ERN RARE-LIVER has categorized them as autoimmune, infectious (viral, bacterial, and parasitic), genetic, hereditary, vascular, neoplastic, and others of unknown etiology like biliary atresia (7). The network meanwhile covers 14 different rare liver disease disorders in both adults and pediatrics, which are divided in four main disease pillars: autoimmune liver disease, metabolic and biliary atresia, structural liver disease, and infectious disease (17). These pillars and their corresponding disease categories are shown below in Figure 1.

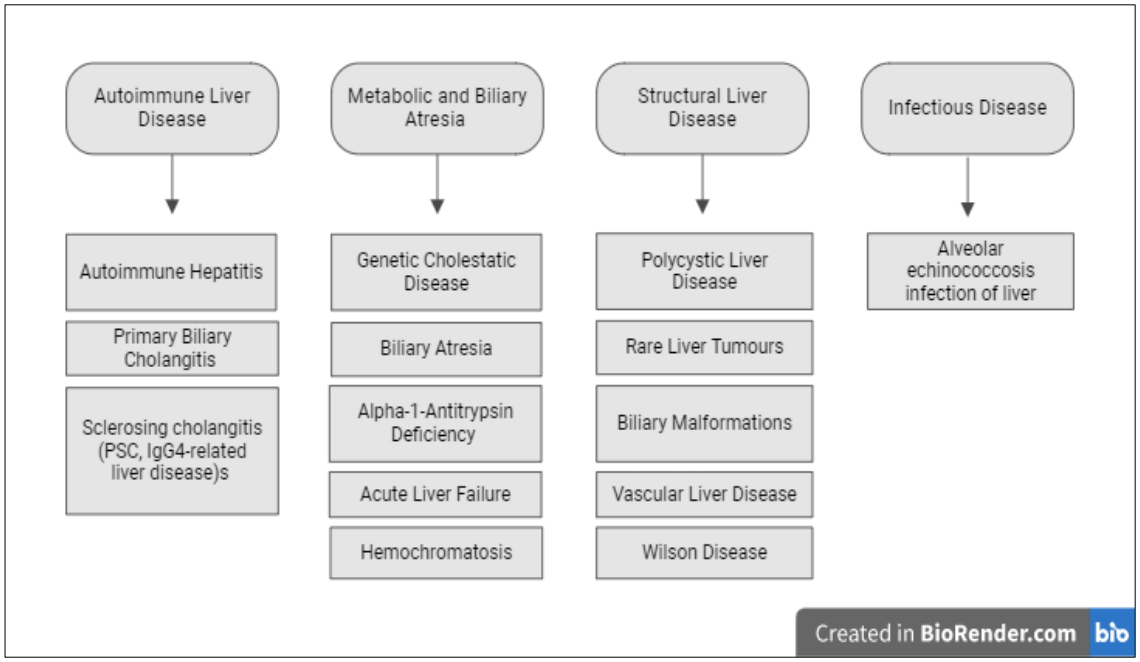

Figure 1 **The 14 rare liver diseases covered by the ERN RARE-LIVER in four pillars**
Own visualization created with BioRender.com

1.3 Quality of life (QoL) and patient satisfaction

In the healthcare landscape for individuals suffering from chronic and complex diseases, understanding both quality of life and patient satisfaction complements the conventional approach of providing medical assessments. This approach serves as a pathway to ensure holistic care is provided to patients throughout their disease journey (19). In addition to providing medical care, this patient pathway ensures that other aspects of patients' lives are also addressed (19). In general, chronic diseases pose a burden on both the physical and mental well-being of patients and require continuous attention (20). For patients living with chronic and complex RDs, limited studies have addressed the impact of the disease on QoL. However, existing literature has identified that complex illnesses have a greater detrimental effect on the psychological functioning of patients than their social or physical functioning (20–22).

To date, healthcare systems have not addressed the burden of RDs on patients. Data show that patients living with RDs and their caregivers are three times more unhappy and depressed than the general population (23). QoL commonly refers to individuals' overall sense of well-being that is influenced by their satisfaction or dissatisfaction with certain domains of life that are essential to them (24). It incorporates holistic dimensions of one's life, such as physical, psychological, spiritual, and emotional health (24).

The rise in unmet medical and social needs for patients with chronic RDs has contributed not only to their decreased QoL but also to their well-being (9). Importantly, it was also reported that seven out of ten patients with a rare condition and/or their caretakers have reduced productivity and reduced working days (9,23). Patients living with RDs are also considered unreliable and are forced by their employers to quit their jobs (9). These factors have attracted the attention of policymakers toward recognizing the challenges faced by all populations living with RDs. The burden of RDs not only affects patients themselves but is also projected onto their families and societies (9).

Additionally, measuring patient satisfaction with healthcare providers and healthcare services is another approach that can assist in determining the overall well-being of patients. Patients with depression or anxiety symptoms are reported to be less satisfied with the healthcare services (25). The effectiveness of medical treatment has been associated with patient satisfaction with the quality of care provided by healthcare providers (21). Patients also have higher satisfaction with healthcare services when there is effective doctor-patient communication and improved patient perceptions of healthcare provider support (19).

Measuring patients' QoL or patient satisfaction is a challenge; both are constructs, and no standardized measuring scale has been adopted by researchers to evaluate them. Therefore, generic scales have been designed to study health problems across different populations and in various contexts and settings. An example of such a scale is the Health Outcomes Short Form (SF-36), which encompasses eight aspects of QoL categorized under physical and psychosocial domains (24). The Patient Satisfaction Questionnaire (PSQ-18) contains seven domains that cover patient satisfaction with healthcare services (26). The

two scales mentioned above are utilized for this thesis and are discussed in further detail in section 3.3 under subsections 3.3.1 and 3.3.2.

1.4 Autoimmune Hepatitis (AIH)

AIH is a chronic and progressive liver disease occurring when the body's immune system attacks liver cells, leading to inflammation and scarring of the liver (27). This scarring eventually leads to liver failure if left untreated (27).

The liver is a vital organ in the human body and is located in the right upper quadrant of the abdomen, on top of the right kidney, stomach, and intestines (28). It has a dual blood supply from the hepatic artery and portal vein to ensure the continuous perfusion and transport of blood (29). The liver is divided into two main lobes (right and left), these lobes are connected to the hepatic duct via the small ducts. The shape of a healthy liver is illustrated by the ERN RARE-LIVER in Figure 2 (30).

The liver is considered the main metabolic organ of the body (31). It performs central functions such as supporting the immune system, protein synthesis, and metabolism of amino acids, carbohydrates, and lipids (29,32). It is also responsible for detoxification and removal of pathogens from systemic circulation (31,32). These harmful substances are excreted in the form of bile by-products outside the body as feces, or in the form of blood by-products that are filtered by the kidneys and excreted outside the body by urine (28). The liver as a metabolic organ increases its risks of exposure to neoantigens, which are proteins present in cancerous cells and are produced from the over metabolic activity of the liver itself (31).

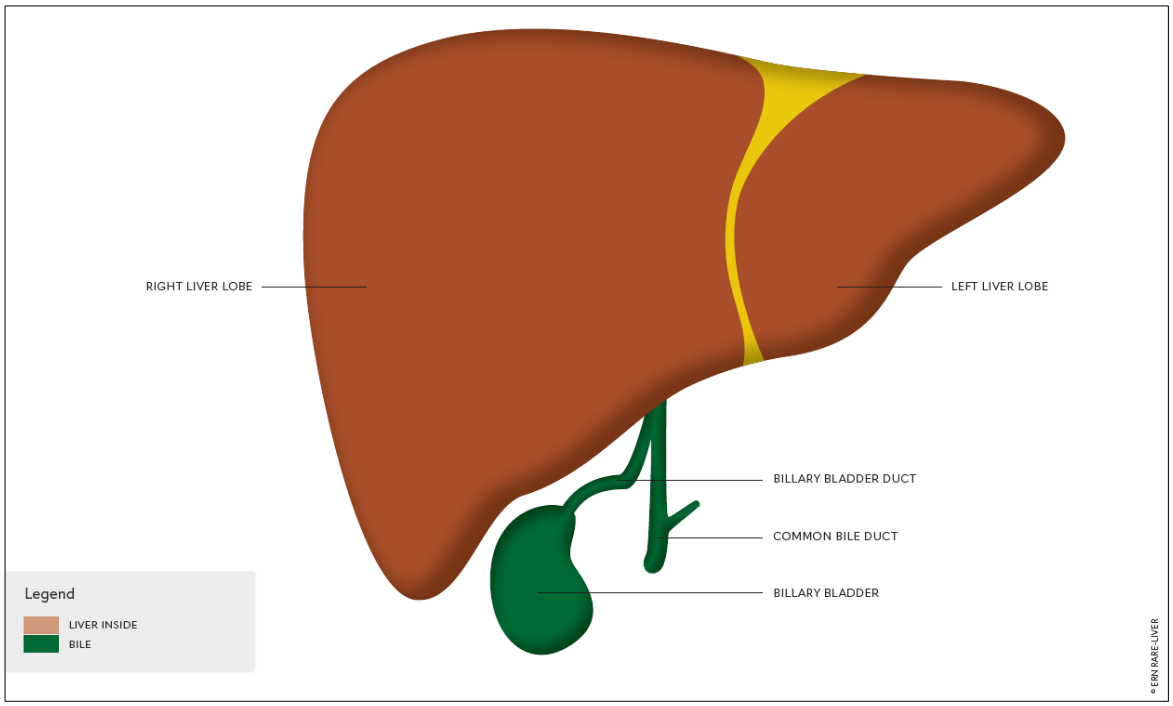

Figure 2 Illustration of healthy liver by ERN RARE-LIVER

Different cell types make up the liver, and each has distinct functions. Hepatocytes are the primary cells that comprise the majority of the liver volume and perform the main liver functions, followed by cholangiocytes (32). Hepatic stellate cells exist in an active or dormant state, and their main functions are the synthesis and storage of vitamin A as well as the organization and deposition of collagen in the liver (32). Once liver injury occurs, these cells are activated and proliferate, causing scarring of the liver, which may also advance to cirrhosis (32).

The liver has a reservoir of approximately 500,000 to one million immune cells called lymphocytes (31). These hepatic lymphocytes consist of innate and adaptive immune cells (31). The role of the different immune cells found in the liver is still vague. Some are protective against external pathogens, others against liver failure, and some cells play an immunoregulatory role, which seems to increase in patients diagnosed with AIH and other autoimmune diseases (31). Furthermore, the liver contains natural killer T cells (NKT),

which regulate innate and adaptive immunity (33). However, NKT cells also induce inflammation, liver injury and fibrosis (31,33). Therefore, these liver-related lymphocytes not only maintain homeostasis but also trigger immune-mediated liver injuries, and AIH is an exemplary case (33).

AIH is a unique rare liver disease and has special features upon presentation in comparison with other rare liver diseases (34). It may also rapidly progress to liver failure in patients with severe disease presentation (34). AIH mostly occurs in young or middle-aged patients (35,36). Around 20 percent of adult patients present with AIH after the age of 60-years and the majority of these patients between 60 percent and 75 percent are females (35). Females have higher incidence and prevalence of AIH compared to men, with a reported male-to-female ratio 1:4 to 1:6 (36). Half of the AIH patients have liver fibrosis on diagnosis and one-third have cirrhosis, regardless of being symptomatic (34).

Worldwide, a drastic increase in the incidence and prevalence of AIH is observed, affecting both pediatrics and adults, all genders and different ethnicities in various geographical locations (34,36). The disease prevalence in European and American populations is higher than that in Asian populations (37). In Caucasian Europeans and North Americans, the reported AIH prevalence is approximately 1/6,000 (34). Furthermore, the point prevalence in European countries is reported to be 10 to 25 per 100,000 population while in the Asia-Pacific region, it ranges from 5 to 25 per 100,000 population (36). The shape of the AIH liver is illustrated by the ERN RARE-LIVER in Figure 3 (30).

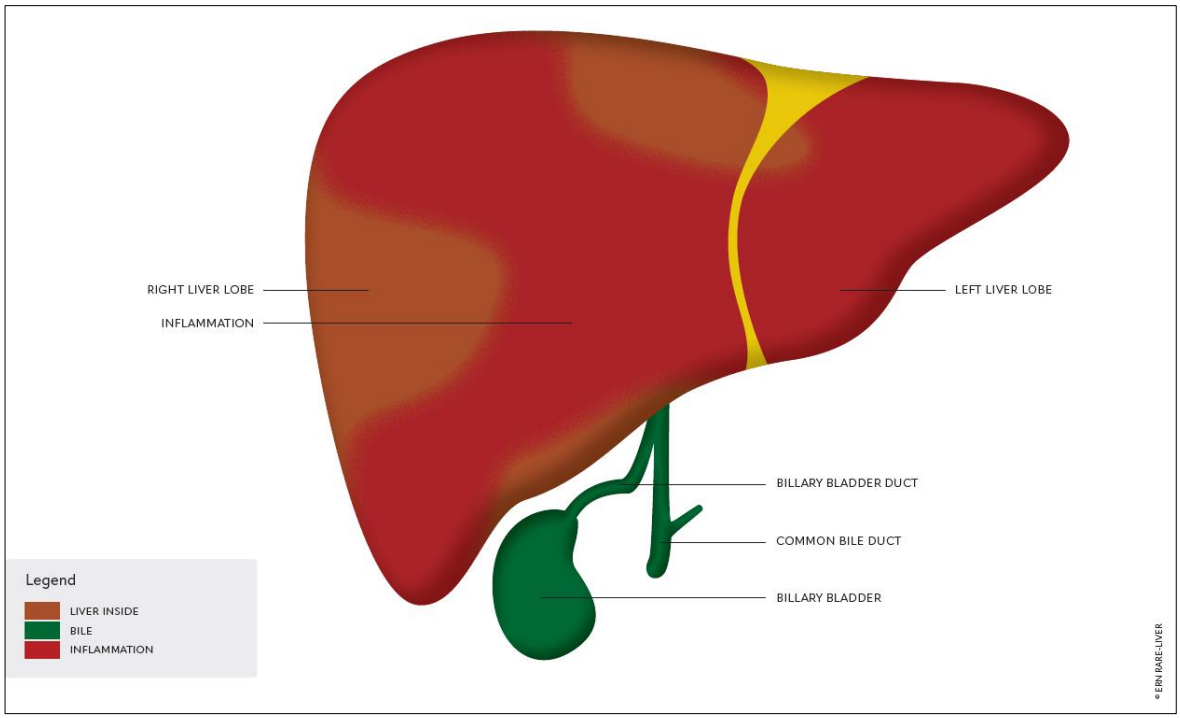

Figure 3 Illustration of AIH liver by ERN RARE-LIVER

1.4.1 Etiology and pathology

The disease etiology up to date is unclear, but AIH is often diagnosed in patients with a certain genetic background triggered by environmental factors like drugs or biological agents (38). Another discussed risk factor for AIH is viral infections (39).

There are two types of AIH, and their classification is primarily dependent on serological findings. AIH type-1 is identified by the presence of antinuclear antibodies (ANA) with or without anti-smooth muscle antibody (SMA) (40). It is more common and can be diagnosed in both pediatric and adult patients (40). On the other hand, type-2 AIH is mostly diagnosed in pediatric cases by the presence of anti-liver/kidney microsomal antibody type-1 (anti-LKM) with or without anti-liver cytosol type-1 antibody (anti-LC) (39). The disease progression in both types of AIH has been shown to be similar (41).

AIH can occur in three forms: acute, severe, or acute liver failure (ALF) (36). Clinically, it can range from being asymptomatic to end-stage liver disease (37). The acute form of AIH doesn't have a strict definition but it commonly lacks the conventional characteristics of AIH such as positive autoantibodies, elevated gamma-immunoglobulin (IgG) and elevated transaminases (36,37). It is a problematic form of AIH and is often not considered by physicians if only elevated serum transaminases are present (36). This is challenging because it delays early diagnosis and treatment initiation, allowing the disease to progress to severe hepatitis and ALF (36). The European Association for the Study of the Liver (EASL) clinical practice guidelines indicated that approximately 25 percent of patients present with an acute-onset form of AIH (36).

The course of AIH is unpredictable and is often coupled with frequent relapses (16). Its presentation is also variable, and in the majority of the cases it coexists with other liver diseases such as primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) (35). Accurate diagnosis of AIH is complicated because there are multiple overlapping features in the signs and symptoms, as well as the biochemical and immunological tests between AIH and PBC or PSC (35). In addition to the overlap with other rare liver diseases, approximately 20 to 50 percent of AIH patients are affected by extrahepatic autoimmune diseases (39). These diseases are: rheumatoid arthritis, Sjögren's syndrome, inflammatory bowel diseases (ulcerative colitis, Crohn's disease), Hashimoto thyroiditis, hemolytic anemia and gastritis (38). Moreover, tumors and psychiatric disorders such as depression were also found to be concomitant with AIH (38).

1.4.2 Clinical presentation and diagnosis

The diagnosis of AIH is complex due to heterogeneity in the biochemical and clinical presentation, and it is very challenging for clinicians to diagnose. There is no specific diagnostic test, and hepatologists rely on a combination of clinical, biochemical, immunological, and histological readings to determine a correct diagnosis (16,27). Additionally, the exclusion of other viral infections such as hepatitis B, C, and E or other liver diseases of known causes, such as Wilson's disease or nonalcoholic steatohepatitis (NASH), is also part of the diagnostic process (39). Diagnosis is sometimes established

based on the clinical features identified and presented in other extrahepatic autoimmune diseases (39).

AIH has non-specific manifestations with ranging severities. Its symptoms include fatigue, nausea, malaise, abdominal pain, arthralgia, jaundice, weight loss, anorexia (36,39). Amenorrhea is sometimes present in young women (39). Cirrhosis has been reported to be present in one-third of cases at the initial diagnosis (39). Clinically, AIH is characterized by elevated serum transaminase levels, aspartate aminotransferase (AST) and alanine transaminase (ALT), elevated serum IgG, and the presence of autoantibodies, all of which are captured by blood testing (27,36). Elevated levels of these markers indicate active inflammation of the liver (42,43). Once a patient is suspected to have AIH based on the presenting symptoms and has elevated levels of the liver surrogates AST, ALT, and IgG, physicians follow a scoring system developed by the International Autoimmune Hepatitis Group (IAIHG) to confirm the diagnosis of AIH.

In 1993, the IAIHG introduced diagnostic criteria for AIH patients, which were modified in 1999 to include testing for changes in AST, ALT, alkaline phosphatase (ALP), liver histology, drug history, and response to therapy (44). Moreover, the exclusion of hepatotropic viruses such as cytomegalovirus (CMV) or Epstein-Barr Virus (EBV) other than hepatitis A, B, and C was also part of the diagnostic criteria (44). In 2008, the criteria were revised and simplified for use as a tool in clinical practice, focusing on four items: IgG levels, autoantibody titers, absence of viral hepatitis, and certain histological features of the liver (37,39).

Given the fluctuating course of the disease, monitoring of liver function tests (LFTs), commonly known as transaminases (ALT and AST) and IgG, is recommended every three to six months for early detection of possible disease flares (16). This process has been largely utilized in order to avoid further disease progression and complications (16).

It is estimated that 25 to 75 percent of AIH cases present in acute form which is characterized by the absence or undetectable autoantibodies and normal IgG values at the time of diagnosis (46). Of the acute cases, 39 percent have undetectable serum autoantibodies,

and between 25 to 39 percent have normal IgG values (46). In contrast, biochemical elevation of liver enzymes (AST and ALT) and/or liver fibrosis are common manifestations of the chronic form of AIH (44). The transaminases are often increased three to ten-fold compared to the normal ranges (35). The normal reference values of AST and ALT set by the IAIHG are <50 IU/L in male patients and <35 IU/mL in female patients (38). Similarly, the normal range of IgG is <16 g/l in both males and females (47).

It was mentioned in different publications that the proposed AIH scoring system by the IAIHG is insufficient to diagnose acute cases of AIH due to the absence of autoantibodies (ANA and SMA) or elevated IgG, thus, it is nowadays recommended to confirm suspected AIH cases by also taking a liver biopsy (36,38,44). Liver biopsy is a key diagnostic technique used to confirm the diagnosis of suspected AIH, specifically in acute onset cases (36). Viral hepatitis signs and symptoms also mimic those of AIH, and distinguishing between them is almost impossible (44). It is therefore mandatory to test for hepatitis A, B, C, and E, EBV, and CMV in patients undergoing liver biopsy to confirm the diagnosis of AIH (44).

Liver histology is also an important visual indicator for establishing the diagnosis of AIH (40). Hepatocytes are visualized under a microscope following a biopsy. Hepatic cells in patients with AIH are surrounded by inflammatory cells that appear swollen (40). Moreover, the histological studies identify as well the extent of fibrosis and presence of other concomitant diseases (40).

1.4.3 Treatment and prognosis

There is no cure for AIH, the treatments available are primarily to manage the condition, delay the progression of fibrosis to cirrhosis, and improve prognosis (16,38). The chronic cycle of liver inflammation must be interrupted to prevent worsening of liver injury. Evidence suggests that liver fibrosis or even liver cirrhosis may be reversed if the critical ‘point of no return’ has not surpassed (38). Cirrhosis has been confirmed to be present in approximately 30 percent of patients at diagnosis, indicating a disease course of months or sometimes years prior to diagnosis, and is associated with poorer prognosis (16). AIH

patients with cirrhosis have an increased mortality rate compared to those without cirrhosis (36).

The standard treatment which has been in use for the past forty years is immunosuppressive therapy, as it not only improves the values of the liver surrogate markers but also improves overall symptoms and prolongs patient survival (16,27). In the guidelines of the American Association for the Study of the Liver Disease (AASLD), corticosteroids (prednisone 60 mg/day) are recommended as monotherapy or a combination of prednisone 30 mg/day with azathioprine 50 mg/day (36). On the contrary, EASL suggests an initial treatment with prednisone 0.5-1 mg/kg/day) accompanied by azathioprine 50 mg/day (36). As an alternative to prednisone, budesonide has been suggested to have fewer adverse events and a hepatic clearance rate of 90 percent (36). In a double-blinded randomized trial, the use of budesonide in combination with azathioprine has been reported to induce biochemical remission in AIH patients more effectively than with prednisone (36). However, therapeutic options are dependent on the histological presentation and severity of scarring of the liver, and the simplified scoring system of the IAIHG is user-friendly and helps in determining the course of corticosteroid treatment (36).

While treatment is extremely important to prevent progression of the disease, approximately 15 percent of patients may experience insufficient response to treatment, which is evident by the failure to achieve normal histological or complete normalization of biochemical parameters (16). Normalization or attainment of biochemical remission of LFTs is a fundamental part of improving patient prognosis and journey with the disease; patients who achieve biochemical remission have excellent outcomes (36).

The IAIHG defines complete biochemical remission as the attainment of normal transaminases and IgG levels within six to twelve months of immunosuppressive treatment initiation (16,38). In contrast, incomplete biochemical remission is defined as the incomplete normalization and persistent elevation of one or two of the liver surrogates (ALT, AST or IgG) after six to twelve months after treatment (43,47). Assessment of liver histology is also recommended to assess liver health and overall progression of the disease alongside primary blood surrogate markers (43). Histological remission of the liver is the modified

hepatitis activity index value <4/18, a value higher than four points is associated with long-term progression of AIH regardless if biochemical remission was achieved (43).

AIH is clinically challenging, and patients may experience frequent relapses even after achieving complete remission (16). A relapse may occur in 50 percent to 90 percent of the cases (45). The international guidelines do not favor frequent biopsies to monitor the patients' liver health, it is rather advised to rely on obtaining repeated measurements of normal serum transaminases and normal serum IgG levels (16). Monitoring of transaminases and IgG levels is recommended to be continued for at least six months after achieving complete biochemical remission (16). Treatment is also recommended to be continued for at least 24 months after attainment of complete remission (45).

Another important component to be considered while treating patients with AIH is health-related quality of life (HrQoL). Interestingly, the HrQoL of patients with AIH is highly impacted, with depression being the predominant symptom reported to affect patients' well-being (36). Both depression and anxiety in patients with AIH have been associated with a high degree of treatment non-adherence (47).

1.5 R-LIVER registry

The cohort for this study included AIH patients registered in the database of the R-LIVER registry at the University Medical Center Hamburg-Eppendorf (UKE). R-LIVER is a prospective registry provided by the ERN RARE-LIVER, covering patients diagnosed with rare liver diseases (48). The R-LIVER is coordinated by the UKE. It collects uniform clinical data from individual patients with different rare liver diseases (48). These data undergo ongoing monitoring in order to fulfill the quality benchmarks established by the ERN RARE-LIVER. The registry is a platform for clinicians to closely monitor patients, measure the success of clinical management, and provide follow-ups and quick interventions to improve the quality of care for patients with rare liver disorders (15). Among the quality measures outlined, a key measure is to ensure that more than 70 percent of AIH patients have reached complete remission within 1-year of diagnosis (15). The R-LIVER

registry focuses on different rare liver disease areas, nevertheless, the cohort chosen for this thesis paper is only from the autoimmune liver diseases patient registry. It constitutes 281 patients diagnosed with AIH, and these patients are covered by private and public health insurance schemes.

2. Research aims and objectives

The aim of this master's thesis is to study the impact of the two different main health insurance schemes in Germany, private and public health insurance, on liver health in patients with autoimmune hepatitis (AIH), a chronic autoimmune disease of the liver. Furthermore, the overall experiences of AIH patients at UKE with the different healthcare services will be assessed. Patient experiences with the healthcare system vary and may depend on several aspects. However, the target of this study was to assess health-related quality of life and satisfaction with aspects related to doctor-patient communication, medical care, and medical services (26).

Research questions:

i. What is the impact of private and public health insurance schemes on liver health in patients with autoimmune hepatitis?
ii. How does the type of health insurance relate to the experiences and satisfaction with healthcare for patients with autoimmune hepatitis?

As stated previously, the liver surrogates AST, ALT, and IgG are pivotal biomarkers to assess the inflammatory activity of AIH and guide treatment decisions. Therefore, biochemical remission was measured using LFTs and IgG as proxies for liver health. The hypotheses listed below are investigated in this study.

1. Patients with PvtHI have better liver health than PubHI at baseline and after 1-year of treatment.
2. There is improvement in liver health within the same insurance groups after 1-year of treatment.

3. AIH patients with PvtHI have a better quality of life compared to those with PubHI.
4. AIH patients with PvtHI report higher levels of satisfaction with their healthcare compared to those with PubHI.

3. Methodology

3.1 Study design

This is a cross-sectional study, exploring the difference in liver health and patient satisfaction of AIH patients with PvtHI and PubHI. This study will help to understand the potential differences in the clinical health outcomes, quality of life, and experiences of patients with AIH to improve the quality of care provided at UKE. This is achieved by gathering and comparing the measurements of the laboratory values of the transaminases (ALT and AST) and IgG at different time points. These are the standard surrogate markers of liver inflammation. As per the recommendations of the international guidelines to attain the treatment goals, UKE adopts the same procedure for monitoring and early detection of possible disease flares. To gather insight into patient experiences, a survey will be circulated to collect information on patients' health-related quality of life and their satisfaction with their healthcare and health insurance.

3.2 Participants

The study sample included patients with AIH in the R-LIVER prospective registry at UKE, Hamburg. All study participants provided written informed consent abiding by privacy regulations and legislation set by the EU General Data Protection Regulation (GDPR) (15). The GDPR is a European law established to protect and empower EU citizens data privacy (49). The study protocol was approved by the local ethics committee (Ethikkommission der Ärztekammer Hamburg, Germany) and was registered under ethical approval number PV5548.

The R-LIVER registry comprises a total of 281 AIH patients diagnosed between 2017 and 2022. This is the number of patients registered as of November 2023 during the running time of this thesis research. Of the total number of AIH patients included in the registry, 22 had PvtHI and 259 had PubHI. Therefore, for this thesis, given the variability in group sizes, the sample was formed of two equal group sizes, and a total of 34 participants were selected: 17 PvtHI and 17 PubHI. The participants were matched by sex to ensure an equal distribution of males and females in both groups. There were 12 females in PubHI and 12 in PvtHI. Similarly, there were 5 males in PubHI and 5 males in PvtHI. A nurse from UKE who was not familiar with the study matched the two groups. The eligibility criteria used in selecting participants in the research study is displayed below in Table 1. The criteria were assessed based on the patient's diagnosis date, age, insurance type, and informed consent.

Table 1 Inclusion and exclusion criteria for the study participants

Eligibility criteria for participants in the study
Inclusion criteria • Patients participating in the R-LIVER registry. • Patients have a signed informed consent. • Patients have private or public insurance. • Diagnosis of Autoimmune Hepatitis.
Exclusion criteria • Rejected to sign the informed consent. • Other insurance types: self-payers. • Uninsured patients. • Other rare liver diseases. • Other diseases overlapping with AIH. • Diagnosis less than 1 year ago. • Younger than 18 years of age.

3.3 Data collection

Data for this study was obtained from the R-LIVER registry at UKE spanning from 2017 until 2022, including laboratory values (ALT, AST and IgG), patient demographics such as height, weight, body mass index (BMI) and patient disease information. Some of the patients at baseline had missing laboratory values. In PubHI, four different patients had missing ALT and IgG values, and two PvtHI patients had missing IgG values. Additionally, a survey using close-ended questions was systematically distributed among participants in November 2023, during the thesis writing process. The survey aims to gather standardized responses in order to collect quantitative data related to the differences in patient experiences and health outcomes in the private and public insurance. Although interviews offer more flexibility with open responses, the focus of the discussion may deviate from the primary hypothesis being investigated, hence, survey is the optimal data gathering tool for this study (50).

The survey is divided into three sections. The first section included demographic and socioeconomic questions (Appendix D), the second section was the Short Form Health Survey (SF-36) (Appendix E), and the last section was the Standard Patient Satisfaction Questionnaire (PSQ-18) (Appendix F). The online EU-Survey tool was used for the compilation of these survey questions (51). The survey titled “Studie zu Lebensqualität und Patientenzufriedenheit” was administered to the study participants by creating an online link that was shared online via email or sent by post (51). The method, whether online or on paper, through which the survey was completed, was influenced by the participants’ preferences and the availability of email addresses for all subjects. This approach offers the benefits of privacy, ensuring confidentiality for participants, and allowing patients to conveniently participate at their own pace (50).

The purpose of the study was explained to patients in a one-sheet document attached to the main survey. The timeframe in which the respondents were requested to answer the survey questions was between November 9, 2023, and December 9, 2023. It took approximately seven minutes for the participants to complete the survey. The survey was sent to the entire recruited cohort (n=34), and 29 surveys were returned. In the current study, the

original PSQ-18 questionnaire (Appendix G) was translated into the local language, German, employing a translation-retranslation procedure. Additionally, irrespective of the survey response rate, the laboratory values of 34 participants were included in the analysis.

3.3.1 Short form health-related quality of life questionnaire (SF-36)

The SF-36 is a generic questionnaire offered to patients to self-report on their health-related quality of life (HrQoL). It was developed in 1992 as part of the instruments used in the Medical Outcome Study (MOS) and is generic because it measures health concepts that correspond to basic values in an individual's well-being (52–54). HrQoL is normally associated with subjective health indicators, such as physical and social functioning or mental health, as these are directly affected by the disease course (53,54). This tool was initially introduced in the United States but was later translated into different languages, including German, and has been tested and proven to have internal consistency and is applicable and valid for use in German populations (53,55).

The questionnaire contains 36 items to measure health attributes in both physical and psychosocial well-being by using eight multi-item subscales, each containing 2-10 items (24,53). Physical function items cover limitations in daily life secondary to health-related problems. Body pain measures the pain severity and frequency with the day-to-day tasks. General health items cover the individual's general health perception. Vitality items assess fatigue and energy levels. Social functioning measures the extent to which health problems affect one's social roles and activities. Role emotional assesses limitations due to emotional problems, and mental health includes psychological stressors. Table 2 displays the detailed contents of the eight domains of the SF-36 adapted from the SF-36 manual and interpretation guide (54). An edited version of this questionnaire containing an extra question was distributed to the patients, but the analysis was solely performed for the 12 main categories containing 36 questions in total. Additionally, in the analysis of this questionnaire, one patient was excluded for missing more than half of the questionnaire items.

Table 2 SF-36 scales and scales content

Items	SF-36 Scales	Scale content and items description
9a&9e	Vitality	Feeling lots of energy
9g		Feeling worn out
9i		Tired
5a	Role emotional	Cut down the time spent on work/activities
5b		Accomplished less than wanted
5c		Didn't do work or other activities as usual
6	Social function	Health problems interfered with normal social activities
10		Frequent health problems interfered with social activities
9b	Mental health	Been nervous
9c		Feeling down
9d		Feeling calm and peaceful
9f		Feeling downhearted and sad
9h		Been happy
1&2	General health	Health is: excellent, very good, good, fair, poor
11a		My health is excellent
11b		I am healthy like everyone I know
11c		I seem to get sick easier than others
11d		I expect my health to get worse
7	Body pain	Intensity of body pain
8		Pain interfered with normal work/activities
3a	Physical function	Vigorous activities: running, lifting heavy objects
3b		Moderate activities: moving a table, vacuuming
3c		Lifting or carrying groceries
3d		Climbing multiple flights of stairs
3e		Climbing one flight of stairs
3f		Bending, stooping of kneeling
3g		Walking more than 1 kilometer
3h		Walking several blocks
3i		Walking one block
3j		Bathing or dressing
4a	Role physical	Limited in work/activities
4b		Cut down the amount of time spent on work/activities
4c		Accomplished less than wanted
4d		Difficulty performing the work/activities

Table adapted from SF-36 manual and interpretation guide by John E.Ware

Likert's scoring method was used for this questionnaire. Although this scoring algorithm is complicated, it generates scores that can be used to compare groups or across other studies (54). Participants had the option to answer each domain using a predefined response choice. Table 3 shows two example questions on the pain and social functioning domains of the SF-36. Pain having three response levels: yes severely restricted, yes somewhat restricted, no not restricted at all. Social functioning having five response levels: not at all, slightly, moderately, quite a bit, extremely. The detailed questionnaire questions and response options are presented in Appendix E.

Table 3 SF-36 example questions and scoring method

Questions and response choices	Assigned score	Recoded score
Q. Sind Sie durch Ihren derzeitigen Gesundheitszustand bei diesen Tätigkeiten eingeschränkt ? Wenn ja, wie stark?		
- anstrengende Tätigkeiten, z.B. schnell laufen, schwere Gegenstände heben, anstrengenden Sport treiben		
☐ Ja, stark eingeschränkt	1	1
☐ Ja, etwas eingeschränkt	2	2
☐ Nein, überhaupt nicht eingeschränkt	3	3
Q. Wie sehr haben Ihre körperliche Gesundheit oder seelischen Probleme in den vergangenen 4 Wochen Ihre normalen Kontakte zu Familienangehörigen, Freunden, Nachbarn oder zum Bekanntenkreis beeinträchtigt?		
☐ Überhaupt nicht	1	5
☐ Etwas	2	4
☐ Mäßig	3	3
☐ Ziemlich	4	2
☐ Sehr	5	1

These response levels were assigned scores ranging from 1 to 5. Following the entry of original responses of the participants (step 1, Figure 4), reverse numbering of some items occurs. This technique ensures that higher values will always indicate better health in all scales of the SF-36 (54). In fact, ten items in the SF-36 are worded to reflect that a higher score indicates a poor health state. Therefore, these items were reverse-coded or numbered (step 2, Figure 4). An example question that underwent this recording method is presented in Table 3.

Missing values were scored using mean imputation, in which a missed/unanswered response by participants was replaced by the mean average of the item's corresponding scale (step 3, Figure 4). After items are recoded and missing values are recalibrated, average scores of each item scale are completed (step 4, Figure 4). Low scores indicate poor health, and higher scores indicate better health (Appendix H). Then the overall average score of the two dimensions, physical and psychosocial, is calculated (step 4 i, Figure 4). Lastly, the overall score of all items per participant is calculated (step 4 ii, Figure 4). Figure 4 shows the flow chart of SF-36 questionnaire scoring used in this thesis.

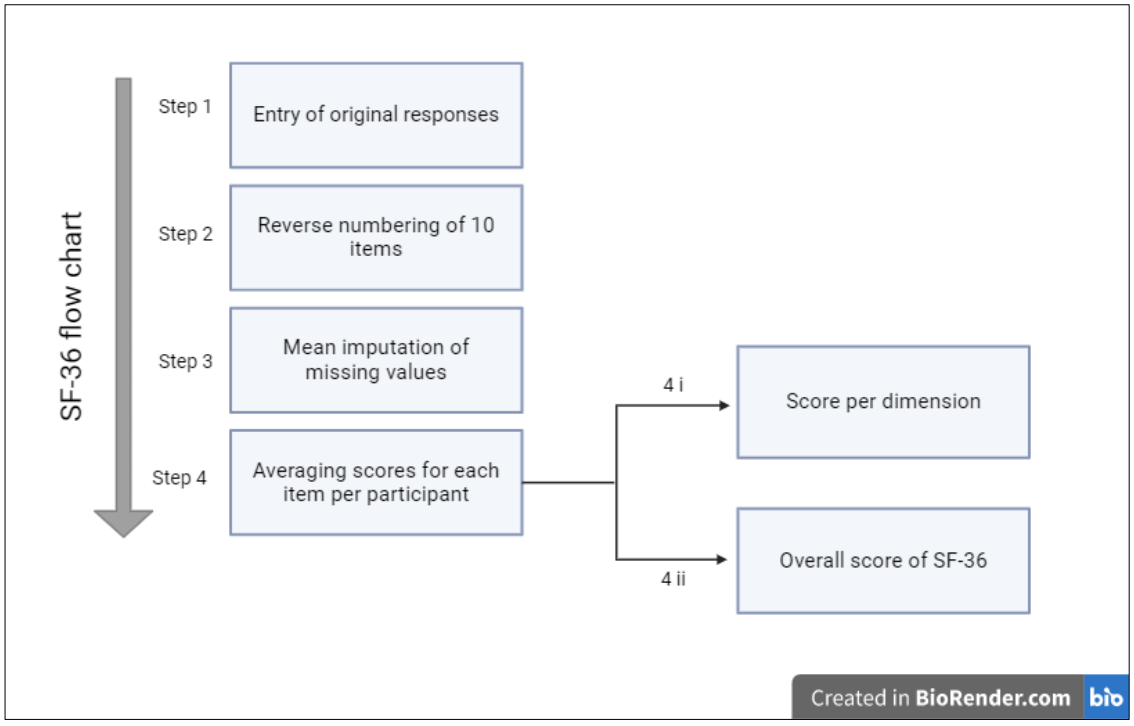

Figure 4 **Flow chart of the SF-36 questionnaire**
Own visualization created with BioRender.com

3.3.2 Patient satisfaction questionnaire (PSQ-18)

The PSQ-18 is a tool used to evaluate patient satisfaction with healthcare services and to assess the quality of care. These services include aspects such as doctor-patient relationships, communication, financial affordability, accessibility and convenience (26). The PSQ-18 is a revised version of the original PSQ and contains only 18 items to answer. The original version was 80-items long, it was shortened to 50-items in the PSQ-III for more convenience and practicality related to time constraints while participants are answering the long survey (26).

The PSQ-18 assesses the satisfaction and dissatisfaction of patients in different domains of healthcare services. The domains are then tested with different related questions, generating scores for seven sub-scale areas to identify gaps within healthcare (26). These seven subscales are general satisfaction, communication, technical quality, time spent with doctor, interpersonal manner, accessibility and convenience, and financial aspects (26,56).

Items 3 and 17 were used to assess general patient satisfaction with healthcare. Technical quality (items 2, 4, 6, and 14) evaluates the quality of medical care, proficiencies, and competencies of healthcare providers. The interpersonal manner (items 10 and 11) focuses on effective communication between patients and their clinicians, aspects such as empathy, patient involvement in decision making, and the clinician's ability to listen. Communication (items 1 and 13) addresses clinicians' ability to communicate and explain medical conditions and treatment options and the patient's ability to understand the plan of care (26,56,57).

The financial scale (items 5 and 7) covers the aspects of patients being satisfied with insurance coverage and affordability of care. The time spent with the doctor (items 12 and 15) assesses satisfaction with the duration and quality of interaction provided to the patient by the healthcare provider. Accessibility and convenience (items 8, 9, 16, and 18) addresses availability and accessibility of healthcare services, it covers items of waiting times, location and appointments scheduling (26,56,57).

In this questionnaire, the phrasing of the questions is done in such a way that agreement with a question reflects either satisfaction or dissatisfaction with healthcare. A 5-point Likert scale ranging from 1 to 5 was used to score the original responses of the participants (26,56) (steps 1&2, Figure 5). Respondents were given multiple options to answer questions at a five-response level: [1] strongly agree, [2] agree, [3] uncertain, [4] disagree, and [5] strongly disagree (57). Table 4 shows example questions with the response choices and the items scoring. Reverse coding of the original responses follows (step 3, Figure 5), where items reflecting satisfaction (step 3i, Figure 5), and dissatisfaction (step 3ii, Figure 5), are separated, and their values are recoded accordingly (see Table 4). The detailed questionnaire questions are displayed in Appendix F.

Table 4 PSQ-18 example questions and scoring

Questions and response choices	Assigned score	Recoded score
Q. Es ist mir möglich, medizinische Versorgung zu erhalten wann immer ich sie brauche. *(item reflecting dissatifaction)*		
☐ Ich stimme voll und ganz zu	1	1
☐ Ich stimme eher zu	2	2
☐ Unsicher	3	3
☐ Ich stimme eher nicht zu	4	4
☐ Ich stimme gar nicht zu	5	5
Q. Manchmal frage ich mich, ob die Diagnose meiner Ärzte die richtige ist. *(item reflecting satisfaction)*		
☐ Ich stimme voll und ganz zu	1	5
☐ Ich stimme eher zu	2	4
☐ Unsicher	3	3
☐ Ich stimme eher nicht zu	4	2
☐ Ich stimme gar nicht zu	5	1

The final scoring was performed by averaging items of the same sub-scale together (step 4, Figure 5). The higher the score, the higher is the satisfaction, and vice versa. As per the PSQ-18, the overall sum score of the subscales ranges from 18 to 90 points; 18 reflects the lowest evaluation, and 90 is the best evaluation (57). If an item was not answered by the respondent, the averaging is done by calculating the total responses of this item and ignoring the missing one (26). The scoring algorithm and PSQ-18 flow chart used in this thesis are presented in Figure 5. This questionnaire is validated to and proven to be reliable and have internal consistency to be used in various settings but only on the American population (26,56). However, for the German population it is merely an experimental analysis.

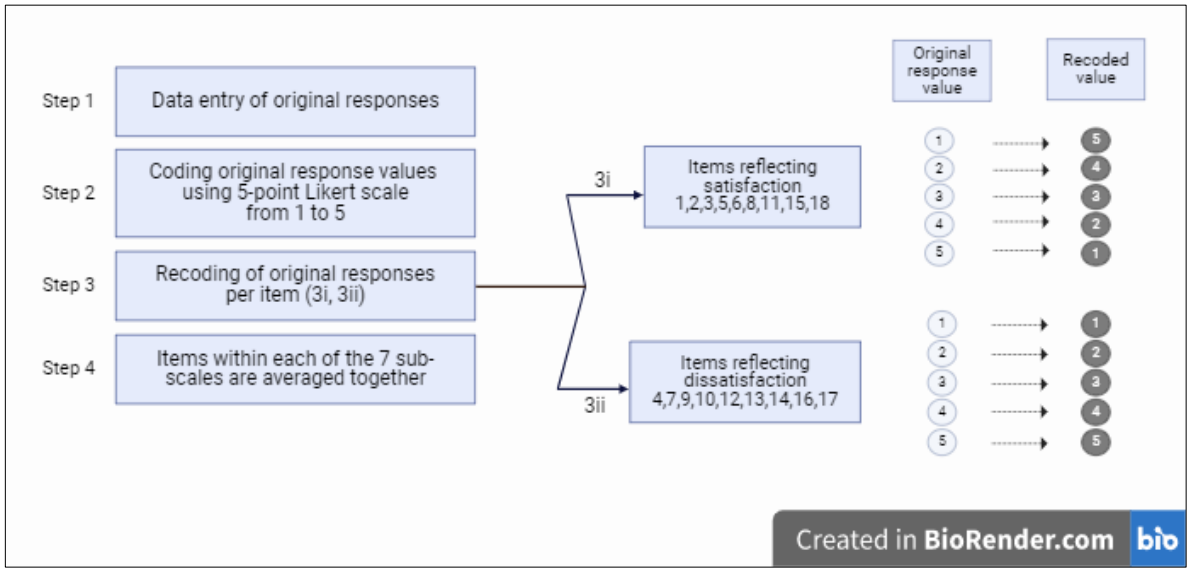

Figure 5 **Scoring algorithm of PSQ-18 questionnaire**
Own visualization created with BioRender.com

3.3.3 R-LIVER registry data

All patients with AIH as the initial and main diagnosis and a minimum 1-year follow-up were reviewed. In order to compare the liver health outcomes between the two groups, AST, ALT, and IgG laboratory values were obtained from the R-LIVER registry. Data

from two different time points were analyzed. Baseline and 1-year after treatment initiation, irrespective of the patient's diagnosis date. Additional data extracted included height, weight, and BMI. Other comorbidities include cancer, diabetes mellitus, hypertension, pulmonary diseases such as asthma, cardiac diseases, inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, and other autoimmune diseases such as rheumatoid arthritis, Hashimoto's thyroid disease, and multiple sclerosis.

3.4 Data analysis and statistical testing

All variables were tested for normal distribution using the Kolmogorov-Smirnov test. Descriptive statistics was used to present data in frequencies with percentages for nominal variables and medians (Mdn) with interquartile ranges (IQR) for categorical variables. Differences between two independent groups were compared using the non-parametric Mann-Whitney U test. The Wilcoxon paired signed-rank test was used for comparison of paired groups. The survey data were analyzed using the Mann-Whitney U test. The PSQ-18 comprising 18 questions and the SF-36 containing 12 main questions, each with sub-questions totaling 36 overall.

Statistical analyses were performed using the IBM SPSS software (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY, USA).
Graphics were created using Prism (GraphPad Software, Prism 10 for Windows, Version 10.1.2, December 12, 2023, San Diego, CA, USA).

4. Results

Demographic data

Extracted from the R-LIVER registry database, 34 adult AIH patients being diagnosed between 2017 and 2022 were included. The majority of the patients were females (n=24, 70.6%) and males (n=10, 29.4%). The sample comprised two groups: 50% of the cohort had PubHI, and the other 50% had PvtHI. Other comorbidities were diagnosed in 94.1% and 82.4% of PubHI and PvtHI patients, respectively. Table 5 displays the baseline characteristics of the study participants.

Table 5 Demographic characteristics of AIH patients with PubHI and PvtHI

Total (N=34)	PubHI	PvtHI	P-value
Disease duration, years, Median (IQR)	3 (4)	3 (3)	0.888
Age at diagnosis, years, Median (IQR)	57 (20)	64 (19)	0.352
BMI, kg/m^2, Median (IQR)	27 (7)	24 (8)	0.220
Education, n (%)			
Kein Schulabschluss: Without school-leaving degree	0	0	**0.027**
Volks- oder Hauptschulabschluss: 9 years of education	1 (5.9%)	1 (5.9%)	
Mittlere Reife: 10 years of education	11 (64.7%)	2 (11.8%)	
Fachabitur: 11 years of education	1 (5.9%)	0	
Abitur: High school diploma: 12-13 years of education	1 (5.9%)	2 (11.8%)	
Hochschul-/Fachhochschulabschluss: University/technical degree	2 (11.8%)	8 (47.1%)	
Employment status, n (%)			
Full time	3 (17.6%)	2 (11.8%)	0.340
Part time	4 (23.5%)	3 (17.6%)	
Retired:			
Due to age	6 (35.3%)	8 (47.1%)	
Due to illness	3 (17.6%)	0	
Apprenticeship	0	0	
Unemployed	0	0	
Other comorbidities, n (%)			
Yes	16 (94.1%)	14 (82.4%)	0.287
No	1 (5.9%)	3 (17.6%)	

Nominal variables are presented as frequencies and percentages. Continuous variables are presented as medians (IQR). Bold denotes significance.

Other comorbidities: cancer, diabetes mellitus, hypertension, pulmonary diseases, cardiac diseases, inflammatory bowel diseases and other autoimmune diseases.

4.1 Liver health

As mentioned above, LFTs and IgG are used as proxies for liver health. The laboratory data extracted from the R-LIVER registry included baseline measurements of ALT, AST, and IgG levels at the initial diagnosis, as well as follow-up measurements at 1-year after treatment initiation. The statistical analysis carried out for this dataset is elucidated in sections (4.1.1) and (4.1.2), addressing hypotheses 1 and 2.

4.1.1 Comparison of liver health between the two insurance schemes (hypothesis 1).

A non-parametric Mann-Whitney U test was used to assess the difference in liver health between the two insurance schemes. Comparisons were performed at baseline and after 1-year (n=34).

When comparing AST levels at baseline between patients with PubHI and PvtHI, there was no difference between the two groups (see Figure 6A). Similarly, the same was observed when comparing ALT levels and IgG levels at baseline between the groups (see Figures 6B, 6C). Detailed results of the statistical analysis can be found in Appendix A.

When comparing LFTs and IgG values after 1-year follow-up, no differences were observed between the two groups in any of the biochemical markers (AST, ALT, and IgG) (see Figure 6). Detailed description of the statistical findings can be found in Appendix B.

In summary, no differences were observed in the three examined laboratory measurements (AST, ALT, and IgG) between PubHI and PvtHI patients at baseline and after 1-year follow-up. The transaminases and IgG levels were above the normal range in the vast majority of patients at baseline, indicating the presence of liver inflammation (Table 6). The overall findings of these biochemical parameters are shown in Figure 6 A, B, and C.

Table 6 Number of abnormally elevated biochemical values in PubHI and PvtHI at baseline

Baseline biochemical values	PubHI (n=17)	PvtHI (n=17)
AST	17	17
ALT	15	17
IgG	9	9

4.1.2 Comparison of liver health within the two insurance schemes over time (hypothesis 2).

A non-parametric Wilcoxon paired signed-rank test was performed to compare the differences within groups over time. The aim was to check for differences in laboratory values within groups of PvtHI (n=17) between baseline and 1-year follow-up and PubHI (n=17) between baseline and1-year follow-up following treatment initiation.

For PubHI patients, the measured AST levels were higher at baseline (Mdn= 458 U/L) than after 1-year follow-up (Mdn=36 U/L). The test yielded a p-value of <0.001 and Z= -3.621 U/L. These results show an improvement in AST levels for PubHI over time (see Figure 6A).

For patients with PvtHI, the AST levels were also higher at baseline (Mdn= 280 U/L) than after 1-year follow-up (Mdn=31 U/L). The test yielded a p-value of <0.001 and Z= -3.621 U/L. These results similarly show improvement in the AST levels for PvtHI over time (see Figure 6A).

The same pattern was observed for the ALT values. For PubHI patients, the measured ALT levels were higher at baseline (Mdn= 577 U/L) than after 1-year follow-up (Mdn=42 U/L); p <0.001 and Z= -3.408 U/L (see Figure 6B).

Additionally, for patients with PvtHI, the collected ALT values were higher at baseline (Mdn= 455 U/L) than after 1-year follow-up (Mdn=33 U/L); p <0.001, Z= -3.621 U/L (see Figure 6B).

Finally, the IgG values for PubHI patients were also higher at baseline (Mdn=18 g/l) than after 1-year follow-up (Mdn=11 g/l); $p < 0.001$, Z= -3.408 g/l (see Figure 6C).

For PvtHI patients, IgG levels were similarly higher at baseline (Mdn=19 g/l) than after 1-year follow-up (Mdn=10 g/l); $p = 0.003$, Z= -2.970 g/l (see Figure 6C).

In summary, significant improvements in AST, ALT, and IgG levels were observed over time in both insurance groups. It can be deduced from the above that the higher reported values of AST, ALT, and IgG at baseline indicate the presence of liver inflammation in the two groups. However, after 1-year of treatment, the follow-up results of these laboratory measurements showed a significant drop in their levels, indicating improvement in the liver inflammation in the two groups and the success of treatment. Figure 6 A, B, and C present significant differences within the insurance groups over time. Detailed description of the statistical findings is presented in Appendix C.

As a summary, in this cohort, complete remission after 1-year of treatment was achieved in 5/17 PubHI and 10/17 PvtHI patients. Incomplete remission was observed in 12/17 of the PubHI patients and 7/17 of the PvtHI patients, where a persistent elevation in one or two of the biochemical markers was still observed after 1-year of treatment. Table 7 displays the number of patients with individual normalized laboratory values after 1-year, in addition to the number of patients who achieved complete remission (normalization of all three biochemical markers) between the two groups. No significant difference was observed between the number of PubHI and PvtHI patients with complete remission.

Table 7 Number of patients achieving biochemical remission after 1-year

Biochemical values at 1-year	PubHI (n=17)	PvtHI (n=17)
AST	12	11
ALT	6	11
IgG	15	15
Complete remission	5	10

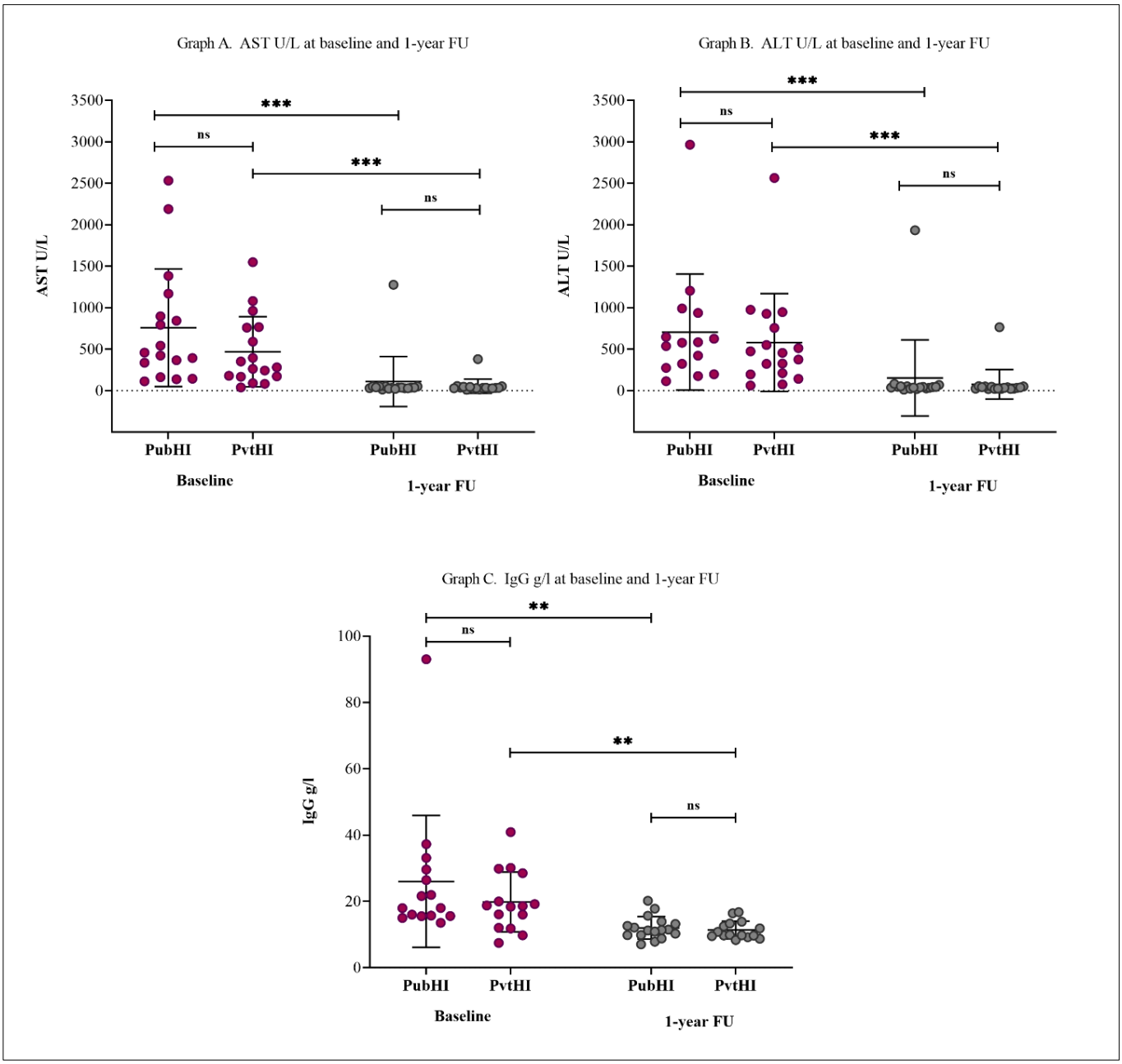

Figure 6 **Liver function tests and IgG at baseline and 1-year follow-up (FU) of PubHI and PvtHI patients**

Displays biochemical markers AST (A), ALT (B), and IgG (C). Individual data points, mean and SD are presented. Purple circles denote lab values at baseline and grey circles denote lab values at 1-year follow-up. *** P-value <0.001, ** P-value <0.01 and ns indicates non-significance. Significance tested by Mann-Whitney-U test between groups and Wilcoxon paired test within groups over time.

4.2 Survey data

A total of 34 surveys were distributed to the study participants, and 29 responses were received. The majority of responses (20 surveys) were submitted online, while only nine were returned by post. Of the total respondents, 16 had PubHI, and 13 had PvtHI. The analysis of the survey responses was carried out using the Mann-Whitney U test.

4.2.1 Health-related quality of life (HrQoL)

The patients' HrQoL was tested in eight subscales covering two dimensions: physical and psychosocial health. The average scores on each subscale of these two dimensions were compared between the two groups. There was no difference in overall HrQoL between the two groups (see Figure 7).

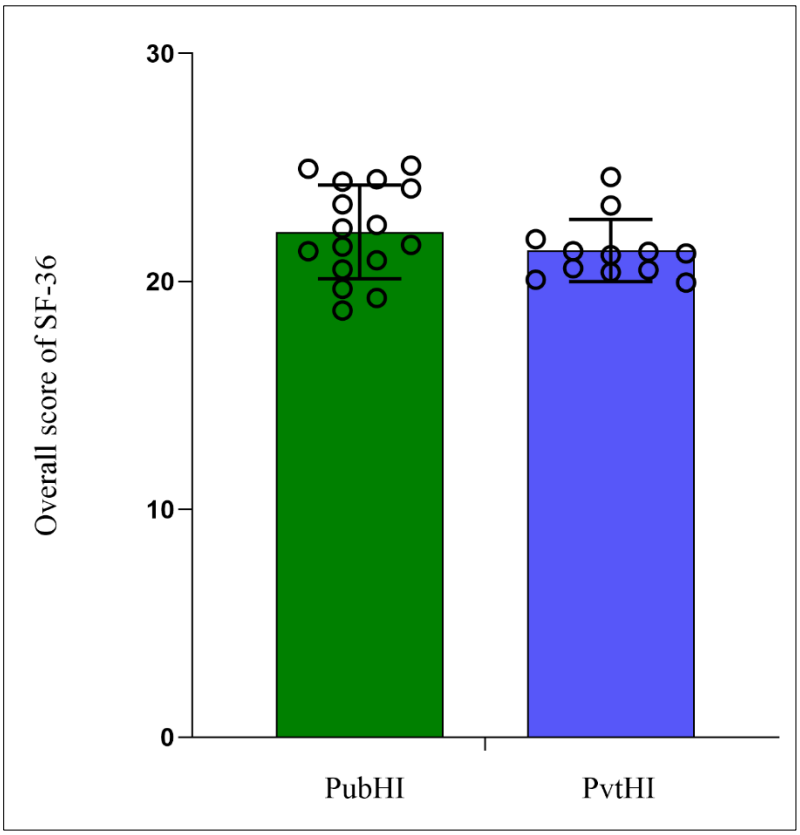

Figure 7 HrQoL overall score of PubHI and PvtHI patients

Displayed are individual data points with mean and SD of the overall score of SF-36 questionnaire for PubHI (green) and PvtHI (blue).

However, within the two dimensions, there was an observed difference in the physical dimension (p= 0.033, Z= -2.136) (see Figure 8).

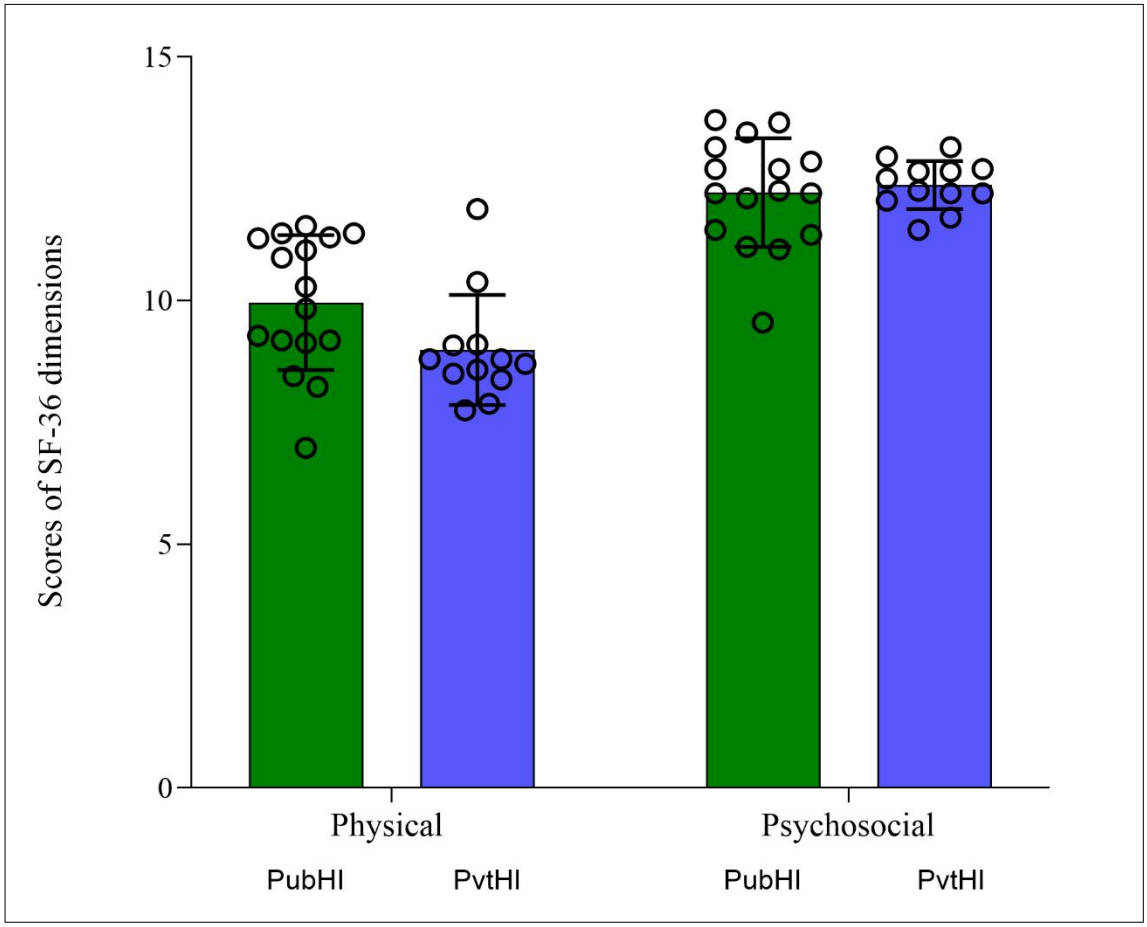

Figure 8 **SF-36 overall scores of the two dimensions**

Displayed are individual data points with mean and SD of the SF-36 questionnaire dimensions for PubHI (green) and PvtHI (blue).

The values of each subscale of the SF-36 questionnaire are displayed in Figure 9. High scores indicate better outcomes and performance in one group than in the other.

PubHI patients have better mean score value reported in the subscales “vitality” (p= 0.008, Z= -2.655) and “body pain” (p= 0.014, Z= -2.452) than PvtHI patients (see Figure 9).

Whereas, PvtHI patients have a better mean score reported in the subscales “role emotional” (p= 0.019, Z= -2.346) and “physical function” (p= 0.009, Z= -2.605) than PubHI patients (see Figure 9).

No differences were found in “social function”, “mental health”, “role physical”, and “general health” subscales between the two groups (see Figure 9).

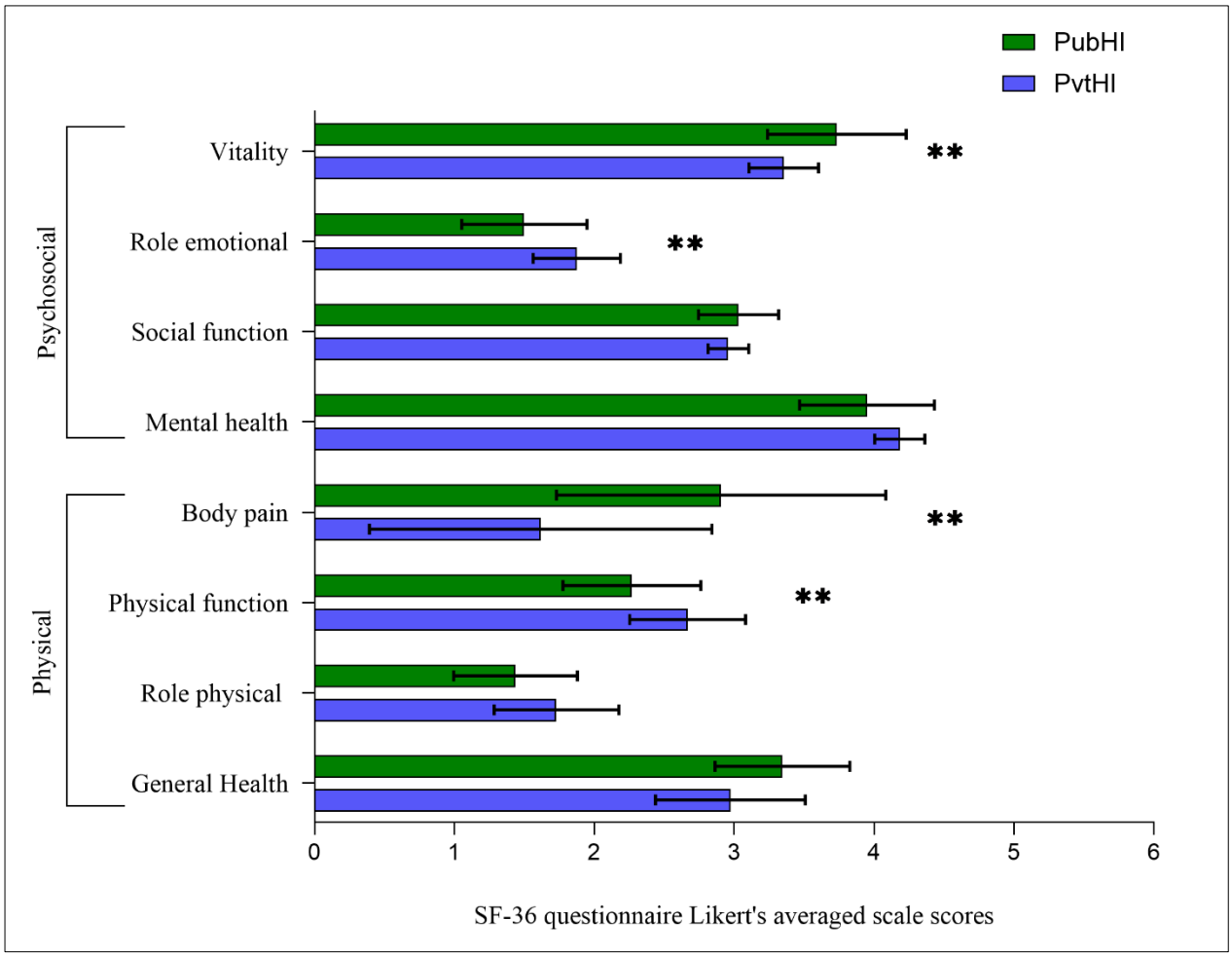

Figure 9 **Subscales of patients HrQoL in PubHI and PvtHI**

Displayed are group mean scores and SD of the 8 subscales of SF-36 questionnaire for PubHI (green) and PvtHI (blue). The lower 4 subscales belong to the physical dimension, the upper 4 subscales belong to the psychosocial dimension. ** P-value <0.01

4.2.2 Patient satisfaction

Patient satisfaction overall score was calculated and presented in Figure 10. Additionally, scores per subscale were calculated on a 5-point scale and compared between the two groups. With 1 reflecting lowest satisfaction and 5 reflecting highest satisfaction.

There was a difference in the overall satisfaction between the two groups (p= 0.031, Z = -2.154), suggesting that PvtHI patients tend to experience higher satisfaction with their healthcare than PubHI patients (see Figure 10).

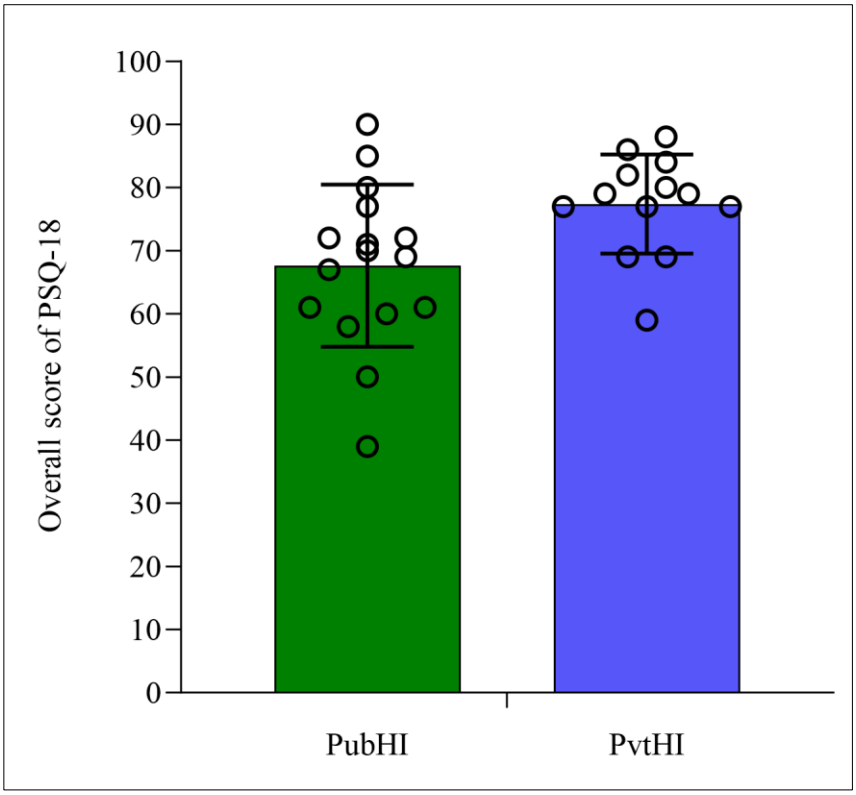

Figure 10 **Patient satisfaction with their healthcare for PubHI and PvtHI**

Displayed are individual data points with mean and SD of the PSQ-18 questionnaire for PubHI (green) and PvtHI (blue).

Descriptively, PvtHI patients displayed higher satisfaction with their healthcare than PubHI patients in three of the seven subscales. These subscales are “accessibility and convenience”, “financial aspect” and “technical quality”. No differences were observed

in “general satisfaction”, “interpersonal manner”, “communication”, and “time spent with the doctor” between the two groups (see Figure 11).

These observed differences in accessibility and convenience (p= 0.049, Z= -1.966), financial aspect (p= 0.031, Z= -2.162), and technical quality (p= 0.012, Z = -2.524), indicate that PvtHI patients report higher satisfaction in these subscales than PubHI patients (see Figure 11).

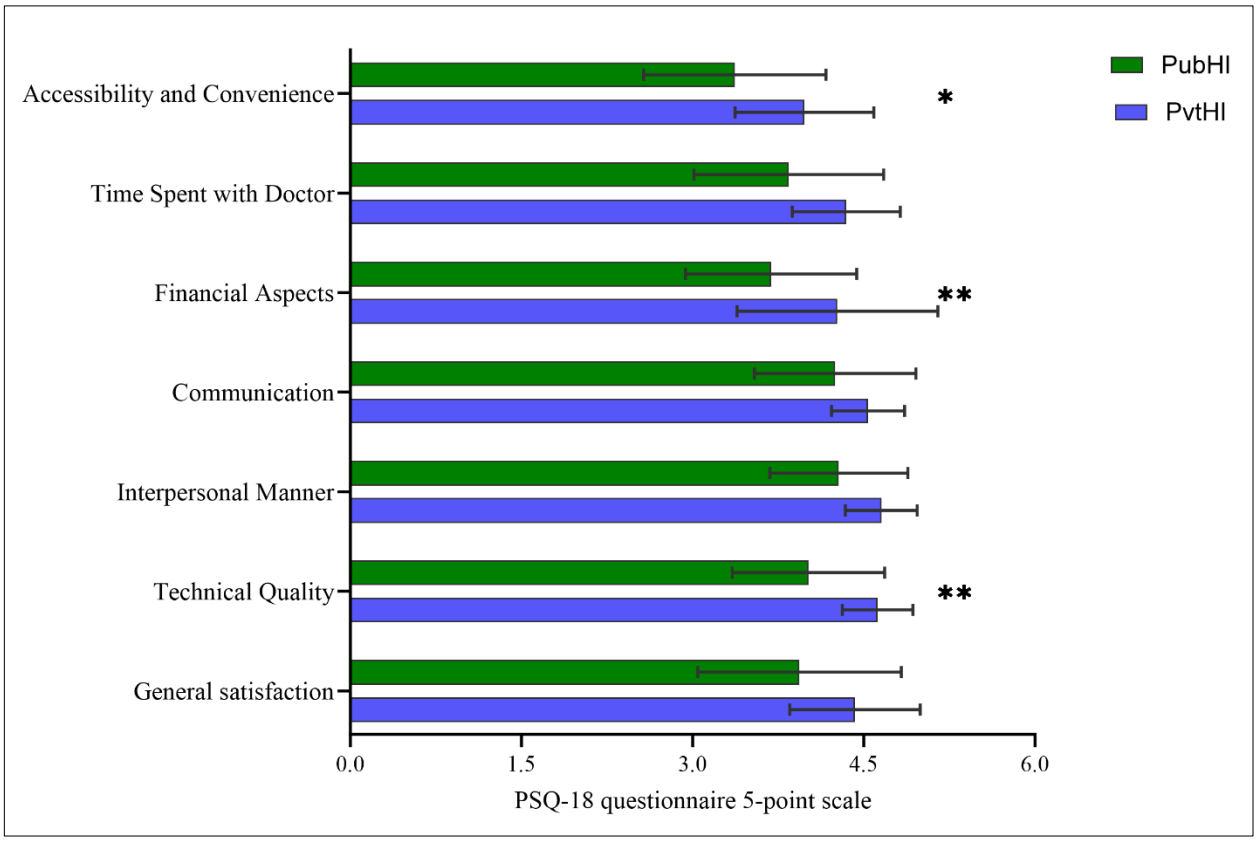

Figure 11 **Subscales of patient satisfaction with their healthcare in PubHI and PvtHI**

Displayed are group mean scores and SD of the 7 subscales of PSQ-18 questionnaire for PubHI (green) and PvtHI (blue). ** P-value <0.01, * P-value <0.05

4.2.3 Influence of biochemical remission on patient reported HrQoL and satisfaction

In addition to the above analysis of both surveys, this study also re-grouped patients to examine if participants’ HrQoL and satisfaction differed depending on their biochemical remission status. Group differences in survey results were analyzed between patients who

achieved complete remission and those with incomplete remission, irrespective of the insurance type.

Analysis of the PSQ-18 using Mann-Whitney U test revealed no significance in all subscales of this questionnaire except in "accessibility and convenience" subscale (p= 0.010, Z= -2.563). Indicating that patients with complete remission report to have better access to healthcare services than patients with incomplete remission.

Analysis of the SF-36 using Mann-Whitney U test revealed no significance in all subscales of this questionnaire.

4.3 Comparison of biochemical values

Displayed below are laboratory values of all PubHI patients in incomplete remission (Table 8) and PvtHI patients in incomplete remission (Table 9), obtained at baseline and after 1-year of treatment. Bold values are above normal threshold and indicate failure to achieve complete remission after 1-year.

Table 8 Biochemical values of PubHI patients with incomplete remission

AIH patients	AST U/L		ALT U/L		IgG g/l	
	Baseline	1-year	Baseline	1-year	Baseline	1-year
Patient 1- Male	842	49	1204	**52**	37,23	**20,16**
Patient 2- Male	144	49	322	**82**	16	9,85
Patient 3- Male	162	20	113	22	93	**17,78**
Patient 4-Female	1383	**37**	989	**47**	16	7,84
Patient 5- Female	112	32	196	**42**	16	11
Patient 6-Female	792	**49**	536	**37**	26,4	11
Patient 7- Female	542	**36**	647	**45**	21,93	11
Patient 8- Female	896	**40**	937	**38**	33,12	12
Patient 9- Female	392	**37**	273	**36**	29,6	13
Patient 10-Female	2532	**1276**	2965	**1934**	16	15

Normal reference range: AST and ALT: <50 U/L in males, and <35 U/L in females. IgG <16 in both. Bold denotes abnormal values after 1-year.

Table 9 Biochemical values for PvtHI patients with incomplete remission

AIH patients	AST U/L		ALT U/L		IgG g/l	
	Baseline	1-year	Baseline	1-year	Baseline	1-year
Patient 1- Male	961	**379**	2564	**764**	16	16
Patient 2- Female	1549	**55**	926	**49**	28,5	10,82
Patient 3- Female	262	34	326	**47**	30,1	8,73
Patient 4- Female	171	**51**	210	**41**	18	9,76
Patient 5- Female	1080	**45**	**947**	33	40,87	16

Normal reference range: AST and ALT: <50 U/L in males, and <35 U/L in females. IgG <16 in both. Bold denotes abnormal values after 1-year.

5. Discussion

This study investigated the impact of the two main health insurance schemes in Germany on the liver health of AIH patients. AIH patients with PvtHI were expected to have better liver health at baseline and at 1-year follow-up as compared to PubHI patients. However, the findings of this thesis showed that there were no differences in liver health between the two insurance groups at the two studied time points. However, the difference was observed within the same groups over time. This was demonstrated by the improved values of the liver surrogates after 1-year of treatment in both groups. This finding is inconsistent with what is already known from previous literature that patients with PvtHI in Germany are healthier than PubHI patients (3,58).

Patients with PvtHI have timely access to their doctors and are offered more innovative treatments and services (58). However, in the case of AIH, all patients are offered and treated with the same standard immunotherapy irrespective of the insurance type (27). This is because previous studies could show that this treatment delays disease progression, prolongs patient survival and is effective in the majority of patients (16,46).

The results of this thesis relate to a study investigating whether the advanced features of the PvtHI in Germany ensure better health. It was concluded that the health outcomes of PvtHI and PubHI patients did not differ (59). On the other hand, another study reported

that patients with PvtHI tend to be healthier and have fewer doctor visits because of the broad alternative treatments being prescribed compared to patients with PubHI (58). Doctors treating patients with PvtHI are compensated by the type and number of treatments prescribed to the patient, and not by the number of visits (58). Consequently, based on these findings, one could speculate that PvtHI patients experience better health outcomes than PubHI secondary to the more comprehensive healthcare services available under the PvtHI scheme.

Biochemical remission is the standard benchmark used by clinicians to reflect the regression of liver inflammation and improvement of the general health of the liver (16). But the low number of PubHI patients (5/17) who achieved full remission in this study compared to PvtHI patients (10/17) does not necessarily imply that PvtHI patients have better liver health than PubHI patients (see Table 7). Statistically, no difference was observed between the two insurance groups. This may have risen by chance, because while testing for significance of all patients who have complete remission and incomplete remission with the subscales of the satisfaction questionnaire, irrespective of the insurance type, the only observed difference was in "accessibility and convenience" subscale. This indicates that patients with complete remission in both insurance types are able to get appointments with the specialists fast, therefore, any disease progression or flares are detected early. This is not in line the common practice in the German health insurance system, where the waiting time for PvtHI patients to get an appointment is shorter than that for PubHI patients (59). In Germany, patients of both insurance types are entitled to out-of-hours services in cases of emergencies, and these services are covered by the state (1). However, patients with PvtHI still benefit from more advanced services that are paid separately by their insurance scheme (1,59).

Interestingly, the laboratory values of the patients who failed to achieve complete remission were elevated from the normal range only at a small margin (see Tables 8 and 9). Evidently, these patients showed a significant decline in their LFTs and IgG levels from the baseline. While these findings suggest improvement in liver inflammation, some patients did not attain complete biochemical remission as the serum levels of their LFTs and/or IgG remained above the normal threshold levels. Although the IAIHG have strict

protocols indicating that failure to achieve complete remission calls for treatment changes, such as dose escalation or switch of immunosuppressive drug, this may not be the most relevant indicator in clinical practice. In daily practice, hepatologists at UKE also consider other factors such as side effects, presence of other comorbidities, drug intolerance, poor treatment adherence or failure and disease history to decide on the need to intensify or change treatment (16,38). In fact, out of the 17 patients from the PubHI, only one patient had strongly elevated LFTs results after 1-year (Patient 10- Female, Table 8). The same is observed in the PvtHI patients, only one patient had high laboratory values after 1-year (Patient 1- Male, Table 9).

There is increasing evidence that patients with AIH suffer from symptoms that affect their general well-being (60). It is commonly known that the QoL of patients is affected by the disease course over time, presence of other comorbidities, or even treatment side effects (47). The reported or perceived HrQoL of AIH patients is an important measure impacting treatment decisions (61). The PvtHI has been reported to positively impact health (59) and it can be assumed that this also improves HrQoL. However, in this study, this was not the case, as no difference in HrQoL was detected between the two insurance groups. This does not align with previous data revealing that patients with PvtHI tend to rate their health status more positively than patients with PubHI (58).

In four of the eight subscales of the SF-36 questionnaire significant differences between the two groups were found. The difference observed in the vitality subscale between the two insurance groups is a possible indication that patients with PubHI have higher vitality than PvtHI, meaning that PubHI patients are less fatigued and have better energy than PvtHI patients. Despite that more patients in the PvtHI showed complete remission in response to treatment than the PubHI. Studies have reported fatigue to be one of the prominent symptoms in chronic liver diseases, specifically in patients with AIH (45,47,60). Furthermore, the difference observed in body pain between the two groups revealed that patients with PubHI tend to experience less pain and have less pain-related limitations than PvtHI patients.

The same pattern was observed in role emotional subscale, the group difference suggests that patients with the PvtHI have fewer problems with work and with their daily activities. Unlike PubHI patients, whose illness impacts their ability to work and their day-to-day activities more. No difference was found between the two groups in this study when comparing employment status between the PvtHI and PubHI. However, three patients from PubHI reported retiring due to illness compared to none from PvtHI (see Table 5). Finally, the last group difference was observed in physical function, patients with PubHI are limited in performing some of their daily life activities, such as bathing or dressing. In contrast, patients with PvtHI seem to perform better and experience less limitations in daily life.

A central finding observed in this study was that HrQoL of AIH patients was not affected by either complete remission or incomplete remission. Both groups (complete and incomplete remission) showed no differences in QoL. In contrast to a recent study that reported higher HrQoL in AIH patients with complete remission than in those with incomplete remission (47).

Overall, no difference was detected between the two groups in HrQoL. Interestingly, a single-center study using the SF-12 questionnaire reported that the physical well-being of patients with AIH is less severely impacted than their mental well-being (61). This does not match the finding of this study. Since it was found that on average all patients reported higher scores for the psychosocial dimension than the physical dimension. In a Polish study using different questionnaires to evaluate health outcomes and satisfaction of AIH patients, it was also found that the HrQoL of AIH patients was impaired compared to the healthy group, and they scored worse in almost all studied domains of these questionnaires (60). The most pronounced significant findings of this study were impairment by depression, fatigue, and anxiety (60).

Similarly, the analysis of the PSQ-18 questionnaire showed that a difference is present in the overall satisfaction of the two insurance groups, where PvtHI patients have a higher score than PubHI, but the absolute difference in mean values is moderate. This contradicts

the study reporting that the type of healthcare insurance does not have a significant influence on patient satisfaction (62).

For instance, the majority of the patients in the two groups had overall scores ranging between 50 and 90 points in the PSQ-18 questionnaire. Among them, only one patient in the PubHI group had the least favorable overall score of 39 points. While exploring the patient's individual survey responses and comparing with his laboratory values, he had incomplete remission after 1-year, with only ALT above the normal range (82 U/L) (Patient-2 Male, Table 8). In comparison, a patient from the PvtHI who scored 77 in the overall PSQ-18 questionnaire, had worse laboratory values were worse. He did not achieve remission after 1-year and had persistently elevated levels of AST (379 U/L) and ALT (764 U/L) (Patient 1- Male, Table 9). This opens the possibility to speculate that satisfaction is not related to illness severity, which is in line with a study reporting that reasons seeking medical attention (sickness, treatment, or preventative measures) do not have a significant correlation with satisfaction (62). However, such a hypothesis would have to be tested for systematically across a cohort.

The difference in subscale "accessibility and convenience" observed in this study may not reflect the true picture if patients with PubHI are not satisfied because they are unable to receive medical care when needed and have to wait longer for doctors' appointments as compared to PvtHI. But the finding relates to the reported results of a Chinese study, where convenience of healthcare centers was reported to have a significant effect on patient satisfaction (62). Moreover, a typical practice in the German health insurance system is that PvtHI patients are preferentially selected by physicians and given faster appointment times than PubHI patients (3,56).

Interestingly, it was found while testing for group differences of PSQ-18 subscales between patients with complete remission and incomplete remission, without taking into consideration the insurance type, that "accessibility and convenience" showed a significant difference. This indicates that patients with complete remission might have received better access to healthcare services than patients with incomplete remission.

The financial aspect was shown to affect satisfaction to a certain extent between the two groups of this study. This aligns with a study reporting that reimbursement is an important factor to patient satisfaction, but the outcome did not show a strong influence on the overall patient satisfaction (62). Furthermore, in this study, the resulting difference in technical quality is probably because AIH patients with PubHI are treated by general and junior doctors (58). Whereas, the PvtHI patients are treated by senior specialists or head doctors (58). A Chinese study investigating factors that influence patient satisfaction reported that competencies and attitudes of medical staff have a significant effect on patient satisfaction (62). Moreover, physicians tend to choose to treat PvtHI patients first because of the higher tariffs received from them (3,58). If patients are satisfied with their doctors, they tend to adhere more to their treatment (21). In this study, PvtHI patients have higher remission rates than PubHI and they reported better overall satisfaction with the healthcare services than PubHI.

A limitation of this study is the inclusion of the study cohort from a single center, the University Medical Center Hamburg-Eppendorf, and the small sample size. Thus, there is a risk of bias. The sample may not be sufficient to represent actual differences between groups and does not allow for generalization. Some of the differences may have occurred only by chance. Additionally, other liver tests could have been used to assess the differences in liver inflammation between the two groups, however, due to the short period of time for the completion of this thesis study, only the primary laboratory values (AST, ALT, and IgG) were used. Therefore, for the future, in order to have robust findings, bigger sample size, possibly collecting data from multiple centers need to be used. In addition, it would be advisable to expand the parameters to monitor liver health, such as autoantibodies and liver histology findings.

Moreover, the survey to assess satisfaction and QoL was distributed during the running time of this master's thesis, without considering the diagnosis date of patients, which ranged from 2-6 years. Hence, the responses likely reflect current patients experience with their healthcare system and not upon initial diagnosis. Therefore, creating a mismatch in time between measurements of liver inflammation and survey data. To tackle this in future

research, the implementation of a prospective study can be useful. Patients can be systematically monitored and tracked from the diagnosis date while simultaneously being surveyed to collect data on their experiences with the healthcare system and their liver health. This is helpful to better understand how patient experiences, quality of life and liver health evolve during the provision of the healthcare services over time. Moreover, internal and external validity of the PSQ-18 questionnaire was validated in the US population but not in the German population and has been used for this study solely for experimental analysis. Finally, there was a higher response rate of PubHI patients to the survey than PvtHI patients.

6. Conclusion

This thesis investigated AIH patients' QoL and experiences with their healthcare and the impact of insurance on the remission of liver inflammation. A key finding is that AIH patients of both PvtHI and PubHI have an overall improvement in the liver inflammation. This is a positive outcome indicating successful treatment and close monitoring of these patients at UKE. Effective care and improvement of health for patients with AIH is a substantial goal of the ERN RARE-LIVER. And from this study, UKE can obtain preliminary feedback on the services and care provided to patients.

Other findings of this thesis showed that PvtHI reported higher satisfaction with their healthcare. QoL differed in some aspects between groups, whereas overall QoL did not differ. Instead, it is bound to inform future research on the need to consider exploring other factors affecting patient satisfaction with healthcare services. Such as investigating patient perceptions and personal experiences with the healthcare services. Hence, pushing healthcare systems to develop patient care pathways, especially for patients with rare diseases. To standardize care and switch from a disease-centered approach to patient-centered care will aim to improve the provision and quality of healthcare services of AIH patients. This can be applied to UKE in the meantime, but it can also serve other ERN RARE-LIVER centers in Europe and support their patients in the future.

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Declaration of academic honesty

I hereby declare that I have completed this thesis paper entirely on my own, and without any other materials and resources than those specified and enlisted. I further declare that I have fully referenced all ideas and verbatim quotations taken from other works.

Hamburg, 08.03.2024

_____

Nagham Issa

Appendices

Appendix A. Non-parametric Mann-Whitney U test output of lab values showing differences between groups at baseline

Statistics at baseline	AST U/L	ALT U/L	IgG g/l
Mean	613	638	23
SD	593	637	16
Median	393	492	19
Mann-Whitney U	107	106	101
Z	-1.292	-.812	-.477
Asymp. Sig (2-tailed)	.196	.417	.633

P-value <0.05

Appendix B. Non-parametric Mann-Whitney U test output of lab values showing differences between groups at 1-year follow-up

Statistics at 1-year FU	AST U/L	ALT U/L	IgG g/l
Mean	80	114	12
SD	220	345	3
Median	34	38	11
Mann-Whitney U	128	113	107
Z	-.586	-1.103	-.774
Asymp. Sig (2-tailed)	.558	.270	.439

P-value <0.05

Appendix C. Non-parametric Wilcoxon-related test output of laboratory values showing differences within groups at baseline and 1-year follow-up

Insurance	Statistics	AST U/L		ALT U/L		IgG g/l	
		base-line	1-year FU	base-line	1-year FU	base-line	1-year FU
Private	Median	280	31	455	33	19	10
	Mean	468	53	580	76	20	11
	SD	423	85	591	178	9	3
Z (*baseline vs 1-year FU PvtHI)*		-3.621		-3.621		-2.970	
P-value (*baseline vs 1-year FU PvtHI)*		**<.001**		**<.001**		**.003**	
Public	Median	249	36	577	42	18	11
	Mean	757	108	704	152	26	12
	SD	709	301	700	459	20	3
Z (*baseline vs 1-year FU PubHI)*		-3.621		-3.408		-3.408	
P-value (*baseline vs 1-year FU PubHI)*		**<.001**		**<.001**		**<.001**	

P-values in bold denote significance ($p<0.05$)

Appendix D. Demographic data collected in survey

2 Allgemeine Informationen

Vorname und Nachname:

Datum:

In welchem Jahr sind Sie geboren?

Welches Geschlecht haben Sie?

- männlich
- weiblich
- divers

Was ist Ihr höchster Schulabschluss?

- Kein Schulabschluss
- Volks- oder Hauptschulabschluss
- Mittlere Reife
- Fachabitur
- Abitur
- Hochschul-/Fachhochschulabschluss

Sind Sie aktuell angestellt oder freiberuflich tätig?

- Ja, in Vollzeit
- Ja, in Teilzeit
- Nein, in Rente
- Nein, in Ausbildung oder Umschulung
- Nein, Arbeitslos
- Nein, anderes

Nein, in Rente

- Altersrente
- Erwerbsunfähigkeit

anderes

Wie sind Sie krankenversichert?

- gesetzlich versichert
- privat versichert

Falls Sie gesetzlich versichert sind, sind Sie

- gesetzlich pflichtversichert
- freiwillig gesetzlich versichert
- weiß nicht

Falls Sie privat versichert sind, sind Sie Beamter?

- Ja
- Nein

Bei welcher Krankenkasse sind Sie versichert?

Appendix E. SF-36 questionnaire. German, original

Universitätsklinikum Hamburg-Eppendorf

Fragebogen zum Gesundheitszustand (SF-36)

In diesem Fragebogen geht es um Ihre Beurteilung Ihres Gesundheitszustandes. Der Bogen ermöglicht es, im Zeitverlauf nachzuvollziehen, wie Sie sich fühlen und wie Sie im Alltag zurechtkommen.

Bitte beantworten Sie jede der folgenden Fragen, indem Sie bei den Antwortmöglichkeiten die Zahl ankreuzen, die am besten auf Sie zutrifft.

1. Wie würden Sie Ihren Gesundheitszustand im Allgemeinen beschreiben ?

(Bitte kreuzen Sie nur eine Zahl an)

Ausgezeichnet..... 1

Sehr gut..... 2

Gut..... 3

Weniger gut..... 4

Schlecht..... 5

2. Im Vergleich zum vergangenen Jahr, wie würden Sie Ihren derzeitigen Gesundheitszustand beschreiben ?

(Bitte kreuzen Sie nur eine Zahl an)

Derzeit viel besser als vor einem Jahr..... 1

Derzeit etwas besser als vor einem Jahr..... 2

Etwa so wie vor einem Jahr..... 3

Derzeit etwas schlechter als vor einem Jahr..... 4

Derzeit viel schlechter als vor einem Jahr..... 5

3. Im folgenden sind einige Tätigkeiten beschrieben, die Sie vielleicht an einem normalen Tag ausüben. Sind Sie durch Ihren derzeitigen Gesundheitszustand bei diesen Tätigkeiten eingeschränkt ? Wenn ja, wie stark ?

(Bitte kreuzen Sie in jeder Zeile nur eine Zahl an)

TÄTIGKEITEN	Ja, stark eingeschränkt	Ja, etwas eingeschränkt	Nein , überhaupt nicht eingeschränkt
a. anstrengende Tätigkeiten, z.B. schnell laufen, schwere Gegenstände heben, anstrengenden Sport treiben	1	2	3
b. mittelschwere Tätigkeiten, z.B. einen Tisch verschieben, staubsaugen, kegeln, Golf spielen	1	2	3
c. Einkaufstaschen heben oder tragen	1	2	3
d. mehrere Treppenabsätze steigen	1	2	3
e. einen Treppenabsatz steigen	1	2	3
f. sich beugen, knien, bücken	1	2	3
g. mehr als 1 Kilometer zu Fuß gehen	1	2	3
h. mehrere Straßenkreuzungen weit zu Fuß gehen	1	2	3
i. eine Straßenkreuzung weit zu Fuß gehen	1	2	3
j. sich baden oder anziehen	1	2	3

4. Hatten Sie in den vergangenen 4 Wochen aufgrund Ihrer körperlichen Gesundheit irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten im Beruf bzw. zu Hause ?

(Bitte kreuzen Sie in jeder Zeile nur eine Zahl an)

SCHWIERIGKEITEN	JA	NEIN
a. Ich konnte nicht so lange wie üblich tätig sein	1	2
b. Ich habe weniger geschafft als ich wollte	1	2
c. Ich konnte nur bestimmte Dinge tun	1	2
d. Ich hatte Schwierigkeiten bei der Ausführung (z.B. ich mußte mich besonders anstrengen)	1	2

5. Hatten Sie in den vergangenen 4 Wochen aufgrund seelischer Probleme irgendwelche Schwierigkeiten bei der Arbeit oder anderen alltäglichen Tätigkeiten im Beruf bzw. zu Hause (z.B. weil Sie sich niedergeschlagen oder ängstlich fühlten) ?

(Bitte kreuzen Sie in jeder Zeile nur eine Zahl an)

SCHWIERIGKEITEN	JA	NEIN
a. Ich konnte nicht so lange wie üblich tätig sein	1	2
b. Ich habe weniger geschafft als ich wollte	1	2
c. Ich konnte nicht so sorgfältig wie üblich arbeiten	1	2

6. Wie sehr haben Ihre körperliche Gesundheit oder seelischen Probleme in den vergangenen 4 Wochen Ihre normalen Kontakte zu Familienangehörigen, Freunden, Nachbarn oder zum Bekanntenkreis beeinträchtigt?

(Bitte kreuzen Sie nur eine Zahl an)

Überhaupt nicht..... 1

Etwas..... 2

Mäßig..... 3

Ziemlich..... 4

Sehr..... 5

7. Wie stark waren Ihre Schmerzen in den vergangenen 4 Wochen ?

(Bitte kreuzen Sie nur eine Zahl an)

Ich hatte keine Schmerzen..... 1

Sehr leicht 2

Leicht..... 3

Mäßig..... 4

Stark..... 5

Sehr stark..... 6

8. Inwieweit haben die Schmerzen Sie in den vergangenen 4 Wochen bei der Ausübung Ihrer Alltagstätigkeiten zu Hause und im Beruf behindert ?

(Bitte kreuzen Sie nur eine Zahl an)

Überhaupt nicht..... 1

Ein bißchen..... 2

Mäßig..... 3

Ziemlich..... 4

Sehr..... 5

9. In diesen Fragen geht es darum, wie Sie sich fühlen und wie es Ihnen in den vergangenen 4 Wochen gegangen ist. (Bitte kreuzen Sie in jeder Zeile die Zahl an, die Ihrem Befinden am ehesten entspricht). Wie oft waren Sie in den vergangenen 4 Wochen...

(Bitte kreuzen Sie in jeder Zeile nur eine Zahl an)

BEFINDEN	Immer	Meistens	Ziemlich oft	Manch-Mal	Selten	Nie
a. ...voller Schwung	1	2	3	4	5	6
b. ...sehr nervös	1	2	3	4	5	6
c. ...so niedergeschlagen, daß Sie nichts aufheitern konnte ?	1	2	3	4	5	6
d. ...ruhig und gelassen	1	2	3	4	5	6
e. ...voller Energie?	1	2	3	4	5	6
f. ...entmutigt und traurig	1	2	3	4	5	6
g. ...erschöpft	1	2	3	4	5	6
h. ... glücklich	1	2	3	4	5	6
i. ...müde	1	2	3	4	5	6

9. Wie häufig haben Ihre körperliche Gesundheit oder seelischen Probleme in den vergangenen 4 Wochen Ihre Kontakte zu anderen Menschen (Besuche bei Freunden, Verwandten usw.) beeinträchtigt?

(Bitte kreuzen Sie nur eine Zahl an)

Immer..... 1

Meistens..... 2

Manchmal..... 3

Selten..... 4

Nie..... 5

10. Inwieweit trifft jede der folgenden Aussagen auf Sie zu ?

(Bitte kreuzen Sie in jeder Zeile nur eine Zahl an)

AUSSAGEN	Trifft ganz zu	Trifft weit-gehend zu	Weiß nicht	Trifft weitgehend nicht zu	Trifft überhaupt nicht zu
a. Ich scheine etwas leichter als andere krank zu werden	1	2	3	4	5
b. Ich bin genauso gesund wie alle anderen, die ich kenne	1	2	3	4	5
c. Ich erwarte, daß meine Gesundheit nachläßt	1	2	3	4	5
d. Ich erfreue mich ausgezeichneter Gesundheit	1	2	3	4	5

11. Wie würden Sie Ihren derzeitigen Gesundheitszustand beschreiben ?

sehr gut o gut o mittelmäßig o schlecht o sehr schlecht o

12. Im Folgenden finden Sie eine Reihe von Aussagen. Bitte Kreuzen (X) Sie in jeder Reihe an, ob diese für Sie zutrifft oder nicht.

	JA	NEIN
Ich bin andauernd müde	0	0
Ich habe nachts Schmerzen	0	0
Ich fühle mich niedergeschlagen	0	0
Ich habe unerträgliche Schmerzen	0	0
Ich nehme Tabletten, um schlafen zu können	0	0
Ich habe vergessen, wie es ist Freude zu empfinden	0	0
Ich fühle mich gereizt	0	0
Ich finde es schmerzhaft, meine Körperposition zu verändern	0	0
Ich fühle mich einsam	0	0
Ich kann mich nur innerhalb des Hauses bewegen	0	0
Es fällt mir schwer mich zu bücken	0	0
Alles strengt mich an	0	0
Ich wache in den frühen Morgenstunden auf	0	0
Ich kann überhaupt nicht gehen	0	0
Es fällt mir schwer, zu anderen Menschen Kontakt aufzunehmen	0	0
Die Tage ziehen sich	0	0
Ich habe Schwierigkeiten Treppen hinauf- und hinunterzugehen	0	0
Es fällt mir schwer nach Gegenständen zu greifen	0	0
Ich habe Schmerzen beim Gehen	0	0
Mir reißt derzeit oft der Geduldsfaden	0	0
Ich fühle, daß ich niemanden nahestehe	0	0
Ich liege nachts die meiste Zeit wach	0	0
Ich habe das Gefühl, die Kontrolle zu verlieren	0	0
Ich habe Schmerzen, wenn ich stehe	0	0
Es fällt mir schwer mich selbst anzuziehen	0	0
Meine Energie läßt schnell nach	0	0
Es fällt mir schwer lange zu stehen (z.B. am Spülbecken, an der Bushaltestelle)	0	0
Ich habe andauernd Schmerzen	0	0
Ich brauche lange zum Einschlafen	0	0
Ich habe das Gefühl für andere Menschen eine Last zu sein	0	0
Sorgen halten mich nachts wach	0	0
Ich fühle, daß das Leben nicht lebenswert ist	0	0
Ich schlafe nachts schlecht	0	0
Es fällt mir schwer mit anderen Menschen auszukommen	0	0
Ich brauche Hilfe, wenn ich mich außer Haus bewegen will (Stock oder jemand, der mich stützt)	0	0
Ich habe Schmerzen, wenn ich Treppen hinauf- und hinuntergehe	0	0
Ich wache deprimiert auf	0	0
Ich habe Schmerzen, wenn ich sitze	0	0

Appendix F. PSQ-18 questionnaire, German, translated

KURZFRAGEBOGEN ZUR PATIENTENZUFRIEDENHEIT (PSQ-18)

Bei den nachfolgenden Fragen geht es darum, wie Sie die medizinische Versorgung empfinden die Sie erhalten.
Auf den folgenden Seiten finden Sie einige Dinge, die Menschen über die medizinische Versorgung sagen. Bitte lesen Sie jede Aussage sorgfältig durch und denken Sie dabei an die medizinische Versorgung, die Sie selbst zurzeit in unserem Zentrum erhalten. (Wenn Sie in letzter Zeit nicht behandelt wurden, überlegen Sie, was Sie erwarten würden, wenn Sie heute behandelt werden müssten).
Wir sind daran interessiert, wie Sie Ihre medizinische Versorgung, –empfinden, die guten und die schlechten Aspekte.

Wie sehr stimmen Sie jeder der folgenden Aussagen zu?

1. Die Ärzte sind gut darin, zu erklären, warum medizinische Untersuchungen gemacht werden.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu

11

   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

2. Ich denke, meine Arztpraxis Verfügt über alles, was benötigt wird, um meine vollständige medizinische Versorgung zu gewährleisten.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

3. Die medizinische Versorgung, die ich erhalten habe ist perfekt.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

4. Manchmal frage ich mich, ob die Diagnose meiner Ärzte die richtige ist.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

5. Ich bin mir sicher, dass ich die medizinische Versorgung, die ich brauche, bekommen kann, ohne finanzielle Einbußen zu fürchten.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

6. Wenn ich zur medizinischen Versorgung gehe, wird alles sorgfältig überprüft.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher
   - Ich stimme eher nicht zu
   - Ich stimme gar nicht zu

7. Ich muss mehr für meine medizinische Versorgung bezahlen als ich es mir leisten kann.
   - Ich stimme voll und ganz zu
   - Ich stimme eher zu
   - Unsicher

12

- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

8. Ich habe einen einfachen Zugang zu den Fachärzten, die ich brauche.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

9. Dort, wo ich medizinische Versorgung erhalte, müssen die Menschen bei Notfällen zu lange auf Behandlung warten.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

10. Ärzte benehmen sich mir gegenüber zu geschäftsmäßig und zu unpersönlich.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

11. Meine Ärzte gehen mit mir sehr freundlich und höflich.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

12. Diejenigen, die mich medizinisch betreuen, nehmen sich zu wenig Zeit für mich.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

13. Die Ärzte ignorieren manchmal, was ich ihnen.
- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

14. Ich habe Zweifel an der Fähigkeit, der Ärzte, die mich behandeln.

- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

15. Ärzte nehmen sich in der Regel viel Zeit für mich.

- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

16. Ich finde es schwierig, für eine schnelle medizinische Versorgung einen Termin zu bekommen.

- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

17. Ich bin mit einigen Dingen unzufrieden die meine medizinische Versorgung betreffen.

- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

18. Es ist mir möglich, medizinische Versorgung zu erhalten wann immer ich sie brauche.

- Ich stimme voll und ganz zu
- Ich stimme eher zu
- Unsicher
- Ich stimme eher nicht zu
- Ich stimme gar nicht zu

Fragen, Anregungen oder Kritik

Vielen Dank

Appendix G. PSQ-18 questionnaire, English, original

SHORT-FORM PATIENT SATISFACTION QUESTIONNAIRE (PSQ-18)

These next questions are about how you feel about the medical care you receive.

On the following pages are some things people say about medical care. Please read each one carefully, keeping in mind the medical care you are receiving now. (If you have not received care recently, think about what you would expect if you needed care today.) We are interested in your feelings, good and bad, about the medical care you have received.

How strongly do you AGREE or DISAGREE with each of the following statements?

(Circle One Number on Each Line)

	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
1. Doctors are good about explaining the reason for medical tests	1	2	3	4	5
2. I think my doctor's office has everything needed to provide complete medical care	1	2	3	4	5
3. The medical care I have been receiving is just about perfect	1	2	3	4	5
4. Sometimes doctors make me wonder if their diagnosis is correct	1	2	3	4	5
5. I feel confident that I can get the medical care I need without being set back financially	1	2	3	4	5
6. When I go for medical care, they are careful to check everything when treating and examining me	1	2	3	4	5
7. I have to pay for more of my medical care than I can afford	1	2	3	4	5
8. I have easy access to the medical specialists I need	1	2	3	4	5

How strongly do you AGREE or DISAGREE with each of the following statements?

(Circle One Number on Each Line)

	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
9. Where I get medical care, people have to wait too long for emergency treatment	1	2	3	4	5
10. Doctors act too businesslike and impersonal toward me	1	2	3	4	5
11. My doctors treat me in a very friendly and courteous manner	1	2	3	4	5
12. Those who provide my medical care sometimes hurry too much when they treat me	1	2	3	4	5
13. Doctors sometimes ignore what I tell them	1	2	3	4	5
14. I have some doubts about the ability of the doctors who treat me	1	2	3	4	5
15. Doctors usually spend plenty of time with me	1	2	3	4	5
16. I find it hard to get an appointment for medical care right away	1	2	3	4	5
17. I am dissatisfied with some things about the medical care I receive	1	2	3	4	5
18. I am able to get medical care whenever I need it	1	2	3	4	5

Appendix H. SF-36 description of low and high scores

Concepts	No. of Items	No. of Levels	Low	High
Physical Functioning	10	21	Limited a lot in performing all physical activities including bathing or dressing due to health	Performs all types of physical activities including the most vigorous without limitations due to health
Role–Physical	4	5	Problems with work or other daily activities as a result of physical health	No problems with work or other daily activities as a result of physical health
Bodily Pain	2	11	Very severe and extremely limiting pain	No pain or limitations due to pain
General Health	5	21	Evaluates personal health as poor and believes it is likely to get worse	Evaluates personal health as excellent
Vitality	4	21	Feels tired and worn out all of the time	Feels full of pep and energy all of the time
Social Functioning	2	9	Extreme and frequent interference with normal social activities due to physical or emotional problems	Performs normal social activities without interference due to physical or emotional problems
Role–Emotional	3	4	Problems with work or other daily activities as a result of emotional problems	No problems with work or other daily activities as a result of emotional problems
Mental Health	5	26	Feelings of nervousness and depression all of the time	Feels peaceful, happy, and calm all of the time