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Quality of Life and Psychosocial Outcomes in Adults with Congenital Heart Disease

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Abstract

Due to medical advances in treatment and care of congenital heart defects (CHD), the survival rate of adults with congenital heart disease (ACHD) has increased substantially. Despite these improvements, nearly all ACHD remain chronically ill with challenges reaching far beyond physical limitations. In particular, mental health problems, such as depression, anxiety, and post-traumatic stress disorder (PTSD) can become a serious burden. Yet, knowledge of the psychological situation in ACHD and their need for psychological support remains limited. This dissertation contains one narrative review and three subsequent studies conducted in quantitative-based cross-sectional design in order to investigate quality of life (QOL) and psychological outcomes explicating novel indices of adaption to CHD. The narrative review synthesizes the current state of knowledge on the prevalence of emotional distress in ACHD and provides the basis for further quantitative studies in this field. The second study investigates the correlation of QOL in over 4,000 German ACHD with various patient-related and clinical variables. To identify psychological effects of illness on a patient's self-perception, the third study investigates the novel framework of illness identity and its effects on psychological outcomes among ACHD. A fourth study was conducted to evaluate QOL in a distinct subset of patients with Marfan syndrome (MFS), which is an inherited multiorgan disease with far-reaching psychosocial consequences. Widely held assumptions among clinicians are that chronic illness inevitably causes diminished well-being. However, present findings suggest that ACHD do experience a generally good QOL. Remarkably, the severity of CHD was positively associated with QOL overall. However, specific subgroups, especially patients affected by MFS, may require additional attention and support to cope with disease-related challenges. A patient's illness identity might play an important role in psychological adjustment to CHD. Unique differences in depression and anxiety among ACHD were revealed by in-depth investigation of illness identity. Maladaptive illness identity states (i.e., engulfment and rejection) predicted higher levels of emotional distress, whereas adaptive illness identity states (i.e., acceptance and enrichment) were linked to better psychological functioning. The overall extent of emotional distress differed in relation to a patient's self-rated health, but not as a function of CHD complexity.

This dissertation provides novel insights into clinical and psychosocial factors associated with psychological well-being within a considerable sample of ACHD. The findings strengthen the hypothesis that the subjective burden of illness constitutes a stronger determining factor of overall psychological adjustment than the actual illness. This dissertation generated crucial findings for guiding future research and, especially, clinical practice for ACHD. More importance needs to be directed towards assessing a patient's health perception, illness identity, and psychological functioning, independent of the cardiac condition. To this end, ACHD require an integrated concept for holistic care in which multidisciplinary professionals collaborate closely to meet the complex psychosocial needs of ACHD and to provide a complete and effective treatment. Practical and theoretical insights acquired within this dissertation could also be applied to the study and potential management of other types of chronic illness.

Keywords: adults with congenital heart disease; psychological situation; psychocardiology; prevention

Zusammenfassung

Dank moderner Behandlungsmethoden ist die Überlebensrate von Erwachsenen mit angeborenen Herzfehlern (EMAH) erheblich gestiegen. Dennoch ist die Mehrzahl von ihnen als chronisch krank einzustufen. Die Herausforderungen ihrer Erkrankung gehen weit über die körperlichen Einschränkungen hinaus. Aktuellen Erkenntnissen zufolge, weisen EMAH ein signifikant höheres Risiko für psychische Komorbiditäten, wie Depression, Angst und posttraumatischer Belastungsstörung (PTBS) auf. Derzeit ist das Wissen um die psychische Situation bei EMAH relativ begrenzt und der Bedarf an psychologischer Betreuung nur minimal gedeckt. Die vorliegende Dissertation untersucht Auswirkungen des angeborenen Herzfehlers (AHF) auf die Lebensqualität und das psychische Wohlbefinden bei EMAH. Außerdem werden Muster der Krankheitsverarbeitung bei EMAH zum tieferen Verständnis ihrer psychischen Situation erhoben. Die Dissertation umfasst einen Literaturreview, auf dem drei weiterführende Studien in quantitativ-basierten Querschnittsdesigns aufbauen. Der Literaturreview fasst den aktuellen Kenntnisstand zur Prävalenz psychischer Belastungsstörungen bei EMAH zusammen. Die zweite Studie untersucht die Lebensqualität von EMAH innerhalb einer Kohorte von über 4.000 Patienten unter Berücksichtigung verschiedener patientenbezogener und klinischer Variablen. Die dritte Studie untersucht erstmals psychische Auswirkungen des AHF auf die Selbstwahrnehmung der Patienten anhand des Konzeptes der Krankheitsidentität. Eine vierte Studie wurde durchgeführt, um die Lebensqualität innerhalb einer bestimmten Subgruppe von Patienten zu bewerten, die an einer genetisch bedingten Multiorganerkrankung (Marfan Syndrom) mit weitreichenden psychosomatischen Folgen erkrankt sind. Entgegen weit verbreiteter Annahmen unter Klinikern, dass chronische Erkrankungen grundsätzlich mit einem verminderten psychischen Wohlbefinden einhergingen, attestieren vorliegende Ergebnisse EMAH eine allgemein gute Lebensqualität. Während der Schweregrad der Erkrankung insgesamt positiv mit der Lebenszufriedenheit assoziiert ist, weisen bestimmte Untergruppen, insbesondere Marfan Patienten, deutliche psychische Beeinträchtigungen auf. Die Krankheitsidentität spielt in der Krankheitsverarbeitung eine wesentliche Rolle. Dabei lassen sich günstige und ungünstige Dimensionen differenzieren, die jeweils in unmittelbarem Zusammenhang zu Angst und Depression bei EMAH stehen. Das Gesamtausmaß psychischer Beeinträchtigungen konnte nur zu einem geringen Anteil über objektive Krankheitsfaktoren, wie die Komplexität des Herzfehlers, erklärt werden.

Die vorliegende Dissertation liefert neue Einblicke in klinische und psychosoziale Faktoren, die mit dem psychischen Wohlbefinden bei EMAH in Verbindung stehen. Vorliegende Ergebnisse bestärken die Hypothese, dass Anpassungsprozesse bei EMAH weniger mit objektiven Krankheitsvariablen, als vielmehr mit subjektiven Bewertungs- und Wahrnehmungsprozessen korrelieren. Die vorliegende Dissertation ist wegweisend für die Weiterentwicklung der Forschung und Praxis auf dem Gebiet der AHF. In einem modernen Verständnis einer ganzheitlichen Behandlung gewinnen künftig verhaltensbezogene und affektive Krankheitskomponenten, wie das subjektive Gesundheitsempfinden und die Krankheitsidentität, immer mehr an Bedeutung. EMAH benötigen daher ein ganzheitliches, integriertes Behandlungskonzept, das multidisziplinäre Fachkräfte gleichermaßen miteinschließt, um ihren komplexen psychosozialen Bedürfnissen gerecht zu werden und eine effektive, umfassende Behandlung zu gewährleisten. Praktische und theoretische Einblicke in diese spezielle Patientenpopulation dienen als potentielle Inspirationsquelle für das interdisziplinäre Vorgehen bei vielen weiteren chronischen Erkrankungen.

Schlüsselwörter: Erwachsene mit angeborenem Herzfehler; psychische Situation; Psychokardiologie; Prävention

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Abbreviations

ACHD	Adults with Congenital Heart Disease
ACHD-AP	Adult Congenital Heart Disease – Anatomic and Physiological Classification
AHA	American Heart Association
APPROACH-IS	English acronym for study on Patient-Reported Outcomes in ACHD
ASD	Atrial Septal Defect
ASMR	Age Standardized Mortality Rate
CBT	Cognitive Behavioral Therapy
CHD	Congenital Heart Defect/Disease
EQ-5D-5L	Measure of Quality of Life developed by the EuroQol Group
EQ-VAS	EuroQol- Visual Analogue Scale
HADS	Hospital Anxiety and Depression Scale
HADS-D	Hospital Anxiety and Depression Scale - Deutsch
HRQOL	Health-Related Quality of Life
MFS	Marfan syndrome
NYHA	New York Heart Association
OR	Odds Ratio
PROM	Patient Reported Outcome Measure
PTSD	Posttraumatic Stress Disorder
QOL	Quality of Life
SDI	Socio-Demographic Index
VAS	Visual Analogue Scale
VEMAH	German acronym for "Medical Care Situation of ACHD"
VSD	Ventricular Septal Defect

1 Introduction

"The impact of congenital heart disease on the individual would not be limited to the physiological alteration in the heart's functioning but would affect the whole individual.'
-Doucet, 1981

As early as 1981, the eminent physician Stella Doucet suggested links between psychological and cardiac issues in the management of adults with congenital heart disease (ACHD). While recognition of psychosocial implications of congenital heart disease (CHD) is not a novel concept (Doucet, 1981), this has not translated to definitive research or updates to patient care. Advances in cardiology and cardiac surgery over the past few decades have created a rapidly increasing number of ACHD, and therefore a critical need to better understand psychosocial implications of CHD. With an approximate incidence of 1 % and a prevalence of 5-10 per 1,000 live births, more than 90% of children with CHD reach adulthood and the overall number of ACHD currently exceeds the number of children with CHD. Accordingly, CHD has been transformed from a lethal disease to a manageable chronic condition (Marelli, 2012). Yet, almost all ACHD are chronically ill and have lifelong psychosocial challenges, such as heart-focused anxiety, adherence concerns, problematic life-stage transitions or adjustment difficulties, all of which add another layer of complexity to their healthcare needs (Bang et al., 2013). ACHD providers now face a collective responsibility to achieve optimal outcomes beyond improved survival and life expectancy (Kovacs & Bellinger, 2021). As a result, the psychological dimension of CHD is receiving increasing attention. Current evidence suggests that ACHD are at a significantly higher risk for developing serious mental health problems, such as depression, anxiety and post-traumatic stress disorder (PTSD) (Andonian et al., 2018). The psychological burden of disease is especially high in patients with Marfan syndrome (MFS) due to the far-reaching consequences of the multiorgan disease (Nielsen et al., 2019). Frequently unrecognized and untreated, chronic emotional distress is a significant predictor of poor quality of life (QOL) and adverse cardiovascular outcomes (Benderly et al., 2019; Gleason et al., 2019), yet present findings are seldom applied in clinical settings and only a minority of patients with CHD receive psychological treatment (Kovacs et al., 2009a). There are several possible reasons for this paradox, including a lack of scientific rigor in this field and a lack of awareness and productive dialogue between medical professionals (Kovacs et al., 2009a).

To date, the majority of studies on QOL among ACHD is compromised by methodological and conceptual flaws. Present findings are hard to compare due to the lack of a clear conceptual background, varying methods, and heterogenous target samples (Bratt & Moons, 2015). The present dissertation aims to improve upon these studies by investigating QOL and psychosocial outcomes among a representative sample of ACHD. It further attempts to explain variability of these outcomes in psychological functioning by elucidating pathways mediating the novel framework of illness identity among ACHD. It involves four studies, including one narrative review and three quantitative-based studies conducted in cross-sectional designs. Present findings indicate a vital need to direct more attention towards assessing a patient's subjective well-being, independent of his or her factual cardiac condition. These findings provide productive avenues for future research and important psychocardiological interventions for this particular patient population. According to this new integrated vision, ACHD require a holistic, multidisciplinary treatment approach in order to promote disease management and ensure seamless comprehensive care.

2 Clinical and Scientific Background

2.1 Congenital Heart Disease: Medical Overview

Understanding the mechanisms and psychosocial implications of ACHD implies a general understanding of CHD from a medical perspective. CHD are inborn cardiovascular malformations characterized by an impaired pattern of blood circulation (Brickner et al., 2000). There are various types of CHD ranging from simple to life-threatening conditions. While simple defects can go without treatment, more complex defects require cardiovascular surgery. Over the past decades, MFS, a hereditary connective tissue disorder, has also been linked to CHD. Although MFS adversely affects various organs, it is highly associated with cardiovascular abnormalities (Meester et al., 2017). Early diagnosis and timely treatments are therefore essential in preventing cardiac events. Although medical interventions have substantially improved and up to 97% of babies born with heart defects survive into adulthood, CHD still remains the leading cause of infant mortality, which creates a heavy disease burden on a global scale (Brickner et al., 2000; Mandalenakis et al., 2020; Neidenbach et al., 2017). Considering that surgeries and interventional procedures are not curative, patients with CHD require lifelong management to improve not only survival rate but overall quality of life (Wu et al., 2020; Zimmerman et al., 2020).

2.1.1 Current Classification Systems of Congenital Heart Disease and Subtypes

CHD can be classified either physiologically (cyanotic and acyanotic) or anatomically (simple, moderate and severe) (***Table A1 (Appendix)***, ***Figure 2.1***).

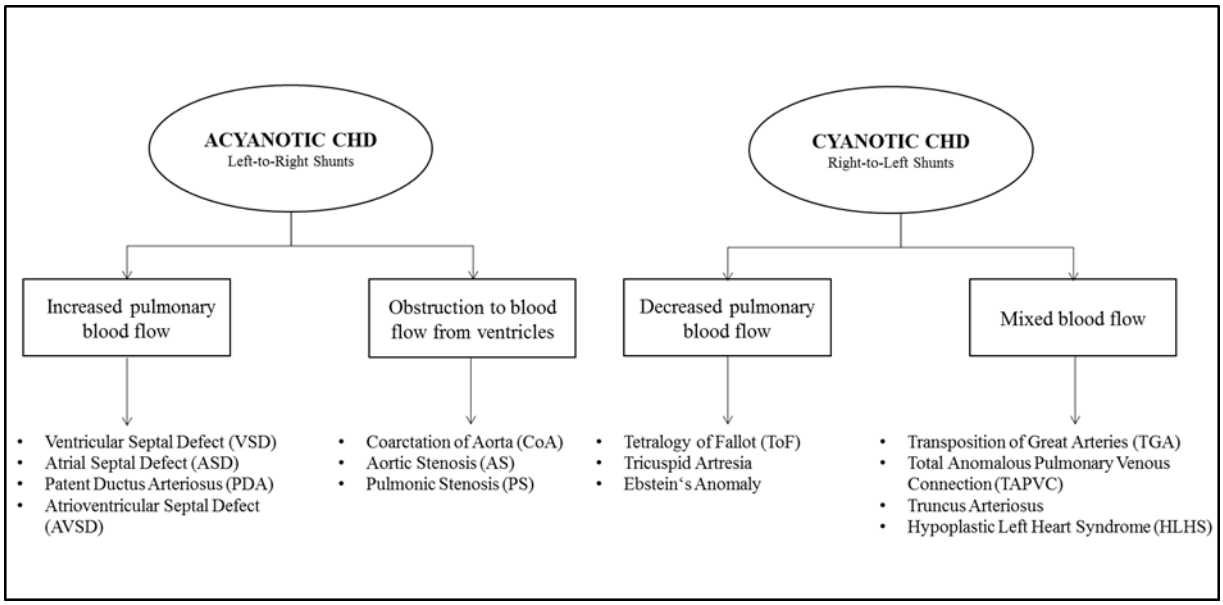

Figure 2.1: Classification of CHD pathology, modified according to Thiene & Frescura, 2010

Acyanotic lesions account for 79% of all forms of CHD (Khan, 2011). Of these, the most common are ventricular septal defects (VSD) (Gabriels et al., 2017), atrial septal defects (ASD) (Menillo et al., 2020) and patent ductus arteriosus with a prevalence of 37%, 25%, and 5-10% (Miranović, 2014; Moodie, 2002; Schneider & Moore, 2006), respectively. Cyanotic heart defects, on the other hand, are considered the most severe forms of CHD (Ratti et al., 2012), including tetralogy of Fallot (Bailliard & Anderson, 2009), transposition of the great arteries (Digilio et al., 2001), and truncus arteriosus with a prevalence of 7-10%, 5-7%, and 0,5-0,8%, respectively (Lindinger et al., 2010), which are among the most complex forms of CHD. While the need for intervention in acyanotic cases is largely determined by the severity of the cardiac anomaly, most cyanotic CHDs require immediate surgery (Diller et al., 2011; Rao, 2019).

With an overall prevalence rate of 0,3%, almost all patients with MFS are affected by some kind of cardiac pathology, ranging from aortic regurgitations and aortic root dilatations to life-threatening aortic dissections (Behr et al., 2019; Kumar & Agarwal, 2014). Additionally, individuals with MFS have to cope with visible physical features of their genetic condition which include an abnormally thin physique, disproportionately long limbs, and skeletal deformities (Peters et al., 2005).

Endeavors to divide patients with CHD into groups have led to a second classification system which categorizes patients into simple, moderate, and severe cases according to the anatomy of their heart defects and the overall complexity of their disease (Webb & Williams, 2001) (see ***Table A1, Appendix***). However, anatomic and physiological severity are not necessarily correlated. Thus, a classification system like the new Adult Congenital Heart Disease Anatomic and Physiological classification (ACHD-AP) that considers the complex interplay between anatomic and physiologic variables is vital to categorize CHD severity and predict the needs of this growing and evolving patient population (Ombelet et al., 2020; Stout et al., 2018; Wichert-Schmitt & Oechslin, 2019). For reasons of simplicity and lack of extensive data on the validity of the new ACHD-AP, this dissertation refers to the universal classification systems based upon the complexity of heart defects and the physiology of systemic circulation (Thiene & Frescura, 2010; Warnes et al., 2001).

2.1.2 Global Burden of Congenital Heart Disease

The worldwide epidemiology of the incidence and prevalence of CHD is not yet fully determined and remains a challenge to this day. Steadily increasing 18.7% since 1990, it is estimated that nearly 12 million people are living with CHD as of 2017. This increase is due to early detection and technological advances in cardiovascular care. CHDs count among the most common congenital anomalies with a slightly higher incidence in male than female patients (Zimmerman et al., 2020). By comparison, MFS affects males and females equally (Kumar & Agarwal, 2014).

Globally, the Age Standardized Mortality Rate (ASMR) of CHD declined from 6.3 per 100,000 in 1990 to 3.9 per 100,000 in 2017 which accounts for a drastic decrease of 38.1%. Nevertheless, CHD remains the leading cause of mortality from birth defects, which creates an enormous disease burden on a global scale regardless of sex, age, and socio-demographic index (SDI) regions (Wu et al., 2020; Zimmerman et al., 2020). Globally, CHD-related death primarily occurs in children under 5 years (Wu et al., 2020). There are only minor differences in the incidence of subtypes of CHD among different countries. An

overall decreasing trend in the prevalence of VSD and ASD could be noted due to the increasing number of repaired lesions coupled with an ageing population. However, Asian countries report a higher prevalence of VSD than the rest of the world (Hoffman, 2013). As expected, the highest CHD incidence rates are found in developing countries with low SDIs, whereas the lowest rates are found in developed countries with high SDIs. Although overall mortality rates declined on a global level, the ASMR is in fact more than four times higher in developing countries with low SDIs than it is in high SDI countries due to higher economic and medical status (Wu et al., 2020). Infant mortality has declined by 60% in all regions with a high SDI (Zimmerman et al., 2020). No ethnic or geographical bias has been observed related to the incidence of mutations that cause MFS (Kumar & Agarwal, 2014). Respective of the above findings, more focus should be put on CHD in less developed countries in order to alleviate the burden of CHD on a global scale. More importantly, the worldwide data on the inequities of CHD can function as a resource to improve survival rates and QOL for this patient population.

Table 2.1: Global incidence and mortality rate of CHD between 1990 and 2017, modified according to Wu and Zimmermann, 2020

	1990	**2017**
Incidence rate of CHD (per 1,000)		
Total	17.2	17.9
Male	18.3	19.1
Female	16.0	16.6
Birth prevalence	9.1	9.4
Ventricular septal defect and Atrial septal defect	5.4	5.3
Age Standardized Mortality Rate (per 100,000)		
Total	6.3	3.9
Male	6.4	3.9
Female	6.2	3.8
Children (< 5 years)	54.2	31.5
High SDI regions *[1]	3.1	1.2
Low SDI regions *[2]	9.7	4.9

*[1] High SDI regions, e.g. Europe
*[2] Low SDI regions, e.g. Africa & Asia

2.2 Changing Patterns of Health: Quality of Life in Adults with Congenital Heart Disease

Dramatic medical and technological advances have led to decreasing mortality and a growing number of ACHD over the past decades (Marelli, 2012). Traditionally, clinical research has focused on objective medical outcomes, such as mortality, morbidity, or functional status. At the same time, there has been a corresponding increase in recognition of psychosocial factors affecting the etiology and the prognosis of CHD, as demonstrated by the burgeoning body of articles on QOL in ACHD over the past 40 years (Bratt & Moons, 2015; Moons et al., 2021b). Therefore, interest has turned toward examining patient-reported outcome measures (PROM) in order to genuinely understand health and well-being in ACHD (Hunter & Swan, 2016; Nordenfelt, 2013). In support of this paradigm shift, the following section examines evidence on biopsychosocial determinants that impact QOL in ACHD. Understanding and improving both physical and psychosocial risk factors in ACHD has therefore become an ethical obligation in the context of a holistic approach to cardiac care (Callus et al., 2020).

2.2.1 Conceptual Definitions

Since its introduction in the medical literature in the 1960s, the term "quality of life" has become increasingly popular (Post, 2014). The concept of QOL dates back to the World Health Organization (WHO) definition of health as a "state of complete physical, mental and social well-being, and not merely the absence of disease" (World Health Organization, 1947). The use of the term "well-being" in this context has thereby contributed to a conceptual confusion. Despite much disagreement, health and medical sciences have adopted this definition and incorporated at least three dimensions in any index measuring QOL: physical health, mental status, and ability to engage in social activities (Post, 2014).

Two common threads in the structure and content of QOL research have been identified (Aaronson, 1988). First, measurements of QOL tend to reflect a multifactorial approach with a wide ranging array of dimensions, i.e. physical health (somatic sensations, disease symptoms, treatment side effects), mental health (nonpathological forms of psychological distress to diagnosable psychiatric disorder), social health (social contacts and interactions) and functional health (self-care, mobility) (Aaronson, 1988). Second, beyond these dimensions, many studies concentrate on variables specific to a given disease or treatment and therefore inadvertently focus on health-related QOL (HRQOL) (Drotar, 2014). Consequently, many authors use the terms QOL, HRQOL, health perception and functional status interchangeably.

Within the context of the present research, QOL is operationalized as *"the degree of overall life satisfaction that is positively or negatively influenced by an individual's perception of certain aspects of life, including matters both related and unrelated to health"* (Moons et al., 2005). According to this definition, QOL is a holistic umbrella term describing a person's overall sense of well-being, which is influenced by various biopsychosocial factors. Moons et al. conclude that this definition is the most reasonable as it takes all conceptual problems into consideration (Moons et al., 2005). In contrast, HRQOL concentrates on the impact of, in this case, CHD on a patient's daily life (Drotar, 2014). Other

related constructs, such as functional status or health perceptions, are considered subordinate since none adequately reflect QOL or HRQOL as a whole (Rumsfeld et al., 2013).

Despite this growing field of research, conceptual and methodological aspects of QOL were largely disregarded and a universally accepted definition of QOL does not exist (Apers et al., 2015). Concepts often vary depending on the applied instruments. An evaluation of existing QOL research in ACHD by Bratt & Moons (2015) revealed that a large majority of studies is compromised by methodological weaknesses and inappropriate definitions (Bratt & Moons, 2015), and calls for further conceptually and methodologically diligent QOL research to allow for reliable conclusions and correct translations into clinical practice (Moons et al., 2004).

2.2.2 Current Evidence and Biopsychosocial Determinants of QOL

There is considerable evidence that an interplay of biopsychosocial factors contributes to QOL in ACHD. This has given rise to the development of psychocardiology, which highlights the importance of a holistic multidisciplinary approach for ACHD (Callus et al., 2020). Over the past ten years, 47 primary studies on QOL in ACHD have been identified and findings are comprehensively summarized below (see ***Appendix: Table A2, Table A3, Table A4***). Compared to healthy participants, some studies found that ACHD present a significantly lower QOL than healthy controls (Apers et al., 2015; Cotts et al., 2012; Eslami et al., 2015). Other findings indicate a similar or even higher QOL among ACHD, when compared to control subjects (Moons et al., 2021b; Opić et al., 2012). Studies that examined different subscales of QOL, showed equally diverging results among ACHD and controls (Enomoto et al., 2012; Mokhles et al., 2011; Vigl et al., 2011). Remarkably, the severity of the heart defect only impacted the physical dimension of QOL. Psychosocial factors revealed much stronger associations with QOL than disease factors (Vigl et al., 2011).

To date, the study on Patient-Reported Outcomes in ACHD (APPROACH-IS) is the largest with the most extensive power, including 4,028 ACHD among 15 countries from 5 continents (Moons et al., 2021b). Results indicate that QOL among ACHD is generally good, but compromised by different medical, sociodemographic, behavioral, psychological and social factors (Moons et al., 2021b). Adverse medical factors included worse functional status, atrial arrhythmias, cyanotic heart disease or Eisenmenger syndrome, implanted cardiac devices, higher hospitalization rates or physical inactivity (Bay et al., 2017; Casteigt et al., 2021; Lévesque et al., 2020; Moons et al., 2021b; Moons et al., 2021c). However, medical characteristics only explained a minor proportion of total variability in QOL indicating that subjective factors may be more important contributors to QOL than objective medical parameters (Apers et al., 2016). The most compromising sociodemographic correlates of QOL included older age, single status, economic instability and low educational attainment (Apers et al., 2016; Moons et al., 2018a; Moons et al., 2021b). QOL was further impaired by psychological factors, such as poor illness perceptions, emotional distress and lower scores on illness coherence and personal control (Holbein et al., 2018; Rassart et al., 2017). Conversely, QOL was positively associated with higher social and family support, higher education, better functional class, absence of cardiac surgery, greater knowledge of CHD, as well as a stronger sense of coherence (Chen et al., 2011; Eslami et al., 2015;

Moons et al., 2021a; Müller et al., 2014; Teixeira et al., 2011). High perceived social support has consistently emerged as an important resource for high QOL in ACHD (Kovacs et al., 2005). Findings remain inconsistent in regard to sex, disease severity, CHD subtype, diagnosis and the duration of illness, although these variables appeared to be the most frequently investigated determinants (Apers et al., 2015).

In contrast to the diverging QOL results in ACHD, findings in MFS patients consistently indicated decreased levels of QOL, which were mostly triggered by biobehavioral variables including chronic pain and fatigue, difficulties in executive functioning and psychological distress (Moon et al., 2016; Nielsen et al., 2019). Predictors of better QOL were analogous to those in ACHD mostly relating to better social inclusion, material and employment conditions, as well as higher levels of education (Goldfinger et al., 2017). Additionally, fewer surgical interventions, less comorbidities, and less severe manifestations of MFS were found to be associated with higher levels of QOL (Goldfinger et al., 2017).

Despite the large body of literature published on QOL, it is difficult to compare the present findings as they vary greatly in methods and sample sizes. Apart from APPROACH-IS, which constitutes one of the largest international landmark studies to examine inter-country variations of QOL in ACHD (Moons et al., 2021b), the majority of studies had sample sizes below 100 patients. In addition, eight different tools were used to assess QOL with the 36-Item Short Form Health Survey (SF-36) being the most frequently applied instrument (Bratt & Moons, 2015). The population of patients also differed substantially in regard to their congenital heart lesions. Furthermore, with regard to MFS, almost half of the studies reported findings of patients without a verified diagnosis of MFS (Vanem et al., 2020). Almost all studies were conducted in a cross-sectional design making it impossible to draw firm conclusions about the directionality of effects. Although a recent review of QOL studies over the past 40 years confirms temporal improvements in the quality of QOL studies, the majority of studies still fail to meet scientific quality criteria (Bratt & Moons, 2015).

2.3 Psychological Adjustment to Congenital Heart Disease

With increased awareness of the biopsychosocial dimensions of CHD, there is growing emphasis on comprehensively assessing and managing the mental health needs of patients (Roseman & Kovacs, 2019). The database on psychological distress in ACHD has expanded enormously during the past decades. A search of “anxiety and depression in adult congenital heart disease” on PubMed yielded 190 entries, including many citations in medical and cardiology journals. In stark contrast to the extensive database linking psychiatric comorbidities to CHD, is the remarkably small number of clinical trials (Tesson et al., 2019). There is a large disparity between efforts to investigate CHD-related psychological distress and attempts to ameliorate them, which contributes to the striking gap in psychosocial care for ACHD (Kovacs et al., 2009a). The following chapter summarizes the current research status on psychological functioning in ACHD and introduces the novel concept of illness identity which potentially provides a valuable tool to predict psychological outcomes in ACHD. Since elevated rates of emotional distress have been associated with worse clinical outcomes (Benderly et al., 2019), this section reviews reciprocal effects of psychological distress on physiological outcomes.

2.3.1 Anxiety, Depression and Post-traumatic Stress in Adults with Congenital Heart Disease

Living with CHD can create a major challenge in a patient's life as it comes with a great burden in various domains of private and professional life (Nagdyman et al., 2016). Psychosocial challenges can be classified as intrapersonal (e.g. self-esteem, body-image insecurities, uncertainties about the future) and interpersonal (feeling different, difficulties in social interaction) (Roseman & Kovacs, 2019). Recent trends in research have indicated a significantly higher prevalence of emotional distress in ACHD, a finding that is the specific focus of this research (Jackson et al., 2018; Pauliks, 2013).

A recent synopsis of studies examining the prevalence of depression and anxiety among ACHD is depicted by ***Figure 2.2*** and ***Figure 2.3.*** A previous review confirms that 33% of ACHD experience symptoms consistent with mood or anxiety disorders with considerably higher prevalence over the lifetime (Roseman & Kovacs, 2019). Another recent study focusing on ACHD survivors at age 50 and beyond rendered similar results, with an incidence of depression or anxiety ranging up to 55% in patients with complex CHD (Rehan et al., 2021). To date, the largest German study conducted by Westhoff-Bleck et al. (n=150) documented that 48% of ACHD present psychiatric disorders, which is significantly above the general population (48.0%; CI: 44.7-60.0 vs. 35.7%; CI: 33.5-37.9) (Westhoff-Bleck et al., 2016). In line with previous studies, mood and anxiety disorders were the leading causes of psychiatric illness. However, authors stress that these disorders are rarely diagnosed, which results in insufficient treatment and a notable decrease in QOL (Westhoff-Bleck et al., 2016). In fact, 39% of ACHD who meet diagnostic criteria for a mood or anxiety disorder, have not received any mental health treatment, despite the fact that 51% reported significant interest in psychological support (Kovacs et al., 2009a).

A possible reason for the psychological underdiagnosis and undertreatment in ACHD might be the atypical clinical presentation of depression and anxiety in cardiac patients as compared to psychiatric patients (Roseman et al., 2021). Fatigue or lack of energy, irritability and avolition are more frequent than typical symptoms, such as flat affect, feelings of guilt, or decreased self-esteem (Martens et al., 2006). Although little research has been conducted specific to this outcome, heart-focused anxiety merits mention in this context (Andonian et al., 2021d; Roseman et al., 2021). It refers to a fear of cardiac-related sensations and is often triggered by perceived negative consequences (Eifert et al., 2000; Roseman et al., 2021). A retrospective review of 100 ACHD that received psychological counselling revealed that heart-related anxiety was among the most frequent psychological concerns (71%) (Ferguson & Kovacs, 2016). Another study similarly demonstrated that ACHD with high anxiety are frequently hypervigilant to heart-related symptoms (Karsdorp et al., 2009). Therefore, CHD providers are encouraged to be aware of the possibility that patients might not report "traditional" psychiatric symptoms (e.g., generalized anxiety or major depression), yet still experience cardiac-related anxiety or coping difficulties that might require mental health treatment (Roseman & Kovacs, 2019).

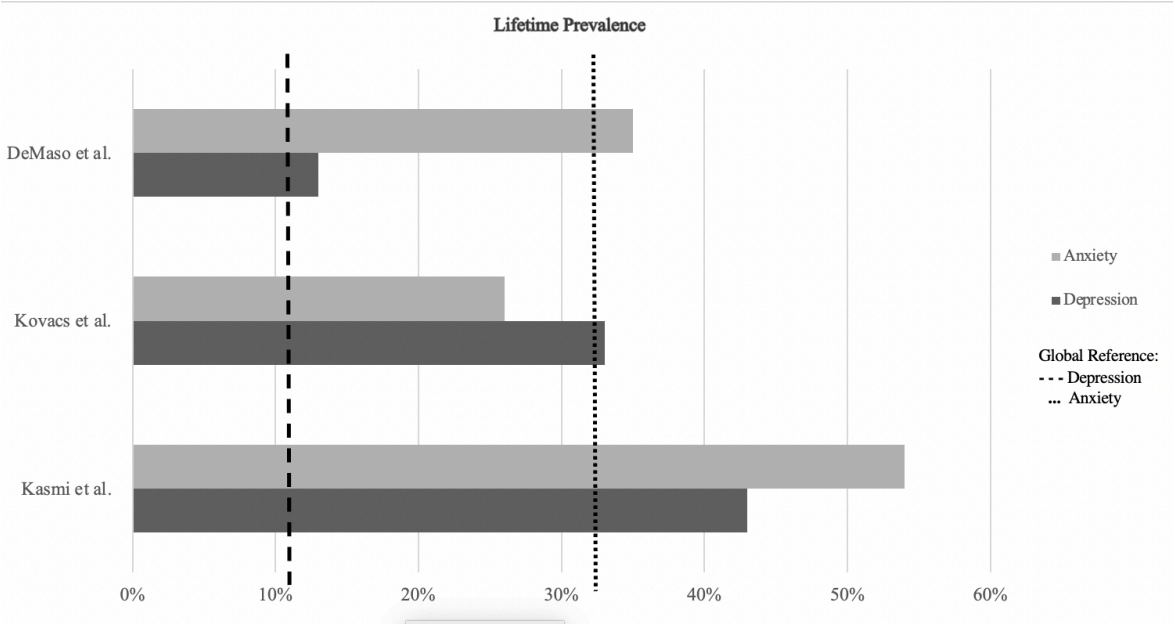

Figure 2.2: Studies examining depression and anxiety in ACHD (lifetime prevalence in %); modified according to Andonian et al., 2018

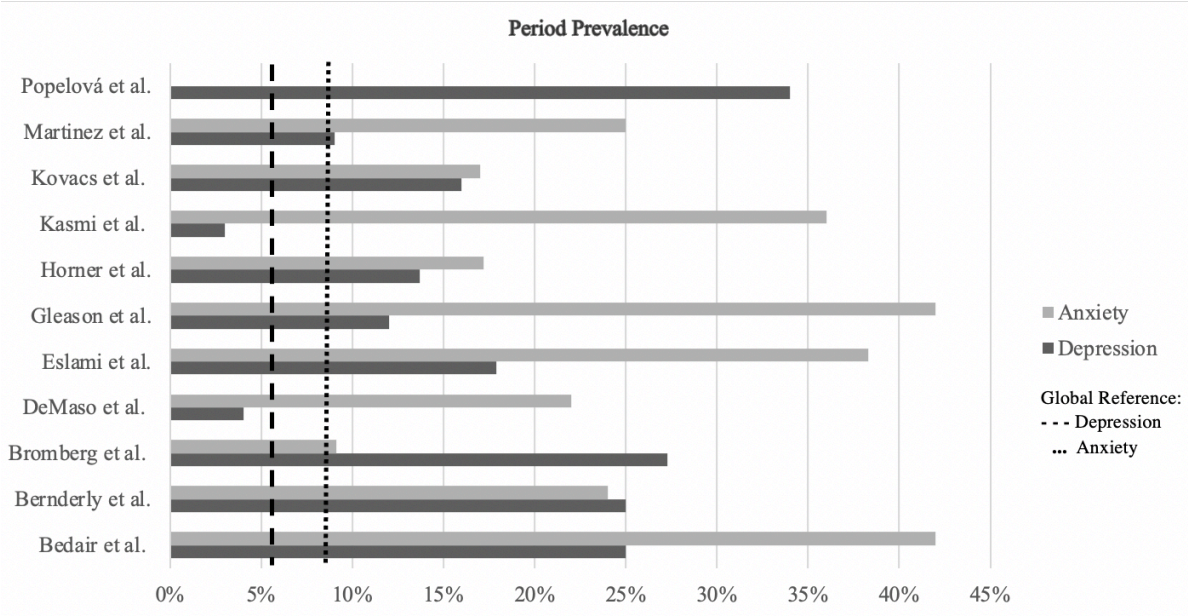

Figure 2.3: Studies examining depression and anxiety in ACHD (current prevalence in %); modified and extended according to Andonian et al., 2018

Studies that specifically addressed features of depression and anxiety in MFS patients are still scarce and inconsistent. Nevertheless, the available findings point toward a higher incidence of overall psychopathology, ranging from 25-98% with depression being the leading mental disorder in MFS patients (Hansen et al., 2020; Moon et al., 2016; Nielsen et al., 2019). An explorative study of 174 adults with MFS found that 44% of study participants reported depression that was significantly associated

with mitral valve prolapse (Peters et al., 2001). A cross-sectional survey of 218 MFS patients documented that anxiety and depression were present in 63.8% and 71.5% of patients, respectively (Moon et al., 2016). Other studies have indicated that female patients were particularly vulnerable to experiencing emotional distress (Rand-Hendriksen et al., 2007; Rao et al., 2016). Furthermore, anxiety was especially present in patients who received a life-saving intervention and had a negative view regarding the controllability of their disease (Benke et al., 2017). Healthcare providers should therefore be aware of the precarious psychosocial situation in individuals with MFS and proactively conduct proper screening in this particular patient population (Nielsen et al., 2019).

Surprisingly, despite the fact that hospitalizations or medical emergencies potentially constitute sources of trauma across the lifespan, PTSD has received limited attention (Roseman et al., 2021). There are currently two studies examining the prevalence and correlates of PTSD. One study found that elevated levels of PTSD were reported by 11-21% of ACHD compared to an average rate of 3.5% in healthy controls. Two factors emerged as significant correlates of PTSD: First, PTSD was uniquely associated with increased depressive symptoms although the causal direction between depression and PTSD remains to be elucidated. Second, the risk of developing PTSD is associated with the amount of time since surgery, with higher rates when surgery occurred more recently (Deng et al., 2016). A second study (n=25) presented in this context revealed that nearly 25% of all participants met clinical criteria for full-blown PTSD. Chronic uncertainty and unpredictability of the course of illness were associated with a higher incidence of PTSD in ACHD (Moreland & Santacroce, 2018). These findings deserve special attention as subjects with PTSD report a significantly lower QOL along with impaired psychosocial functioning and decreased life satisfaction (Deng et al., 2016).

The majority of published literature indicates that psychological functioning in ACHD is irrespective of the objective physical condition (van Rijen et al., 2005). Other variables surfaced as potential correlates of emotional distress, such social isolation, fear of negative evaluation, imposed physical restrictions, and low perceived health status (Callus et al., 2014; Kovacs et al., 2005; Van Rijen et al., 2004). Therefore, possible predictors of emotional distress in ACHD will be further explored within the context of this dissertation in order to incorporate them into clinical practice.

2.3.2 The Concept of Illness Identity

> *"The self is embodied and in order to explore what it means to be a self, we need to explore what it means to have a particular body"* – Zeiler, 2009

Questions around body and identity tap into a long tradition of philosophical inquiry around self-image. However, the exploration of body-mind intersections has not gained much attention in chronic illness research, despite the fact that internal processes are believed to play an important role in how individuals cope with and adjust to their illness (Holmbeck, 2002). While most of the existing literature repeatedly focuses on how patients *perceive* their illness, it fails to fully explore how patients *incorporate* their illness into their identities (Mauthner et al., 2015). It is also striking that most researchers have turned to qualitative methods when it comes to exploring chronic illness experience (Charmaz, 1995, 1999;

Leventhal et al., 1999). This may be due to a fundamental lack of theory and measures available to explore the association between illness and identity.

The novel concept of illness identity, or the degree to which a chronic illness is integrated into one's sense of self, provides a new entry point into rethinking the meaning of living with a CHD (Oris et al., 2018). The underlying phenomenological perspective runs entirely counter to the Cartesian dualism between mind and body, which still influences the way disease, health, and treatment are defined in real-world clinical application (Mehta, 2011). Inspired by the common-sense model of self-regulation, chronic illness is assumed to threaten central feelings about one's self, creating a far different framework of illness experience than that specified by an acute threat (Leventhal et al., 2003). Consequently, individuals form cognitive, affective, and behavioral representations of health threats (Leventhal et al., 1999). However, a major limitation of Leventhal's model is that it was confined to cognitive illness perceptions and failed to represent the complexity of a patient's illness experience (Breland et al., 2020). Building on this, illness identity is not only an expression of the patient's perception of disease, but also how the disease affects the way they think and feel about themselves (Van Bulck et al., 2019). Chronically ill patients need to integrate their illness into their identity in order to achieve a coherent sense of self (Van Bulck et al., 2019). Illness identity comprises four different states, i.e. *engulfment, rejection, acceptance,* and *enrichment* (Oris et al., 2018). While the first two represent maladaptive states of illness integration, the latter two refer to adaptive ways of illness integration (***Figure 2.4***). Related specifically to the topic of this dissertation, each dimension has been linked to different psychological and behavioral outcomes in ACHD (Andonian et al., 2020; Oris et al., 2018; Van Bulck et al., 2018).

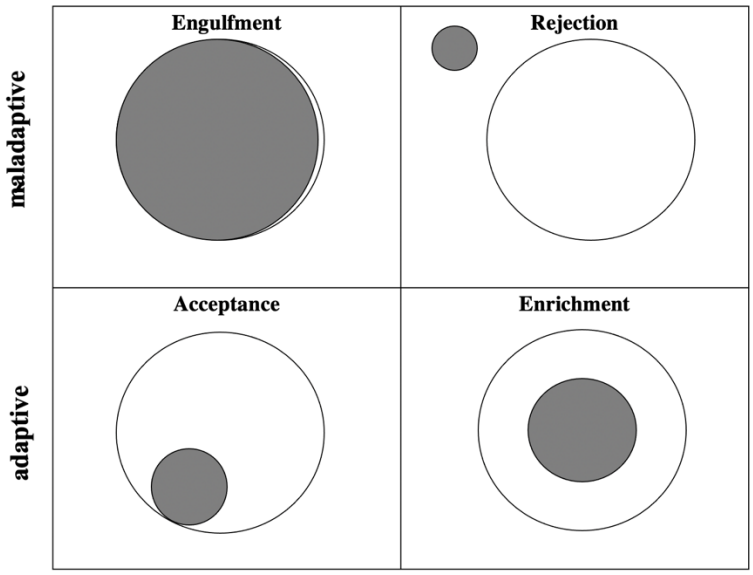

Figure 2.4: Visual depiction of illness identity states; modified according to Van Bulck et al., 2019

Engulfment captures the degree to which patients become self-defined by their chronic illness. An individual's self-concept becomes reorganized entirely around the experience of the chronic illness (Charmaz, 1995; Leventhal et al., 1999; Oris et al., 2018). In contrast to taking responsibility for one's

own health, being overtaken by one's condition occurs without choice (Charmaz, 1995). Engulfment has been associated with worse psychological and physiological outcomes (Andonian et al., 2020; Oris et al., 2018; Van Bulck et al., 2019).

Rejection refers to a state where an individual ignores or minimizes his or her illness in an attempt to preserve the facade of a normal life (Carver & Vargas, 2011). The illness is regarded as an external threat and individuals refuse to acknowledge it as part of themselves (Leventhal et al., 1999). It was previously shown that rejection is unrelated to emotional distress (Andonian et al., 2020). However, passive coping is generally not effective in the long run as it is linked to worse treatment compliance, greater functional impairment and lower general self-efficacy (Carver & Vargas, 2011; Nahlén Bose et al., 2016; Oris et al., 2018).

Acceptance refers to a mode of adaptive illness integration, where individuals adapt to their illness while perceiving the ability to tolerate the unpredictable nature of their condition (Evers et al., 2001; Morea et al., 2008; Oris et al., 2018). Acceptance may have a protective role in the psychological functioning of ACHD as it is associated with beneficial psychological and physiological outcomes (Andonian et al., 2020; Oris et al., 2018). Over the past two decades, research centering on the phenomenon of positive changes as a consequence of illness has expanded (Helgeson et al., 2006; Tedeschi & Calhoun, 2004).

Enrichment addresses ways in which a chronic illness offers possibilities for positive change and identity transformation, in terms of increased life appreciation, personal resilience, more meaningful relationships, or spiritual growth (Stanton & Revenson, 2007; Tedeschi & Calhoun, 2004). Enrichment may be important in ACHD for a number of reasons. It has been associated with QOL after adjusting to several disease-specific and sociodemographic variables (Tomich & Helgeson, 2004). It has also been found to play a moderator role in the relationship between QOL and emotional distress (Morrill et al., 2008). In concrete terms, enrichment appears to play an attenuating role when present, while having a negative impact on QOL and mental health when absent (Moore et al., 2011). Counterintuitively, enrichment is linked to experiencing increased symptoms of illness and pain. However, the concept of post-traumatic growth requires that individuals thoroughly explore their illness in order to form their identities and build valued lives (Oris et al., 2018).

Our previous research on this topic demonstrates that illness identity may provide a valuable tool to predict psychological adaptation to CHD (Andonian et al., 2020). Newer findings indicate that illness identity is stable over time, showing that a one-time examination could provide interesting information for clinical practice (Van Bulck et al., 2021). Currently, there is a gap in understanding how illness identity exerts its effects on psychological outcomes in ACHD. This dissertation will also further investigate explanatory pathways through illness identity in order to generate a deeper understanding and establish targeted psychological interventions for ACHD.

2.3.3 Biobehavioral Mechanisms linking Emotional Distress to Cardiovascular Health

There is emerging evidence that psychological distress goes beyond QOL and extends to medical outcomes among ACHD (Kovacs & Bellinger, 2021). The presence of psychiatric symptoms has been associated with premature mortality, higher healthcare utilization (including higher outpatient and

emergency department visits), and more hospital admissions (Benderly et al., 2019; Kourkoveli et al., 2015). In the field of *acquired* heart disease, the prognostic effect of depression appears to be far greater than that calculated from anxiety and is, for the most part, independent of cardiac pathology (Herrmann-Lingen & Buss, 2007). There is also extensive evidence that depression potentially leads to a greater than two-fold risk for recurrent cardiac events (Cohen et al., 2015; Lichtman et al., 2014; Nicholson et al., 2006; Park et al., 2015; Watkins et al., 2013) and a dose-response relationship between the severity of depression and adverse cardiac outcomes (Lespérance et al., 2002).

Reciprocal influences between body and mind can be partly explained by *indirect* behavioral mechanisms, as well as *direct* pathophysiological disturbances (Herrmann-Lingen & Buss, 2007) (see ***Figure 2.5***). Accordingly, psychological distress is associated with adverse health behaviors including lack of exercise, sleep deprivation, malnutrition, or smoking. These behaviors generally provide short-term stress relief, but ultimately lead to adverse health effects (Carver & Vargas, 2011), and not only result in inappropriate healthcare utilization, but also interact with underlying biological substrates of cardiovascular health (Kop & Plumhoff, 2011). Biological dysregulation linking psychological distress to cardiovascular health involve multiple mutually reinforcing immunosuppressive pathways, related to autonomic dysregulation characterized by increased sympathetic activity, heightened hypothalamic-pituitary-adrenal axis activity, increased release of proinflammatory cytokines, elevated levels of cortisol, and other metabolic alterations (Burg, 2018; Cohen et al., 2015). In one of his earliest works, Hans Selye introduced a theory of stress response and coined the term *general adaptation syndrome* (Selye, 1956). During prolonged emotional distress, the human body resigns and is no longer able to fight against constant damages to the already compromised immune system. Chronic inflammation and vital exhaustion are especially critical to disease progression in ACHD and should be prevented from the outset.

Starting on the reverse side of the model, a CHD itself might constitute a major stressor in afflicted patients and lower the threshold of developing psychological disorders in ACHD. Explanations range from early trauma to aggravating psychosocial factors, including loss of autonomy, professional degradation or financial insecurity (Pauliks, 2013). Besides psychological correlates, inflammatory processes involved in the cardiovascular disease progress may elicit feelings of vital exhaustion and therefore increase the risk of developing long-term psychological distress (Meyer & Herrmann-Lingen, 2014). Therefore, the cause-effect relationship among psychological functioning and physiological dysregulation remains to be determined (Kop & Plumhoff, 2011).

A lack of longitudinal studies, methodological variability, and incomplete adjustments for covariates among publications thus far have raised concerns in attributing causal effects between psychological distress and cardiovascular prognosis. However, these apprehensions have been outweighed considering the extensive amount of data on objective and subjective consequences of psychological variables on cardiovascular endpoints. Preferably, longitudinal research is needed to identify the direction of effects between mental stress and cardiovascular disease. Interestingly, there is evidence that adaptive disease coping is not only related to better health behavior, but also lower levels of cortisol and healthier immune

system functioning (Carver & Vargas, 2011). It may be reasonable to include additional moderator variables, such as illness identity to further refine disease coping for ACHD.

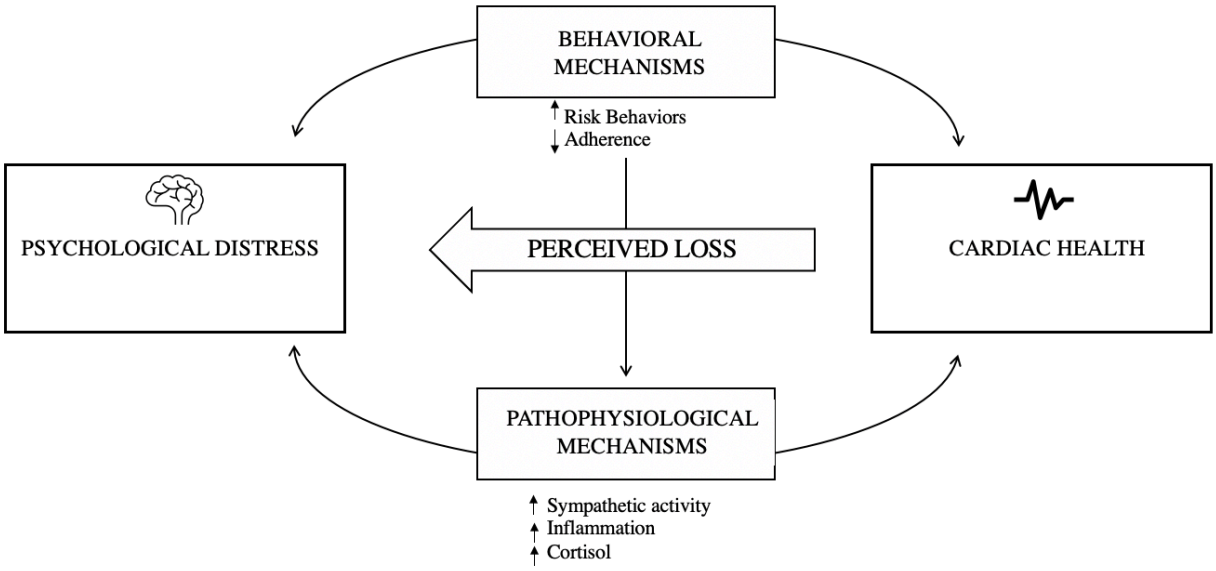

Figure 2.5: Reciprocal mechanisms between mental well-being and cardiac health

2.4 Current Knowledge Gaps

Despite increasing interest in the psychological situation of ACHD, findings on QOL and related psychosocial variables remain *heterogeneous* and partly contradictory due to conceptual and methodological flaws (Moons & Luyckx, 2019). Of the available research on emotional distress in ACHD, there are diverging results due to vast differences of applied instruments and varying sample sizes (Callus et al., 2013). Findings on QOL in MFS patients are equally debatable, since most studies were based on small sample sizes or case reports, and a verified diagnosis of MFS was not required in roughly half of the studies (Nielsen et al., 2019).

In addition, there is little consensus on the *meaning and measurement* of QOL. This lack of a clear conceptual definition has led researchers to measure a wide variety of variables using a range of tools. Consequently, there is great variability of results, making it impossible to draw firm conclusions on the level of QOL or its determinants (Apers et al., 2015). Also, the terms HRQOL, QOL, perceived health status, or functional status are often used interchangeably without prior clarification (see ***Chapter 2.2.1.***). Future studies should therefore build on a solid conceptual basis and choose the most appropriate instrument aligned with the target variable.

Precision and validity of the applied instruments to measure psychological outcomes in ACHD must be questioned. Although the applied psychometric tools are high-quality screening instruments, neither can replace a structured clinical interview to confirm a mental disorder (Stuart et al., 2014). If structured clinical interviews are not feasible in large study populations, at least a thorough clinical assessment should be the natural consequence of critical scores in questionnaires indicating depression or anxiety. There is a vital need to extend current findings to confirmed clinical disorders.

Another complication results from the highly heterogeneous group of ACHD due to the great diversity in anatomical complexity and disease progression. Several studies have therefore focused on a *specific subgroup* of ACHD (Apers et al., 2015). However, it is important to extensively incorporate the whole spectrum of heart defects to account for possible differences in their psychological functioning according to the underlying types of heart disease. This may potentially help clinicians to identify at-risk patients and provide effective prevention strategies.

The majority of published literature demonstrates that psychological functioning in ACHD is often irrespective of the objective cardiac condition (Moons & Luyckx, 2019). Yet, to date, indicators of *psychological adaptation* to CHD have received little attention. From a clinical perspective, such determinants are of particular importance since many are able to be altered and therefore potential targets for effective prevention measures (Andonian et al., 2018; Apers et al., 2015). For these reasons, an in-depth investigation of related psychosocial constructs (i.e., illness identity) will allow for a deeper understanding of chronic disease management in ACHD.

It has been recognized that true excellence in care can only be achieved through rigorous research (Bratt & Moons, 2015). Current gaps in knowledge pave the way for avenues of future research. In addition to conducting more diligent research to eliminate present ambiguities, specific areas relating to chronic disease management should be elaborated. The identification of modifiable correlates of psychological well-being may allow the implementation of considerable changes in the health experience of ACHD.

3 Aims of the Studies

Although rigorous data are lacking, present evidence indicates that a high proportion of ACHD are at increased risk of developing chronic psychological distress (Roseman & Kovacs, 2019). However, mental health issues among ACHD remain undiagnosed and mental health professionals are rarely involved as part of an interdisciplinary care team (Kovacs et al., 2009a). The present dissertation aims to establish a scientifically sound evidence base for psychocardiological intervention planning by prioritizing the following aims:

1) *To summarize the current state of knowledge on the prevalence, etiology, health impact, and treatment of depressive and anxiety symptoms among ACHD*. The narrative review ensured justification for future (empirical) research and raised an overall awareness for the complex psychological situation of ACHD (Andonian et al., 2018). In addition, proposals for handling mental health issues among ACHD in routine clinical settings were considered.
2) *To extensively examine QOL in a representative cohort of ACHD with a special focus on patient-related and clinical determinants*. At present, findings on QOL in ACHD are inconclusive due to a lack of a clear conceptual background as well as inconsistent methods and insufficient sample sizes. Additionally, the high heterogeneity of ACHD constitutes a substantial confounding factor and clinical determinants of QOL have not been sufficiently examined. Identifying correlates of QOL along with special needs of ACHD could improve healthcare for this growing patient population (Andonian et al., 2021a).
3) *To investigate the mediating role of illness identity in the association between perceived health and psychological distress among ACHD*. Although research on the psychological burden of CHD is a growing field, in-depth investigations of the illness experience of ACHD are still in progress (Andonian et al., 2020). This gap in knowledge may contribute to the lack of psychosocial support for this patient population. Given the current evidence that psychological functioning is mainly irrespective of clinical parameters, the third study aimed to seek alternative explanatory variables. These variables have been selected for two major reasons: First, previous research has indicated that symptoms experienced by patients are more important factors to consider than the objective physical condition. Second, there have been no studies to prove the predictive value of illness identity for psychological outcomes in ACHD. The identification of mechanisms that affect emotional outcomes in ACHD may improve early detection and management of mental illness in ACHD (Andonian et al., 2021c).
4) *To systematically assess QOL within a subset of ACHD who have a verified MFS diagnosis and to compare with patients with other types of CHD*. Until now, research on MFS has mainly focused on organ manifestations, molecular pathogenesis, and surgical management, with less attention on psychosocial consequences of MFS (Vanem et al., 2020). Due to the various organ manifestations of MFS, it can be assumed that the diagnosis of MFS alone will likely impact QOL to a far greater extent than observed in other forms of CHD (Andonian et al., 2021b). Therefore, the research aimed to assess whether the phenotypic presentation associated with MFS patients predicts decline in any of QOL subdomains. As treatment has improved and life

expectancy has increased, the present findings offer insight and raise awareness for unique subjective consequences of living with MFS.

The structure and contextual link between the studies is depicted in ***Figure 3.1***.

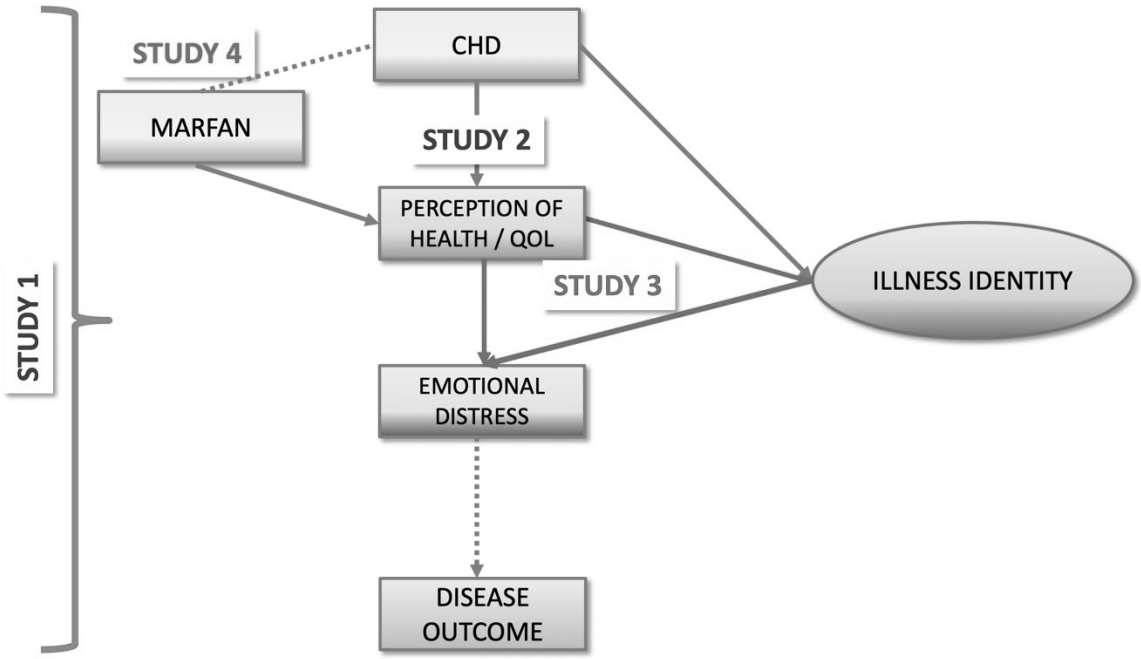

Figure 3.1: Structure of studies

4 Methodology

Since this research project is explorative in nature, a descriptive, cross-sectional study design was chosen for all studies to explore differences in PROMs. A comprehensive overview of the methodology of each study is provided below.

4.1 Study 1

This review provided a comprehensive summary of current research on the prevalence, health impact, and available treatment options of depressive and anxiety symptoms among ACHD. The search was limited to quantitative-based studies that presented original, primary data of patients aged 18 years or older with a confirmed diagnosis of CHD, and that used standardized tools to assess anxiety, depression, or global mental health. Studies which focused on acquired heart disease were excluded. Data that were not directly pertinent to psychological functioning (e.g., neuromotor development, neurocognitive development, QOL) were excluded. Since there are no known differences in regional prevalence rates of CHD, nationality was not considered as an inclusion or exclusion criteria. Medline and PubMed were searched to identify peer-reviewed, English-language studies reporting primary data on depression and anxiety in ACHD. Medical subject heading terms used were combinations of ACHD and depression, depressive disorder, major depressive disorder, mental health, psychosocial outcomes, psychological or emotional distress, anxiety, or emotional exhaustion. Reference lists of retrieved articles were inspected to identify relevant additional articles. Of 16 studies identified from the search, 10 allowed a direct comparison. Demographic information, instruments used, prevalence data on student distress, and reported lifetime- and point prevalence rates were collected. Since most studies relied on self-report measures, this review refers to symptoms of emotional distress rather than formal mood and anxiety disorders as defined by the DSM 5 (American Psychiatric Association, 2013). Although structured clinical interviews are warranted to verify and diagnose mental disorders, preliminary findings provide a comprehensive basis for subsequent empirical research (Andonian et al., 2018).

4.2 Study 2

Using the nationwide cross-sectional VEmaH registry (engl. “Medical Care Situation of ACHD”), this study was conducted as a sub-analysis in an exploratory quantitative manner. VEmaH constitutes the largest ever attempt to comprehensively assess the health care situation of ACHD in Germany (Neidenbach et al., 2021). This is the first study to investigate patient-reported QOL within a German cohort of 4,015 patients encompassing a broad spectrum of CHD (41.8 ± 17.2 [range, 18−97], 46.5% female). Data collection took place between 2016 and 2019 in a cross-sectional design. Eligible patients were required to be at least 18 years old, diagnosed with a CHD, defined as “*a gross structural abnormality of the heart and/or intra-thoracic great vessels that is actually or potentially of functional significance (including mild, moderate, and complex heart defects)*” (Mitchell et al., 1971) and having the necessary physical, cognitive and language capabilities to complete self-report questionnaires. A background questionnaire on demographic and clinical information was specifically devised in close

cooperation with the Chair of Behavioral Epidemiology at the Dresden University of Technology and the German Heart Center Munich to ensure maximum standards of quality and validity. Patients completed the questionnaire either in person, online, or by mail to maximize response. QOL was measured using the updated five-level version of the EQ-5D questionnaire (EQ-5D-5L) (Herdman et al., 2011) consisting of a descriptive system questionnaire and a visual analogue scale (VAS). The descriptive system examines QOL from various angles as it breaks down QOL into five core components: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. In contrast, VAS provides a quantitative measure of a patient's overall health state on the day of questionnaire completion ranging from 0 ("The worst health you can imagine") to 100 ("The best health you can imagine"). Within the context of this research, QOL was predefined as a subjective concept, influenced by multiple causal factors (Moons et al., 2006). This allowed genuine differences in QOL among patients with different backgrounds and clinical characteristics to be revealed (Andonian et al., 2021a). Statistical analysis was performed using IBM SPSS Statistics Version 24.0 (IBM Inc., Chicago, Illinois, USA, 2016). Descriptive measures were calculated for sample characteristics, including patient reported sociodemographic and medical variables (absolute and relative frequencies, mean and standard deviations). Relationships between QOL and patient-reported clinical, as well as sociodemographic variables were quantified using multiple regression analysis and ordinal logistic regression (Andonian et al., 2021a).

4.3 Study 3

Although there is growing research on the psychological situation of ACHD, current data do not sufficiently explain the variability in psychological functioning (Oris et al., 2018). The third study was therefore conducted to examine psychological illness processing of ACHD. The concept of illness identity explains how patients experience and integrate their CHD into their identities. Illness identity was shown to be associated with psychological outcomes in previous research, indicating that this might be a valuable concept to support clinical practice (Oris et al., 2018; Van Bulck et al., 2021). After examining and validating the German version of the illness identity questionnaire within a previously published study (Andonian et al., 2020), the present study investigated illness identity as a mediator of the association between perceived health and psychological distress among ACHD. It was hypothesized that a patient's perceived health status would be related to emotional outcomes (measured by depressive and anxiety symptoms) and that high cardiac disease severity ratings would be related to maladaptive illness identity states, which in turn, would lead to high depression and anxiety. Conversely, low subjective disease severity would be related to adaptive illness identity states, which would be associated with lower depression and anxiety. Due to inconsistent findings on the relationship between objective cardiac parameters and psychological adjustment, the influence of cardiac disease severity on the relationship between perceived health and emotional distress was also investigated. The study was approved by the ethical committee of the Technical University of Munich in June 2019 (56/S6). All study participants were enrolled during their routine waiting period at the German Heart Center Munich between June and September 2019. Inclusion criteria were in accordance with study 2: (1) confirmed diagnosis of CHD, according to the definition of Thiene and Frescura (Thiene & Frescura, 2010); (2)

participants aged 18 years or older; and (3) necessary physical and cognitive capabilities to complete self-report measures. The study was conducted in a cross-sectional design including a representative collective of 229 ACHD (38 ± 12.5 [range, 18−73] years; 45% female). Self-reported measures were assessed on four domains by means of standardized questionnaires: (1) demographics, (2) self-rated health (EQ-5D VAS), (3) illness identity (Illness Identity Questionnaire German (IIQ-D)), and (4) emotional distress (Hospital Anxiety and Depression Scale German [HADS-D]). Since study 1 has indicated that EQ-VAS primarily depicts a patient‘s perceived health, it was used as a reliable single item approach to the measurement of a patient‘s subjective health state. Satisfactory psychometric properties were documented elsewhere (Cronbach’s alpha = 0.87) (De Boer et al., 2004). Moderation and mediation analysis was performed according to procedures described by Hayes and the PROCESS macro for IBM SPSS Statistics 27.0 (IBM Inc., Armonk, NY, USA, 2020). Direct and indirect (i.e. mediated) effects were assessed by evaluation of 95% confidence intervals produced by bootstrapping (bootstrapping=5000) (Andonian et al., 2021c).

4.4 Study 4

Since CHD patients with MFS present a clinically distinct population, the experience of MFS may be subject to unique psychosocial manifestations of the disease (Nielsen et al., 2019). Study 4 constitutes a subgroup analysis of the nationwide VEmaH study, which has been described in detail above (see Study 2). The questionnaire-based survey was initiated and carried out by the Department of Congenital Heart Disease of the German Heart Centre Munich, Technical University Munich, and the Department of Cardiology, University of Erlangen. The insurance company “AOK Bayern” supported the study by sending out questionnaires to their insured ACHD patients in Bavaria. Written informed consent was obtained from all participating patients before the start of documentation. Guidelines on good pharmacoepidemiologic practice and data protection guidelines were followed. In total, 102 MFS patients (39.3 ± 13.1 [range, 20−85]; 40.2% female) were enrolled between 2016 and 2019. Patients were included for sub-analysis according to the following criteria: (1) verified diagnosis of MFS; (2) aged 18 years and older, (3) necessary physical, cognitive, and language capabilities to complete self-report questionnaires, (4) German speaking. Participants were excluded if they did not fulfill age requirements or had severely impaired cognitive abilities. Patients were enrolled consecutively at the clinic. PROMs were assessed by a specifically devised background questionnaire and the updated EQ-5D-5L. For subsequent comparison to other forms of CHD, reference data was ascertained by the same methods to ensure maximum comparability between both populations. Statistical analysis was performed with SPSS 25.0 (IBM Inc., Armonk, NY, USA, 2018). Medical records were reviewed separately for sociodemographics and cardiac and non-cardiac diagnosis. Descriptive statistics were calculated for sociodemographic characteristics. Several logistic regression models were applied to analyse the impact of MFS on QOL domains, using the respective EQ-5D dimensions as dependent variables. Differences between the populations were tested by Chi-square tests. T-tests were applied for comparisons between mean values. Continuous data was expressed as mean ± standard deviation, categorical or interval scaled variables as absolute numbers or percentages. The Crosswalk index value

of the EQ-5D-5L was calculated by using the German value set (Andonian et al., 2021b; Huber et al., 2017).

5 Scientific Publications

5.1 Article 1

Authors: Caroline Andonian, Jürgen Beckmann, Sabina Biber, Peter Ewert, Sebastian Freilinger, Harald Kaemmerer, Renate Oberhoffer, Lars Pieper, Rhoia Clara Neidenbach

Title: Current research status on the psychological situation of adults with congenital heart disease

Journal: *Cardiovascular Diagnosis and Therapy*

Doi: 10.21037/cdt.2018.12.06

Summary:

Due to markedly improved survival rates, the population of ACHD is growing and aging at a rapid pace. Yet, the heterogeneity of disease burden may place some individuals at greater risk for experiencing psychological distress, such as symptoms of depression and anxiety (Jackson et al., 2018). If left untreated, chronic emotional distress has been shown to independently predict QOL and cardiovascular outcomes in ACHD (Benderly et al., 2019). The healthcare perspective for these patients has widened with increased attention for the psychological dimension of CHD (Moons et al., 2018b). However, large-scale research studies on the psychological situation of ACHD and the relation to physiological outcomes are lacking. The present review summarizes the current state of research on the psychological situation in ACHD. According to present findings, ACHD present a higher risk of developing clinical depression (weighted lifetime prevalence ACHD, 24% vs. global prevalence, 11%), and anxiety (weighted lifetime prevalence ACHD, 38% vs. global prevalence, 34%). Estimates on period prevalence rates are similarly elevated in ACHD compared to global reference norms. Etiological explanations range from early trauma to neurological imbalances and aggravating psychosocial factors throughout the course of illness. Reciprocal mechanisms between psychological and physical factors can be partly explained by behavioral pathways and pathophysiological disturbances considering the latest scientific evidence in the field of psychocardiology. To date, there is still insufficient knowledge on the psychotherapeutic treatment of mental health issues in the growing population of ACHD. This review aims to raise awareness of both medical and mental health care professionals on the complex psychological situation of ACHD. It suggests a vital need to further examine the psychological situation of ACHD on a large-scale basis in order to establish consistent psychotherapeutic guidelines as part of a holistic approach to cardiac care.

The article was submitted to the Journal of *Cardiovascular Diagnosis and Therapy* in November 2018 and accepted for publication in December 2018. *Cardiovascular Diagnosis and Therapy* is an open access, peer-reviewed, international journal, which exchanges novel information on diagnosis, prevention, and clinical investigations of cardiovascular diseases among clinicians and investigators (Andonian et al., 2018).

Contribution:

Caroline Andonian was the principal investigator and first author of the published article. She significantly contributed to this study by developing the idea, independently collecting and analyzing relevant articles, reporting data and writing the manuscript. Caroline Andonian received intellectual feedback and linguistic revisions from her co-authors. She was the primary contact during the manuscript submission, peer review, and publication process.

Mini-Review

Current research status on the psychological situation of adults with congenital heart disease

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Contributions: (I) Conception and design: C Andonian, J Beckmann, H Kaemmerer, RC Neidenbach; (II) Administrative support: C Andonian, J Beckmann, H Kaemmerer, RC Neidenbach; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Due to technological and medical advances the population of adults with congenital heart disease (ACHD) is growing. Worldwide, congenital heart disease (CHD) affects 1.35–1.5 million children each year and more than 90% reach adulthood. Given the heterogeneity of CHD, survivors are faced with not only complex medical but also psychological challenges which may manifest in mental health problems, such as depression, anxiety and posttraumatic stress disorder. This review focuses on the emotional dimension of CHD. More precisely, it summarizes the present state of research on the prevalence of emotional distress in ACHD. Theoretical models provide a framework for possible explanations of mental health issues in ACHD. Additionally, the review examines the relation between psychological processes and overall health considering the latest scientific findings on coping with chronic illness (illness identity). There is still insufficient knowledge on the psychosocial treatment of mental health issues in the growing population of ACHD. This review suggests a vital need to further investigate the psychological situation of ACHD on a large-scale basis in order to establish a holistic treatment approach to accommodate the patients' special needs.

Keywords: Congenital heart disease (CHD); adults with congenital heart disease (ACHD); psychological situation, mental health, chronic disease, prevention

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Introduction

Congenital heart diseases (CHDs) are among the most common types of birth defects. Each year 1.35–1.5 million children are born with CHD worldwide. Due to the advances in congenital cardiology and cardiac surgery, survival rates of infants born with CHD have improved substantially (1). More than 90% of all children born with CHD reach adulthood in the industrial world, and the number of adults with CHD (ACHD) meanwhile exceeds the number of children with CHD in the long run. Unfortunately, most of the affected patients are not cured and are chronically ill due to residua, sequelae, complications from the underlying heart disease. Moreover, recent studies uncovered that many of them suffer from cardiac and non-cardiac comorbidities, and are at increased risk of psychological distress, neurocognitive deficits, and social challenges (2-4). Therefore, the need for an ongoing, lifelong holistic care for these patients is undisputed (5,6).

Given the heterogeneity of CHD, patients are faced with unique and often complex medical and psychological challenges beginning from the day they are born. These life-changing experiences entail early trauma due to numerous hospitalizations, continuous medical emergencies

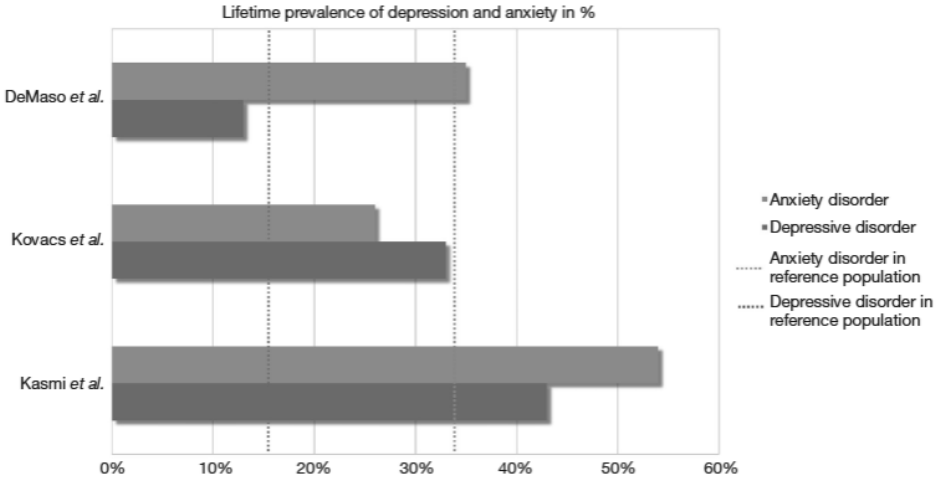

Figure 1 Studies examining depression and anxiety in ACHD (lifetime prevalence in %) (11-13). ACHD, adults with congenital heart disease.

and developmental constraints. It has been found that this patient population tends to have an increased prevalence of mood and anxiety disorders (7,8) and a significantly higher risk of post-traumatic stress disorder (PTSD) (9). However, large-scale research on the psychological situation of ACHD and the relation to physiological health is still insufficient. Given the cross-sectional design of current research, the direction of mechanisms and the progression of psychological symptoms cannot be determined. In addition, no valid statements can be made in regards to the different types of CHD.

The purpose of this article is to raise awareness for the complex psychological situation of patients with CHD. Both medical and mental health care professionals need to provide adequate measures in order to accommodate the patients' special needs. Sensitive communication and adequate education play a vital role in reducing denial and empowering patients to make wise decisions in their healthcare. Furthermore, ongoing research should seek to identify reliable screening tools for early detection and management of mental issues in patients with CHD.

Prevalence of emotional distress [depression, anxiety, PTSD and quality of life (QOL)]

Living with CHD can be a major challenge to a person's life as it is accompanied by a great burden in various aspects of private and professional life (10). Although most patients adjust their individual lifestyles, research shows that a significant number of ACHD experience emotional distress in terms of depression, anxiety and a compromised QOL (7). At present, knowledge of the psychological situation is relatively limited. Accordingly, the need for psychological support is high but currently only minimally covered (11).

Two reviews (7,8) indicate elevated levels of depression and anxiety in ACHD. *Figures 1* and *2* show the prevalence of depression and anxiety among ACHD in recent studies extracted from the reviews. Three out of seven studies present lifetime prevalence rates on depression and anxiety disorders in ACHD (11-13). In comparison to the general population (18,19), ACHD show higher rates in depression (weighted prevalence ACHD: 24% *vs.* global prevalence: 15%) and anxiety (weighted prevalence ACHD: 38% *vs.* global prevalence: 34%). Similarly, current prevalence rates of depression (weighted prevalence in ACHD: 16% *vs.* global prevalence: 6%) and anxiety (weighted prevalence ACHD: 29% *vs.* global prevalence: 8%) are elevated among ACHD compared to reference norms (18,19). The largest German study (14) using structured clinical interviews points to a significantly higher prevalence for overall psychopathology in ACHD when compared to the general population (48.0%, 95% CI: 44.7–60.0 *vs.* 35.7%, 95% CI: 33.5–37.9). The study included only 150 ACHD, mostly of mild or moderate severity.

In this context it is remarkable that PTSD has scarcely been investigated in ACHD although it is qualified by the

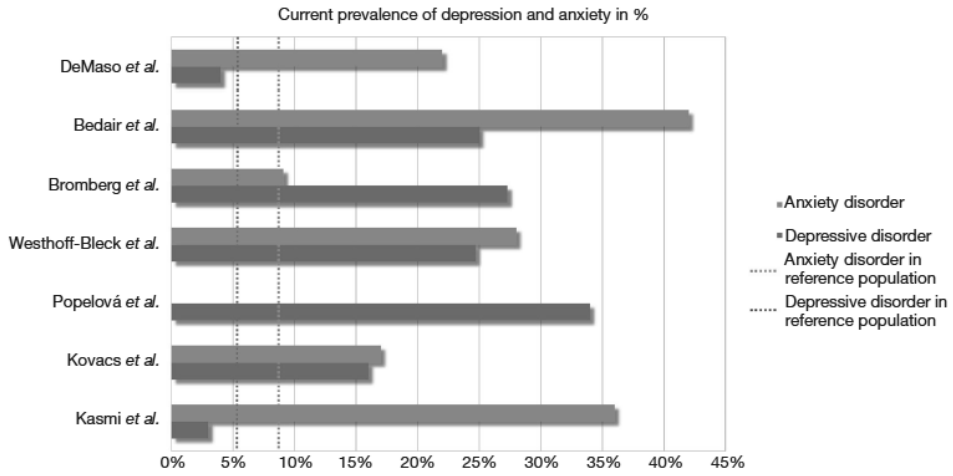

Figure 2 Studies examining depression and anxiety in ACHD (current prevalence in %) (11-17). ACHD, adults with congenital heart disease.

exposure to a traumatic event in childhood (20). A single-center study at The Children's Hospital of Philadelphia which enrolled 134 adult participants found that PTSD was present in 11–21% of ACHD compared to a rate of 3.5% in the general population. The researchers identified two factors that were associated with PTSD: elevated depressive symptoms and the year of most recent cardiac surgery. Accordingly, patients who had undergone cardiac surgery at an earlier stage in life were more likely to develop PTSD. Furthermore, subjects with PTSD reported lower QOL (9). Their findings support the "residual stress" theory of PTSD stating that traumatic events manifest in lasting, chronic stress (21). Their study has important clinical implications as PTSD is known to be linked to serious medical conditions in other cardiac populations (22).

Several studies (23-25) found that ACHD experience a generally good QOL. However, compromising factors entail adverse social and economic circumstances like lack of employment, older age and single life. ACHD tend to differ from healthy individuals in higher financial strain and less social support which in turn results in higher scores of emotional distress (26). A recent large-scale international study conducted by Moons *et al.* (27) identified functional class, higher age, unemployment status, standard of living and healthcare system characteristics as important predictors for a patient's health status and found significant variations across the countries patients live in. Patient-reported health outcomes defined as a composite of psychological well-being, physiological functioning and health behaviors were most favorable in Switzerland, Sweden and the Netherlands and lowest in France, Japan and India. Intercountry variation can be partly attributed to economic differences and healthcare system factors.

Etiology of emotional distress in ACHD

Different psychological disease models can be referred to for an explanation of emotional stress among adult CHD survivors. From a psychoanalytical perspective, the internalization of early psychological trauma due to illness and hospitalizations with the separation from parents at times leads to a higher risk for depression later in life. In fact, van Rijen *et al.* (28) could verify a significant relation between early hospitalizations with reoperations in CHD patients and higher behavioral and emotional problems later in life (28).

According to Bowlby's attachment theory, a secure and trusting mother-infant relationship is essential for a child's social-emotional development. Early mother-child separation due to hospitalizations with reoperations during infancy may disrupt the formation of a secure attachment and result in later psychological maladjustment (29).

The psycho-biological approach to depression provides evidence that repetitive stress events in early childhood lead to a neuro-transmitter imbalance in the brain. These events make individuals more vulnerable for developing

maladaptive psychological responses, such as posttraumatic stress disorder or depression, later on (30).

From a behavioristic perspective depression in CHD patients can be addressed as "learned helplessness". This view holds that because patients are permanently exposed to stressful situations linked to their illness associated with a lack of control they tend to adapt a passive (helpless) role. Learned helplessness contributes to the development of depression (8). Aggravating psychosocial factors, such as financial strain or lack of social support may contribute to the sense of helplessness (26).

Mechanisms and impact of emotional distress on health outcomes

There is sparse evidence on the impact of chronic emotional distress on health outcomes among ACHD. However, the findings on acquired heart disease suggest that high levels of emotional distress increase the risk for adverse medical outcomes and premature mortality (31-33). While depression is clearly linked to mortality in coronary artery disease patients, a meta-analysis (34) also confirmed that anxiety can be detrimental to cardiac health in patients with acquired cardiovascular disease (CVD). Based on the findings in patients with acquired CVD, it is conceivable that unrecognized and hence untreated mental issues may also put individuals with CHD at an increased risk for recurrent cardiac events. However, there is a substantial deficit of research on the interaction of psychological conditions and physiological outcomes in CHD patients. Particularly, longitudinal research on the consequences of emotional distress in CHD patients is needed.

Research among ACHD is mostly observational, identifying possible risk factors for emotional distress and diminished QOL. The research suggests that the relationship between the CHD severity and the patient's QOL is relatively complex (23,24). Holbein *et al.* (35) found that individual illness perceptions are an important mediating factor in the association between the CHD diagnosis and the patients' QOL. However, the relation of depression and anxiety symptoms to illness perceptions and QOL remains unclear and needs to be further investigated (35).

In order to understand how ACHD experience chronic illness, Oris *et al.* (36) went beyond illness perceptions. They examined how ACHD integrate their chronic illness into their sense of self (Illness Identity). Four different illness identity states were identified (i.e., engulfment, rejection, acceptance, and enrichment) and set in relation to psychological and physiological parameters. Oris *et al.* (36) found that engulfment is accompanied by maladaptive psychological and physiological outcomes in line with previous research (37). Rejection was related to more illness symptoms, but unrelated to depression and anxiety. The authors conclude that patients might reject their illness as part of their identity as a self-defense mechanism. Acceptance was linked to better psychological functioning—that is, less depression and anxiety symptoms—and less physical symptoms. Lastly, enrichment was related to more physical symptoms in ACHD as individuals experience the full scope of their illness in order to grow as a person (38). Their findings stress the importance of integrating the illness into one's identity in order to better cope with individual disease related challenges in ACHD. Their research also implies, that providing patients with clear information on their illness (psychoeducation) and how to deal with it can improve the understanding of the illness which is beneficial to the patients' health condition and their QOL.

Research conducted by van Rijen *et al.* suggests that younger patients (20 to 27 years) and female patients show more psychopathology than older patients (28 to 32 years) and male patients. In addition, the assessment of caregivers suggested more problems than the patients' self-reports (39). It is unclear, whether rather optimistic self-reports stem from well-adjusted coping skills, or other states such as overcompensation or denial which might extend the framework of illness identity.

Treatment of emotional distress in ACHD

There is insufficient research on the treatment of mental issues in ACHD. To date, only a small amount of patients receive psychosocial or pharmacological treatment for anxiety and depression (11). According to Kovacs *et al.*, 39% of ACHD who fulfilled diagnostic criteria for a mood or anxiety disorder have not received any psychosocial treatment (11). Preliminary results of their randomized controlled trial examining the efficacy of a cognitive-behavioral treatment in ACHD (n=42) showed reductions in depressive symptoms. Their eight-session group intervention (ACHD-CARE Program) included psychoeducation and cognitive behavioral techniques such as cognitive restructuring, relaxation, self-awareness techniques and soft skills training (40). The authors confirmed the feasibility of conducting a large-scale trial on a broad composition of ACHD to improve psychological well-being (41).

Conclusions and perspectives

Decades ago, CHD was considered a fatal pediatric condition. Due to medical and technological advances, ACHD are now becoming a fast-growing population. As research indicates, a significant number of ACHD suffer from symptoms of depression, anxiety and PTSD. These mental disorders do not only negatively impact patients' QOL but can also put them at greater risk for cardiovascular morbidity and mortality. Explanations range from early trauma to neurological imbalances in the brain and aggravating psychosocial factors later in life. Yet, to date only a minority receives psychosocial treatment.

The influences on the psychological situation of ACHD have received little attention. An in-depth investigation of the unique role of illness identity in the psychological well-being of ACHD needs to be undertaken. It may be reasonable to consider additional psychological constructs (e.g., meaning in life, recovery-stress model) in order to gain a deeper understanding into the relation between psychological processes and physiological outcomes. Considering the tremendous heterogeneity of ACHD large-scale population-based studies are feasible to help caregivers identify crucial indicators for diagnosis and treatment.

Acknowledgements

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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5.2 Article 2

Authors: Caroline Andonian, Sebastian Freilinger, Stephan Achenbach, Peter Ewert, Ulrike Gundlach, Jürgen Hoerer, Harald Kaemmerer, Lars Pieper, Michael Weyand, Rhoia Neidenbach, Jürgen Beckmann

Title: The "Well-being paradox" revisited: A cross-sectional study of quality of life in over 4,000 adults with congenital heart disease

Journal: *BMJ Open*

Doi: 10.1136/bmjopen-2021-049531

Summary:

Since findings on QOL among ACHD are highly heterogeneous due to conceptual and methodological flaws, the present study aimed to extensively examine QOL on a sound conceptual basis. As part of the ongoing nationwide VEmaH registry, 4,014 ACHD (41.8 ± 17.2 [range, 18−97], 46.5% female) encompassing a broad spectrum of CHD (mild, moderate and severe disease complexity) were included. QOL was analysed with a special focus on patient-related and clinical determinants, since these variables have not yet been sufficiently examined to account for potential differences in QOL. In conceptual alignment with the target variable, EQ-5D-5L was applied to provide a simple, generic measure of a patient's perceived QOL. Sociodemographic and medical information was obtained by a self-devised questionnaire. Associations of QOL with patient-reported clinical and sociodemographic variables were analysed by multiple regression analysis and multiple ordinal logit models. Overall, the results suggest that ACHD report a fairly satisfactory QOL which is comparable to general German population norms. However, the dimensions pain/discomfort (mean: 16.3, SD: $p<0.001$) and anxiety/depression (mean: 14.3, $p<0.001$) appeared to be the most problematic. QOL differed significantly within diagnostic subgroups based on complex heart defects yielding to more favorable QOL outcomes within the dimensions of self-care (odds ratio [OR] 0.148, 95% CI .04-.58) and mobility (odds ratio [OR] 0.384, 95% CI .19-.76). Older age, female sex, medication, and the presence of comorbidities, were associated with significant reductions in QOL ($p<0.001$). Surprisingly, ACHD generally indicate a high level of subjective well-being. However, present findings also help clinicians to identify specific subgroups of patients who are particularly at risk for decreased QOL and may therefore require extra psychological support. The study therefore constitutes a major step in paving the way towards integrated cardiac care (Andonian et al., 2021a).

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Contribution:

Caroline Andonian was the principal investigator and first author of the published article. She was ultimately responsible and accountable for the idea of the study, the study design, and collecting and reporting data. She chose appropriate methods of analysis with support and feedback of her supervisor. Based on her findings, Caroline Andonian extended existing theories of chronic illness experience exemplified in the ACHD population. Caroline Andonian wrote the published article, while receiving feedback from her co-authors. She served as the primary contact during the submission process.

Open access Original research

BMJ Open

'Well-being paradox' revisited: a cross-sectional study of quality of life in over 4000 adults with congenital heart disease

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ABSTRACT

Objective The present cross-sectional study investigated quality of life (QOL) in a large cohort of German adults with congenital heart disease (ACHDs) in association with patient-related and clinical variables.

Design Cross-sectional survey.

Participants Between 2016 and 2019, a representative sample of 4014 adults with various forms of congenital heart defect (CHD) was retrospectively analysed. Inclusion criteria were confirmed diagnosis of CHD; participant aged 18 years and older; and necessary physical, cognitive and language capabilities to complete self-report questionnaires.

Primary and secondary outcome measures QOL was assessed using the 5-level EQ-5D version (EQ-5D-5L). Sociodemographic and medical information was obtained by a self-devised questionnaire. Associations of QOL with patient-reported clinical and sociodemographic variables were quantified using multiple regression analysis and multiple ordinal logit models.

Results Overall, ACHDs (41.8±17.2 years, 46.5% female) reported a good QOL comparable to German population norms. The most frequently reported complaints occurred in the dimensions pain/discomfort (mean: 16.3, SD: $p<0.001$) and anxiety/depression (mean: 14.3, $p<0.001$). QOL differed significantly within ACHD subgroups, with patients affected by pretricuspid shunt lesions indicating the most significant impairments ($p<0.001$). Older age, female sex, medication intake and the presence of comorbidities were associated with significant reductions in QOL ($p<0.001$). CHD severity was positively associated with QOL within the dimensions of self-care (OR 0.148, 95% CI 0.04 to 0.58) and mobility (OR 0.384, 95% CI 0.19 to 0.76).

Conclusion Current findings temper widely held assumptions among clinicians and confirm that ACHDs experience a generally good QOL. However, specific subgroups may require additional support to cope with disease-related challenges. The negative correlation of QOL with age is especially alarming as the population of ACHDs is expected to grow older in the future.

Trial registration number DRKS00017699; Results.

Strenghts and limitations of this study

- ► First study of its kind exploring quality of life (QOL) among 4014 patients with different medical and patient-related backgrounds.
- ► Uniform conceptualisation of QOL based on EQ-5D-5L, which is a highly reliable and valid outcome measure within the cardiovascular area.
- ► Present findings help clinicians to identify specific subsets of patients who require extra psychological support and therefore constitute a major step in paving the way towards integrative cardiac care.
- ► Causal inferences are not possible due to the cross-sectional design of this study.
- ► Ambiguous findings open new avenues for future research in understanding the construction of self-rated health despite or as a consequence of congenital heart defect.

INTRODUCTION

Congenital heart defects (CHDs) are the most common isolated inborn organ malformations and affect 1.35–1.5 million children each year. Although 90% of patients with CHD survive into adulthood, many of them are not cured and need to adapt to their chronic medical condition throughout their lives.[1] Besides symptoms related to their heart disease, lifelong psychosocial impairments may seriously impact the patients' perceived quality of life (QOL).[2] While clinical research traditionally focused on objective medical outcomes, the relevance of QOL and various related patient-reported outcomes is increasingly recognised in the evaluation of care for adults with congenital heart disease (ACHDs).[3]

Research on QOL in ACHDs is still relatively scarce and not conclusive. Empirical findings indicate that QOL among ACHDs is compromised by sociodemographic factors (unemployment, older age and single status), psychological features (negative illness perceptions and distressed personality) and

medical characteristics (eg, hospitalisation and worse functional status). QOL has been found to be positively associated with higher socioeconomic and educational status, stronger social support, better functional class, better knowledge of CHD, stronger sense of coherence, as well as the absence of cardiac surgery. Existing findings are inconsistent regarding cardiovascular status, medication, age and gender, although these variables appeared to be the most frequently investigated determinants.[4]

These inconsistent results of existing research on QOL in ACHDs can be attributed to a lack of a clear conceptual background, inconsistent methods and insufficient sample sizes.[4] Additionally, the high heterogeneity of ACHDs constitutes a substantial confounding factor due to their great anatomical and clinical disease complexity. Most studies on QOL in ACHDs focused on specific subgroups of patients, which limits their informational value. Consequently, clinical parameters were not sufficiently examined to explain potential differences in QOL by the underlying diagnosis or severity of CHD. Although a recent review attests temporal qualitative improvements in QOL studies over the past decades, the current research situation still fails to meet scientific quality criteria.[5]

The present study aimed to assess QOL within a large sample of ACHDs in Germany and to examine potential determinants of QOL in terms of patient-related and medical characteristics. Identifying determinants of QOL, along with special needs of ACHDs, could advance the improvement of healthcare for this growing patient population.

METHODS

Design

The present study represents a subanalysis of the nationwide VEMAH initiative (Versorgungssituation von Erwachsenen mit angeborenen Herzfehlern, 'Medical Care Situation of ACHD' in English). Detailed information on the rationale, design and methods is documented in a former published paper.[6] VEMAH is a multicentre, cross-sectional study to assess the healthcare situation of ACHDs in Germany. Coordination of VEMAH was initiated and carried out by the German Heart Centre Munich.

Population

A questionnaire package was consecutively addressed to ACHDs presenting at the Department of Congenital Heart Disease and Paediatric Cardiology of the German Heart Centre Munich and the Department of Cardiology of the University of Erlangen. Additionally, the health insurance provider AOK Bayern distributed questionnaires to their policyholders with CHD in Bavaria, and the National Register for Congenital Heart Defects in Berlin, Germany, invited its members to participate in the study online. Guidelines on good clinical practice and data protection guidelines were followed. Inclusion criteria were (1) confirmed diagnosis of CHD according to the definition of Thiene and Frescura[7]; (2) participant age of 18 years and older; and (3) necessary physical, cognitive and language capabilities to complete self-report questionnaires.

Measures

Patients completed a questionnaire either in person, online or by mail. Data collection took place between 2016 and 2019. QOL was measured using the generic questionnaire 5-level EQ-5D version (EQ-5D-5L).[8]

Demographic and clinical information

Sociodemographic and medical information was obtained by a self-devised questionnaire. Medical variables included leading CHD, medication, presence of cyanosis, (non-) cardiac comorbidities and hereditary diseases. Following the recommendations of the American College of Cardiology, patients were divided into three severity groups based on their CHD diagnosis.[9]

QOL (EQ-5D-5L)

QOL was measured using the updated five-level version of the EQ-5D,[8] which provides a simple, generic measure of a patient's perceived health status. The EQ-5D-5L consists of a descriptive system questionnaire and a Visual Analogue Scale (VAS). The descriptive system compromises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each patient was asked to indicate his perceived impairments on a 5-point Likert scale ranging from 'no problems' to 'extreme problems/unable'. Responses were converted into a single weighted index score (EQ-5D Index), which indicates how good or poor the respondent's health status is based on existing population norms. A value set for the EQ-5D-5L, based on a representative sample of the German population, has recently been developed.[10] The VAS indicates a patient's overall health state on the day of the questionnaire completion. It is a scale which ranges from 0 ('the worst health you can imagine') to 100 ('the best health you can imagine') and provides a quantitative measure of a patient's perceived health. The EQ-5D-5L proved to be a reliable and valid method for measuring QOL in cardiovascular populations (Cronbach's alpha=0.856).[11]

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics V.24.0. Descriptive measures were calculated for sample characteristics, including patient-reported sociodemographic and medical variables (absolute and relative frequencies, mean and SD). The relationships between CHD diagnosis groups and EQ-5D-index values, including the underlying dimensions mobility, self-care, usual activities, pain/discomfort and anxiety/depression were analysed. The comparison of ordinally scaled values was based on cumulative frequencies representing the relative proportion of patients with moderate to severe symptoms on the specific dimensions. Kruskal-Wallis tests were applied to reveal significant differences between

EQ-5D-dimensions and metric index values. Furthermore, the relationship between EQ-5D VAS scores and dedicated index values was analysed with respect to various patient characteristics. Multiple regression models using ordinary least squares (OLS) estimates were calculated, while bivariate Pearson coefficients were used to analyse the correlation between VAS and index scores. Finally, multiple ordinal logit models were applied to identify significant predictors of the respective QOL dimensions. For all tests, the statistical significance level was set at a p value of <0.05. Data analysis was currently performed for complete cases on each variable. To rule out a potential distortion of findings, a further comparison between statistically included and excluded patients was conducted and revealed no significant differences concerning their QOL.

Patient and public involvement

Neither patients nor the public were involved in the design and conduct of this research. The methodology of this research was adapted in multidisciplinary collaboration.

RESULTS

Sample characteristics

A total of 4014 patients was analysed (46.5% female) (table 1). The mean age of ACHDs was 41.8±17.2 (18–97) years. Patients were subclassified according to the underlying CHD into six main groups, consisting of complex CHD (n=581), pretricuspid shunts (n=621), post-tricuspid shunts (n=406), right heart or pulmonary artery anomalies (n=526), left heart or aortic anomalies (n=898) and miscellaneous CHD (n=602). Overall, 15.4% of patients (n=602) presented with cyanosis. The severity of CHD was determined according to the Warnes classification system as simple (n=1722, 62.0%), intermediate (n=650, 23.4%) or severe (n=406, 14.6%).[12]

Table 1 Characteristics of the underlying study population

Variables	n (%)
Age group (years) (n=3903)	
18–34	1663 (42.6)
35–64	1733 (44.4)
65+	507 (13.0)
Gender (n=3898)	
Male	2087 (53.5)
Female	1811 (46.5)
Residence (n=3855)	
City	775 (20.1)
Town	590 (15.3)
Rural	2490 (64.6)
Insurance (n=3905)	
Public	3679 (94.2)
Private	219 (5.6)
No insurance	7 (.2)
Type of congenital heart defect (CHD) (n=4014)	
Complex congenital heart defects	581 (14.5)
Primary pretricuspid shunts	621 (15.5)
Primary post-tricuspid shunts	406 (10.1)
Right heart/pulmonary artery anomalies	526 (13.1)
Left heart/aortic anomalies	898 (22.4)
Miscellaneous CHD	602 (15.0)
Unclassifiable	380 (9.5)
Warnes class (n=2778)	
Simple	1722 (62.0)
Moderate	650 (23.4)
Severe	406 (14.6)

QOL and ACHDs

EQ-5D dimensions were found to be differently associated with CHD subgroups. Significant differences between the underlying diagnosis were found on all dimensions (p<0.001). Compared with all other subgroups, pretricuspid shunts were particularly impaired in mobility, daily activities, pain/discomfort and anxiety/depression (table 2). In contrast, complex CHD showed the least problems on the respective descriptive dimensions (figures 1–5).

Similar results were reflected by EQ-5D VAS and index values (p<0.001) with EQ-5D VAS values being highest in patients with right heart/pulmonary artery anomalies and complex CHD and lowest in patients with pretricuspid shunts. Observed differences were less extreme between descriptive EQ-5D Index values. Both EQ-5D values were positively correlated (r=0.623, p<0.001), with coefficients being the lowest for patients with complex CHD (r=0.579, p<0.001) and highest for patients with left heart/aortic anomalies (r=0.653, p<0.001). Variations in QOL were observed, depending on the type of measurement which was applied. Accordingly, the mean VAS score displayed a significantly lower QOL than the descriptive EQ-5D Index value.

Patient-related determinants of QOL

OLS regression models were applied to analyse relationships of sociodemographic variables with EQ-5D VAS and index values (table 3). At the 5% level of significance, age had the highest negative impact on VAS values (β=−0.32) and index values (β=−0.22). Thus, QOL decreased with advancing age. Patients aged 65+ years indicated the lowest values on both scales. Means for both EQ values were slightly higher in male patients than in female patients. Medication intake had significant negative effects on QOL in both measures. Model fit was slightly higher for the dependent variable in VAS values (R^2=0.190) than EQ-5D Index values (R^2=0.112).

CHD-related determinants of QOL

EQ-5D-dimensions were analysed more specifically in regard to different medical features such as connective

Table 2 Leading diagnosis of CHD and EQ-5D-results

EQ-5D	Total	Complex CHDs	Primary pretricuspid shunts	Primary post-tricuspid shunts	Right heart/ pulmonary artery anomalies	Left heart/ aortic anomalies	Unclassifiable	Miscellaneous	P value
Dimension	N=4014	n=581	n=621	n=406	n=526	n=898	n=380	n=602	
Mobility	12.2	8.6	13.6	10.4	9.6	10.5	15.0	16.6	<0.001*
Self-care	3.5	2.0	3.0	2.3	3.2	3.5	4.4	5.4	0.017*
Usual activities	13.2	13.7	13.5	11.2	12.6	11.1	14.1	16.8	<0.001*
Pain/ discomfort	16.3	13.7	20.4	12.3	11.8	14.3	19.5	22.7	<0.001*
Anxiety/ depression	14.3	14.8	17.5	14.2	12.6	12.0	14.4	15.5	0.002*
EQ-5D VAS	n=3761	n=540	n=605	n=388	n=485	n=844	n=351	n=548	<0.001*
Mean	76.15	78.21	73.29	77.28	79.50	77.36	74.32	72.80	
SD	18.97	17.12	19.93	19.90	17.48	18.55	19.56	19.57	
EQ-5D Index	n=3690	n=540	n=583	n=383	n=489	n=828	n=344	n=523	<0.001*
Mean	0.90	0.92	0.89	0.91	0.92	0.91	0.88	0.87	
SD	0.15	0.14	0.15	0.14	0.15	0.14	0.16	0.18	

Data for EQ-5D-dimensions represent relative percentages of patients, who indicated moderate to severe problems with respect to each dimension. Significant differences were calculated using Kruskal-Wallis tests for independent samples.
*P<0.05.
CHD, congenital heart defect; VAS, Visual Analogue Scale.

tissue diseases with cardiovascular involvement, cyanotic status and severity codes of CHD. Several ordered logistic regression models were applied using each of the five dimensions as dependent variables (table 4). Generally, patients with comorbidities had significantly increased odds of reporting problems on all dimensions than patients without comorbidities (p<0.05). Non-cardiac comorbidities accounted for significantly higher odds of having problems than cardiac comorbidities. No significant effects could be observed for cyanotic status. Furthermore, regression models showed no effects for patients with simple or moderate disease severity classes. Apparently, severely classified patients indicated decreased odds of suffering from issues related to mobility or self-care than patients in lower Warnes' classes.

DISCUSSION

QOL is one of the most important measures used to assess the psychosocial impact of chronic disease on a patient's life. This is the first study to investigate patient-reported QOL within a cohort of 4014 patients encompassing a broad spectrum of CHD. QOL in ACHDs was assessed by using the EQ-5D-5L, a highly reliable and valid outcome measure within the cardiovascular area.[13] It compromises

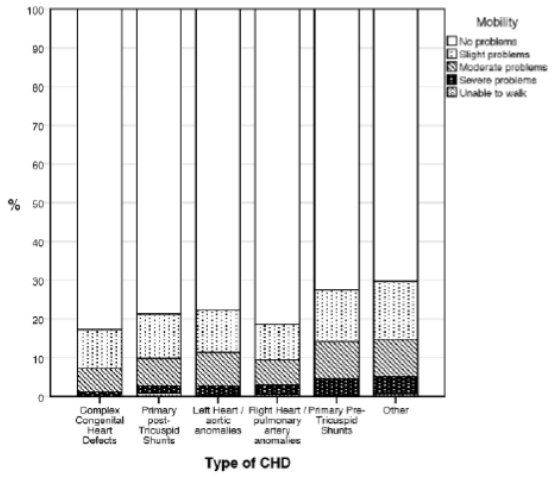

Figure 1 Distribution of scores for mobility. CHD, congenital heart defect.

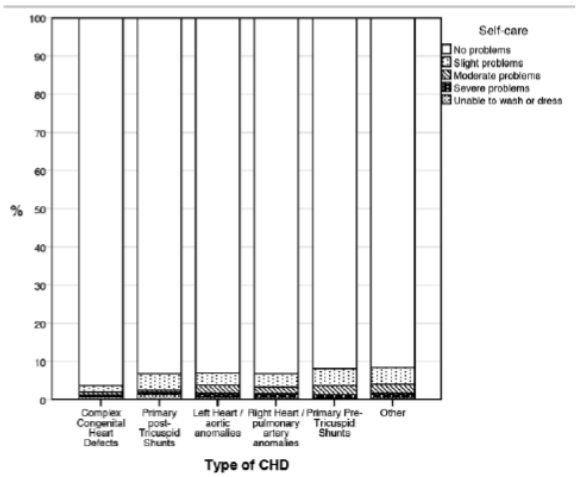

Figure 2 Distribution of scores for self-care. CHD, congenital heart defect.

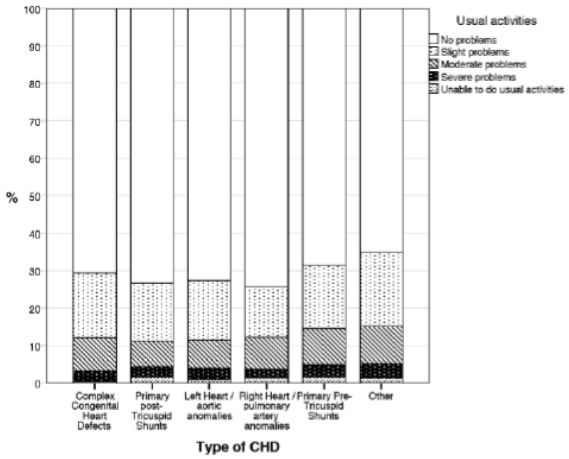

Figure 3 Distribution of scores for usual activities. CHD, congenital heart defect.

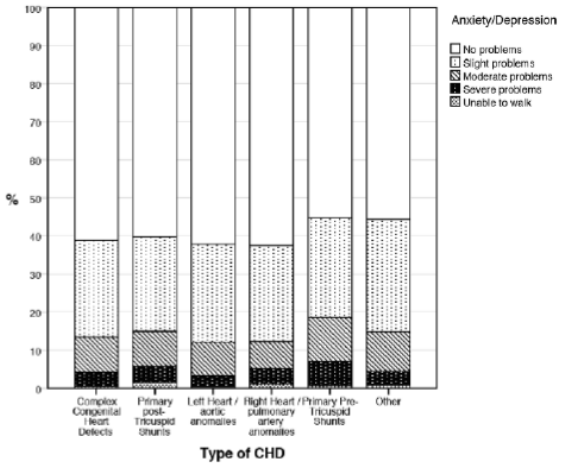

Figure 5 Distribution of scores for anxiety/depression. CHD, congenital heart defect.

two types of measurement and therefore provides a global view on QOL in terms of general life satisfaction. This allowed to revelation of genuine differences in QOL among patients with different medical and socio-demographic backgrounds, regardless of methodological considerations. Within the context of this study, QOL quantifies the influence of CHD on a patient's ability to function and derive personal satisfaction from life.

QOL in ACHDs

In line with previous findings,[14] ACHDs in general reported a good level of well-being which is comparable to German population norms.[15] The twofold measure of QOL revealed that the type of measurement affects QOL scores differently. Apparently, the overall VAS score indicated a significantly lower QOL than the descriptive EQ-5D Index value. One explanation for this discrepancy is differences in the QOL coverage of both measures. It

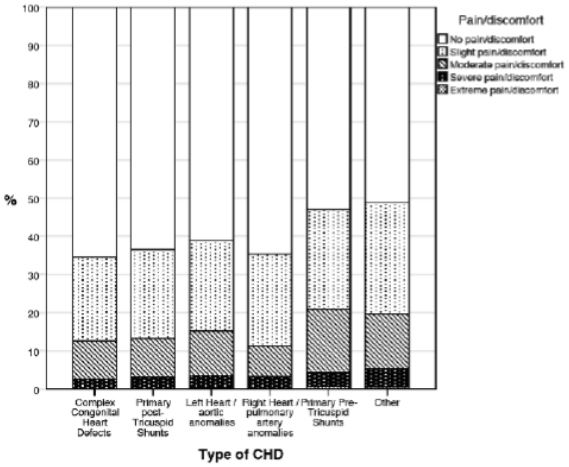

Figure 4 Distribution of scores for pain/discomfort. CHD, congenital heart defect.

can be assumed that the descriptive system encourages a patient to examine QOL from various angles as the system breaks down QOL into various components. Thus, QOL is regarded as a subjective concept being influenced by multiple causal factors.[16] In contrast, VAS picks up a one-dimensional view of perceived health where patients may indicate a higher occurrence of problems by focusing on somatic health restrictions imposed by their CHD. When comparing the quantitative association of CHD with QOL to other chronic disorders, the average reduction in VAS values in the current sample roughly resembles observations of various other heart diseases.[15] In line with previous research, patients most frequently reported problems in the areas of pain/discomfort (16.3%) and anxiety/depression (14.3%).[17] These rates lie considerably above German population standards, which document symptoms of anxiety/depression in 4.7% of the general public. This result further supports previous research showing that ACHDs are specifically prone to increased psychological distress and therefore require additional psychosocial support.[18]

A closer look at different diagnosis groups reveals that patients with pretricuspid shunts were particularly impaired in QOL. Comparable data have previously documented that QOL is not necessarily congruent with the complexity or severity of a heart disease. Even mild primary pretricuspid shunts can have a considerable negative impact on QOL.[19] Clinical reality shows that pretricuspid shunts are often detected incidentally and later in life creating a different psychological situation than diagnosis of CHD early in life. Children who grew up with the awareness of their CHD may acquire a greater sense of appreciation for life and expectations consistent with their capabilities and limitations.[20] Qualitative research on ACHD indicates that patients perceive the awareness of their childhood condition as a ressource to re-evaluate life priorities and develop a new life perspective.[21] A

Table 3 Patient characteristics and their correspondence with EQ-5D vas and index values

	EQ-5D VAS				EQ-5D Index			
Variables	**Mean**	**SD**	**ß**	**p**	**Mean**	**SD**	**ß**	**p**
Age group			–0.32	<0.001*			–0.22	<0.001*
18–34	83.46	14.75			0.94	0.11		
35–64	73.44	18.99			0.89	0.15		
65+	62.23	20.83			0.82	0.21		
Sex			0.01	<0.001*			0.04	0.004
Female	76.11	19.07			0.90	0.15		
Male	76.55	18.85			0.91	0.14		
Residence			0.02	0.084			0.03	0.060
City	76.30	17.49			0.90	0.15		
Town	77.08	18.26			0.90	0.15		
Rural	76.01	19.46			0.90	0.15		
Medication			–0.22	<0.001*			–0.19	<0.001*
No	79.16	17.13			0.92	0.13		
Yes	65.17	20.69			0.83	0.20		

Multivariate analysis was performed using ordinary least squares regression models with EQ-5D VAS and index values as dependent variables.
*P<0.05.
VAS, Visual Analogue Scale.

recent study has further established that sense of coherence is a highly significant predictor of QOL in ACHD.[22] Based on theoretical considerations, Sense of Coherence (SOC) develops during childhood and is thought to be fully developed by the age of 30 years.[23] Patients who may be diagnosed later in life may have missed the chance to develop and refine coping mechanisms and may therefore experience the effects of their CHD more negatively

Table 4 Impact of medical features with respect to EQ-5D dimensions

Variable	**n**	**Mobility n=3070**	**Self-care n=3073**	**Usual activities n=3068**	**Pain/discomfort n=3051**	**Anxiety/ depression n=3061**
Comorbidities						
Cardiac cmorbidities	1463	0.302* (0.25 to 0.36)	0.525* (0.38 to 0.73)	0.348* (0.29 to 0.41)	0.331* (0.28 to 0.39)	0.467* (0.40 to 0.54)
Non-cardiac comorbidities	819	0.263* (0.22 to 0.32)	0.281* (0.20 to 0.39)	0.222* (0.18 to 0.27)	0.311* (0.26 to 0.37)	0.243* (0.20 to 0.29)
Cyanosis						
Cyanotic	744	0.904 (0.49 to 1.68)	0.396 (0.12 to 1.26)	0.880 (0.50 to 1.56)	1.088 (0.65 to 1.82)	0.850 (0.51 to 1.41)
Acyanotic	2176	1.452 (0.70 to 3.02)	0.774 (0.20 to 3.04)	1.207 (0.63 to 2.30)	1.011 (0.58 to 1.77)	0.695 (0.40 to 1.19)
Warnes class						
Simple	1722	1.396 (0.69 to 2.84)	0.707 (0.18 to 2.84)	1.109 (0.60 to 2.06)	0.984 (0.57 to 1.69)	0.739 (0.44 to 1.24)
Moderate	650	0.848 (0.50 to 1.45)	0.538 (0.17 to 1.69)	0.985 (0.60 to 1.61)	0.884 (0.57 to 1.37)	0.921 (0.60 to 1.41)
Severe	406	0.384* (0.19 to 0.76)	0.148* (0.04 to 0.58)	0.710 (0.39–1.30)	0.620 (0.36–1.08)	0.742 (0.43–1.27)

Displayed are ORs and upper and lower bounds (95% CI), respectively, which were obtained from several ordered logistic regressions using EQ dimensions as dependent variable.
*P<0.05.

leading to higher emotional distress. Life-stage variables, such as age at diagnosis or years of survival, need to be further investigated as possible determinants of QOL.

Socioeconomic determinants of QOL

Despite good overall QOL, EQ-5D Index and VAS values deteriorated with increasing age. This might be explained by the uncertainty in disease prognosis manifesting itself in an increased sense of vulnerability in this patient group.[24] Most patients with CHD are known to do well in the first decades of life until they eventually develop unexpected age and disease-related comorbidities. This development deserves special attention as the group of ACHD is expected to grow steadily in the future.[1]

In contrast to previous findings,[14] the present study revealed modest gender-related differences in QOL. Women were more likely to report poor QOL than men. These findings may be attributed to psychosocial factors rather than gender per se.[25] In general, gender is found to influence health expectations, health behaviours and perceived health outcomes.[26] Women may face a triple burden shouldering family responsibility, professional ambition and demands of their chronic disease. Research has demonstrated that women were less likely to return to work, more likely to recline psychological counselling and more socially isolated than men.[27] It has also been argued that women were more willing to disclose problems than men concerning their QOL, which may partly explain the difference in their QOL.[26] Engelfriet *et al* also showed that women with CHD were more often symptomatic and presented functional impairments, despite a higher overall mortality in men over a 5-year period.[28] Gender disparities in patient–provider communication and dissatisfaction with healthcare might be another reason for decreased QOL in women. They might have higher expectations and a stronger demand for more participatory encounters with their healthcare providers.[25] Improved recognition and understanding of these gender-specific differences and challenges among ACHDs is vital to improve their cardiovascular health over the long term.

Reported medication intake was inversely associated with QOL in the present study. This appears plausible because extensive or inappropriate medication can lead to severe side effects and even higher morbidity, which may considerably impair QOL.[29] Aside from incorrect pharmaceutical treatment, the daily intake of medication is a constant reminder of illness and may have a negative impact on life satisfaction. Consequently, medication may be either a facilitator by providing new opportunities or an intensifier of problems by adverse psychological and somatic side effects.

Clinical determinants of QOL

Despite all advances in cardiac care, many patients with CHD are left with significant residua, sequels or complications from the underlying anomaly.[9 30] The impact of comorbidities in ACHD is largely underestimated.[31] The current study indicates that the presence of comorbidities increases the risk of problems on all dimensions of the EQ-5D. It is conceivable that affected patients report a lower health status since they may experience serious restrictions in various life domains. As comorbidities become increasingly dominant with advancing age, they may also explain the recorded deterioration of QOL with age in the present sample.

It is remarkable that patients with a more complex CHD scored significantly better in QOL domains. Until now, research has failed to demonstrate a clear-cut correlation between disease complexity and QOL.[4] Although the present finding may seem counterintuitive at first, there are various possible explanations for a better QOL in the light of a chronic condition. Keyes' two-continua model of mental health[32] provides an important framework for explaining why patients might experience a good QOL despite their CHD. Accordingly, mental health is a complex state resulting from an interplay of environmental and psychological factors that have a profound influence on one's subjective well-being. Keyes' model holds that mental health (sometimes referred to as mental well-being) and mental illness are orthogonally related phenomena and not two endpoints of a single continuum. Although the current state of research confirms elevated levels of mental illness among ACHDs,[18] this does not necessarily imply impaired mental well-being or decreased QOL among these patients. Furthermore, the disability paradox explains why individuals may perceive a high QOL despite serious limitations. Accordingly, QOL depends on finding a balance in life and maintaining harmonious social relationships.[33] The characteristics associated with a severe CHD may potentially include favourable and compromising factors and thus explain both extremes of QOL in ACHDs. Lastly, growing up with a CHD can lead to a so-called 'response shift' in terms of redefining priorities in one's life.[34] It is perceivable that patients develop values different from those of healthy persons in the face of a life-threatening, chronic illness. In this context, Sprangers and Schwartz[35] proposed a theoretical model to clarify and predict changes in QOL as a result of various dispositional characteristics, a patient's health status and mechanisms to accommodate to these changes.[35]

Despite the extensive power of the present study, current results should be interpreted with caution due to certain limitations. The study was retrospective and cross-sectional in nature and does not allow disentanglement of any conclusions about the directionality of effects or the development of QOL over time. Since all information was based on patient-reported outcomes, medical data may have been classified incorrectly due to a patient's limited knowledge of his or her condition. Consequently, surgical status of patients could not be identified. Subsequently, it would be advisable to synchronise these data with medical records in order to disentangle the effects of empirical–medical observations on QOL. As the enrolment was voluntary, selection bias could not be

excluded and may hamper representativeness. Further, this study was performed at a tertiary care centre for ACHD, which does not reflect the typical population of CHD. Further doubts must be raised about whether the applied EQ-5D-5L provides an accurate tool to evaluate QOL among AHCDs. Although the updated 5L version demonstrates superior performance compared with its predecessor, psychometric properties in terms of high ceiling effects and weak discriminatory power have previously been questioned.[36] It has further been shown that the choice of value set has an impact on EQ-5D scores.[37] Since the present study used a population-based value set to construct QOL estimates, we strongly encourage to re-evaluate current findings on the basis of experience-based value sets. Further, the inventory was administered in three different ways. However, measurement invariance across the survey methods was not tested, and the equivalence across the survey methods remains questionable. Since the primary aim of this study was to assess clinical determinants of QOL, sociodemographic variables were not explicitly reviewed within the present analysis. Based on the German healthcare system, the depicted sociodemographic variables are crucial indicators of access to medical supply and were therefore separately analysed. Given previously documented associations between sociodemographic factors and QOL, generalisation of the conclusions and transmission to patients from differing socioeconomic conditions are debatable. The present survey assessed biological sex with a binary value. Given the increasing incidence of transgender and gender non-binary individuals and that large health disparities exist for this population,[38] future research should increasingly expand measures of sex/gender to be trans-inclusive. Finally, no control group was involved, and data could only be compared with published national EQ-5D studies.

CONCLUSION

The present study shows that ACHD experience—on aggregate—a good QOL which is indistinguishable from healthy individuals. Against expectation, patients with complex CHD scored higher on QOL. However, specific subgroups of patients indicate significant reductions in QOL and may require extra support in their care to cope with challenges associated with their underlying CHD. The negative correlation with age deserves particular attention as it could lead to a decrease in QOL with the growing median age of this patient population.

QOL is regarded as a central target in the treatment of chronically ill patients. This study supports the need to further assess and promote mental well-being in ACHDs to safeguard surgical successes of the past decades which have ensured the survival of patients with CHD into adulthood. Successful treatment implies not only an increased length of survival but also enhanced subjective well-being and QOL.

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Patient consent for publication Not required.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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5.3 Article 3

Authors: Caroline Andonian, Sebastian Freilinger, Harald Kaemmerer, Jürgen Beckmann

Title: Psychological Well-being in Adults with Congenital Heart Disease: Testing the Predictive Value of Illness Identity

Journal: *Heart and Mind*

Doi: 10.4103/hm.hm_32_21

Summary:

Although the healthcare perspective for ACHD has widened with increased attention for psychological outcomes, in-depth investigations on illness experience of ACHD are still pending (Moons, 2021). This gap in knowledge may contribute to the lack of psychosocial support for this patient population. Previous research has shown significant associations between illness identity and psychological outcomes in ACHD (Andonian et al., 2020). Since differences in psychological functioning among ACHD could not be sufficiently explained by objective clinical parameters, the third study aimed to investigate the role of illness identity in the association between perceived health and psychological outcomes in ACHD. Self-report outcomes on sociodemographics, health perception, illness identity, and emotional distress were assessed in combination with verified clinical information on cardiac parameters. 229 (38 ± 12.5 [range, 18-73] years; 45% female) study participants were recruited at the outpatient clinic of the German Heart Center Munich. Moderation and mediation analysis were performed according to procedures described by Hayes and the PROCESS macro for IBM SPSS Statistics 27.0 (IBM Inc., Armonk, NY, USA, 2020). The hypothetical model explained 42% of variance in total emotional distress (R^2=0.416). Illness identity was a consistent mediator of the relationship between perceived health and emotional distress ($p<0.05$). The mediating effect varied between different dimensions of illness identity with engulfment presenting the strongest correlation to emotional outcomes. These results corroborated previous studies showing that the extent of emotional distress did not differ as a function of CHD complexity. This study further scrutinized the prognostic value and clinical relevance of illness identity in ACHD. Adaptation to CHD was affected by psychosocial factors, in particular, how patients evaluate and integrate their condition into their identities. Consequently, patients might benefit from early psychological support consisting of both psychoeducational components to enhance their education around their condition and emotion-focused strategies to address difficult emotional patterns associated with their CHD, especially in cases of engulfment. The current findings contribute to a better understanding of the psychological situation in ACHD and may be a useful starting point for establishing psychotherapeutic interventions in ACHD (Andonian et al., 2021c).

The manuscript was submitted to the journal *Heart and Mind* in May 2021 and accepted and published in June 2021. *Heart and Mind* is an international peer reviewed journal that specifically focuses on the relationship between cardiovascular and mental health. The incidence of ACHD in cardiology and cardiac surgery is on the rise and therefore, psychocardiological research in this particular area has become indispensable.

Contribution:

Caroline Andonian was the principal investigator and first author of this manuscript. She developed the research idea, adapted the study design and collected data. Caroline Andonian independently conducted data analyses, wrote the submitted manuscript, and received methodological and content-based feedback from her supervisor and the co-authors. She took primary responsibility of the submission and publication process.

Original Article

Psychological Well-being in Adults with Congenital Heart Disease: Testing the Predictive Value of Illness Identity

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Abstract

Background: Due to advances in medical care and treatment of congenital heart disease (CHD), the number of adults with CHD (ACHD) is constantly growing. The psychological situation of ACHD has recently received increasing attention. There is evidence that adaptation to CHD may be affected by psychological factors, especially in how patients integrate their illness into their identities. The present study examined illness identity as a mediator of the association between a self-rated health and emotional distress among ACHD. **Materials and Methods:** The study used a cross-sectional design. A sample of 229 ACHD (38 ± 12.5 [18–73] years; 45% female) provided background data and completed three questionnaires on self-rated health (EuroQol group's visual analog scale), illness identity (Illness Identity Questionnaire), and emotional distress (Hospital Anxiety and Depression Scale) at the German Heart Center Munich. Serial multiple mediator models were tested using PROCESS macro for SPSS. **Results:** Perceived health had a direct and indirect effect on emotional distress which was mediated by illness identity ($P < 0.05$). Compared to all other dimensions of illness identity, engulfment fully mediated the relationship between self-rated health and emotional distress, when adjusted for sociodemographic and clinical confounders. The model explained 42% of variance in total emotional distress ($R^2 = 0.416$). The extent of emotional distress did not differ as a function of CHD complexity. **Conclusions:** Illness identity emerged as a strong mediating factor between a patient's self-rated health and psychological outcomes. More importance needs to be directed toward assessing a patient's health perception and psychological state, independently of cardiac severity. Based on present findings, targeted psychocardiological interventions should include psychoeducational components and emotion-focused strategies.

Keywords: Adults, congenital heart disease, illness identity, psychocardiology, psychological situation

Introduction

Due to technological and medical advances, over 90% of patients with congenital heart disease (CHD) reach adulthood.[1] However, many adults with CHD (ACHD) face ongoing medical complications and psychosocial disadvantages.[2] In recognition of this fact, increasing attention has been devoted to patient-reported outcomes in ACHD in terms of quality of life (QOL) and related psychological outcomes.[3] Existing findings indicate that ACHD presents a significantly higher risk for developing psychological disorders.[4-7] This is alarming given the fact that chronic emotional distress is known to negatively influence cardiovascular health even leading to premature mortality.[8] However, the current data can not sufficiently explain the variability in their psychological functioning. This gap in knowledge may contribute to the striking lack of psychosocial support for this patient population.[9]

Most of the literature demonstrates that psychological functioning in ACHD is irrespective of their objective physical condition indicating that symptoms experienced by patients are relevant factors to consider.[10] Illness identity provides a novel framework for understanding how patients integrate their illness into their sense of self. One can differentiate

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between four different states of illness identity: rejection, engulfment, acceptance, and enrichment. Previous research has demonstrated a link between negative illness identity states and emotional distress in ACHD.[11,12] Yet, there have been no mediational studies to prove the predictive value of illness identity for psychological adjustment and long-term health outcomes in ACHD. A necessary step is to identify modifiable risk factors that predict emotional distress in ACHD. Therefore, the aim of the present study was to ascertain whether illness identity is a reliable predictor of emotional outcomes to detect patients at risk and consequently establish appropriate psychotherapeutic interventions.

Figure 1 depicts hypothetical pathways among self-rated health, illness identity, and psychological distress. We hypothesized that a patient's self-rated health status would be related to psychological adjustment (measured by depression and anxiety) and that illness identity would mediate this relationship in different ways. Given the inconsistent findings on the relationship between objective medical parameters and psychological adjustment, it was also investigated on how cardiac disease severity and illness identity interact to influence the relationship between perceived health and emotional distress. The identification of mechanisms that affect psychological well-being in ACHD is necessary to establish adequate psychocardiological interventions for this patient population.

Materials and Methods

Population

The present study was part of the nationwide, cross-sectional MERLIN-CHD initiative which investigates the health situation of ACHD in Germany. Study participants were recruited at the German Heart Center Munich, which covers a large spectrum of ACHD ranging from simple to complex CHD. Inclusion criteria were (1) confirmed diagnosis of CHD;[13] (2) participant age 18 years and older; (3) necessary physical, cognitive, and language capabilities to complete self-report questionnaires.

Procedures

The study was approved by the ethical committee in June 2019 (158/19 S). The protocol is in line with ethical guidelines established by the Declaration of Helsinki.[14] Informed consent was obtained from all participants. All patients received a study package consisting of (1) study information, (2) informed consent, and (3) set of questionnaires. Medical records were reviewed for each patient for verified medical information. Data on primary CHD diagnosis, disease complexity, and functional status were extracted and recorded separately.

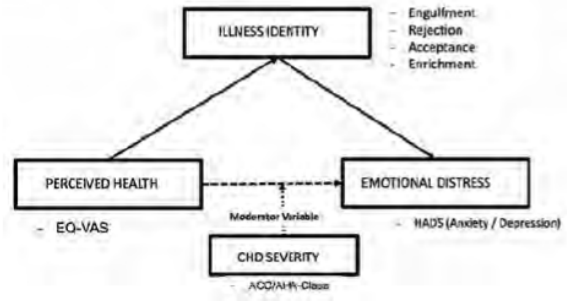

Figure 1: Conceptual framework

Measures

Four domains were measured: (1) demographics, (2) self-rated health, (3) illness identity, and (4) emotional distress. All outcome variables were assessed by standardized questionnaires.

Demographic and clinical information

Patient demographic information was obtained with a background questionnaire. Medical data (CHD diagnosis, functional status, surgical status, cyanosis) were gathered using medical chart reviews. CHD diagnosis was divided into three groups according to the classification of CHD severity by Warnes *et al*.[15]

Independent variable: Perceived health status

Self-rated health was assessed as part of the EQ-5D-5L[16] which provides a simple, generic measure of a patient's perceived health status. For reasons of feasibility, this study used the EuroQol group's visual analog scale (EQ-VAS) as a single-item approach for the measurement of a patient's perceived health status. The EQ-VAS seeks the respondents` overall rating of their health.[17] It is presented as a vertical scale, marked from 0 ("the worst health you can imagine") to 100 ("the best health you can imagine"). Studies generally report high levels of validity and reliability compared to multi-item questionnaires (Cronbach's alpha = 0.87).[18] Satisfactory psychometric properties to assess both, perceived health status and QOL, specifically among ACHD, have been documented by Moons *et al*.[19]

Mediator variable: Illness identity

The Illness Identity Questionnaire (IIQ) reflects how individuals integrate their chronic illness into their sense of self. Items are rated on a 5-point Likert scale ranging from 1 – strongly disagree to 5 – strongly agree. The 25-item IIQ assesses four different illness identity states: rejection (5 items), engulfment (8 items), acceptance (5 items), and enrichment (7 items). To maintain high equivalence between the original English questionnaire and the translated German version, forward and back translation was performed by two independent bilingual translators.[12] Cronbach's alpha values for ACHD were 0.79 for rejection, 0.88 for acceptance, 0.93 for engulfment, and 0.90 for enrichment. All factor correlations are below 0.8 and indicate high discriminant validity.[12]

Dependent variable: Psychological functioning

The Hospital Anxiety and Depression Scale (HADS) was used to assess perceived emotional distress in terms of depressive and anxiety symptoms.[20,21] Cronbach's alphas indicate high internal consistency for all measures (0.83 to 0.87.) The HADS

is a 14-item self-report questionnaire which combines 7-item subscores for depression (HADS-D) and anxiety (HADS-A). Each item is scored on a 4-point Likert scale ranging from 0 (not present) to 3 (considerable). The item scores are summed to provide subscale scores on the HADS-D and the HADS-A which may range from 0 to 21. Studies most commonly employ a cut-off point of ≥8 for each of the respective subscales to indicate a probable case.[22]

Statistical analysis

All statistical calculations. Were carried out using SPSS Statistics 27.0 (IBM, 2020). Descriptive statistics were calculated measuring univariate coefficients of central tendency and distribution. To evaluate the applied instruments, psychometric properties of the underlying scales were analyzed by measuring reliability and minimal selectivity. Pearson product-moment correlations were applied to test bivariate correlations between the main variables. To test direct and indirect effects of perceived health on emotional distress, serial multiple mediator models were used in accordance with procedures described by Hayes and the PROCESS macro for SPSS. Direct and indirect (i.e., mediated) effects were assessed by evaluation of 95% confidence intervals produced by bootstrapping (bootstrapping = 5000). Absolute correlation coefficients did not exceed 0.8 which provides no indication for multicollinearity. For all tests, the statistical significance level was set at $P < 0.05$.

Results

Patient characteristics

Sociodemographic and clinical characteristics are presented in Table 1. Out of 300 distributed questionnaires, 241 questionnaires were returned (response rate: 80.3%). After exclusion for reasons of ineligibility or incompleteness, the remaining 229 ACHDs were retained for final analysis (45% female and 55% male). The mean age of ACHD was 38.2±12.5 [18-73] years.

The severity of CHD was determined according to the Warnes *et al*. classification system as simple ($n = 56$, 24.5%), intermediate ($n = 88$, 38.4%), and severe ($n = 85$, 37.1%).[15] Patients were subclassified according to their functional status based on their symptomatic restrictions (100). 218 patients were in FC I/II (95.2%), 9 patients in FC III (3.9%), and 2 in FC IV (9%).

Table 1: Sociodemographic and clinical characteristics of adults with congenital heart disease

Variables	Value
Age (years)	38.2±12.5 (18-73)
Gender (*n*=229), *n* (%)	
Female	103 (45.0)
Male	126 (55.0)
Marital status (*n*=221), *n* (%)	
Married	94 (42.5)
Divorced	4 (1.8)
Engaged	42 (19.0)
Single	80 (36.2)
Widowed	1 (.5)
Level of education completed (*n*=217), *n* (%)	
No schooling completed	11 (5.1)
Primary school degree	55 (25.3)
Secondary school degree	60 (27.6)
Vocational/polytechnic degree	28 (12.9)
General university entrance qualification	63 (29.0)
Financial standing (*n*=223), *n* (%)	
Poor	21 (9.4)
Fair	61 (27.4)
Good	141 (63.2)
Functional Class (*n*=229), *n* (%)	
I/II	218 (95.2)
III	9 (3.9)
IV	2 (.9)
Severity code of CHD (*n*=214), *n* (%)	
Simple	56 (24.5)
Intermediate	88 (38.4)
Severe	85 (37.1)
Leading diagnosis (*n*=229), *n* (%)	
Complex congenital heart defects	75 (32.8)
Posttricuspid shunts	18 (7.9)
Left heart malformation	44 (19.2)
Right heart malformation	39 (17.0)
Pretricuspid shunts	35 (15.3)
Other	18 (7.9)

CHD=Congenital heart disease

Bivariate correlations between main study variables

Bivariate correlations among the study variables are presented in Table 2. Higher self-rated health was associated with functional illness identity dimensions and lower emotional distress. Functional illness identity states were also inversely correlated with emotional distress. Older age was consistently associated with higher emotional distress, as well as lower self-rated health.

Multiple mediator model

The suggested conceptual model explained 42% of the variance in total emotional distress (adjusted $R^2 = 0.416$). The highest coefficients of determination were found for depression and anxiety through the mediator variable engulfment (depression $R^2 = 0.564$, anxiety $R^2 = 0.405$). In contrast, rejection indicated the weakest coefficients of determination, especially in explaining the variance of anxiety ($R^2 = 0.339$).

Different interactions between the paths self-rated health – illness identity (α) and illness identity – emotional distress (β) were analyzed, and respective regression weights are depicted in Table 3. All effects were significant indicating that self-rated health and illness identity met the criteria for mediational analysis. Moderated mediation models were tested, such that clinical variables were applied as moderators and removed as model covariates. Neither of the moderated mediation models produced significant effects ($P > 0.05$), suggesting that the association between all three variables did not differ as a function of CHD severity.

Table 2: Bivariate Pearson correlations

	1	2	3	4	5	6	7
1. Age							
2. Rejection	0.005						
3. Acceptance	−0.088	−0.486**					
4. Engulfment	0.118	0.376**	−0.415**				
5. Enrichment	−0.047	−0.281**	0.365**	−0.135*			
6. EQ-5D VAS	−0.272**	−0.205**	0.324**	−0.616**	0.213**		
7. HADS anxiety	0.164*	0.388**	−0.389**	0.613**	−0.259**	−0.489**	
8. HADS depression	0.223**	0.304**	−0.401**	0.685**	−0.338**	−0.662**	0.671**

*P<0.05, **P<0.01. VAS=Visual Analog Scale, HADS=Hospital Anxiety and Depression Scale

Table 3: Mediation models for the relationship between perceived health status (EQ-VAS) and emotional distress (Hospital Anxiety and Depression Scale)

Mediation models	Coefficient A VAS-illness Id (α*)	Coefficient B illness Id-HADS (β*)	Direct effect C VAS-HADS (c*)	Indirect effect C' (CI) (c*')
3.1 Rejection anxiety	−0.2161**	0.3352**	−0.3961*	−0.0724 (−0.1311-−0.0254)
3.2 Engulfment anxiety	−0.06160**	0.5163**	−0.2021	−0.3180 (−0.4369-−0.2062)
3.3 Acceptance anxiety	0.3220**	−0.2744**	−0.3549*	−0.0884 (−0.1611-−0.0338)
3.4 enrichment anxiety	0.2200**	−0.1721*	−0.4709**	−0.0379 (−0.0791-−0.0064)
3.5 Rejection depression	−0.2161**	0.2056**	−0.5755**	−0.0444 (−0.0880-−0.00124)
3.6 Engulfment depression	−0.6160**	0.4508**	−0.3857**	−0.2777 (−0.3784-−0.1846)
3.7 Acceptance depression	0.3220**	−0.2414**	−0.5183**	−0.0777 (−0.1383-−0.0317)
3.8 Enrichment depression	0.2200**	−0.2193**	−0.6188**	−0.0482 (−0.0894-−0.0141)

*P<0.05, **P<0.01, Model shows standardized regression weights demonstrating that illness identity dimensions mediate the association between perceived health (EQ-VAS) and emotional distress (HADS); α*, β*, c*, c*'=Standardized regression coefficient. VAS=Visual Analog Scale, HADS=Hospital Anxiety and Depression Scale, CI=Confidence interval, EQ-VAS= visual analog scale

After illness identity was included into the model, perceived health (x) significantly predicted illness identity, which, in turn, significantly predicted emotional distress (y). Coefficient A was negative in the association between self-rated health and maladaptive illness identity (α_{eng}* = −0.06160; α_{rej}* = −0.2161, $P < 0.001$) but turned positive in interaction with anxiety and depression (β_{eng}* = 0.5163, β_{rej}* = 0.3352, P = 0.001). Accordingly, high self-rated health predicted higher values in functional illness identity dimensions (acceptance and enrichment), which consequently lead to lower scores on emotional distress. On the contrary, low self-rated health leads to higher values in dysfunctional illness identity states (rejection and engulfment), which resulted in higher emotional distress ($P < 0.05$).

For the direct pathways, after controlling for demographic and clinical variables, self-rated health was inversely related to emotional distress. Schematic illustrations of the effects of perceived health on emotional outcomes through the mediator variable engulfment are depicted in Figures 2 and 3. All submodels showed significant negative effects, except for engulfment anxiety (c_{eng}* = −0.2021, $P > 0.05$) [Figure 3]. Throughout the entire analysis, the relationship between self-rated health (x) and emotional distress (y) was partially mediated by illness identity. Engulfment fully mediated the association between self-rated health and anxiety. In accordance with previous calculations, all indirect effects were negative with anxiety engulfment showing the highest values.

Summary of analyses

In sum, illness identity constituted a significant predictor of outcome in the relationship between self-rated health and emotional distress satisfying the criteria for a mediator. High self-rated health was related to increase in functional illness identity states, which in turn lead to less emotional distress. In contrast, low subjective health was associated with increase in dysfunctional illness identity dimensions which consequently compromised psychological functioning. Compared to all other dimensions, engulfment showed the strongest effects on psychological outcomes. Objective medical parameters were unrelated to psychological outcomes and therefore did not qualify for moderation testing.

Discussion

The present study offers valuable insights into mediating psychological factors associated with emotional distress in ACHD. To our knowledge, there have been no mediation studies on the recently developed concept of illness identity. The present findings support the proposed conceptual framework, suggesting that illness identity mediates the relationship between individual perceptions of health and emotional distress among ACHD. The mediating effect varied between different dimensions of illness identity with engulfment presenting the highest correlations to emotional distress. The present study further echoed previous findings

that did not confirm a relationship between objective medical parameters and psychological functioning in ACHD.[23] Furthermore, it corroborates findings by Callus *et al*. who confirmed that a patients' subjective disease severity rating had a profound effect on psychological outcomes. The present study expands Callus *et al*.'s findings in several significant ways.[23]

The concept of illness identity provides a new perspective on life with CHD. Existing literature focused on illness perceptions[3] but failed to explore how patients incorporate their illness into their identities.[24] In the present study, illness identity accounted for unique differences in emotional distress among ACHD. Consistent with prior findings, dysfunctional illness identity states were associated with higher emotional distress, while functional illness identity states correlated with lower emotional distress. Engulfment fully mediated the relationship between self-rated health and emotional distress regardless of potential confounders. In ACHD, the predictive role of engulfment had thus far only been associated with the occurrence of excessive health-care encounters.[25] However, in preceding studies, no mediational analysis could be performed due to insufficient data variability. Therefore, underlying mechanisms of psychological well-being in ACHD could not be scrutinized.[3]

The constellation of depression and anxiety in highly engulfed patients is especially alarming due to a 3-fold increased risk of all-cause mortality.[8] Engulfment was defined as the degree to which a patient's self-concept is dominated by his or her CHD. It is claimed that engulfment is determined by both, the individual's perception of his or her illness and the individual's perception of his or her self.[26] Closer inspection of the IIQ revealed that engulfment-related items mainly refer to the impact of illness on the self without considering subjective perceptions of illness. Exemplary items of the IIQ read as follows, i.e., "My illness has a strong impact on how I see myself," "It seems as if everything I do, is influenced by my illness." However, the present results provide evidence that individual perceptions of the severity and permanence of their CHD may play an equally important role in either hampering or promoting ways of adapting to CHD. Future research should acknowledge both dimensions of illness experience to further extend the currently introduced framework of illness identity in ACHD.

In contrast to all other forms of illness identity, the global model fit for rejection displayed the lowest scores within the present study. This could be explained by inherent psychometric weaknesses for the rejection dimension confirmed in an earlier validation study.[12] From a psychological standpoint, rejection might be used by patients who perceive their illness as an external threat to their identity and engage in avoidance behaviors aimed at reducing the seriousness of their CHD.[13] Indeed, avoidance has often been shown to be unrelated to depressive and anxious symptoms in the general population which could potentially explain the weak correlations within the present study.[27]

The present findings are consistent with the shifting perspectives model of chronic illness by Paterson.[28] In their model, the perception of reality, not reality itself, influences how patients adjust to their chronic illness. This is strongly reflected by present results which found significant correlations with subjective health ratings regardless of objective parameters. Furthermore, the authors describe chronic illness experience as a continually shifting process, in which either illness or wellness prevails in a patient's perception. Similarly, the current findings indicate that perceptions of high disease severity have patients pay increased attention to the burden associated with their CHD. In contrast, perceptions of low disease severity allow a shift from "victim of circumstances to creator of circumstances" enabling patients to take ownership of their health and actively manage their chronic condition as a consequence of functional illness integration.[28]

Implications for clinical practice

Given the fact that subjective perception and not objective parameters predict emotional outcomes in ACHD, medical professionals should pay particular attention to educating patients on their condition. Especially in light of the striking supply deficits in ACHD,[29] patients would benefit from ongoing assessments of their illness identity within comprehensive cardiac care. Based on the present results, especially engulfed patients may benefit from emotion-focused interventions by restructuring and transforming problematic emotions on the basis of a caring, client-centered relationship.[30] Although psychotherapeutic interventions have been shown to improve emotional distress in adults with acquired heart disease,[31] there are currently no evidence-based interventions to address psychological well-being in ACHD. However, a recent pilot study conducted by Kovacs *et al*. demonstrated significant effects of cognitive-behavioral group intervention (called ACHD-CARE Program, $n = 42$) on psychological distress in ACHD.[29] Large-scale trials are strongly encouraged to eventually establish manualized interventions for ACHD.

Limitations

Some caution is warranted in the interpretation of current findings. First, due to the cross-sectional design, the direction of the relationship between predictor variables and psychological outcomes cannot be determined. Within the present study, the relationship between self-rated health, illness identity, and psychosocial adjustment might not be one directional and all variables reflect instantaneous, interactional processes. Longitudinal research is needed to further disentangle the pathways. Second, it remains unclear whether illness identity is dynamic or fixed in nature. In accordance with the shifting perspectives model of chronic illness,[28] some patients might assume one predominant dimension but not a static entity. Further influencing factors need to be explored to develop a more accurate understanding of illness identity. Third, disease severity, derived from the Warnes *et al*. classification system, was selected as a central parameter.[15] However, the informational value of this categorization might be limited, and various other indicators of CHD severity need to be considered

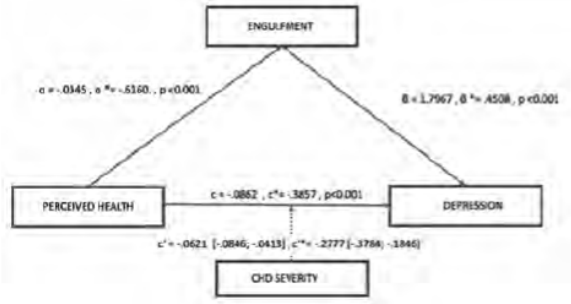

Figure 2: Schematic illustration of the effect of perceived health (visual analog scale) on depression (Hospital Anxiety and Depression Scale-D) through the mediator variable engulfment

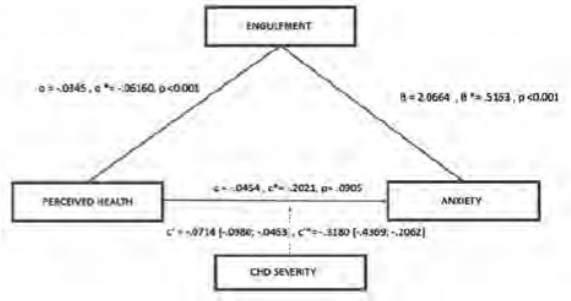

Figure 3: Schematic illustration of the effect of perceived health on anxiety (Hospital Anxiety and Depression Scale-A) through the mediator variable engulfment

to draw valid conclusions on the impact of potential medical confounders. Fourth, this study was based on self-report measures and obtained results were therefore subject to biased responses. Furthermore, patients were not blinded to the aim of the study which might involve the risk of the frequently discussed Hawthorne effect.[32] Fifth, doubts could be raised regarding sufficient precision of the applied instruments for research and screening purposes. Even though the applied psychometric tools are high-quality screening instruments, neither of them can replace a structured clinical interview. We eagerly await studies to extend our findings to confirmed clinical disorders. Sixth, the included sample may not necessarily be fully representative of the population of ACHD. Although patients were equally distributed according to their CHD complexity, patients with higher functional limitations were underrepresented in the sample (FCIII and IV: 4.8%). Whether this underrepresentation has affected, the results of this study need to be clarified.

Conclusions

There have been several calls in the literature for the investigation of explanatory factors in the psychological adjustment of ACHD. The present study provides novel insights into clinical and psychosocial factors associated with emotional distress in ACHD. It strengthens the hypothesis that adaption to CHD is affected by psychological factors, especially how patients appraise their condition and integrate their illness into their identities. The present findings are crucial for guiding future research and, especially, clinical practice. CHD patients might benefit from early psychological support consisting of both, psychoeducational components to enhance the understanding of their condition, and emotion-focused strategies to address difficult thoughts and emotions associated with their CHD to facilitate adaptive ways of illness integration. This might be a useful starting point for establishing psychotherapeutic interventions for ACHD.

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Conflicts of interest

There are no conflicts of interest.

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5.4 Article 4

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Title: Quality of Life in Patients with Marfan Syndrome: A cross-sectional study of 102 adult patients with a verified diagnosis.

Journal: *Cardiovascular Diagnosis and Therapy*

Doi: 10.21037/cdt-20-692

Summary:

Among the various forms of CHD, medical and technological success has improved survival rates and health status of patients with MFS over the past decades. However, MFS patients are still susceptible to severe medical complications throughout their lifetime (Moon, 2016). Living with this risk along with the distinct physical characteristics of MFS potentially results in psychological and psychosocial burden for this patient population which has sparsely been addressed until now (Vanem et al., 2020).

The present study investigated QOL in a representative cohort of 201 adults with a verified diagnosis of MFS (39.3 ± 13.1 [range, 20−85]; 40.2% female). Findings were subsequently put in context with other types of CHD by conducting comparisons to reference data that were ascertained with equal methods. The findings provide evidence that patients with MFS are at particularly high risk for a diminished QOL (mean EQ-VAS: 72.58 ± 15.95) and major mental and physiological impairments. Compared to ACHD, individuals with MFS scored significantly lower in dimensions pain/discomfort, anxiety/depression, mobility and usual activities ($p<0.05$). The present study stresses the need to consider the psychosocial burden of MFS that comes with a cost of resources for both patients and professionals. Clinicians can help patients with MFS to reduce this cost by making mental health issues and psychosocial support an integral part of routine cardiac care for MFS (Andonian et al., 2021b).

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Contribution:

Caroline Andonian was the principal investigator and first author of this article. Together with her experienced medical team members, she developed the research idea and was responsible for conducting the research along with the on-site support of her colleagues at the German Heart Center Munich. Again, she was responsible for collecting and analysing the data. Caroline Andonian prepared and wrote the final manuscript with guidance from her supervisor. She was the primary source of contact for the submission and review process.

Original Article on Current Management Aspects in Adult Congenital Heart Disease (ACHD): Part III

Quality of life in patients with Marfan syndrome: a cross-sectional study of 102 adult patients

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Background: Marfan syndrome (MFS) is a genetically determined multiorgan disease that leads to severe physiological and psychological impairments in adult life. Little consensus exists regarding quality of life (QOL) in individuals with MFS. The present study sought to investigate QOL in a representative cohort of adults with MFS.

Methods: Patient-reported outcome measures from a representative sample of 102 adults with MFS (39.3±13.1 years of age; 40.2% female) were retrospectively analyzed and compared with those from adults with different congenital heart defects (CHD), at the German Heart Center Munich. QOL was assessed using the updated five-level version of the EQ-5D.

Results: Differences between both populations were analyzed. Subjects affected by MFS reported an overall reduced QOL. Compared to CHD patients, individuals with MFS scored significantly lower in the dimensions of pain/discomfort, anxiety/depression, mobility and usual activities ($P<0.05$).

Conclusions: Patients with MFS are at high risk for impaired QOL, especially in mental and physical domains. Psychosocial consequences of MFS cost resources for both, patients and professionals. Current findings highlight the great importance of additional psychological support to cope with disease-related challenges. Increased attention should be directed towards enhancing their subjective wellbeing to potentially improve their QOL and long-term health outcomes.

Keywords: Marfan syndrome (MFS); psychological situation; quality of life; prevention; EQ-5D

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Introduction

Marfan syndrome (MFS) is a genetically determined multiorgan disease that affects the connective tissue throughout the body, including the skeletal, ocular, pulmonary, cardiovascular, and central nervous systems. An estimated proportion of 0.002% to 0.017% of the population is affected by MFS (1). The most severe complications from a medical perspective include aneurysm formation and dissection of the aorta. Consequently, most patients are closely monitored, with serial cardiovascular assessments from early childhood (2-5). Additionally, patients with MFS often have to cope with skeletal or ocular abnormalities leading to a characteristic appearance, which is not only subjectively perceived by themselves, but is also visible to others (6,7). Recent studies have indicated that the combination of physiological and psychological symptoms may lead to a decreased quality of life (QOL) in individuals with MFS (3).

Despite the growing interest in psychosocial consequences for patients with congenital heart defects (CHD), research on the particular psychological concerns of individuals with MFS is still scarce (8). While clinical research has traditionally focused on "hard" outcome measures, such as morality, morbidity, and functional status, the concept of QOL has become increasingly recognized as an important patient-reported outcome measure in the evaluation of care and treatment (9). Patients with MFS present an elevated risk for adverse psychosocial outcomes, including decreased QOL, particularly in the psychological domain (3,4,10-12). Some patients with MFS also experience symptoms of emotional distress, such as depression and anxiety (4,7,13). Emotional distress can impact a patient's overall health and lead to increased cardiovascular morbidity and premature mortality (14,15).

The present study aimed to (I) systematically assess QOL within a large sample of patients affected by MFS and (II) compare the results with findings on patients with other types of CHD. In an attempt to raise awareness for the psychosocial implications of MFS, this study should encourage clinicians to evaluate the psychological status of patients with MFS and, on the basis of this status, enhance treatment options. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/cdt-20-692).

Methods

Population

The present study represents a subgroup analysis of the nation-wide VEMAH study (www.vemah.info) which constitutes the first large-scale attempt to comprehensively assess the health care situation of a large cohort of adults with congenital heart disease (ACHD) in Germany. The questionnaire-based survey was initiated and carried out by the Department of Congenital Heart Disease of the German Heart Centre Munich, Technical University Munich, and the Department of Cardiology, University of Erlangen. The insurance company "AOK Bayern" supported the study by sending out our questionnaires to their insured ACHD patients in Bavaria. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and under the approval of the Ethics Committee of the Technical University of Munich (157 / 16 S). Data collection took place between May 2017 and July 2020. Written informed consent was obtained from all participating patients before the start of documentation. Guidelines on good pharmacoepidemiologic practice and data protection guidelines were followed.

Patients were selected for sub-analysis according to the following inclusion criteria: (I) confirmed diagnosis of MFS; (II) participant age 18 years or older; (III) necessary physical, cognitive and language capabilities to complete self-report questionnaires; (IV) German speaking. Participants were excluded if they did not fulfill age requirements or had severely impaired cognitive abilities. Patients were consecutively included in the order that they presented at the institution and were not selected in prior.

Measures

Patient-reported outcome measures were assessed by a specifically devised questionnaire in cooperation with the Chair of Behavioral Epidemiology at the Technical University of Dresden and the German Heart Center Munich. The questionnaire was completed in person, online or by mail. Data collection took place between 2016 and 2019. QOL was measured using the updated five-level version of the EQ-5D (EQ-5D-5L) which provides a simple, generic measure of a patient's perceived health status. Research has shown that this version presents a significantly higher reliability and discriminatory power and reduces ceiling effects, , compared with the original EQ-5D (16). The EQ-5D-5L is a paper-based, self-complete questionnaire consisting of two sections: a descriptive system questionnaire and a visual analogue scale (VAS). The descriptive system compromises five dimensions: mobility, self-care, usual activities, pain/discomfort and

anxiety/depression. The patient is asked to indicate his or her perceived impairments on a 5-point Likert scale ranging from "no problems" to "extreme problems/unable". Responses are coded as single-digit numbers expressing the severity of impairment on each dimension. Responses can be converted into a single weighted index score (EQ-5D index) using population preference scores. A value set for the EQ-5D-5L based on a representative sample of the German population has recently been developed (17). The EQ-VAS indicates a patient's overall health state on a vertical scale which ranges from 0 ("The worst health you can imagine") to 100 ("The best health you can imagine"). It therefore provides a quantitative measure of a patient's perceived health.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 (IBM Inc., Armonk, NY, USA). Medical records were reviewed for patient demographics, cardiac and non-cardiac diagnoses. Statistical evaluations were pseudonymized and not linked to individual person. Descriptive measures were calculated for sociodemographic sample characteristics. Several logistic regression models were calculated to analyse the impact of MFS on descriptive QOL dimensions, using the EQ-dimensions of the EQ-5D-5L as dependent variables. Differences between the populations were evaluated using the chi-squared tests. *T*-tests were used for comparisons between mean values. Continuous data was expressed as mean ± standard deviation, categorical or interval scaled variables as absolute numbers or percentages. The crosswalk-index-value (utility index) of the EQ5D-5L was calculated using the German value set (17). All occurring P values and tests for significance were performed in a two-sided manner. Statistical significance was indicated by a P value <0.05.

Results

Sample characteristics

Out of 3,885 patients, a total of 102 patients with MFS were retained for the final analysis (40.2% female) (*Table 1*). The mean age of the patients with MFS was 39.3±13.1 (range, 20–85) years. The remaining 3,783 ACHD [42.0±17.3 (range, 18–97) years; 46.6% female] were consulted to offer a point of reference consisting of non-MFS ACHD. Both populations were comparable in their age distribution, residential zone and insurance status.

QOL in patients with MFS

Table 2 shows the impact of MFS on all five QOL dimensions. Having MFS significantly decreased the odds of experiencing no difficulties on all respective dimensions (P<0.05), except for self-care. Similar results are reflected in *Table 3*, which compares the subscales of the EQ-5D-5L for the MFS sample and for the chosen comparison group of ACHD.

Compared to the larger ACHD group, patients with MFS reported significantly worse QOL in usual activities (P=0.002), pain/discomfort (P≤0.001), and anxiety/depression (P=0.022). Observed differences were most extreme on the pain/discomfort dimension. No significant differences were observed on the self-care (P=0.483) or mobility (P=0.059) dimensions. *Figure 1* is a graphic representation of the comparison between the 5 dimensions of the EQ-5D-5L for both samples.

When comparing the combined measures of QOL between patients with MFS and non-MFS ACHD (*Table 4*), patients with MFS scored markedly lower on the VAS (P=0.073) and also had lower descriptive index values (P=0.025). However, the observed differences between the populations were less extreme in regard to the VAS scores. Additionally, the observed variations in QOL depended on the type of measurement applied. Accordingly, the mean VAS score was markedly lower than the descriptive index value for QOL.

Discussion

In recent decades, substantial medical advancements have improved the lives of individuals with MFS. Consequently, many clinicians count MFS among the most manageable of genetic conditions today (7). However, many affected patients do not share this view and describe considerable impairments in their QOL (4). Remarkably few studies have been undertaken to assess psychosocial consequences of MFS. The major purpose of this study was to explore QOL among individuals with MFS and elaborate on previous findings by utilizing the EQ-5D-5L, a highly reliable and valid outcome measure within the cardiovascular area (18). It includes two types of measurement, a short descriptive system questionnaire and a VAS, and therefore holds a more global view on QOL in terms of general life satisfaction. The current study provides evidence that patients with MFS are at particularly high risk for a diminished QOL and

Table 1 Characteristics of the study populations

Demographics	Marfan (n=102)	ACHD (n=3,783)
Age (in years)	39.3±13.1 [20–85]	42.0±17.3 [18–97]
Sex (female), n (%)	41 (40.2%)	1,763 (46.6%)
Age group (in years), n (%)		
18–34	41 (40.2)	1,604 (42.4)
35–64	55 (53.9)	1,678 (44.4)
65+	6 (5.9)	501 (13.2)
Missing (n)	0	111
Residence n (%)		
City	26 (25.7)	747 (20.0)
Town	14 (13.9)	571 (15.3)
Rural	61 (60.4)	2,418 (64.7)
Missing (n)	1	158
Insurance n (%)		
Public	93 (93.0)	3,570 (94.3)
Private	7 (7.0)	210 (5.5)
No insurance	0 (0.0)	7 (0.2)
Missing (n)	2	107

ACHD, adults with congenital heart defects; n, absolute number.

Table 2 Impact of Marfan-diagnosis with respect to EQ-5D-dimensions

EQ-5D-dimensions	Value
Mobility	0.600* (0.37–0.96)
Self-Care	1.070 (0.41–2.77)
Usual activities	0.487* (0.32–0.75)
Pain/discomfort	0.370* (0.25–0.55)
Anxiety/depression	0.598* (0.40–0.90)

Displayed is the odds ratio, upper and lower bounds (95% CI) respectively which was obtained from several ordered logistic regressions using EQ-dimensions as dependent variable. *, P<0.05.

present major mental and physiological impairments.

The study encompassed a nationwide sample of patients with MFS recruited by the German Heart Center Munich. It was ensured that the reference data were ascertained with the same methods to ensure maximum comparability between the two populations.

Nonetheless, the present study may be subject to certain limitations. First, the study was cross-sectional in nature and does not allow any conclusions to be drawn regarding the etiology of psychological and physiological effects or the development in QOL over time. Second, as data were assessed retrospectively, it was not possible to determine precise response rates among the respondents. Third, the study relied on self-report outcomes and might be subject to recall and self-presentation bias. Fourth, as the enrolment was voluntary, selection bias could not be excluded and may limit representativeness. Fifth, this study was performed at tertiary care centers for ACHD which does not reflect the typical population of CHD patients, who most often present to non-specialized physicians. Sixth, the data derived only from patients living in Germany and generalization of the conclusions to the greater, global MFS population is debatable. Finally, since no control group was involved in the original study design, data could only be compared to the remaining respondents affected by a variety of types of CHD. In order to put findings into appropriate perspective, control group designs are conceivable in future clinical trials.

Table 3 Distribution of EQ5D-dimensions

EQ-5D dimensions	Marfan		ACHD		P value
	n	%	n	%	
Mobility					
No problems	62	66.7	2,820	76.0	0.059
Slight problems	18	19.4	449	12.1	
Moderate problems	10	10.8	309	8.3	
Severe problems	2	2.2	117	3.2	
Unable to walk	1	1.1	17	0.4	
Missing	9	–	182	–	
Self-care					
No problems	88	94.6	3,442	92.8	0.483
Slight problems	3	3.2	141	3.8	
Moderate problems	1	1.1	70	1.9	
Severe problems	1	1.1	33	0.9	
Unable to wash/dress	0	0.0	25	0.7	
Missing	9	–	183	–	
Usual activities					
No problems	51	54.8	2,599	70.2	0.002*
Slight problems	23	24.7	619	16.7	
Moderate problems	13	14.0	320	8.6	
Severe problems	6	6.5	119	3.2	
Unable to do	0	0.0	44	1.2	
Missing	9	–	193	–	
Pain/discomfort					
No pain	30	32.6	2,154	58.7	<0.001*
Slight pain	39	42.4	922	25.1	
Moderate pain	16	17.4	450	12.3	
Severe pain	7	7.6	130	3.5	
Extreme pain	0	0.0	15	0.4	
Missing	10	–	223	–	
Anxiety/depression					
Not anxious/depressed	43	46.2	2,181	59.2	0.022*
Slightly anxious/depressed	33	35.5	981	26.6	
Moderately anxious/depressed	14	15.1	346	9.4	
Severely anxious/depressed	3	3.2	148	4.0	
Extremely anxious/depressed	0	0.0	31	0.8	
Missing	9	–	207	–	

*, significant finding. ACHD, adults with congenital heart defects; n, absolute number.

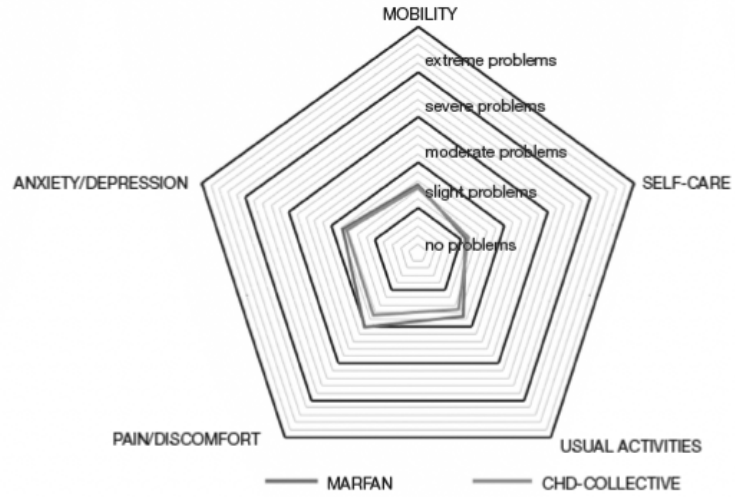

Figure 1 EQ-5D-5L values in the Marfan syndrome patients *vs.* the ACHD comparison group. Each dimension consists of 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. Average values were calculated for all dimensions and accordingly depicted. ACHD, adults with congenital heart defects.

Table 4 Crosswalk Index Value *vs.* Visual Analog Scale (VAS)

	Marfan (mean ± SD)	ACHD (mean ± SD)	P value
Crosswalk	86.97±15.12	90.67±15.51	0.025*
VAS	72.58±15.95	76.23±19.04	0.073

*, significant finding. ACHD, adults with congenital heart defects; SD, standard deviation.

QOL in patients with MFS

Pain/discomfort

Current findings indicate that QOL of patients with MFS is significantly compromised in the physical domain compared to counterparts with other forms of CHD. Indeed, previous research has demonstrated that the percentage of MFS patients suffering from chronic pain ranges from 47% to 92% and that this is a significant and persistent problem in MFS (19). According to recent findings related to pain in individuals with MFS, pain is a major contributor to decreased QOL (4). The most severe types of pain include back pain followed by neck pain and headaches (20). Clinical manifestations of MFS, such as dural ectasia, degenerative disk disease, kyphosis and early osteo-arthritis frequently cause great pain (4). However, treatment options for chronic pain management are still lacking and research efforts in this area appear fragmented. In a survey of 993 patients with MFS, Nelsen *et al.* noted that very few patients receive medical procedures for pain and less than a half of them are satisfied with their current pain treatment (21). These findings are especially worrying since chronic pain is linked to profound disability and significant psychological burden (19). Further research is needed to characterize, in greater depth, the directionality of pain, mental well-being and QOL in patients with MFS. Better management could potentially improve an individual's satisfaction with life by facilitating work participation and everyday activities.

Usual activities

According to the present findings, having MFS increased the risk of reporting problems with usual activities (e.g., work, study, housework, family or leisure activities). Generally, emotional distress and physical inactivity have been found to be significantly correlated with work participation (22,23). Studies confirm that the employment

rate among patients with MFS is considerably below that of the general population (24,25). Workplace discrimination and stigma are further factors that compound other difficulties in the daily lives of patients with MFS (26). Peters *et al.* found that 32% of adults with MFS reported feeling socially discriminated against and 20% of patients perceived instances of workplace discrimination. For this reason, these patients chose to withdraw from social situations or keep their illness secret (7,26). Eighty percent of patients also reported reducing work hours due to MFS or missing on average of 6.5 to 7 months of work because of their treatment (20). Social stigmatization is significantly correlated with mental illness, pessimistic outlook towards MFS and low self-esteem (26). These findings indicate the necessity of offering individuals with MFS psychological assistance in order to facilitate their coping strategies and improve long-term outcomes.

Mobility

MFS was significantly associated with the occurrence of mobility impairments which is hardly surprising given the findings related to pain in patients with MFS. Symptoms commonly associated with MFS, such as chronic pain and fatigue, may lead to restricted mobility and lower QOL in the physical domain (27). Physical QOL issues have been found to be particularly related to age and the presence of scoliosis. Additionally, chronic pain was correlated with severe mental and physical fatigue which is ranked as one of the highest complaints in patients with MFS (20). Until now, it is unclear whether fatigue is linked to medication use, or inherent symptoms related to MFS itself (4). Further research is needed to investigate the exact etiology of fatigue in patients with MFS and eventually reveal modifiable features of MFS which could be considered in their treatment to improve their QOL.

Anxiety/depression

In accordance with earlier findings, patients with MFS experienced considerable impairments in the emotional area. Anxiety and depression have been recognized as bio-behavioral variables, that have the strongest and most direct effects on QOL among all disease-related factors (28). Peters *et al.* found that over 40% of their study cohort had a significant degree of depressive symptoms (7). Emotional distress is known to have far-reaching implications for adverse psychological outcomes, such as body image dissatisfaction, negative illness perceptions and decreased self-esteem (4,29), as well as negative cardiovascular consequences, including increased morbidity and premature mortality (14,15). As patients sometimes present no observable physical signs, they frequently report feeling invisible in the health care system and struggle to find adequate treatment (7). Based on these findings, clinicians need to consider that psychological features that may lie beyond cardinal features of MFS may potentially play an equally important role in a patient's quality of life.

Visual Analog Scale vs. Index values

The two-fold measure of the EQ-5D-5L made it possible to investigate variations in QOL as determined by each of these two types of measurement. Apparently, the overall VAS score indicated a significantly lower QOL than that demonstrated by the descriptive index value, for both populations. It is conceivable that the descriptive system encourages a patient to examine QOL from different perspectives as it breaks down QOL into psychological, social, physical components. This goes along with Moons' operationalization of QOL as: "*the degree of overall life satisfaction that is positively or negatively influenced by an individual's perception of certain aspects of life that are important to them, including matters both related and unrelated to health*" (30). Thus, QOL is regarded as a multidimensional concept that is influenced by subjective evaluations of both positive and negative aspects of life (31). On the contrary, VAS picks up a one-dimensional view of perceived health, in which patients may be primarily focused on somatic health restrictions associated with their MFS.

Conclusions

Remarkably few studies have been undertaken to systematically assess psychosocial aspects of MFS. The present results provide evidence that individuals with verified MFS are likely to experience diminished QOL, in both mental and physical domains. Considerable restrictions in their QOL become even more evident when comparing the study group to patients with other forms of CHD. It is therefore important to consider the psychosocial consequences of MFS which cost resources for both, patients and professionals (e.g., time, money and emotional energy). Clinicians can help patients with MFS to reduce this cost by making mental health and psychosocial support an integral part of cardiac care for MFS.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The survey has been approved by the institutional review boards of the Technical University Munich (157/16 S) and written informed consent was obtained from all participating patients before the start of documentation.

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6 General Discussion

In recent years, the psychological situation of ACHD has received increasing attention. Despite notable heterogeneity, alarming results have been uncovered with respect to the psychological well-being of ACHD (Moons & Luyckx, 2019). However, to date, appropriate measures have not been developed or implemented into the practice of psychocardiology for this patient population (Kovacs et al., 2009a; Roseman & Kovacs, 2019). Examination of psychological adjustment to CHD is particularly important (Bombardier et al., 1990). First, previous research demonstrated that the magnitude of physiologic or structural abnormalities of the heart was not predictive of psychological outcomes (Moons & Luyckx, 2019). Second, for most patients the magnitude of their CHD will remain constant whereas psychosocial impairment constitutes the most modifiable and important area of intervention (Bombardier et al., 1990). This dissertation provides a substantial contribution to a holistic care system for ACHD by identifying new markers to detect, prevent, and treat concomitant psychological distress in ACHD. These findings indicate important starting points for establishing tailored psychosocial interventions to help close the striking psychosocial healthcare gap in this patient population.

The literature review forms the basis for subsequent quantitative studies for this thesis by consolidating the current state of knowledge on the prevalence of emotional distress in ACHD (Andonian et al., 2018). To date, study 2 is the first to investigate patient-reported QOL within a cohort of 4,015 ACHD in Germany (Andonian et al., 2021a). Study 3 provides a new perspective on the psychological dimension of CHD by examining the predictive and mediating role of illness identity within an innovative framework of psychological adjustment (Andonian et al., 2021c). Study 4 compares QOL findings in ACHD to a particularly vulnerable subset of patients with MFS, which is a hereditary multiorgan disease with far-reaching psychosocial consequences (Andonian et al., 2021b).

The findings of this dissertation expand existing knowledge on psychological well-being in ACHD in several significant ways. First, ACHD experienced an unexpectedly good QOL. Paradoxically, patients with a higher CHD-severity reported an improved level of well-being (Andonian et al., 2021a). However, MFS patients had a particularly high risk for a diminished QOL compared to patients with other forms of CHD (Andonian et al., 2021b). Results gained from study 3 indicate that illness identity and a patient's subjective health perception emerged as reliable factors affecting the risk for mental illness in ACHD (Andonian et al., 2021c). This identification of mechanisms mediating mental health outcomes among ACHD contributes to an enhanced understanding of psychological processes and potentially facilitates the choice of primary target variables for intervention (Nahlén Bose et al., 2016). Findings suggest that the subjective burden of illness constitutes a stronger determining factor of overall adjustment than does the illness itself (Andonian et al., 2021c). Chronic psychological burden might lead to an exacerbation of physical health and resource utilization for both patients and professionals (i.e., time, money and emotional energy) (Benderly et al., 2019). This dissertation has important implications for policy, practice, and research in the field of psychocardiology for ACHD. The present findings will help clinicians with early detection of patients at risk for a diminished psychological well-being and consequently identify both, preventive and psychotherapeutic targets. The following section discusses and expands on the influential theories of psychological adaptation to chronic illness based on

present findings in the example of ACHD. Finally, the data obtained as part of these studies can enable the generation of strategies to translate findings into practice and enhance meaningful patient outcomes. While maximizing the physical status of ACHD must remain a priority, it is inevitable to make psychocardiological care an integral part of cardiac care to ensure optimal use of resources and to reduce healthcare disparities for both patients and professionals.

6.1 Mental Illness and overall Well-being? Building on Keyes' Two Continua Model

Present findings demonstrate that ACHD generally experienced high levels of overall well-being, currently referred to as QOL (Andonian et al., 2021a). At first glance, this stands in stark contrast to previously reported elevated signs of emotional distress in this patient population (Kovacs & Bellinger, 2021). Taken together, findings suggest that the data best fit a 'two factor' model, indicating that overall well-being and psychopathology are two moderately related, yet distinct contributions to our understanding of human health (Iasiello & Van Agteren, 2020; Renshaw & Cohen, 2014). These results further validate Keyes' two-continua model of mental health (***Figure 6.1***) (Iasiello & Van Agteren, 2020; Keyes, 2005).

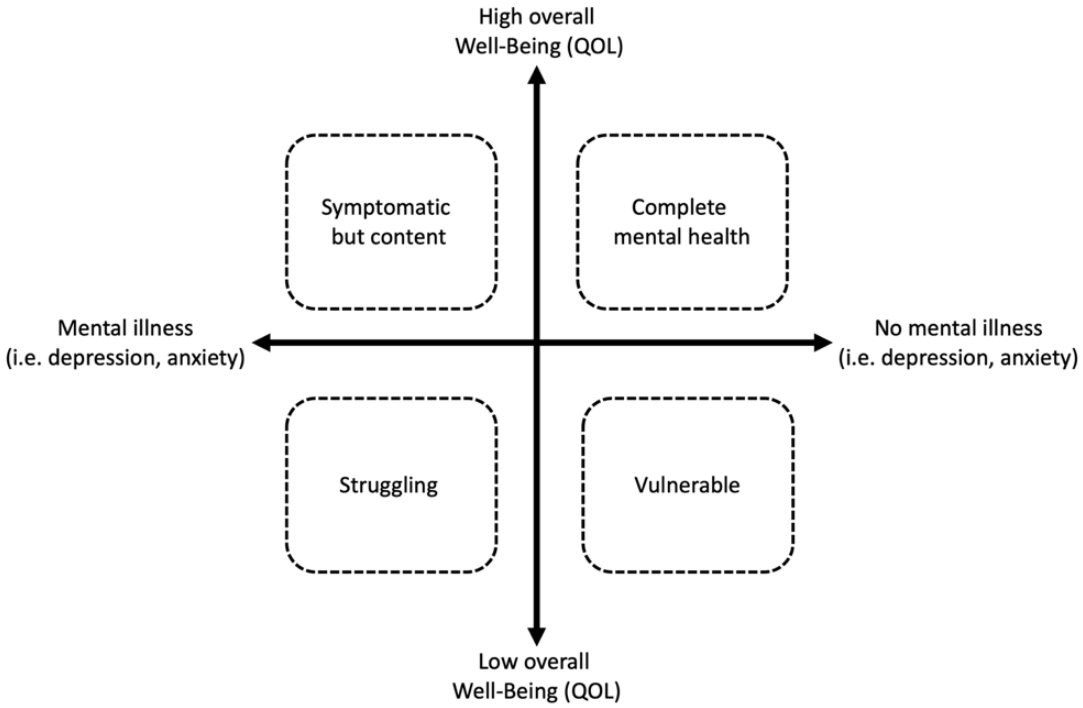

Figure 6.1: Two continua model according to Keyes (2005); terminology adapted to context of dissertation

Unlike traditional pathogenic oriented approaches, the two-continua model represents a more comprehensive concept of psychological well-being. In this model, psychological well-being and mental illness reflect distinct continua rather than extreme ends of one single spectrum (Iasiello & Van Agteren, 2020). This approach allows a person to be considered more or less distressed in some regards, while

simultaneously more or less well in others. Accordingly, most patients enrolled within the present study could be classified as symptomatic, yet content (Renshaw & Cohen, 2014). Taken together, overall well-being and mental illness were each associated with shared and unique psychosocial and medical predictors which is a strong indication that the constructs are distinct, but related due to some degree of overlap (***Figure 6.2***) (Iasiello & Van Agteren, 2020). According to present findings, age could be seen as a major risk factor for less favorable outcomes in both domains, QOL and mental illness. A recently published longitudinal study on illness identity in ACHD revealed that older patients were more likely to be either overwhelmed by their disease, or to reject their disease over time (Van Bulck et al., 2021). Similarly, APPROACH-IS found that older age led to worse PROMs in ACHD (Moons et al., 2021b). Based on the proposed working hypothesis, this may explain diminished psychological outcomes on both scales.

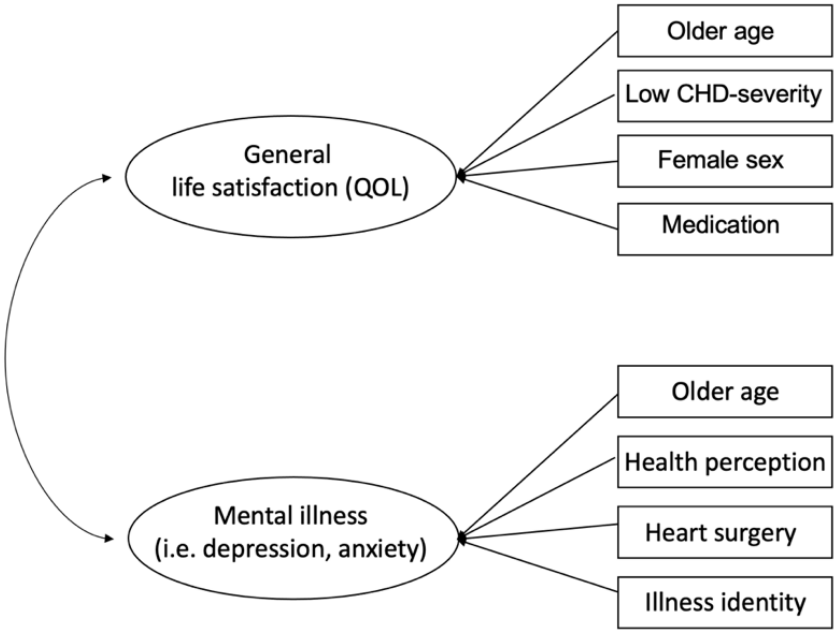

Figure 6.2: Differential predictors of general life satisfaction (QOL) and mental illness using multiple regression analysis

Regarding somatic determinants of QOL, it is remarkable that patients with higher CHD severity described their overall well-being as significantly superior to those with rather simple heart lesions, when considering both psychological and physical health domains in conjunction. This finding suggests an extension to Keyes' two-continua model by a tri-axial framework (Keyes, 2005). Research on the psychological impact of objective somatic parameters in ACHD has yielded inconsistent results leading to the assumption that no somatopsychic correlation exists (Moons & Luyckx, 2019). However, these findings have not been investigated within the context of a dual-or three-dimensional framework and future in-depth investigations might reveal characteristic somatopsychic patterns among ACHD. ***Figure 6.3*** illustrates a range of conditions investigated within this dissertation by using a novel three-dimensional model. It attempts to capture the diversity of subjective health presentations among ACHD

along three different continua: an axis of physical health, an axis of mental illness or emotional distress, and one of overall subjective well-being. Although this framework does not entirely account for interindividual variability, it allows for a differentiated perspective on contributing factors and appropriate conclusions in the mental health management of ACHD.

Core features of the diagram are currently divided into eight broad groupings (***Table 6.1***). This table represents different types of presentations one can routinely find when working with ACHD, from the least impaired clients (*cell 1, top left corner*) to the severely impaired clients (*cell 8, lower right corner*). Of note, that the axes presented in ***Figure 6.3*** are not independent of one another and changes on one might drive changes on another. This has important practical implications, as each cell requires a different psychological treatment approach ranging from preventive (*cell 2, 3, 4*) to reactive interventions (*cell 5, 6, 7, 8*) (James, 2015). Since this representation is simplified, it does not address mechanisms to explain why the majority of patients within the current research presented themselves in cells 5 and 6 (i.e., varying physical parameters, good overall well-being, high levels of mental distress). Explanations of arising paradoxes for patients falling into cell 6 (i.e., severe physical impairment, good overall well-being) will be further discussed in the following sections.

Table 6.1: Grid outlining eight cells of the hypothetical three axes model of mental health in ACHD, modified acc. to James, 2015

	No mental illness		**Severe mental illness**	
Good physical health	1. High general well-being	3. Poor general Well-being	5. High general well-being	7. Poor general well-being
Poor physical health	2. High general well-being	4. Poor general Well-being	6. High general well-being	8. Poor general well-being

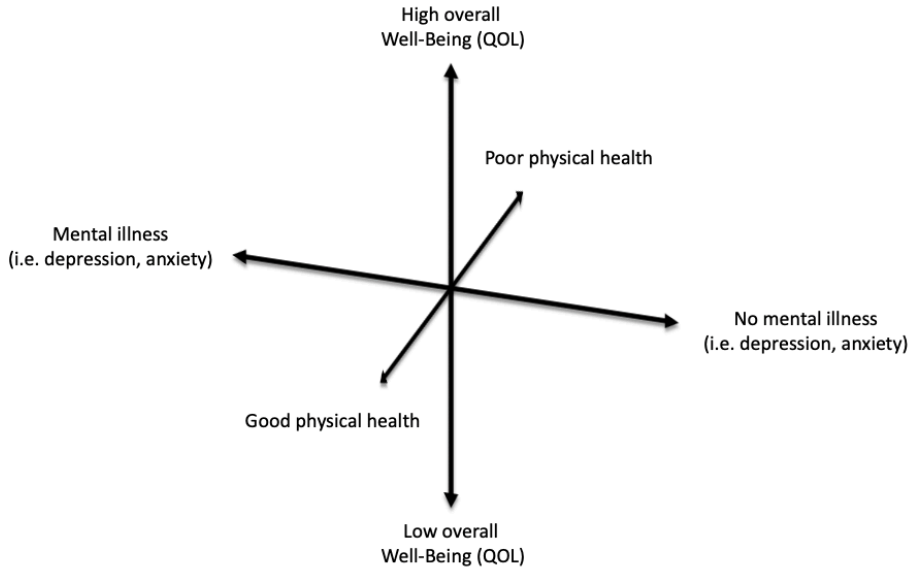

Figure 6.3: Three-dimensional framework of mental well-being in ACHD, modified according to James, 2015

6.2 Revisiting the "Paradox of Well-being": An Integrated, Multidimensional Model

The empirical phenomenon that individuals often maintain or increase their subjective well-being despite (or even because of) their chronic illness, is known as the paradox of well-being (Herschbach, 2002; Swift et al., 2014). In other words, objectively negative factors in one's life often have relatively little impact on the subjective QOL (Herschbach, 2002). This was also strongly supported by findings in this dissertation, which revealed that patients with higher CHD complexity had higher levels of QOL, and were more capable of adapting to their CHD (Andonian et al., 2021a). Accordingly, patients with more complex heart defects showed decreasing tendencies of rejection, as well as higher acceptance rates (Andonian et al., 2020). Higher disease complexity was further associated with better QOL, especially within the dimensions of self-care and mobility (Andonian et al., 2021a). While illness identity has presently emerged as both a risk- and protective factor in the prevention of mental illness, its role in the context of overall well-being must be further clarified (Andonian et al., 2021c). Therefore, an open question remains: which kind of mechanisms generate high overall well-being in ACHD? As each illness trajectory is unique, understanding a patient's lived experience and its effects on health and well-being is essential to quality care (Christensen, 2015).

One potential mechanism essentially lies in the experience of a CHD and the personal *meaning* assigned to this experience. Due to decades of nearly exclusive concern with negative emotions in the context of chronic illness, less is known about positive well-being in affected individuals (Folkman & Moskowitz, 2000). Lazarus's early stress coping model dealt primarily with the negative appraisal of threat, and highlighted that coping was mainly directed towards the regulation of distressing emotions (Folkman & Moskowitz, 2000; Folkman & Moskowitz, 2007; Lazarus & Folkman, 1984). Coping mechanisms have been traditionally classified as problem- or emotion-focused. Problem-focused coping involves active strategies to alter the stressor, while emotion-focused coping involves processing and expressing distressing feelings in order to reduce psychological burden (Lazarus & Folkman, 1984; Riley & Park, 2014). Research on illness identity conducted in the dissertation provides strong evidence that positive reappraisals of CHD can lead to positive affective states (i.e., less emotional distress) and may therefore be equally important in understanding emotional responses in ACHD. In this context, recent coping theories put forth a third type of coping, namely meaning-focused coping (Riley & Park, 2014). It implies that the positive reinterpretation of a stressor consequently leads to better psychological adjustment and overall well-being (Riley & Park, 2014). From this perspective, the concept of illness identity shares important similarities with core elements of emotion-focused and meaning-focused coping as it concentrates on the adaptational significance of both negative and positive ways of illness integration.

Another potential explanation is a patient's unique *perception* of his or her condition, regardless of objective disease parameters (Andonian et al., 2021c). As indicated by present findings, there is considerable evidence that adjustment to chronic illness may be affected by subjective health perceptions to a far greater extent than the actual medical diagnosis itself (Bombardier et al., 1990;

Kovacs & Bellinger, 2021; Paterson, 2001). The shifting perspectives model of chronic illness holds that a patient's perspective on his or her condition influences how he or she interprets symptoms and responds to the illness. A metasynthesis of 292 qualitative research studies revealed that it is irrelevant whether the illness actually was as significant as the perception of the illness. The experience of a chronic illness is constantly changing with a perception of either illness or wellness prevailing. Paterson's findings expand the currently applied framework of illness identity by incorporating a dynamic component, making it possible to explain some variability in research outcomes (Paterson, 2001). Remarkably, this stands in contrast to recently published findings on the longitudinal development of illness identity showing that a patient's illness identity was stable over time (Van Bulck et al., 2021). However, this cannot be widely applied due to the exclusion of patients diagnosed after the age of 10 years, and data collection over a short period of time. It would be ideal to replicate these findings over a broader time frame in order to disentangle effects of different phases in illness trajectory (Van Bulck et al., 2021).

Within the context of the research conducted in this dissertation, a negative perception of health occurred in recently diagnosed patients (i.e., primary pre-tricuspid shunts) and patients with MFS who indicated significantly impaired levels of well-being. Although not specifically addressed within the context of this research, social stigma deserves particular attention when it comes to evaluating the psychological situation of MFS patients. Given the characteristic physical features of MFS including disproportionately long extremities, tall and leptosomal body types, serious scoliosis, or crowded teeth, patients with MFS constitute a considerably distinct patient population compared to other cardiac populations. In this respect, they might remain vulnerable to social stigmatization similar to individuals with other visible genetic conditions (Peters et al., 2005). Indeed, 32% of MFS patients have previously reported feeling socially discriminated because of their illness, which was significantly correlated with increased depression, lower self-esteem, pessimistic perceptions around their illness, and negative body image (Hansen et al., 2020; Peters et al., 2005). Since research on MFS has primarily focused on organ affections and surgical management, future studies should be directed toward psychosocial long-term consequences of MFS (Vanem et al., 2020).

In contrast, positive connotations of CHD in the form of favorable health ratings might reinforce successful adaptation to CHD, presently indicated by high levels of acceptance and enrichment (Andonian et al., 2021c). In light of these findings, two fields of research have been recognized as clinically meaningful and useful to understand the discrepancy between expected and perceived evaluations of QOL in individuals with a chronic health condition: response shift and transformative learning. Both constructs refer to a process of personal change in internal values (response shift) leading to new perspectives and identity change (transformative learning) (Barclay-Goddard et al., 2012). The currently investigated connections between subjective health perceptions and illness identity share a number of features. Accordingly, all frameworks require a trigger (i.e., CHD or other chronic physical illness) to initiate positive reconceptualization. While the response shift theory does not include procedural matters, the concept of *illness identity* parallels so-called *meaning perspectives* in transformative learning theory, which both refer to general beliefs that influence the integration of new

events. Different from transformational learning theory, the presently applied framework does not cover the aspect of readiness to change – which is considered integral to change. Since transformative learning has not been tested beyond the qualitative retrospective approach, future research is encouraged to identify indicators and mechanisms of change in ACHD (Barclay-Goddard et al., 2012). The following integrated model (***Figure 6.4***) illustrates multidimensional relationships between biopsychosocial determinants of well-being that have surfaced during this research. Potential challenges that ACHD face in achieving well-being include biomedical (i.e., individual fitness, disease-related factors, surgical interventions), psychological (i.e., illness perception, identity formation, emotional distress), and social (i.e., cultural considerations, employment, feeling different) components (Kovacs & Bellinger, 2021). The interplay between biomedical and psychological factors was demonstrated within present findings in which individual health perceptions and illness identity were stronger predictors of emotional outcomes, than CHD diagnosis or lesion complexity. Although much has been learned about biopsychosocial relationships within this dissertation, the translation of mechanisms into somatic outcomes among ACHD remains to be elucidated. Since this topic has sparsely been addressed in the literature, it should remain a priority for future investigations.

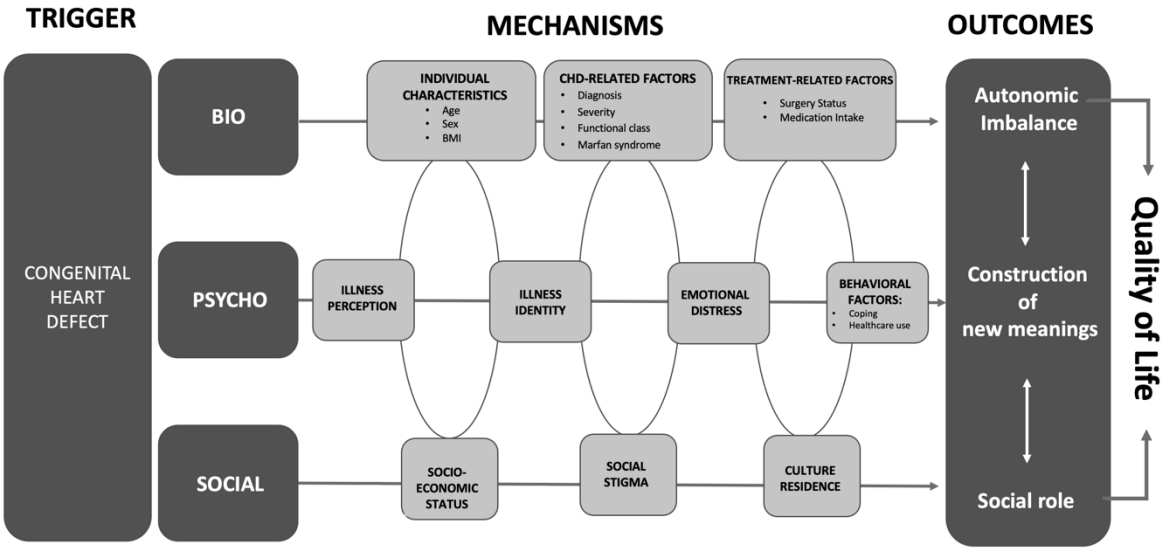

Figure 6.4: Hybrid model of change in ACHD, modified according to Andonian et al., 2021

6.3 Translating Research intro Practice: An Integrated Cardiac Care Service for Adults with Congenital Heart Disease

The increased awareness of biopsychosocial challenges associated with CHD has come to the forefront and thus makes it necessary to reflect upon psychocardiological elements in managing mental health care needs of ACHD (Callus et al., 2010; Roseman & Kovacs, 2019). Although psychocardiology has become an established discipline, no specialized programs for ACHD exist (Kovacs et al., 2015). This is especially problematic, given that psychological needs of ACHD differ not only from their healthy peers, but also from adults with acquired heart disease in several significant ways. First, ACHD are still

considerably younger, although the adult population is continuously on the rise (Callus et al., 2010). While adults with acquired heart disease may focus on recovery following a cardiac infarction, ACHD need support in coping with their chronic health condition that has been present since birth (Kovacs et al., 2015). Specific challenges include psychological disturbances, body image concerns, as well as impaired peer relationships, delayed progression into independent adulthood, and unique considerations in regard to education, employment, and family planning (Kovacs et al., 2005).

The findings of this dissertation provide insights into unique elements of psychocardiological care for ACHD that will be further discussed. Based on the hypothetical framework of study 3, psychological support should ideally encompass a stepped care approach ranging from preventative to reactive strategies. From this perspective, assessing psychological well-being indicators in conjunction with psychological distress is warranted in order to obtain optimal results in ACHD (Renshaw & Cohen, 2014).

Regardless of the mental health status of a patient, *psychoeducation* remains an indispensable component of CHD-specific interventions in which patients learn about their diagnosis and common emotional reactions across the course and progression of their CHD (Callus et al., 2010). ACHD often present to healthcare providers with knowledge and expectations based on misinformation (Neidenbach et al., 2021). A recently published study demonstrated that ACHD who perceived greater competence in managing their condition were less likely to experience depression and anxiety in the future (Leslie et al., 2020). Another smaller study demonstrated that preprocedural education significantly reduced anxiety symptoms in ACHD (Boyer et al., 2020). Based on the framework of the current investigation, improving health literacy becomes an integral component of supporting a patient's self-management and preventing any incidence of mental distress (Schulman-Green et al., 2012).

ACHD who are not yet experiencing mental distress (see *cell 1-4*, ***Table 6.1***) might not require specific clinical interventions, but should take active steps to identify available resources in order to foster positive illness identity states and increase their QOL (Keyes, 2007). In this context, *positive psychology* interventions deserve particular attention as they are aimed at strengthening positive feelings and behavior instead of reducing to what is wrong or dysfunctional (Bolier et al., 2013; Callus et al., 2010). Indeed, these findings show that the ongoing awareness of one's CHD might lead to increased levels of overall well-being and positive illness identity, presumably through a process of change in internal values (response shift), new perspectives, and more clarity of purpose and meaning in life (*see* **Figure 6.4**) (Barclay-Goddard et al., 2012; Callus et al., 2010).

Notwithstanding, one third up to one half of ACHD meet diagnostic criteria for mood and/or anxiety disorders which can adversely impact QOL and cardiovascular outcomes if left untreated (Kovacs & Bellinger, 2021). These patients (see *cells 4-8*, ***Table 6.1***) require specialist input to address their mental health needs and facilitate effective coping strategies. *Cognitive behavioral therapy* (CBT) is based on the assumption that emotions and behaviors are influenced by one's perceptions of events (Beck & Haigh, 2014). This assertion has also proven true within the context of this research showing that the patients' perceptions of their condition, and not the factual diagnosis itself, influence how they respond to their CHD (Andonian et al., 2021c). A major component of CBT is to identify and challenge

dysfunctional perceptions that may generate adjustment problems in accordance with the confirmed framework of study 3 (Doering et al., 2016). To date, there is one feasibility trial with promising results on the effectiveness of a CBT group-intervention in ACHD (ACHD-CARE) (Kovacs et al., 2015). The ACHD-CARE program was based upon a comprehensive needs assessment in ACHD (Kovacs et al., 2009a) and encompassed behavioral interventions including cognitive restructuring to challenge dysfunctional thoughts, behavioral activation to elevate effects (e.g., pleasant activity scheduling), in combination with relaxation training to reduce chronic tension and social skills training to improve communication skills of ACHD (Callus et al., 2010; Eifert & Lau, 2001; Kovacs et al., 2015). Despite an established evidence-base for psychological interventions in other chronic illness populations, efficacy data for ACHD is still limited and full-scale clinical trials are highly encouraged (Kovacs et al., 2018).

Findings obtained within this dissertation have encouraged the active incorporation of novel knowledge into routine care by triggering the demand for a *specialized psychological ACHD service* at the German Heart Center Munich. Given a programmatic commitment, psychological treatment, mental health screening, and psychocardiological counselling have become an integral part of standard care. In view of the data outlined in this dissertation, a treatment algorithm for use in ACHD has been developed. The algorithm starts with a comprehensive psychological assessment applying validated psychometric screening tools in conjunction with a structured clinical interview in order to evaluate whether formal diagnostic criteria are met. Feedback is then provided including a standardized case conceptualization and the communication of psychiatric diagnoses. If treatment is indicated and agreed upon, treatment recommendations and appropriate referrals (out-patient consultations, hospital day-care, inpatient treatment, pharmacotherapy) are reviewed in the next step of the algorithm. Continued follow-up and monitoring of symptoms are offered to determine the effectiveness of treatment or whether further treatment efforts are necessitated. All behavioral care takes place in the same medical setting within the context of coordinated visits, which conveys a holistic message to patients and potentially increases their confidence in the system of interdisciplinary ACHD care (Burg, 2018). Given the known overlap between many cardiac and psychological symptoms, this also has the advantage of follow-up consultations between ACHD providers and mental health professionals (Roseman & Kovacs, 2019). A schematic illustration of the treatment algorithm is shown in ***Figure 6.5***.

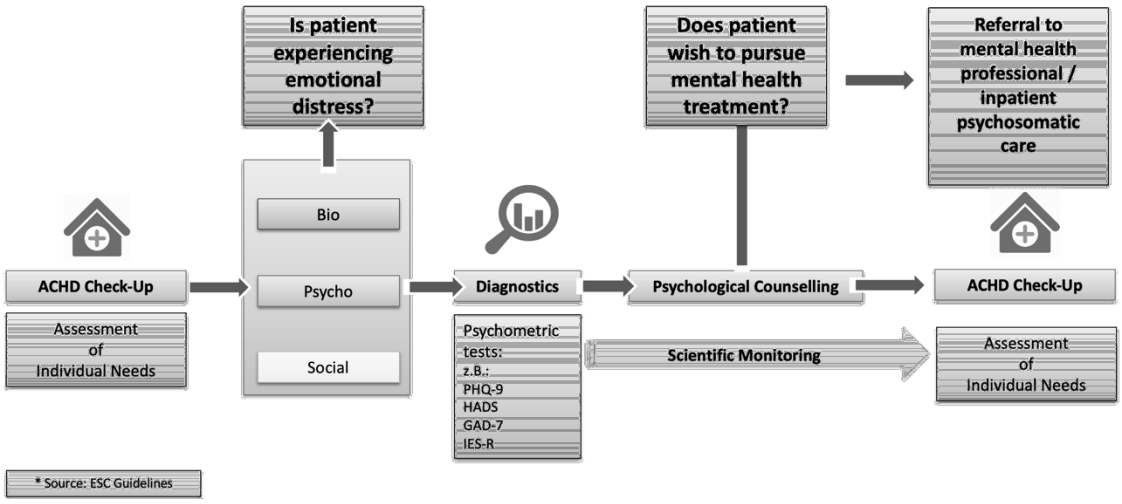

Figure 6.5: Treatment algorithm applied at the German Heart Center Munich

7 Conclusion

Recent advances and developments in cardiovascular medicine have revolutionized the landscape of ACHD care. What was once considered a fatal pediatric condition, can now be successfully treated, and affected children survive at much higher rates today than a few decades ago. With over 90% of children born with CHD surviving into adulthood, the number of ACHD is quickly outnumbering children with CHD (Kovacs & Bellinger, 2021). Given the unique physical and psychosocial challenges inherent to an aging CHD population, it is essential to expand the definition of meaningful ACHD outcomes to include QOL and various related psychosocial outcomes. However, many patients with psychological distress remain unrecognized and therefore are at greater risk for diminished QOL and adverse cardiovascular outcomes (Benderly et al., 2019; Westhoff-Bleck et al., 2016). It is high time that the recommendations of the 32nd Bethesda Conference in 2001 are taken seriously and those responsible start implementing what is long overdue:

> *„The emotional health of adults with CHD should be a priority in the overall care of this patient population. Appropriate screening and referral sources for treatment should be available at all regional ACHD centers. Tools for screening for psychosocial problems in this population should be developed and tested. Data should be developed to assess the effectiveness of regular follow-up care on the long-term physical and psychosocial health of adults with CHD."* (Warnes et al., 2001)

This dissertation provides a significant contribution to a holistic, multidisciplinary care system by identifying novel markers to detect, prevent, and treat concomitant psychological distress in ACHD. Patients experienced a generally good QOL, whereby objective health markers played a subordinate role compared to the subjective burden of disease in determining psychological well-being. These findings will help clinicians to identify specific subgroups of patients who are particularly at risk for an impaired psychological well-being and may therefore require extra psychological support. Illness identity was found to be a novel and consistent predictor of emotional distress in ACHD and should be considered when trying to understand and improve psychological well-being. The present findings also open up avenues for productive future research and, in particular, advance the evolving practical field of psychocardiological care for this particularly vulnerable patient population. Future tasks involve the development of psychosocial interventions tested in scientifically rigorous trials to enhance the provision of mental health care for patients with CHD of all ages (Tesson et al., 2019). Practical and theoretical insights acquired in this pioneering field of research could further serve as a source of inspiration for managing other chronic health conditions.

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Appendix

Appendix 1: Tables

Table A1: Classification of CHD complexity modified according to Warnes et al., 2001

SIMPLE	MODERATE	SEVERE
Native disease: - Isolated congenital aortic valve disease - Isolated congenital mitral valve disease (e.g. except parachute valve, cleft leaflet) - Isolated patient foramen ovale or small atrial septal defect - Isolated small ventricular septal defect (no associated lesions) - Mild pulmonic stenosis Repaired conditions: - Previously ligated or occluded ductus arteriosus - Repaired secundum or sinus venosus atrial septal defect without residua - Repaired ventricular septal sefect without residua	Repaired or unrepaired conditions: - Aorto-left ventricular fistulae - Anomalous pulmonary venous drainage (partial or total) - Atrioventricular canal defects (partial or complete) - Coarctation of the aorta - Ebstein's anomaly - Infundibular right ventricular outflow obstruction of significance - Ostium primum atrial septal defect - Patent ductus arteriosus (not closed) - Pulmonary valve regurgitation (moderate to severe) - Pulmonic valve stenosis (moderate to severe) - Sinus of Valsalva fistula/aneurysm - Sinus venosus atrial septal defect - Subvalvar or supravalvar aortic stenosis (except HOCM) - Tetralogy of Fallot - Ventrical septal defects with Absent valve(s) Aortic regurgitation Coarctation of the aorta Mitral disease Right ventricular outflow tract obstruction Straddling tricuspid/ mitral valve Subaortic stenosis	- Cyanotic CHD (all forms) - Conduits (valved or nonvalved) - Double-outlet ventricle - Eisenmenger syndrome - Fontan procedure - Mitral atresia - Single ventricle - Pulmonary atresia (all forms) - Pulmonary vascular obstructive diseases - Transposition of the great arteries - Tricuspid atresia - Truncus arteriousis/hemitruncus - Other abnormalities of atrioventricular or ventriculoarterial connection (not included above)

Table A2: Biopsychosocial Determinants of QOL in ACHD, Part 1

	Chen et al., 2011	Overgaard et al., 2011	Silva et al., 2011	Teixeira et al., 2011	Vigl et al., 2011	Cotts et al., 2012	Müller et al. , 2012	Opic et al., 2012	Schoormans et al., 2012	Bang et al., 2013	Eslami et al., 2013	Kahya Eren et al., 2013	Müller et al., 2013	Schoormans et al., 2014	Kovacs et al., 2014	Dean et al., 2015	Eslami et al., 2015	Eren et al., 2015	Gierat-Haponiuk et al., 2015
Demographic Variables																			
▪ Higher age			↑		↓						↓			=			↓		
▪ Female	↓		=	=	↓						↑			↓			↑		
▪ Children				=							↑								
▪ Education				↑	↑						↑	↑							
▪ Employment					↑						↑						↑		
▪ Financial strain											↑								
▪ Annual Income											=								
▪ Marriage																			
Clinical Variables																			
▪ Cardiac surgery			↓	↓							↓							↑	
▪ Hospitalisation											↓								
▪ Medication			=	↓							=								
▪ Severity of CHD	↓			=	↓								=			↑	=		
▪ Severity of comorbidity				=															
▪ CHD diagnosis				=						=	=								
▪ Higher NYHA functional class	↓	↓	↓											↓					
▪ Cyanosis																			
▪ Physical activity							↑												
▪ Time of diagnosis																			
▪ Higher BMI											↑								
▪ Implantable defibrillator								↓											
▪ Fontan procedure																			
▪ Duration of illness										=	=								
Psychosocial Variables																			
▪ Social support	↑		↑	↑								↑					↑		
▪ Emotional distress	↓										↓								
▪ Religion										↑	↑								
▪ Information on CHD										↑								↑	
▪ Type D Personality									↓										
▪ Poor illness perceptions														↓					
▪ Extraversion																			
▪ Sense of Coherence													↑		↑				
▪ Cardiac rehabilitation																			↑
▪ Negative illness perceptions																			
▪ Control perceptions																			
▪ Self-blame																			
▪ Self-efficacy																			

* adapted and extended according to Apers et al., 2015 (Apers et al., 2015)

Table A3: Biopsychosocial Determinants of QOL in ACHD, Part 2

	Bedair et al., 2015	Kahr et al., 2015	O'Donocan et al., 2016	Jackson et al., 2016	Fteropoulli et al., 2016	Apers et al., 2016	Müller et al., 2017	Eaton et al., 2017	Bay et al., 2017	Heck et al., 2017	Thomet et al., 2018	Smas-Suska et al., 2018	Holbein et al., 2018	McKillop et al., 2018	Rometsch et al., 2019	Gleason et al., 2019
Demographic Variables																
▪ Higher age			↑		↑	↓			↓	↓			=			
▪ Female											↓		=		↓	
▪ Children																
▪ Education															↑	↑
▪ Employment					↑	↑					↑					↑
▪ Financial strain																
▪ Annual Income				↑												
▪ Marriage						↑										
Clinical Variables																
▪ Cardiac surgery										↑						
▪ Hospitalisation																
▪ Medication				↓					↓							
▪ Severity of CHD		↓	↓		↑			=	=		=		↓			
▪ Severity of comorbidity				=					↓						=	
▪ CHD diagnosis																
▪ Higher NYHA functional class				↓		↓			↓		↓	↓				
▪ Cyanosis																
▪ Physical activity							↑							↑	↑	
▪ Time of diagnosis																
▪ Higher BMI																
▪ Implantable defibrillator	↓															
▪ Fontan procedure												↓	↓			
▪ Duration of illness			↓													
Psychosocial Variables																
▪ Social support														↑	↑	
▪ Emotional distress			↓		↓			↓						↓		↓
▪ Religion																
▪ Information on CHD																
▪ Type D Personality																
▪ Poor illness perceptions			↓		↓								↓			
▪ Extraversion																
▪ Sense of Coherence			↑					↑								
▪ Cardiac rehabilitation																
▪ Personal control perceptions			↑													
▪ Self-blame					↓											
▪ Self-efficacy											↓					

Table A4: Biopsychosocial Determinants of QOL in ACHD, Part 3

	Sandström et al., 2019	Moons et al., 2019	Tay et al., 2019	Enomoto et al., 2019	Huang et al., 2020	Casteigt et al., 2020	Lopez Barreda et al., 2020	Soufi et al., 2021	Jackson et al., 2021	Truong et al., 2021	Rosenberg et al., 2021	Moons et al., 2021
Demographic Variables												
▪ Higher age	↓	↓		↓	↓						↓	↓
▪ Female					↓		↓			↓		↓
▪ Children												
▪ Education					↑			↑				↑
▪ Employment		↑		↑				↑		↑		↑
▪ Financial strain							↓		↓			
▪ Annual Income												
▪ Marriage		↑			↑					↑		
Clinical Variables												
▪ Cardiac surgery			=		↑							↑
▪ Hospitalisation			=									↓
▪ Medication	↓											
▪ Severity of CHD		↓					=	=				
▪ Severity of comorbidity				↓								
▪ CHD diagnosis												
▪ Higher NYHA functional class	↓	↓						↓				↓
▪ Cyanosis												
▪ Physical activity	↑											
▪ Time of diagnosis												
▪ Higher BMI												
▪ Implantable defibrillator												↓
▪ Fontan procedure												
▪ Duration of illness									↓		↓	
▪ Atrial arrhythmia						↓						↓
Psychosocial Variables												
▪ Social support												
▪ Emotional distress							↓			↓		↓
▪ Religion												↑
▪ Information on CHD												
▪ Type D Personality												
▪ Poor illness perceptions												↓
▪ Extraversion												
▪ Sense of Coherence							↑					↑
▪ Cardiac rehabilitation												
▪ Personal control perceptions												
▪ Self-blame												
▪ Self-efficacy												↑

Appendix 2: Questionnaires

VEmaH Patient Questionnaire

Information

Sehr geehrte Patientinnen, Sehr geehrte Patienten!

wir bitten Sie herzlich, an einer wissenschaftlichen Untersuchung der Klinik für angeborene Herzfehler und Kinderkardiologie des Deutschen Herzzentrums München i teilzunehmen.

Dieser Fragebogen untersucht die **aktuelle Versorgungssituation von Erwachsenen mit angeborenen Herzfehlern (EMAH)**. Mit der Teilnahme leisten Sie einen sehr wichtigen Beitrag für die Versorgungsituation der Zukunft! Die Bearbeitung dauert maximal 10 Minuten!

Ihre Daten dienen ausschließlich zur statistischen Auswertung und zur Abfassung von wissenschaftlichen Publikationen. Sie erfolgt nach gesetzlichen Bestimmungen und setzt Ihre Einwilligung voraus.

Vielen Dank für Ihre Unterstützung!

Dr. Rhoia Neidenbach Prof. Dr. Dr. H. Kaemmerer

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Post:
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Einwilligungserklärung / Datenschutzerklärung gemäß Europäischer Datenschutz-Grundverordnung (DSGVO)[1]

Im Rahmen des Forschungsprojekts „Versorgungssituation von Erwachsenen mit angeborenen Herzfehlern (VEmaH)" soll die aktuelle Versorgungssituation von Erwachsenen mit angeborenen Herzfehlern (EmaH) untersucht werden. Alleinig für vorgenannten Forschungszweck sollen Daten durch das **Studienzentrum*** verarbeitet werden (Verarbeitung im Sinne von Erhebung, Speicherung, Veränderung und Nutzung).

Hierzu ist eine freiwillige und informierte Einwilligung erforderlich.
Die Datenerhebung erfolgt nicht personenbezogen. Das bedeutet, dass auf Grund der erhobenen Daten keine Rückschlüsse auf Sie gezogen werden können. Die Forschungsergebnisse werden in wissenschaftlich üblicher Form veröffentlicht. Wir sichern zu, dass aus den Veröffentlichungen keinerlei Rückschlüsse auf natürliche Personen möglich sind.

Rechtsgrundlage: Die Rechtsgrundlagen zur Verarbeitung der Sie betreffenden personenbezogenen Daten bilden bei Studien Ihre freiwillige schriftliche Einwilligung gemäß DSGVO sowie die Deklaration von Helsinki (Erklärung des Weltärztebundes zu den ethischen Grundsätzen für die medizinische Forschung am Menschen) und die Leitlinie für Gute Klinische Praxis. Zeitgleich mit der DSGVO treten in Deutschland das überarbeitete Bundesdatenschutzgesetz (BDSG-neu) und landesdatenschutzrechtliche Regelungen in Kraft.
Einwilligung zur Verarbeitung personenbezogener Daten und Recht auf Widerruf der Einwilligung: Die Teilnahme am Forschungsprojekt ist freiwillig. Eine Nichtteilnahme hat keine Folgen! Die Verarbeitung Ihrer personenbezogenen Daten ist nur mit Ihrer Einwilligung rechtmäßig. Diese Einwilligung kann jederzeit schriftlich und formlos bei der datenerhebenden Stelle (Deutsches Herzzentrum München) und mit Wirkung auf die Zukunft widerrufen werden. Alle personenbezogenen Daten werden nach Abschluss des Forschungsprojektes unwiderruflich gelöscht. Mir ist bekannt, dass ich mich jederzeit an den Datenschutzbeauftragten des Deutschen Herzzentrum München (Herrn Robert Kraus; datenschutz@dhm.mhn.de) sowie an die zuständige Aufsichtsbehörde für den Datenschutz wenden kann.
Recht auf Auskunft: Mir ist bekannt, dass ich jederzeit Auskunft über die zu meiner Person verarbeiteten Daten sowie die möglichen Empfänger dieser Daten, an die diese übermittelt wurden, verlangen kann und mir eine Antwort mit der Frist von einem Monat nach Eingang des Auskunftsersuchens zusteht.
Recht auf Berichtigung: Sie haben das Recht, Sie betreffende unrichtige personenbezogene Daten berichtigen zu lassen.
Recht auf Löschung: Sie haben das Recht auf Löschung Sie betreffender personenbezogener Daten, z. B. wenn diese Daten für den Zweck, für den sie erhoben wurden, nicht mehr notwendig sind und der Löschung keine gesetzlichen Aufbewahrungsfristen entgegen stehen.
Recht auf Einschränkung der Verarbeitung: Unter bestimmten Voraussetzungen haben Sie das Recht auf Einschränkung der Verarbeitung zu verlangen, d. h. die Daten dürfen nur gespeichert, nicht verarbeitet werden. Dies müssen Sie beantragen. Wenden Sie sich hierzu bitte an Ihre Studienleitung.
Recht auf Datenübertragbarkeit: Sie haben das Recht, die Sie betreffenden personenbezogenen Daten, die Sie dem Verantwortlichen für die Studie bereitgestellt haben, zu erhalten. Damit können Sie beantragen, dass diese Daten entweder Ihnen oder, soweit technisch möglich, einer anderen von Ihnen benannten Stelle übermittelt werden.
Widerspruchsrecht: Sie haben das Recht, jederzeit gegen konkrete Entscheidungen oder Maßnahmen zur Verarbeitung der Sie betreffenden personenbezogenen Daten Widerspruch einzulegen. Eine Verarbeitung findet anschließend grundsätzlich nicht mehr statt, es sei denn, die Verarbeitung ist gesetzlich weiterhin gefordert.

Hiermit bestätige ich, dass ich diese Datenschutzerklärung gelesen und verstanden habe und unter diesen Bedingungen freiwillig am Forschungsprojekt „Versorgungssituation von Erwachsenen mit angeborenen Herzfehlern (VEmaH)" teilnehmen möchte.

....
Ort, Datum **Unterschrift**

[1] Verordnung (EU) 2016/679 des Europäischen Parlaments und des Rates vom 27. April 2016 zum Schutz natürlicher Personen bei der Verarbeitung personenbezogener Daten, zum freien Datenverkehr und zur Aufhebung der Richtlinie 95/46/EG (Datenschutz-Grundverordnung)

Beginn des Fragebogens

1. Ihr Alter: _____ Ihr Geschlecht: ❑ männlich ❑ weiblich Ihre Postleitzahl: _____

2. Sie leben in einer:
   - ❑ Großstadt (> 100.000 Einwohner)
   - ❑ Mittelstadt (> 20.000 – 100.000 Einwohner)
   - ❑ Kleinstadt (5.000 – 20.000 Einwohner)
   - ❑ Landgemeinde (< 5.000 Einwohner)

3. Welche Form von angeborenen Herzfehlern haben Sie?
   - ❑ Aortenisthmusstenose
   - ❑ Aortenklappenstenose/ Aortenklappeninsuffizienz
   - ❑ Atrioventrikulärer Septumdefekt
   - ❑ Fallot´sche Tetralogie
   - ❑ Hypoplastisches Linksherzsyndrom
   - ❑ Persistierender Ductus Arteriosus Botalli
   - ❑ Pulmonalklappenstenose/ Pulmonalklappeninsuffizienz
   - ❑ Transposition der großen Arterien
   - ❑ Univentrikuläres Herz
   - ❑ Ventrikelseptumdefekt
   - ❑ Vorhofseptumdefekt
   - ❑ Ich habe mehrere Herzfehler, nämlich: _____
   - ❑ Einen anderen Herzfehler, und zwar: _____

4. Leiden Sie an einer der folgenden Erkrankung?

Marfan - Syndrom	Ja ❑	Nein ❑	Weiß nicht ❑
Ehlers - Danlos - Syndrom	Ja ❑	Nein ❑	Weiß nicht ❑
Turner - Syndrom	Ja ❑	Nein ❑	Weiß nicht ❑
Morbus Fabry	Ja ❑	Nein ❑	Weiß nicht ❑

5. Leiden Sie unter einer der folgenden typischen Begleit- oder Folgeerkrankungen Ihres Herzfehlers?
   - ❑ Herzschwäche
   - ❑ Herzrhythmusstörungen
   - ❑ Herzinnenhautentzündung (Endokarditis)
   - ❑ Koronare Herzerkrankung
   - ❑ Veränderungen im Blutbild
   - ❑ Weiß nicht
   - ❑ Gerinnungsstörungen
   - ❑ Psychische Einschränkungen
   - ❑ Thrombosen
   - ❑ Lungenhochdruck
   - ❑ Neurologische Komplikationen
   - ❑ Nein, ich leide an keiner Begleit-/ Folgeerkrankung

6. Wer ist Ihr erster Ansprechpartner bei allgemeinmedizinischen/gesundheitlichen Problemen, die nicht in Zusammenhang mit Ihrem Herzfehler gebracht werden, und welche Fachrichtung hat dieser Arzt?
   - ❑ Allgemeinarzt
   - ❑ Praktischer Arzt
   - ❑ Internist
   - ❑ Eine andere Fachrichtung, und zwar: _____

7. Führt dieser niedergelassene Arzt auch eine Zusatzbezeichnung? Wenn ja, welche?
   - ❑ Kardiologie
   - ❑ Gastroenterologie
   - ❑ Hämatologie
   - ❑ Angiologie
   - ❑ Pneumologie
   - ❑ Endokrinologie
   - ❑ Rheumatologie
   - ❑ Nephrologie
   - ❑ Keine Zusatzbezeichnung
   - ❑ Weiß nicht
   - ❑ Eine andere Schwerpunktbezeichnung, und zwar: _____

8. Ist diesem Arzt bekannt, dass Sie einen angeborenen Herzfehler haben?
   - ❑ Ja ❑ Nein ❑ Weiß nicht

9. Wer ist Ihr erster Ansprechpartner bei Problemen in Zusammenhang mit Ihrem angeborenen Herzfehler, und welche Fachrichtung hat dieser Arzt?
   - ❑ Allgemeinarzt
   - ❑ Praktischer Arzt
   - ❑ Internist
   - ❑ Eine andere Fachrichtung, und zwar: _____

10. Führt dieser niedergelassene Arzt auch eine Zusatzbezeichnung? Wenn ja, welche?
    - ❑ Kardiologie
    - ❑ Gastroenterologie
    - ❑ Hämatologie
    - ❑ Angiologie
    - ❑ Pneumologie
    - ❑ Endokrinologie
    - ❑ Rheumatologie
    - ❑ Nephrologie
    - ❑ Keine Zusatzbezeichnung
    - ❑ Weiß nicht
    - ❑ Eine andere Schwerpunktbezeichnung, und zwar: _____

11. Handelt es sich bei dem Arzt, den Sie bei **allgemeinmedizinischen/gesundheitlichen Problemen** und bei **Problemen in Zusammenhang mit Ihrem angeborenen Herzfehler** aufsuchen, **um denselben Versorger?**
    ❑ Ja ❑ Nein

12. Welchen **Versicherungsstatus** haben Sie aktuell?
    ❑ Gesetzliche Krankenversicherung ❑ Private Krankenversicherung ❑ Keine ❑ Weiß nicht

13. Besteht aus Ihrer Sicht ein Bedarf an **spezifischer Beratung** für Patienten mit angeborenen Herzfehlern bezüglich folgender Themen?

Krankenversicherung	❑ Ja	❑ Nein	❑ Weiß nicht
Lebensversicherung	❑ Ja	❑ Nein	❑ Weiß nicht
Alterssicherung	❑ Ja	❑ Nein	❑ Weiß nicht

14. Welchen **Grad der Behinderung** haben Sie? _____ (in 10er Schritten von 0-100)

15. Besteht aus Ihrer Sicht der **Bedarf an spezifischer Beratung, vor allem** hinsichtlich **Behinderung und folgender Themen?**
    ❑ Ja, bezüglich Rente ❑ Ja, bezüglich Schwerbehindertenausweis ❑ Nein

16. Werden Ihnen regelmäßig **sehr teure Medikamente** verordnet?
    ❑ Ja, Medikamente wegen Lungenhochdruck ❑ Ja, Gerinnungshemmer ❑Nein
    ❑ Weiß nicht ❑ Sonstige, und zwar: _____

17. Hat Ihr Hausarzt **Probleme bei der Verordnung** Ihrer Medikamente? (z.B. auf Grund hoher Kosten?)
    ❑ Ja ❑ Nein ❑ Weiß nicht ❑ Ich nehme keine Medikamente

18. Bitte bewerten Sie mit Schulnoten Ihre aktuelle **Versorgungslage in Zusammenhang mit Ihrem Herzfehler!**
    ❑ Sehr gut ❑ Gut ❑ Befriedigend ❑ Ausreichend ❑ Mangelhaft ❑ Ungenügend

19. Bitte bewerten Sie mit Schulnoten Ihre aktuelle allgemeinmedizinisch-ärztliche **Versorgungslage!**
    ❑ Sehr gut ❑ Gut ❑ Befriedigend ❑ Ausreichend ❑ Mangelhaft ❑ Ungenügend

20. Besteht aus Ihrer Sicht ein **Bedarf an spezifischer Beratung** für Patienten mit angeborenen Herzfehlern bezüglich folgender Punkte? Wenn ja, bitte ankreuzen! (Mehrfachantworten möglich)
    ❑ Rehabilitationsmaßnahmen ❑ Bildungsformen (Schule, Studium, Beruf)
    ❑ Berufsfähigkeit ❑ Belastbarkeit im Alltag
    ❑ Führerscheinerwerb ❑ Flugtauglichkeit
    ❑ Leistungsfähigkeit, sportliche Betätigung ❑ Genetische Beratung
    ❑ Ernährung und Bewegung ❑ Prävention
    ❑ Schwangerschaft ❑ Sonstige, und zwar: _____

21. Ist Ihnen bekannt, dass es **zertifizierte Kliniken/ Zentren** für **Erwachsene mit angeborenen Herzfehlern** gibt? (Mehrfachantworten möglich)
    ❑ Ja, und zwar niedergelassene Kinderkardiologen mit EMAH-Zertifizierung
    ❑ Ja, und zwar niedergelassene Kardiologen mit EMAH-Zertifizierung
    ❑ Ja, und zwar zertifizierte EMAH-Schwerpunktkliniken, EMAH-Zentren
    ❑ Nein, mir sind keine zertifizierten Kliniken/Zentren für EMAH bekannt

22. Hat Sie Ihr niedergelassener Arzt in der **Vergangenheit** an eine **EMAH-zertifizierte Institution** überwiesen?
    ❑ Ja, bei kardialen Probleme in Zusammenhang mit meinem Herzfehler
    ❑ Ja, bei Problemen/ Erkrankungen, deren Verlauf von meinem Herzfehler beeinflusst werden kann
    ❑ Nein, ich wurde noch nie in eine EMAH-Institution überwiesen

23. Sind Sie über die **spezifischen Versorgungszentren ausreichend informiert?**
    ❑ Ja ❑ Nein ❑ Weiß nicht

24. Sind Ihnen **Selbsthilfeorganisationen für EMAH** bekannt? (z.B. Bundesverband JEMAH e.V., Deutsche Kinderherzstiftung, Bundesverband herzkranker Kinder e.V., Herzkind e.V.)
    ❑ Ja ❑ Nein ❑ Weiß nicht

25. Sind Sie bereit an einer vertiefenden **Befragung** teilzunehmen?
    ❑ Ja, bitte **kontaktieren Sie mich** unter folgender Emailadresse: _____
    ❑ Nein danke, ich bin an einer Befragung nicht interessiert

Bitte füllen Sie im Anschluss 5 Fragen zur Lebensqualität aus!

Bitte **kreuzen** Sie unter jeder Überschrift DAS Kästchen an, das Ihre Gesundheit HEUTE am besten beschreibt.

BEWEGLICHKEIT / MOBILITÄT

Ich habe keine Probleme herumzugehen ❑
Ich habe leichte Probleme herumzugehen ❑
Ich habe mäßige Probleme herumzugehen ❑
Ich habe große Probleme herumzugehen ❑
Ich bin nicht in der Lage herumzugehen ❑

FÜR SICH SELBST SORGEN

Ich habe keine Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe leichte Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe mäßige Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe große Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen ❑

ALLTÄGLICHE TÄTIGKEITEN *(z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)*

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe leichte Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe mäßige Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe große Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen ❑

SCHMERZEN / KÖRPERLICHE BESCHWERDEN

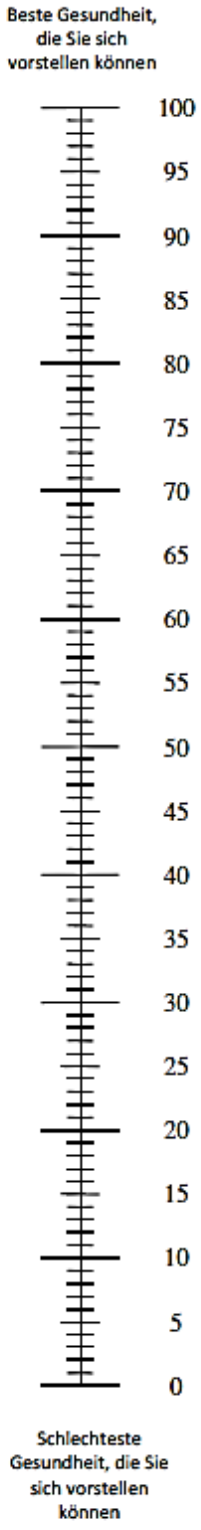
Ich habe keine Schmerzen oder Beschwerden ❑
Ich habe leichte Schmerzen oder Beschwerden ❑
Ich habe mäßige Schmerzen oder Beschwerden ❑
Ich habe starke Schmerzen oder Beschwerden ❑
Ich habe extreme Schmerzen oder Beschwerden ❑

ANGST / NIEDERGESCHLAGENHEIT

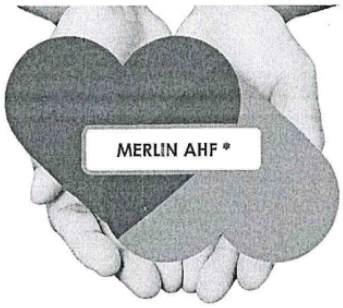
Ich bin nicht ängstlich oder deprimiert ❑
Ich bin ein wenig ängstlich oder deprimiert ❑
Ich bin mäßig ängstlich oder deprimiert ❑
Ich bin sehr ängstlich oder deprimiert ❑
Ich bin extrem ängstlich oder deprimiert ❑

- Wir wollen herausfinden, wie gut oder schlecht Ihre Gesundheit HEUTE ist.
- Diese Skala ist mit Zahlen von 0 bis 100 versehen.
- 100 ist die beste Gesundheit, die Sie sich vorstellen können.
  0 (Null) ist die schlechteste Gesundheit, die Sie sich vorstellen können.
- Bitte kreuzen Sie den Punkt auf der Skala an, der Ihre Gesundheit HEUTE am besten beschreibt.
- Jetzt tragen Sie bitte die Zahl, die Sie auf der Skala angekreuzt haben, in das Kästchen unten ein.

IHRE GESUNDHEIT HEUTE = ☐



MERLIN Patient Questionnaire



Patienteninformationsblatt

Sehr geehrte Patientinnen, sehr geehrte Patienten!

Wir bitten Sie herzlich an der wissenschaftlichen Studie "Analyse des Gesundheitsverhaltens von Erwachsenen mit angeborenen Herzfehlern (EmaH) als Grundlage für die Etablierung primär-präventivmedizinischer Maßnahmen zur Reduktion von Gesundheitsrisiken" teilzunehmen. Dafür möchten wir Sie bitten heute und bei Ihrem nächsten routinemäßigen Ambulanzbesuch nachfolgende Fragbögen auszufüllen. Mit Ihrer Teilnahme leisten Sie einen sehr wichtigen Beitrag! Die Bearbeitung wird maximal 20 Minuten in Anspruch nehmen.

Mit der Studienteilnahme treten für Sie keine Risiken oder Belastungen auf. Eine Nichtteilnahme hat keine Folgen. Aus der Studienteilnahme ergibt sich kein unmittelbarer persönlicher Nutzen. Auf dem Boden der erhobenen Daten sollen Informationsprogramme entwickelt werden, die primär den Patienten, Familienangehörigen, aber auch versorgenden Ärzten gesundheitsrelevantes Wissen vermitteln.

Die Ergebnisse der Routineuntersuchung werden pseudonymisiert in eine Forschungsdatenbank aufgenommen. Zusätzlich wird während der typischerweise anfallenden Wartezeiten im Rahmen des Ambulanzbetriebes eine Fragebogenuntersuchung zu den Themen Lebenstil, Gesundheitsverhalten, Ernährung und psychische Situation durchgeführt.

In dieser Studie ist Herr Prof. Dr. Dr. Harald Kaemmerer, Klinik für angeborene Herzfehler und Kinderkardiologie, Deutsches Herzzentrum München Lazarettstr. 36, 80636 München, Mail: vemah@dhm.mhn.de (Studienzentrum) für die Datenverarbeitung verantwortlich. Die Verarbeitung Ihrer Daten setzt Ihre Einwilligung voraus (Rechtsgrundlage). Ihre Daten werden ausschließlich im Rahmen dieser Studie verwendet. Dazu gehören personenidentifizierende Daten wie Name, Anschrift und sensible personenbezogene Gesundheitsdaten. Alle unmittelbar Ihre Person identifizierenden Daten (Name, Geburtsdatum) werden durch einen Identifizierungscode ersetzt (pseudonymisiert). Dies schließt eine Identifizierung Ihrer Person durch Unbefugte weitgehend aus. Ihre Daten werden an der Klinik für angeborene Herzfehler und Kinderkardiologie, Deutsches Herzzentrum München Lazarettstr. 36, 80636 München gespeichert. Sie werden nach Ablauf der gesetzlichen Löschfristen gelöscht.

Die Einwilligung zur Verarbeitung Ihrer Daten ist freiwillig, Sie können jederzeit die Einwilligung ohne Angabe von Gründen und ohne Nachteile für Sie widerrufen. Sie haben das Recht, Auskunft über die Sie betreffenden Daten zu erhalten, auch in Form einer unentgeltlichen Kopie. Darüber hinaus können Sie die Berichtigung oder Löschung Ihrer Daten verlangen. Wenden Sie sich in diesen Fällen an das Studienzentrum.

Im Falle einer Beschwerde wenden Sie sich an:

Behördlicher Datenschutzbeauftragter
Klinikum rechts der Isar der Technischen Universität München
Ismaninger Str. 22, 81675 München
E-Mail: datenschutz@mri.tum.de

oder:
Bayerischer Landesbeauftragter für den Datenschutz
Postanschrift: Postfach 22 12 19, 80502 München, Hausanschrift: Wagmüllerstr. 18, 80538 München
E-Mail: poststelle@datenschutz-bayern.de.

Die Teilnahme an oben genannter Studie ist freiwillig und setzt Ihre Einwilligung voraus (**Bitte lesen Sie sich dazu die Einwilligungserklärung auf der nächsten Seite durch und füllen Sie diese entsprechend aus**).

Das MERLIN-AHF Studienteam bedankt sich für Ihre Mithilfe!

Dr. R. Neidenbach | Prof. Dr. Dr. H. Kaemmerer | Prof. Dr. P. Ewert

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URL: www.vemah.info

Datenschutzerklärung / Allgemeine Einwilligung zur Studienteilnahme
gemäß Europäischer Datenschutz-Grundverordnung (DSGVO)[1]

Datenerhebende Stelle:
Klinik für angeborene Herzfehler und Kinderkardiologie, Deutsches Herzzentrum München
Lazarettstr. 36, 80636 München, Prof. Dr. Harald Kaemmerer, Tel: (089)1218-3055, E-Mail: vemah@dhm.mhn.de

Ich, _____ (Vorname, Nachname) wurde über Wesen, Zielsetzung sowie Ablauf, Bedeutung und Tragweite der geplanten Längsschnittstudie *„Analyse des Gesundheitsverhaltens von Erwachsenen mit angeborenen Herzfehlern (EmaH) als Grundlage für die Etablierung primär-präventivmedizinischer Maßnahmen zur Reduktion von Gesundheitsrisiken"* aufgeklärt. Eine Kopie dieser Einwilligungserklärung sowie eine schriftliche Probandeninformation wurden mir ausgehändigt und ich hatte ausreichend Zeit, diese zu lesen und Fragen zu stellen. Den Inhalt habe ich verstanden und meine Fragen wurden vollständig geklärt. Weitere Informationen kann ich jederzeit beim Studienpersonal erfragen.
Ich erkläre, dass ich aus freier Entscheidung darin einwillige, an dieser Studie teilzunehmen. Mir ist bekannt, dass ich meine Einwilligungserklärung zur Teilnahme an der Studie jederzeit ohne Angabe von Gründen zurücknehmen kann, ohne dass mir daraus Nachteile entstehen.

Rechtsgrundlage

Die Rechtsgrundlagen zur Verarbeitung der Sie betreffenden personenbezogenen Daten bilden bei Studien Ihre freiwillige schriftliche Einwilligung gemäß DSGVO sowie die Deklaration von Helsinki (Erklärung des Weltärztebundes zu den ethischen Grundsätzen für die medizinische Forschung am Menschen) und die Leitlinie für Gute Epidemiologische Praxis. Zeitgleich mit der DSGVO treten in Deutschland das überarbeitete Bundesdatenschutzgesetz (BDSG-neu) und landesdatenschutzrechtliche Regelungen in Kraft.

Einwilligungserklärung zum Datenschutz

Ich willige ein, dass die im Rahmen der oben genannten Studie erhobenen Daten (Fragebögen) pseudonymisiert, d.h. mit einem Zahlencode versehen (ohne Namens- oder Initialnennung) aufgezeichnet, in Computern gespeichert, ausgewertet und verschlüsselt unter Aufsicht des Studienzentrums* an andere kooperierende wissenschaftliche Einrichtungen weitergegeben werden. Wir sichern Ihnen zu, dass die Daten unverzüglich anonymisiert werden, sobald es der Forschungszweck erlaubt. Insofern dies nicht anders gesetzlich bestimmt ist oder Sie im Einzelfall ausdrücklich eingewilligt haben, erfolgt keine Übermittlung von personenbezogenen Daten an Dritte. Ich bin damit einverstanden, dass die Ergebnisse der Studie in Gruppen zusammengefasst und ohne Bezug auf konkrete natürliche Personen in wissenschaftlich üblicher Form veröffentlicht werden.

Die Teilnahme am Forschungsprojekt ist freiwillig. Eine Nichtteilnahme hat keine Folgen! Die Verarbeitung Ihrer personenbezogenen Daten ist nur mit Ihrer Einwilligung rechtmäßig. Ich bin darüber aufgeklärt worden, dass ich jederzeit ohne Angabe von Gründen schriftlich und formlos bei der datenerhebenden Stelle und mit Wirkung auf die Zukunft die Teilnahme an der Studie beenden kann und die Einwilligung zur Erhebung und Verarbeitung der personenbezogenen Daten widerrufen kann. Im Falle eines solchen Widerrufs meiner Einwilligungserklärung willige ich ebenso ein, dass die bis zu diesem Zeitpunkt gespeicherten Daten weiterhin verwendet werden dürfen, soweit dies erforderlich ist, um die Richtlinien guter wissenschaftlicher Praxis einzuhalten, die eine Aufbewahrung von Studiendaten für mindestens zehn Jahre vorsehen.

Alle personenbezogenen Daten werden nach Abschluss des Forschungsprojektes unwiderruflich gelöscht.

Mir ist bekannt, dass ich mich jederzeit an den Datenschutzbeauftragten des Deutschen Herzzentrum München (Herrn Robert Kraus; datenschutz@dhm.mhn.de) sowie an die zuständige Aufsichtsbehörde für den Datenschutz (https://www.datenschutz-bayern.de/vorstell/impressum.html) wenden kann und gegen konkrete Entscheidungen oder Maßnahmen zur Verarbeitung der Sie betreffenden personenbezogenen Daten Widerspruch einlegen kann.

Außerdem haben Sie das Recht, Beschwerde bei der/den Datenschutzaufsichtsbehörde/n einzulegen, wenn Sie der Ansicht sind, dass die Verarbeitung der Sie betreffenden personenbezogenen Daten gegen die Datenschutzgrundverordnung (DSGVO) verstößt. Wollen Sie von diesem Recht Gebrauch machen, wenden Sie sich bitte an eine der oben genannten Datenschutz-Aufsichtsbehörden.

Mir ist bekannt, dass ich jederzeit Auskunft über die zu meiner Person verarbeiteten Daten sowie die möglichen Empfänger dieser Daten, an die diese übermittelt wurden, verlangen kann und mir eine Antwort mit der Frist von einem Monat nach Eingang des Auskunftsersuchens zusteht. Wenden Sie sich hierzu bitte an Ihre Studienleitung.

[1] Verordnung (EU) 2016/679 des Europäischen Parlaments und des Rates vom 27. April 2016 zum Schutz natürlicher Personen bei der Verarbeitung personenbezogener Daten, zum freien Datenverkehr und zur Aufhebung der Richtlinie 95/46/EG (Datenschutz-Grundverordnung)

Sie haben das Recht, Sie betreffende unrichtige personenbezogene Daten berichtigen zu lassen. Sie haben das Recht auf Löschung Sie betreffender personenbezogener Daten, z. B. wenn diese Daten für den Zweck, für den sie erhoben wurden, nicht mehr notwendig sind und der Löschung keine gesetzlichen Aufbewahrungsfristen entgegen stehen. Unter bestimmten Voraussetzungen haben Sie das Recht auf Einschränkung der Verarbeitung zu verlangen, d. h. die Daten dürfen nur gespeichert, nicht verarbeitet werden. Dies müssen Sie beantragen. Wenden Sie sich hierzu bitte an Ihre Studienleitung. Sie haben das Recht, die Sie betreffenden personenbezogenen Daten, die Sie dem Verantwortlichen für die Studie bereitgestellt haben, zu erhalten. Damit können Sie beantragen, dass diese Daten entweder Ihnen oder, soweit technisch möglich, einer anderen von Ihnen benannten Stelle übermittelt werden.

***Studienzentrum:**
Klinik für angeborene Herzfehler und Kinderkardiologie,
Deutsches Herzzentrum München
Prof. Dr. Dr. Harald Kaemmerer
Lazarettstr. 36, 80636 München

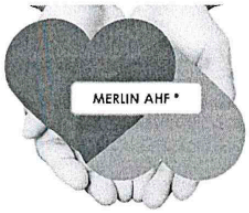
Kooperierende wissenschaftliche Einrichtungen
Medizinische Klinik II
Universitätsklinikum Erlangen
Ulmenweg 18, 91054 Erlangen

Darüber hinaus willige ich ein, dass ein autorisierter und zur Verschwiegenheit verpflichteter Beauftragter der Ethikkommission der Technischen Universität München in die personenbezogenen Daten Einsicht nimmt, soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der Studie notwendig ist. Für diese Maßnahme entbinde ich die Studienmitarbeiter von ihrer Schweigepflicht.

Hiermit bestätige ich, dass ich diese Datenschutz-/Einwilligungserklärung gelesen und verstanden habe und unter diesen Bedingungen freiwillig am Forschungsprojekt " Analyse des Gesundheitsverhaltens von Erwachsenen mit angeborenen Herzfehlern (EmaH) als Grundlage für die Etablierung primär-präventivmedizinischer Maßnahmen zur Reduktion von Gesundheitsrisiken " teilnehmen möchte.

_____ _____
Ort, Datum Unterschrift des/der Teilnehmer/in

_____ _____
Ort, Datum Unterschrift des/der aufklärenden Mitarbeiter/in



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***MERLIN-AHF: Medizinische Erfolge langfristig bewahren durch integrierte Versorgung angeborener Herzfehler**

Liebe Patienten!
In diesem Fragebogen geht es um Ihren Lebensstil und Ihr Gesundheitsverhalten! Ziel der Befragung ist es, herauszufinden, welche Maßnahmen etabliert werden müssen, um ggf. Ihre Gesundheitsrisiken zu erkennen und Sie dabei unterstützen, diese langfristig zu reduzieren. Die Teilnahme ist freiwillig und dauert nur wenige Minuten. Bitte geben Sie den ausgefüllten Fragebogen am Schwesternstützpunkt ab!
Vielen Dank für Ihre Mithilfe!

Beginn des Fragebogens

1.) Wie alt sind Sie? _____
2.) Welches Geschlecht haben Sie? ❑Männlich ❑Weiblich ❑anderes ❑keine Angabe
3.) Wie groß sind Sie? _____cm
4.) Wie viel wiegen Sie? _____kg

5.) Wie ist Ihr Familienstand?
❑Verheiratet und zusammenlebend ❑Verheiratet und getrennt lebend ❑geschieden
❑In fester Partnerschaft ❑keine feste Partnerschaft ❑verwitwet

6.) Wie ist der Familienstand Ihrer Eltern?
❑Verheiratet und zusammenlebend ❑Verheiratet und getrennt lebend ❑geschieden
❑In fester Partnerschaft ❑keine feste Partnerschaft ❑verwitwet

7.) Haben Sie Kinder? ❑Nein ❑Ja

8.) Falls Frage 7 auf Sie zutrifft, wie viele Kinder haben Sie? _____ Kinder

9.) Wie schätzen Sie persönlich Ihre momentane finanzielle Lage im Vergleich zu anderen Personen Ihrer Altersgruppe ein? ❑sehr gut ❑gut ❑weder gut noch schlecht ❑schlecht ❑sehr schlecht

10.) Welchen höchsten Schulabschluss haben Sie?
❑Schule beendet ohne Abschluss ❑Hauptschulabschluss/Volksschulabschluss ❑Realschulabschluss
❑Fachhochschulreife ❑Allg. Hochschulreife/Abitur

11.) Welchen beruflichen Ausbildungsabschluss haben Sie?
❑noch in Ausbildung (Student/in, Auszubildende/r)
❑keinen beruflichen Abschluss und nicht in beruflicher Ausbildung
❑Beruflich-betriebliche Ausbildung (Lehre)
❑Beruflich-schulische Ausbildung (Berufsfachschule, Handelsschule)
❑Abschluss von einer Fach-, Meister-, Technikerschule, Berufs- oder Fachakademie
❑Fachhochschulabschluss
❑Hochschulabschluss
❑anderer beruflicher Abschluss, und zwar: _____

12.) Welche berufliche Tätigkeit üben Sie zurzeit aus? Bitte geben Sie die Berufsbezeichnung so genau wie möglich an. _____

13.) Wie oft waren Sie in den letzten 12 Monaten beim Hausarzt, praktischen Arzt, Allg. Internisten? _____Mal

14.) Wie oft waren Sie in den letzten 12 Monaten beim Facharzt (nicht Zahnarzt)? _____Mal

15.) Wie oft waren Sie in den letzten 12 Monaten beim Zahnarzt? _____Mal

16.) Wie oft waren Sie in den letzten 12 Monaten in stationärer Behandlung? _____Mal

Studien-ID_._._._._._._

17.) An wie vielen Tagen waren Sie in den letzten 12 Monaten so krank, dass Sie Ihren üblichen Tätigkeiten (z.B. Beruf, Sport, soziale- und Alltagsaktivitäten) nicht nachgehen konnten? _____Mal

18.) Wie oft wurden Sie in den letzten 12 Monaten durch einen Arzt arbeitsunfähig geschrieben? _____Mal

19.) Rauchen Sie zurzeit täglich Zigaretten oder haben Sie früher täglich Zigaretten geraucht?
❑nein, ich habe noch nie geraucht ❑Ja, ich rauche seit _____ Jahren täglich etwa _____ Zigaretten
❑Ja, ich habe früher geraucht, insgesamt _____ Jahre und ca. _____ Zigaretten/Tag

20.) Wie oft trinken Sie alkoholische Getränke (Wein, Bier, Likör, Spirituosen)?
❑nie ❑1-2 mal pro Monat
❑1-2 mal pro Woche ❑3-4 mal pro Woche ❑5-7 mal pro Woche oder mehr

21.) Nehmen Sie regelmäßig Medikamente ein? ❑Nein ❑Ja

22.) Welche Medikamente nehmen Sie regelmäßig ein? (z.B. Antikoagulation, ACE Hemmer, Antibaby Pille, ...)
_____

23.) Konsumieren Sie gelegentlich Drogen? ❑Nein ❑Ja Wenn ja, welche? _____

24.) Treiben Sie regelmäßig Sport? ❑Nein ❑Ja

25.) An wie vielen Tagen/ Woche und wie viele Stunden pro Woche sind Sie körperlich aktiv? (Sport, Gartenarbeit, Gehen,...) _____Tagen/ Woche und ca. ____Stunden/Woche

26.) Welchen Sport/ welche körperliche Aktivität üben Sie gerne aus?

❑Jogging	❑Kampfsport	❑Yoga, Pilates, QiGong
❑Radfahren	❑Fitnesscenter	❑Tennis
❑Schwimmen	❑Reiten	❑Tischtennis
❑Wandern	❑Klettern	❑Badminton
❑Fußball	❑Skifahren, Langlauf	❑Tanz
❑Volleyball	❑Golf	❑Turnen

❑anderen, und zwar:_____

27.) Wann sind Sie während der letzten 4 Wochen gewöhnlich abends zu Bett gegangen?
übliche Uhrzeit: _____Uhr

28.) Wie lange hat es während der letzten 4 Wochen gewöhnlich gedauert, bis Sie nachts eingeschlafen sind?
In Minuten: _____

29.) Wann sind Sie während der letzten 4 Wochen gewöhnlich morgens aufgestanden?
übliche Uhrzeit: _____Uhr

30.) Wie viele Stunden haben Sie während der letzten 4 Wochen pro Nacht tatsächlich geschlafen?
(Das muss nicht mit der Anzahl der Stunden, die Sie im Bett verbracht haben, übereinstimmen)
Effektive Schlafzeit (Stunden) pro Nacht: _____ "h:min" (Bitte geben Sie die Stunden und Minuten, getrennt durch einem Doppelpunkt und zweistellig ein. z.B.: 08:30)

31.) Wie würden Sie insgesamt die Qualität Ihres Schlafes während der letzten 4 Wochen beurteilen?
❑Sehr gut ❑Ziemlich gut ❑Ziemlich schlecht ❑Sehr schlecht

32.) Wie oft am Tag essen Sie normalerweise? (einschließlich aller Mahlzeiten & Snacks) ____ Mal (z.b. 4 Mal)

33.) Haben Sie in den letzten 12 Monaten eine Diät gemacht, Ihre Essgewohnheiten geändert oder etwas anderes getan, um Ihr Gewicht zu kontrollieren?
❑nein ❑ja, ein paar Tage ❑ja, eine Woche ❑ja, mehr als 1 Woche aber weniger als 1 Monat
❑ja, mehr als 1 Monat, aber weniger als 6 Monate ❑ja, mehr als 6 Monate

Studien-ID_._._._._._._

34.) Wie oft haben Sie in den letzten 12 Monaten eine Diät gemacht, um Gewicht zu verlieren? (Mit „Diät" meinen wir, die Essensgewohnheiten so zu verändern, dass man Gewicht verlieren kann.)
❑kein Mal ❑1-2 Mal ❑3-4 Mal ❑5-6 Mal ❑7 Mal oder öfter

35.) Welche Diät oder Ernährungsumstellung haben Sie gemacht? (z.B. Low-Carb, Intermittierendes Fasten, Verzicht auf Fleisch, oder ähnliches....) _____

36.) Wie beurteilen Sie Ihre körperliche Konstitution heute?
❑untergewichtig ❑leicht untergewichtig ❑normalgewichtig ❑leicht übergewichtig
❑übergewichtig ❑stark übergewichtig

37.) Fühlen Sie sich in Ihrer Sexualität beeinträchtigt? ❑nein ❑ja

38.) Wenn Frage 37 auf Sie zutrifft, können Sie hierführ eine mögliche Ursache beschreiben? (z.B Medikation, Stress,Partnerschaft,..)_____

39.) Wie hoch würden Sie Ihre derzeitige Stressbelastung einschätzen?
❑keine ❑gering ❑mäßig ❑hoch ❑sehr hoch

40.) Versuchen Sie, den ursächlichen Anteil bei der Entstehung Ihres Stressproblems in Prozent zu schätzen. (z.B. Arbeit 45%, Freizeit 20%, Familie 25%, Krankheit 10%)
Arbeit_____% Freizeit_____% Familie_____% Krankheit_____%

41.) Erleben Sie bei Stressbelastungen zeitweilig negative körperliche Reaktionen? (z.B. Kopfschmerzen, Angst, Magenbeschwerden, Muskelverspannungen, ...)
❑Nein ❑Ja wenn ja welche? _____

42.) Wie regelmäßig nehmen Sie an Vorsorgeuntersuchungen teil?
❑regelmäßig ❑häufig ❑bei Beschwerden ❑selten ❑nie

43.) Sind Ihre Impfungen auf dem aktuellen Stand und lassen Sie den Impfpass regelmäßig überprüfen?
❑nein ❑ja ❑weiß nicht

44.) Wie oft hatten Sie in den letzten 12 Monaten Probleme die Anweisungen Ihres Arztes Folge zu leisten?
❑nie ❑fast nie ❑selten ❑oft ❑immer

45.) Wie oft hatten Sie in den letzten 12 Monaten Probleme, die Medikamente so einzunehmen, wie sie Ihnen vom Arzt verschrieben wurden?

❑nie ❑fast nie ❑selten ❑oft ❑immer

46.) Wenn ja, was waren die Gründe dafür?
❑ Ich vergesse die Medikamente ❑ Ich halte die regelmäßige Einnahme nicht für wichtig
❑ Ich habe zu viele Nebenwirkungen ❑ Ich halte andere Maßnahmen für besser
❑ Ich habe Angst vor Nebenwirkungen ❑ Ich komme bei den vielen Medikamenten durcheinander

47.) Fühlen Sie sich ausreichend informiert über gesunde Ernährung im Alltag? ❑nein ❑ja

48.) Würden Sie gerne an Workshops teilnehmen, die den Bereich körperliche Aktivität für Sie abhandeln?
❑nein ❑ja wenn ja, haben Sie besondere Wünsche:_____

49.) Würden Sie gerne an Workshops teilnehmen, die den Bereich optimale Ernährung betreffen?
❑nein ❑ja wenn ja, haben Sie besondere Wünsche:_____

50.) Würden Sie gerne an Workshops teilnehmen, die den Bereich Gesundheit (Prävention, Impfungen, Gesundheitsförderung) betreffen?
❑nein ❑ja wenn ja, haben Sie besondere Wünsche:_____

Studien-ID_._._._._._._

Bitte beantworten Sie im Anschluss noch folgende Fragen zur Lebensqualität!

Bitte **kreuzen** Sie unter jeder Überschrift DAS Kästchen an, das Ihre Gesundheit HEUTE am besten beschreibt.

BEWEGLICHKEIT / MOBILITÄT

Ich habe keine Probleme herumzugehen ❑
Ich habe leichte Probleme herumzugehen ❑
Ich habe mäßige Probleme herumzugehen ❑
Ich habe große Probleme herumzugehen ❑
Ich bin nicht in der Lage herumzugehen ❑

FÜR SICH SELBST SORGEN

Ich habe keine Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe leichte Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe mäßige Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich habe große Probleme, mich selbst zu waschen oder anzuziehen ❑
Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen ❑

ALLTÄGLICHE TÄTIGKEITEN *(z.B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)*

Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe leichte Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe mäßige Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich habe große Probleme, meinen alltäglichen Tätigkeiten nachzugehen ❑
Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen ❑

SCHMERZEN / KÖRPERLICHE BESCHWERDEN

Ich habe keine Schmerzen oder Beschwerden ❑
Ich habe leichte Schmerzen oder Beschwerden ❑
Ich habe mäßige Schmerzen oder Beschwerden ❑
Ich habe starke Schmerzen oder Beschwerden ❑
Ich habe extreme Schmerzen oder Beschwerden ❑

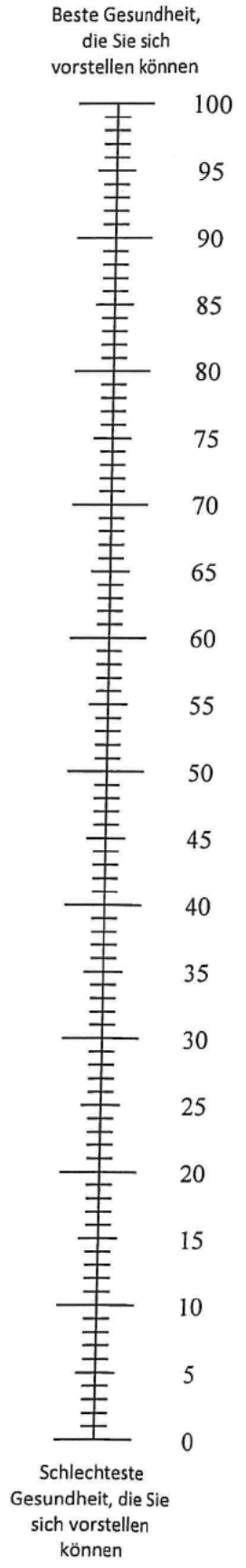
ANGST / NIEDERGESCHLAGENHEIT

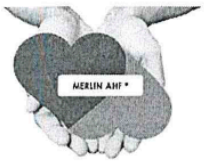
Ich bin nicht ängstlich oder deprimiert ❑
Ich bin ein wenig ängstlich oder deprimiert ❑
Ich bin mäßig ängstlich oder deprimiert ❑
Ich bin sehr ängstlich oder deprimiert ❑
Ich bin extrem ängstlich oder deprimiert ❑

Studien-ID_._._._._._._

- Wir wollen herausfinden, wie gut oder schlecht Ihre Gesundheit HEUTE ist.
- Diese Skala ist mit Zahlen von 0 bis 100 versehen.
- 100 ist die beste Gesundheit, die Sie sich vorstellen können.
  0 (Null) ist die schlechteste Gesundheit, die Sie sich vorstellen können.
- Bitte kreuzen Sie den Punkt auf der Skala an, der Ihre Gesundheit HEUTE am besten beschreibt.
- Jetzt tragen Sie bitte die Zahl, die Sie auf der Skala angekreuzt haben, in das Kästchen unten ein.

IHRE GESUNDHEIT HEUTE = ☐





Klärung des psychischen Zustands von Erwachsenen mit angeborenen Herzfehlern

Information

Sehr geehrte Patientinnen, Sehr geehrte Patienten!

wir bitten Sie herzlich, an einer wissenschaftlichen Untersuchung der Klinik für Kinderkardiologie und angeborene Herzfehler des Deutschen Herzzentrums München teilzunehmen.

Worum geht es?

Bei Ihnen wurde ein angeborener Herzfehler festgestellt, der dank verbesserter Therapiestrategien inzwischen erfolgreich behandelt werden kann. So gehen wir davon aus, dass heute allein in Deutschland 300.000 Erwachsene wie Sie mit angeborenem Herzfehler leben. Bislang ist allerdings nur wenig über die seelischen Auswirkungen der Diagnose bekannt. Um eine optimale und umfassende Versorgung zu gewährleisten, ist es uns ein Anliegen, den psychischen Zustand bei Erwachsenen mit angeborenem Herzfehler zu erheben. Der folgende Fragebogen umfasst Fragen zu ihrem Umgang mit der Erkrankung, ihrem persönlichen Lebenssinn und ihrer wahrgenommenen Belastung und Erholungsfähigkeit.

Als „Experte in eigener Sache" können Sie einen wertvollen Beitrag zur Entwicklung eines ganzheitlichen Therapieprogrammes leisten, welches auf die individuellen Bedürfnisse von Menschen mit angeborenem Herzfehler abgestimmt ist. Die Ergebnisse dieser Studie werden in die Empfehlungen zur Therapie für angeborene Herzfehler miteinfließen und stellen wichtige Entscheidungshilfen bei der Wahl des für den einzelnen Patienten geeigneten Therapieplans dar.

Die Bearbeitung des Fragebogens dauert nur wenige Minuten. Der Fragebogen muss nicht zu einem bestimmten Zeitpunkt ausgefüllt werden. Sie können ihn bearbeiten, wenn es gerade zeitlich für Sie passt. Alle im Rahmen dieses Forschungsprojektes erhobenen Daten sind vertraulich und dienen ausschließlich in anonymisierter Form zur statistischen Auswertung und zur Abfassung von wissenschaftlichen Publikationen.

Vielen Dank für Ihre Mithilfe!

Krankheitsidentitäts-Fragebogen (IIQ-D)

Im Folgenden finden Sie eine Reihe von Aussagen, die sich auf Ihr Verhältnis zu Ihrer Herzkrankheit und Ihren Umgang damit beziehen. Bitte kreuzen Sie jeweils an, wie sehr Sie der entsprechenden Aussage zustimmen oder nicht. Dazu stehen Ihnen 5 Antwortmöglichkeiten zur Verfügung. Machen Sie bitte nur ein Kreuz pro Frage und lassen Sie bitte keine Frage aus.

	Trifft gar nicht zu	Trifft eher nicht zu	Nicht sicher	Trifft eher zu	Trifft genau zu
1. Ich weigere mich, meine Herzkrankheit als Teil von mir zu sehen.	○	○	○	○	○
2. Ich denke lieber nicht an meine Herzkrankheit.	○	○	○	○	○
3. Ich spreche mit anderen nie über meine Herzkrankheit.	○	○	○	○	○
4. Ich hasse es, wenn ich auf meine Herzkrankheit angesprochen werde.	○	○	○	○	○
5. Ich vermeide es,über meine Herzkrankheit nachzudenken.	○	○	○	○	○
6. Meine Herzkrankheit gehört zu mir als Person dazu.	○	○	○	○	○
7. Meine Herzkrankheit ist Teil von mir.	○	○	○	○	○
8. Ich akzeptiere, eine Person mit einer Herzkrankheit zu sein.	○	○	○	○	○
9. Ich kann meiner Herzkrankheit einen Platz in meinem Leben einräumen.	○	○	○	○	○
10. Ich habe gelernt, die Einschränkungen zu akzeptieren, die sich aus meiner Herzkrankheit ergeben.	○	○	○	○	○
11. Meine Herzkrankheit beherrscht mein Leben.	○	○	○	○	○
12. Meine Herzkrankheit beeinflusst stark, wie ich mich selbst sehe.	○	○	○	○	○
13. Ich bin sehr fixiert auf meine Herzkrankheit.	○	○	○	○	○
14. Meine Herzkrankheit beeinflusst all meine Gedanken und Gefühle.	○	○	○	○	○
15. Meine Herzkrankheit zehrt mich vollständig auf.	○	○	○	○	○
16. Es scheint, als ob all mein Tun durch meine Herzkrankheit beeinflusst wird.	○	○	○	○	○

17. Meine Herzkrankheit hält mich davon ab, das zu tun, was ich wirklich gerne tun würde	○	○	○	○	○
18. Meine Herzkrankheit beschränkt mich in vielen Dingen, die mir wichtig sind.	○	○	○	○	○
19. Durch meine Herzerkrankung bin ich als Person gewachsen.	○	○	○	○	○
20. Aufgrund meiner Herzerkrankung weiß ich, was ich vom Leben will.	○	○	○	○	○
21. Durch meine Herzerkrankung bin ich eine stärkere Person geworden.	○	○	○	○	○
22. Aufgrund meiner Herzerkrankung habe ich erkannt, was wirklich wichtig im Leben ist.	○	○	○	○	○
23. Durch meine Herzerkrankung habe ich viel über mich selbst gelernt.	○	○	○	○	○
24. Durch meine Herzerkrankung habe ich gelernt, Probleme durchzustehen und nicht einfach aufzugeben.	○	○	○	○	○
25. Durch meine Herzerkrankung habe ich gelernt, den Augenblick besser zu genießen.	○	○	○	○	○

Fragebogen zu Ihrem Informationsbedürfnis

Im Folgenden finden Sie Aussagen, die sich auf Ihr Informationsbedürfnis zu Ihrer Herzkrankheit beziehen.

	Trifft gar nicht zu	Trifft eher nicht zu	Nicht sicher	Trifft eher zu	Trifft genau zu
26. „Ich fühle mich über meine Krankheit ausreichend informiert."	○	○	○	○	○
27. „Ich möchte gerne mehr über meine Erkrankung erfahren."	○	○	○	○	○
28. „Wenn ich mehr weiß, macht es mich nur nervös."	○	○	○	○	○
29. „Wenn ich mehr weiß, beruhigt es mich."	○	○	○	○	○

HADS-D

Name, Vorname: ..... **Datum:** .....

Geburtsdatum: ..... **Code-Nummer:** .....

Sehr geehrte Patientin, sehr geehrter Patient!

Sie werden von uns wegen körperlicher Beschwerden untersucht und behandelt. Zur vollständigen Beurteilung Ihrer vermuteten oder bereits bekannten Erkrankung bitten wir Sie im vorliegenden Fragebogen um einige persönliche Angaben. Man weiß heute, dass körperliche Krankheit und seelisches Befinden oft eng zusammenhängen. Deshalb beziehen sich die Fragen ausdrücklich auf Ihre allgemeine und seelische Verfassung.

Die Beantwortung ist selbstverständlich freiwillig. Wir bitten Sie jedoch, jede Frage zu beantworten, und zwar so, wie es für Sie persönlich **in der letzten Woche** am ehesten zutraf. Machen Sie bitte nur ein Kreuz pro Frage und lassen Sie bitte keine Frage aus! Überlegen Sie bitte nicht lange, sondern wählen Sie die Antwort aus, die Ihnen auf Anhieb am zutreffendsten erscheint! Alle Ihre Antworten unterliegen der ärztlichen Schweigepflicht.

Ich fühle mich angespannt oder überreizt.

☐ meistens
☐ oft
☐ von Zeit zu Zeit/gelegentlich
☐ überhaupt nicht

Ich fühle mich in meinen Aktivitäten gebremst.

☐ fast immer
☐ sehr oft
☐ manchmal
☐ überhaupt nicht

Ich kann mich heute noch so freuen wie früher.

☐ ganz genau so
☐ nicht ganz so sehr
☐ nur noch ein wenig
☐ kaum oder gar nicht

Ich habe manchmal ein ängstliches Gefühl in der Magengegend.

☐ überhaupt nicht
☐ gelegentlich
☐ ziemlich oft
☐ sehr oft

Mich überkommt eine ängstliche Vorahnung, dass etwas Schreckliches passieren könnte.

☐ ja, sehr stark
☐ ja, aber nicht allzu stark
☐ etwas, aber es macht mir keine Sorgen
☐ überhaupt nicht

Ich habe das Interesse an meiner äußeren Erscheinung verloren.

☐ ja, stimmt genau
☐ ich kümmere mich nicht so sehr darum, wie ich sollte
☐ möglicherweise kümmere ich mich zu wenig darum
☐ ich kümmere mich so viel darum wie immer

Ich kann lachen und die lustige Seite der Dinge sehen.

☐ ja, so viel wie immer
☐ nicht mehr ganz so viel
☐ inzwischen viel weniger
☐ überhaupt nicht

Ich fühle mich rastlos, muss immer in Bewegung sein.

☐ ja, tatsächlich sehr
☐ ziemlich
☐ nicht sehr
☐ überhaupt nicht

Mir gehen beunruhigende Gedanken durch den Kopf.

☐ einen Großteil der Zeit
☐ verhältnismäßig oft
☐ von Zeit zu Zeit, aber nicht allzu oft
☐ nur gelegentlich/nie

Ich blicke mit Freude in die Zukunft.

☐ ja, sehr
☐ eher weniger als früher
☐ viel weniger als früher
☐ kaum bis gar nicht

Ich fühle mich glücklich.

☐ überhaupt nicht
☐ selten
☐ manchmal
☐ meistens

Mich überkommt plötzlich ein panikartiger Zustand.

☐ ja, tatsächlich sehr oft
☐ ziemlich oft
☐ nicht sehr oft
☐ überhaupt nicht

Ich kann behaglich dasitzen und mich entspannen.

☐ ja, natürlich
☐ gewöhnlich schon
☐ nicht oft
☐ überhaupt nicht

Ich kann mich an einem guten Buch, einer Radio- oder Fernsehsendung erfreuen.

☐ oft
☐ manchmal
☐ eher selten
☐ sehr selten

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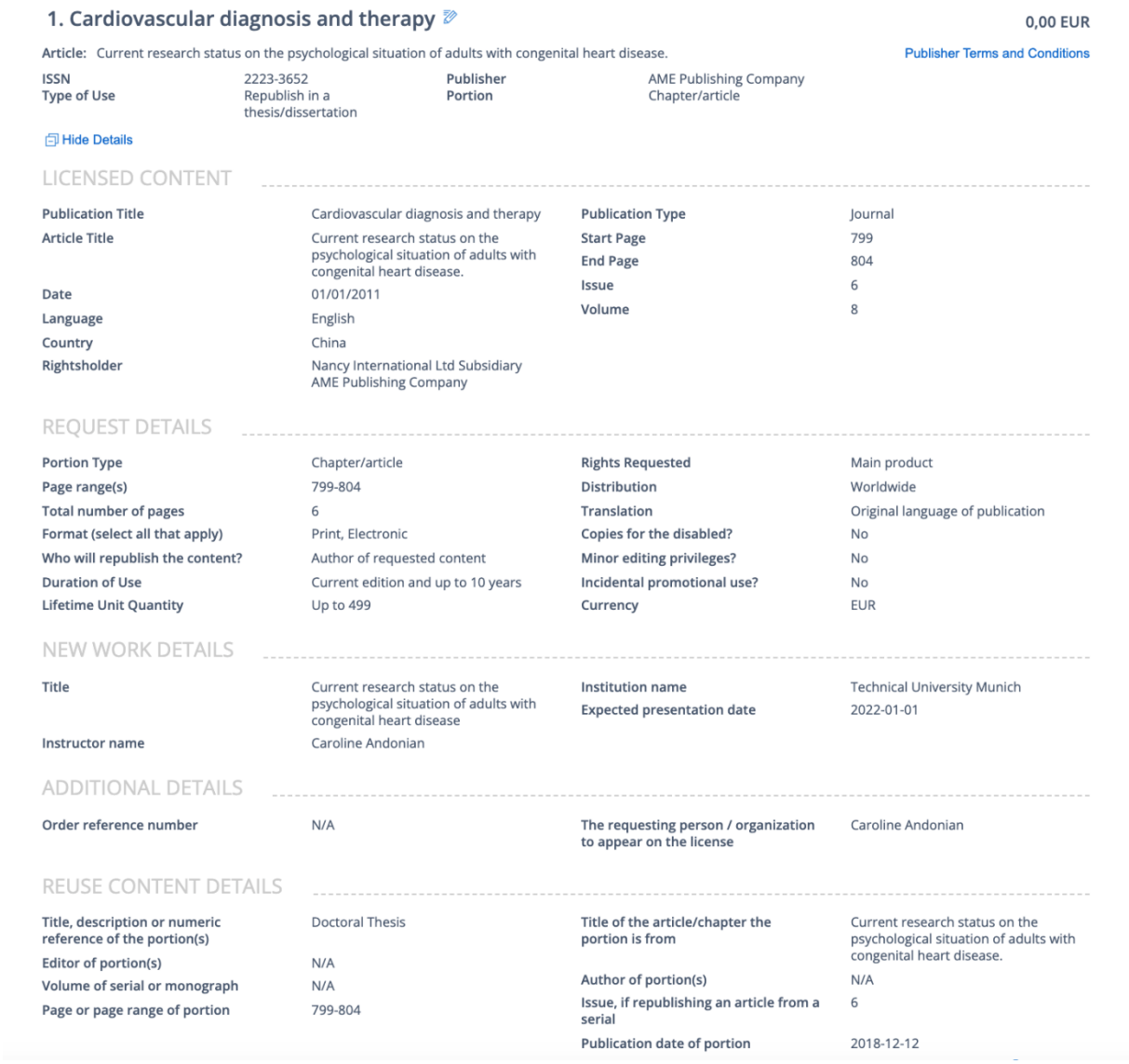

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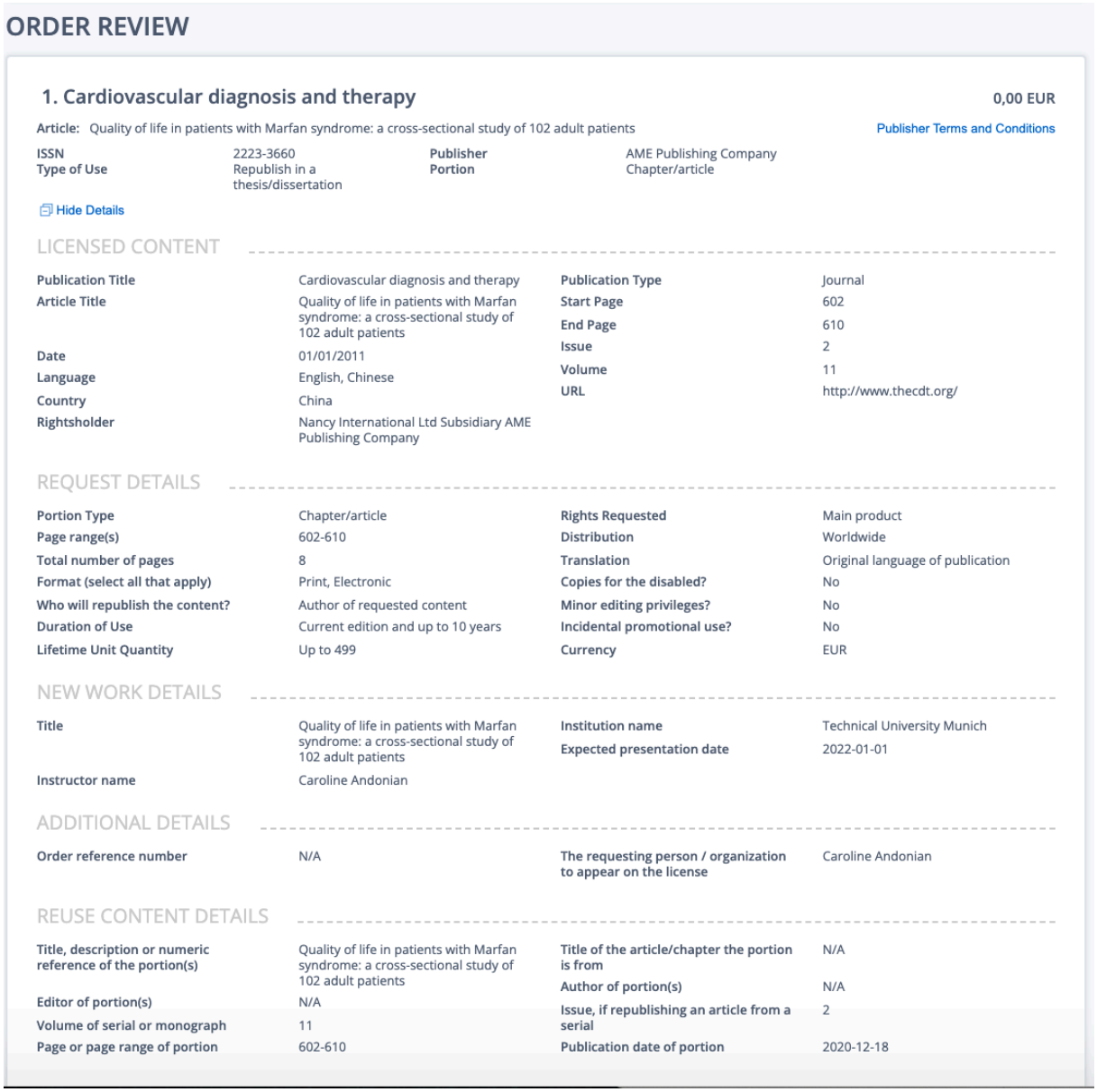
Thank you very much!

Best,
Caroline Andonian

4. Andonian, C., Freilinger, S., Achenbach, S., Ewert, P., Gundlach, U., Kaemmerer, H., ... & Beckmann, J. (2021). Quality of life in patients with Marfan syndrome: a cross-sectional study of 102 adult patients. Cardiovascular Diagnosis and Therapy, 11(2), 602.



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