Quality of Life and patient reported outcomes in Paediatric Cardiac Surgery patients

Key Words: Cardiac, Congenital heart, lifestyle, quality of life, patient reported outcome measures (PROMS)

Introduction

This chapter provides an overview of the literature examining patient reported outcome measures (PROMS) following paediatric cardiac surgery. Unlike adult specialities, the impact of CHD surgery is felt by the whole family. Furthermore, quantifying measures of QoL in a neonate or infant is extremely difficult, where the patient is unable to express themselves. Similarly, in young children, recording subjective measures are difficult where the child and family have no comparison. CHD is also particular in the heterogeneity in presentation. Similarly, there is a large spectrum in outcomes, which are often confounded by other factors. For instance, the association of a syndrome will have a significant impact on outcome and expectations, with a congenital atrio-ventricular septal defect (cAVSD) in a child with Trisomy 21 (T21) significantly different to those of a child without T21. Other unknown factors are also at play, where one tetralogy of fallots (ToF) patient requiring one operation, and another 2 or 3. These factors all require consideration when examining patient reported outcomes (PROs)

Background

Congenital heart disease (CHD) is the most frequently occurring congenital anomaly, affecting around 0.8% of live births.(Bouma and Mulder, 2017) It is a heterogeneous group of cardiac anomalies ranging from innocent malformation to severe anomalies carrying significant risk of neonatal death if not recognized and managed appropriately (Lopes et al. 2018, Marantz

et al. 2013 and Jenkins 2012). Annually, around 5500 operations are performed in the United Kingdom (NICOR, 2017). These may be classed as either corrective or palliative. Whilst corrective surgery has traditionally been viewed as curative, palliative correction is directed to improving functional capacity, often requiring several operations or interventions during the patient's lifetime.

Following the introduction of the cardiopulmonary bypass machine in the early 1950s, cardiac surgery quickly developed as a speciality (Cohn Lawrence, 2003). Nonetheless, developments in CHD surgery lagged behind, with the majority of complex surgical cases treated with palliative procedures, and few options for definitive surgery. As a result, many patients require multiple surgeries, often associated with high morbidity, and poor quality of life (QoL) (Martin and Jonas, 2018). The last two decades have witnessed a significant reduction in both mortality and morbidity following CHD surgery, most noticeable in the treatment of complex, previously incurable conditions (Spector et al., 2018). This has ultimately led to an increased life expectancy for the majority of patients; with most now surviving into adulthood (Ottaviani et al., 2017).

The impact of a chronic disease, on a developing child and their family, is complex, and combined with underline pathology management can have a significant effect on their QoL and their ability to psychologically adjust (Silva et al., 2020, Eiser and Morse, 2001). As mortality decreases, the need for a better understanding of the long-term impact of QoL and other patient reported outcomes in patients following CHD diagnosis has increased (Rometsch et al, 2019).

Patient reported outcomes (PROs) and patient reported outcome measures (PROMs)

PROMS are tools used to measure outcomes that matter to patients; reflecting patients' or caregivers' perspective of the impact of the condition on their lives, including how illness is experienced. (Makrinioti et al., 2020) An example could be 'can I climb my stairs?', rather than 'has my cardiac output improved?' The completion and compilation of PROMS by patients plays an important role in patient assessment, assisting clinical decision-making, and tracking patient progress. There is growing evidence to support the use of PROMS to improve care processes and outcomes in part through supporting communication between clinicians and patients (Nelson et al., 2015) as well as improve patient engagement and satisfaction with care. (Field et al., 2019) PROs can be characterised into five dimensions namely: functional status; symptoms and symptom burden; patient experience; health behaviours; and quality of life or more specifically health related quality of life. (Cella et al., 2015) Despite the growing interest in PROMs, at the time of writing, no PROM for congenital heart disease in children (Algurén et al., 2020) and one newly validated PROM for the adult congenital heart disease (ACHD) population (Cedars et al., 2020) has been identified. Tools identified in the literature are presented in table 1

Quality of life

Quality of life is a multidimensional concept and focusses on the self-perceptions of an individual's current state of mind (Bonomi et al, 2000). It consists of a combination of objective and subjective indicators within a broad range of life domains, including physical, psychological, social and environmental factors, as well as incorporating individual values (Koot and Wallander, 2014). Translating this concept into empirical terms is not simple, and

even less so when examining the concept within the paediatric population (Matza et al., 2004). Children's perceptions and values are likely to differ from those of adults, but will also change as they move from childhood to adolescents and early adulthood. (Bullinger et al., 2002). In addition, the importance of contextual variables, such as family and peer support systems cannot be underestimated (Thiyagarajan et al., 2019).

There are an increasing number of systematic reviews comparing QoL of CHD patients to healthy peers or siblings. These are presented in table 2. CHD patients are heterogeneous in their presentation, with highly conflicting evidence. Findings from studies examining factors such as the complexity of the underline anomaly, and the number of surgical interventions on QoL have come to differing conclusions (Huisenga et al., 2021 and Xu et al, 2020). One recent study demonstrated a lower QoL in those with complex CHD compared with peers with moderate and simple cases (Ladak et al, 2018). However, another study reported impaired QoL in moderate and complex CHD patients only with no difference in simple CHD cases (Kahr et al., 2015). Other studies have demonstrated no difference in QoL between all cohorts of CHD patients when compared to their control peers (Schrøder et al., 2016). However, others suggest that QoL is higher in girls with CHD during childhood, and boys and girls during adolescence, with severity in disease not shown to affect the overall outcomes (Reiner et al., 2019).

Findings appear more consistent and nuanced across the limited evidence examining specific domains of QoL. A study by Rometsch et al. (2019) focusing on QoL within the physical and psychosocial domains, reported impaired physical QoL during young adulthood, but no deficit in the mental and psychological domains. This was exacerbated when associated with a lower

physical exercise tolerance, female gender, reduced social support and lower educational level predictors of reduced overall QoL.

A number of reviews have compared QoL of specific subgroups of the CHD population, to peers. In a review by Dahan-Oliel (2011), disease complexity was associated with a poorer HRQoL. However, this became particularly noticeable in the cohort of patients born preterm, as well as those with additional impairments. This difference remained the case for adolescents and young adults.

Social determinants such as parental unemployed as a result of the child's needs or families who experienced financial difficulties have also been associated with lower QoL, compared to of control groups. (Latal et al., 2009)

Few studies have compared QoL of children with CHD to that of children with other chronic conditions. Again, findings are contradictory, with one study reporting that children with CHD after surgery experience a better proxy-reported QoL than other children with chronic disease (Mussatto and Tweddell, 2005) while the opposite was found in another study (Dunbar-Masterson et al., 2001).

Parents and caregiver prospective

Children with CHD, especially those with complex underline pathologies, may need several operations, and often associated with prolonged hospital stays. This can have significant effect on the parental life, with parents suffering psychological, emotional and financial difficulties, in some instances resulting in post-traumatic stress disorder (PTSD), (Bevilacqua

et al, 2013, Woolf-king et al. 2017 and Landolt et al. 2011). A recent study showed that up to 22% of the parents have persistent psychological issues when they have a child with CHD, regardless of the complexity of the disease (Lawoko et al., 2002). Therefore, maintaining the well-being of the parents can be significant contributing factor in promoting the long-term wellbeing and QoL of the child (Kasparian et al, 2019).

Timing of the diagnosis may also influence the impact on the family. Developments in antenatal testing and diagnosis have meant that many parents will have engaged with the clinical team prior to birth. This provides time to prepare both psychologically and physically for the arrival of a neonate who will require medical intervention. Regular counselling and an understanding of the pathology and the requirement for intervention enables parents to prepare for the birth, and any immediate requirements for intervention (Biber et al., 2019). However, the antenatal journey is paved with uncertainty. Parents-to-be have to work hard to negotiate around the uncertainties associated with diagnosis and prognosis of the suspected anomaly. Parents' capacity to cope with uncertainty, and the way in it is managed by the clinical team will impact on their burden. (Lotto et al., 2018) Ongoing counselling, parents and peer support, and external support can be of great help to reduce the burden on the parents (Ruggiero et al, 2018). The provision of comprehensive information packs, group support, or individual sessions detailing the care needs of a child with CHD throughout their lifetime is therefore essential. Parental perception of QoL peri-operatively may also have an effect on their children's QoL perception (Gonzalez et al., 2017). If parental mental health is affected by their children's condition, it may in turn lead to poor engagement in ensuring that

their children develop according to their milestones, segregation from others, as well as reduced social opportunities.

Whilst the psychological impact on parents is considerable, there is evidence to suggest it reduces over time (Bevilacqua et al., 2013 and Landolt et al., 2011). Nonetheless, such parental stress can have negative implications on the life of the child if not addressed, with some parents becoming defensive and overprotective of the child, resulting in barriers to interaction between the child and other children in the same family or at school (Soulvie et al., 2012). Siblings add to the complexity of the family dynamics (Biber et al., 2019), affecting not only the relationship between parent and child, but between parents, with over 40% of parents reporting strains on their relationships as a result of caring for a child with CHD (Winener et al., 2017 and Darke et al., 1994). By maximizing children's developmental stages, long term poor QoL outcomes may be prevented (Wernovsky et al., 2016).

Functional status

Functional status refers to the ability of a patient to perform age specific activities of daily life. (Cohen and Marino, 2000). Within the context of CHD, neurodevelopmental disability is the most common complication for survivors of surgery for congenital heart disease (CHD), (Cassidy et al., 2018), with the impact reflecting of their functional status.

A limited number of prospective studies are reported in a systematic review addressing neurodevelopmental outcomes in young CHD patients. The included studies consistently revealed cognitive and motor delay in children after cardiac surgery during early infancy. (Snookes et al., 2010) These findings were reflected in a subsequent large scale international

study involving over 1700 participants. (Gaynor et al., 2015) Primary outcome measures included were Psychomotor Development Index (PDI), and Mental Development Index (MDI). Findings suggested that early neurodevelopmental outcomes have improved modestly over time, but only after adjustment for innate patient risk factors. Lower birth weight and genetic or extracardiac anomalies were associated with reduced PDI and MDI. Risk factors for lower PDI also included white race and, for MDI, male gender and lower maternal education.

In addition, age, supplemental tube feeding, longer cardiopulmonary bypass time, and shorter time since last hospitalization have been reported as significant predictors of developmental outcomes.(Mussatto et al., 2014) Lower performance on intelligence and alertness assessment has also been reported, which may contribute to difficulties in daily life and school. (Sterken et al., 2015)

Heterogeneity in assessment methods, small sample sizes, and substantial heterogeneity in the group with CHD are likely to limit the interpretation and go some way to explain the different findings reported. The neurodevelopmental outcomes of infants with single-ventricle CHD is generally reported to be inferior to those with two-ventricle CHD. Similarly, those with complex CHD are at increased risk of impaired developmental outcome. (Huisenga et al., 2020).

Whilst literature around long term impact is generally lacking, there is some evidence to suggest that children with two-ventricle CHD gradually grow out of their initial developmental impairment. (Huisenga et al., 2020). However, these are often still pertinent as the child commences school, with a range of developmental difficulties often present at school entry

which enhance the risk of learning challenges and subsequent decreased social participation.(Majnemer et al., 2008)

Symptom and symptom burden

Symptoms are defined as “the subjective evidence of disease or physical disturbance observed by a patient.” Websters English Dictionary The negative nature of symptoms is implicit, as is the requirement for the symptoms to be observed and experienced by the patient and can only be known through patient reporting. Symptom burden captures the combination of both symptom severity and impact experienced with a specific disease or treatment. (Cleeland, 2007) The most commonly described symptoms in children with CHD are anorexia, difficulty in activities, palpitations, shortness of breath, weakness, and fatigue. (Bektas et al., 2020) Symptoms such as chest pain, fatigue and breathlessness, have been described as living “at war with” and “against the body” (Gantt, 1992, p. 246). (Gantt, 1992). These symptoms impact on physical and educational development, with many experiencing concentration and memory difficulties at school (Cornett and Simms, 2014, Birks et al., 2007) This is exacerbated by hospital appointments and procedures that resulted in missed school and academic assessments (Chong et al., 2018). The impact of symptom burden is clearly reflected within the patient experience discussed below.

Patient experience

Over the past two decades, patient satisfaction and experience has become a key dimension of patient-centered care. (Lapin et al., 2019) They have been used as measures to reflect quality, inform patient choice, and drive change, (van Velthoven et al., 2018, Coulter, 2016) Measurement of this concept is complex and relates to perceived needs, expectations as well as experience of care (Williams, 1994). Literature relating to patient experience of paediatric congenital cardiac surgery patients is extremely limited. Of the papers available, the focus is predominantly on parental perceptions, with some literature around adolescents and young adulthood, in particular the transition period.

Becoming a parent of a child with CHD can be traumatic, with the need to manage a chronic condition, interspersed with acute medical crises. (Sjostrom-Strand and Terp, 2017). Parents have to manage the long term implications of a CHD but also aspects of life-threatening treatments such as surgery followed by high-technology intensive care (Franich-Ray et al., 2013). Research examining the lived experience of parents suggests they encounter intense and fluctuating emotions (McMahon and Chang, 2020), with increased levels of distress leading up to surgery (Wray and Sensky, 2004). Significant differences in experience have been recorded between mothers and fathers (Lotto et al., 2019a, Lotto et al., 2019b)

Mothers, in particular, are at risk of psychological distress, presenting with symptoms of anxiety, depression, hopelessness, as well as posttraumatic stress symptoms. (Woolf-King et al., 2018, Lotto et al., 2019a) This may subsequently influence the mother's responsiveness to her child. (Kolaitis et al., 2017). Long term, most parents successfully adapt, but approximately 40% report a need for psychosocial care (Kolaitis et al., 2017), with around 30% of parents of children with critical CHD presenting with posttraumatic stress (PTS) symptoms

(Woolf-King et al., 2018). In addition, parents face numerous additional physical, financial, and practical challenges (Kolaitis et al., 2017), requiring the whole family to undergo a stressful adjustment process (Lan et al., 2007). Parents describe financial costs as broader than monetary terms, including family burden and emotional burdens. (Connor et al., 2010) Disease complexity, as well as parental socioeconomic status appear to be linked to higher levels of financial cost, and associated emotional and family burden.(Connor et al., 2010) The difficulties experienced by parents following the birth of a child with CHD are widely documented. However, the degree of burden reported varies considerably. These inconsistencies may again reflect different approaches to how and what to measure.(Wei et al., 2015) Indeed, reliance on quantitative measures is drawn into question, where qualitative approaches have been shown to provide a 'more complete' picture. (Utens et al., 2000)

A small, predominantly qualitative literature base was identified examining childhood experiences. This included a recent narrative synthesis, drawing the studies together (Chong et al., 2018) The findings highlight the difficulties encountered by children, and is presented across six themes: disrupting normality; powerlessness in deteriorating health; enduring medical ordeals; warring with the body; hampering potential; and establishing one's own pace. These themes highlight the vulnerability of the children as they oscillate between health and illness, burdened by physical symptoms, and traumatised by invasive interventions, whilst coping with treatment failure and preoccupation with mortality.

Many of these themes are reflected in the literature exploring the experiences of adolescents, particularly in relation to transition to adult services, Qualitative literature discusses the

'ambivalence' experienced by adolescents in relation to daily life and encounters with the health care system. (Berghammer et al., 2006) Similar themes run through much of the literature, describing the needs of adolescents to strike a balance between being different and not being different; being sick and being healthy; revealing or hiding their congenital heart disease, and therefore living with a hidden handicap (Chiang et al., 2015) (Berghammer et al., 2006, Lee et al., 2014, Berghammer et al., 2015). Despite this, adolescents stressed the importance of "seeing possibilities instead of restrictions" (McMurray et al., 2001)

Health behaviours

Data derived from health behaviour PROMs may serve several important clinical purposes. They enable clinicians to monitor risk behaviours and intervene early, but also identifies areas for implementing (and subsequent evaluation of) risk reduction and health promotion interventions (Cella et al., 2015).

CHD is a chronic condition requiring life-long follow-up, and as such, patients are at increased risk of a number of health concerns, such as cardiac related morbidities including coronary artery disease and heart failure, as well as endocarditis, stroke, and pregnancy complications (Jackson et al., 2015). In order to optimise long-term outcomes, health-promoting behaviours are recommended (Janssens et al., 2016). However, few studies have examined health behaviours in young people with CHD (Reid et al., 2008, Uzark et al., 1989, Lunt et al., 2003, Chen et al., 2007, Massin et al., 2007).

Those available have reported increased levels of 'risky behaviour' including frequent poor oral health care practices (Chen et al., 2007), relatively high rates of substance use (Uzark et

al., 1989, Massin et al., 2007), and low levels of physical activity, particularly as patients age (Lunt et al., 2003)

Physical activity (PA) is an important part of normal childhood development, promoting healthy growth and improving the child's general fitness (Malina, 2001). Even children who have undergone the Fontan procedure (series of operations performed in children born with only one ventricle) may obtain beneficial effects from PA participation and exercise interventions, with improvements in their cardiovascular fitness and quality of life (Moola et al., 2009, Takken et al., 2007a, Takken et al., 2007b). However, children with CHD (regardless of the severity of their condition) show lower PA levels and a higher proportion of sedentary time compared to their peers (Voss et al., 2017), something that worsens with age and that especially affects girls, those with siblings, younger children, and those from areas of higher deprivation (Voss et al., 2017). Maternal anxiety and depression negatively impacts the self-efficacy of these children with CHD, with consequential negative impact on their activity level (Dulfer et al., 2015). Different barriers to participation, such as social stigma and parental overprotection, make engaging this group of children and adolescents in physical activities more complex (Moola et al., 2009), and currently no consensus on what constitutes optimal PA levels in this population has been reached. However, as with other chronic diseases, it is likely that physical activity programmes require tailoring to individual needs and abilities and are likely to change over the life-course.

Tools and Measures

QOL has been increasingly studied amongst the CHD population, with notable heterogeneity of QOL scores (Drakouli et al., 2015, Ernst et al., 2018). Any QoL measures should conform to scientific standards, and should be reliable and valid, reflecting quality. In addition, they should reflect, or be combined to reflect, the multiple domains associated with QoL. There is some debate over the validity of adult based tools when examining the QoL in a paediatric population, with specific paediatric tools perceived as preferable (Eiser and Morse, 2001). Rationale includes the potential failure of adult measures to explore specific aspects of QoL that are important to a child, but also the accessibility of adult based measures that impose considerable response burden for children, in terms of length, reading skills and response scale. (Eiser and Morse, 2001) Nonetheless, there is evidence to suggest that children are able to self-report of their QoL from as early as 5 years of age (Sluys et al., 2015). Calls to improve the rigour and methodological approach to assessing QoL in the CHD population have been made, with many of the studies assessed deemed to be of a poor quality or exhibiting methodological flaws (Moons et al., 2004, Bratt and Moons, 2015).

Whilst there is some debate within the wider literature around the validity of parental proxy measures (Fayed et al., 2019, Cohen et al., 2019), evidence from cardiac based studies, supports the use of these tools, with patients and parents broadly in agreement on the impact of congenital heart disease on the QoL of children and adolescents (Marino et al., 2009).

A number of tools for measuring QoL and health related QoL (HRQoL) were identified within the literature. The majority of measures employed are generic QoL andreliant on parents to complete on behalf of the child. Only one CHD specific measure was identified, which could be completed by older children or adolescents (Kamphuis et al. 2004). The heterogeneity of

the tools applied makes inter-study comparisons difficult. However, all the measure include some form of measure of a physical, mental and social component.[63] Despite this, the lack of validated CHD specific measures is likely to impact on our understanding of the QoL of this population. (Latal et al., 2009)

Tools employed are presented in table 1.

Summary and Conclusion

Despite the variability of the evidence available, children with complex CHD appear to be at higher risk of lower QoL than their peers. This is reflected in their lower exercise levels and poorer general health. However, issues with the quality and comparability of evidence is clear. Few studies examine the same risk factors, and heterogeneity of sample populations make comparisons difficult. This is compounded by the use of a number of different tools, most of which are not validated specifically within the CHD population. Quality of papers has been criticized previously, further obscuring our understanding.

Table 2. Summary of Key systematic review and meta-analyses studies and their findings in QoL in cardiac surgery patients 598

Study	Focus of the study	Summary of key findings
Clancy et al. (2020)	Psychosocial outcomes of infants and young children with CHD who had cardiac surgery early in life.	The study found a high prevalence of low severity emotional and behavioural dysregulation. Comorbidity was shown to increase impairment, with evident externalisation. The study encouraged assessment and monitoring of behaviour and social development to enable early detection and intervention.
Drakouli et al. (2015)	Assessing the QoL in children and adolescents with CHD.	QoL is determined by factors such as parental support, economic support, physical ability and overall mental health.

Dulfer et al. (2014)	QoL in children and adolescents with CHD.	No clear relationships were found between exercise capacity, physical activity and QoL in children and adolescents with CHD.
Fteropoulli et al. (2013)	Relationship between disease severity and QoL in patients with CHD.	The QoL of adult congenital heart disease patients can be compromised in physical disease.
Golfenshtein et al. (2015)	Parental stress and experience of raising children with CHD, pediatric cancer, and ASD.	Future research and assessment of parenting stress should account for the illness course and family needs should be addressed.
Gregory et al. (2018)	Review of how parental QoL may be affected with children diagnosed with CHD.	The main factors which affected parental QoL included: severity of illness, age at which child was diagnosed, perceived levels of support and financial resources available.

Huisenga et al. (2021)	Developmental outcomes from infancy to adolescence with children with CHD who underwent surgery.	Children with complex CHD can beat increased risk of poorer developmental outcomes. Single-ventricle CHD has worse outcomes than two-ventricle CHDs. There is no constant association between preoperative factors and patient outcomes.
Jackson et al. (2015)	Familial impact and coping with CHD.	Holistic approach and early psychological intervention should be implemented in order to allow for better coping mechanisms.
Journiac et al. (2020)	Psychosocial outcomes and experiences of young adult cardiac patients (18-55 years old).	In comparison to the general population, young adult cardiac patients demonstrated worse health behaviour profiles. Women were shown to have increased levels of depression, stress and distress and overall a lower QoL.

Kahr et al. (2015)	QoL in CHD patients.	QoL is impaired in moderate or complex CHD.
Ladak et al. (2019)	General and cardiac-related HRQOL.	HRQOL was worse in patients with CHD postoperatively vs non-CHD participants. The largest difference in HRQOL was for physical function.
Lip et al. (2003)	Psychological interventions in children with CHD with depression.	Depression can exacerbate the physical impact of CHD. There has been no efficacy proven in non-pharmacological treatments.
Schrøder et al. (2016)	QoL in adolescents and young adults.	Social functioning was found to be comparable, or better compared with controls. In some subdomains, patients appeared to have reduced QoL. Overall, adolescents and young adults do not have reduced QoL.

Tesson et al. (2019)	Review of psychological interventions for children adolescents and adults with CHD and their family's efficacy-wise.	Patient focus interventions allowed for alleviation of anxiety and worry maternal mental health wise and better coping and family functioning.
Vo et al. (2018)	Systematic review of the literature available on the psychosocial impact of 22q11deletion syndrome.	Study found that a lot of complex and conflicting emotions were experienced by family members of those with 22q11 deletion syndrome.
Xu et al. (2020)	Post-op effects of exercise training on QoL, biomarkers, exercise capacity and vascular function in CHD.	NT-proBNP levels were lower in individuals who engaged in exercise training. Exercise interventions were also shown to increase the score in QoL from the score prior to intervention.

References:

ALGURÉN, B., COENEN, M., MALM, D., FRIDLUND, B., MÅRTENSSON, J. & ÅRESTEDT, K. 2020. A scoping review and mapping exercise comparing the content of patient-reported outcome measures (PROMs) across heart disease-specific scales. *Journal of patient-reported outcomes,* 4**,** 7.

BEKTAS, İ., KıR, M., YıLDıZ, K., GENÇ, Z., BEKTAS, M. & ÜNAL, N. 2020. Symptom Frequency in Children with Congenital Heart Disease and Parental Care Burden in Predicting the Quality of Life of Parents in Turkey. *J Pediatr Nurs,* 53**,** e211-e216.

BERGHAMMER, M., DELLBORG, M. & EKMAN, I. 2006. Young adults experiences of living with congenital heart disease. *International journal of cardiology,* 110**,** 340-347.

BERGHAMMER, M. C., BRINK, E., RYDBERG, A. M., DELLBORG, M. & EKMAN, I. 2015. Committed to Life: Adolescents' and Young Adults' Experiences of Living with F ontan Circulation. *Congenital heart disease,* 10**,** 403-412.

BIRKS, Y., SLOPER, P., LEWIN, R. & PARSONS, J. 2007. Exploring health-related experiences of children and young people with congenital heart disease. *Health Expectations : An International Journal of Public Participation in Health Care and Health Policy,* 10**,** 16-29.

BOUMA, B. J. & MULDER, B. J. 2017. Changing landscape of congenital heart disease. *Circulation research,* 120**,** 908-922.

BRATT, E. L. & MOONS, P. 2015. Forty years of quality-of-life research in congenital heart disease: Temporal trends in conceptual and methodological rigor. *Int J Cardiol,* 195**,** 1-6.

BULLINGER, M., SCHMIDT, S., PETERSEN, C. & GROUP, D. 2002. Assessing quality of life of children with chronic health conditions and disabilities: a European approach. *International Journal of Rehabilitation Research,* 25**,** 197-206.

CASSIDY, A. R., ILARDI, D., BOWEN, S. R., HAMPTON, L. E., HEINRICH, K. P., LOMAN, M. M., SANZ, J. H. & WOLFE, K. R. 2018. Congenital heart disease: a primer for the pediatric neuropsychologist. *Child Neuropsychology,* 24**,** 859-902.

CEDARS, A. M., KO, J. M., JOHN, A. S., VITTENGL, J., STEFANESCU-SCHMIDT, A. C., JARRETT, R. B., KUTTY, S. & SPERTUS, J. A. 2020. Development of a Novel Adult Congenital Heart Disease–Specific Patient-Reported Outcome Metric. *Journal of the American Heart Association,* 9**,** e015730.

CELLA, D., HAHN, E. A., JENSEN, S. E., BUTT, Z., NOWINSKI, C. J., ROTHROCK, N. & LOHR, K. N. 2015. Patient-reported outcomes in performance measurement.

CHEN, C.-W., CHEN, Y.-C., CHEN, M.-Y., WANG, J.-K., SU, W.-J. & WANG, H.-L. 2007. Health-promoting behavior of adolescents with congenital heart disease. *Journal of Adolescent Health,* 41**,** 602-609.

CHIANG, Y. T., CHEN, C. W., SU, W. J., WANG, J. K., LU, C. W., LI, Y. F. & MOONS, P. 2015. Between invisible defects and visible impact: the life experiences of adolescents and young adults with congenital heart disease. *Journal of Advanced Nursing,* 71**,** 599-608.

CHONG, L. S., FITZGERALD, D. A., CRAIG, J. C., MANERA, K. E., HANSON, C. S., CELERMAJER, D., AYER, J., KASPARIAN, N. A. & TONG, A. 2018. Children's experiences of congenital heart disease: a systematic review of qualitative studies. *European journal of pediatrics,* 177**,** 319-336.

CLEELAND, C. S. 2007. Symptom burden: multiple symptoms and their impact as patient-reported outcomes. *J Natl Cancer Inst Monogr*, 16-21.

COHEN, M. E. & MARINO, R. J. 2000. The tools of disability outcomes research functional status measures. *Arch Phys Med Rehabil,* 81, S21-9.

COHEN, M. L., TULSKY, D. S., BOULTON, A. J., KISALA, P. A., BERTISCH, H., YEATES, K. O., ZONFRILLO, M. R., DURBIN, D. R., JAFFE, K. M. & TEMKIN, N. 2019. Reliability and construct validity of the TBI-QOL communication short form as a parent-proxy report instrument for children with traumatic brain injury. *Journal of speech, language, and hearing research,* 62, 84-92.

COHN LAWRENCE, H. 2003. Fifty Years of Open-Heart Surgery. *Circulation,* 107, 2168-2170.

CONNOR, J. A., KLINE, N. E., MOTT, S., HARRIS, S. K. & JENKINS, K. J. 2010. The meaning of cost for families of children with congenital heart disease. *Journal of Pediatric Health Care,* 24, 318-325.

CORNETT, L. & SIMMS, J. 2014. At the 'heart'of the matter: An exploration of the psychological impact of living with congenital heart disease in adulthood. *Journal of health psychology,* 19, 393-406.

COULTER, A. 2016. Patient feedback for quality improvement in general practice. British Medical Journal Publishing Group.

DRAKOULI, M., PETSIOS, K., GIANNAKOPOULOU, M., PATIRAKI, E., VOUTOUFIANAKI, I. & MATZIOU, V. 2015. Determinants of quality of life in children and adolescents with CHD: a systematic review. *Cardiology in the Young,* 25, 1027.

DULFER, K., DUPPEN, N., VAN DIJK, A. P., KUIPERS, I. M., VAN DOMBURG, R. T., VERHULST, F. C., VAN DER ENDE, J., HELBING, W. A. & UTENS, E. M. 2015. Parental mental health moderates the efficacy of exercise training on health-related quality of life in adolescents with congenital heart disease. *Pediatric cardiology,* 36, 33-40.

DUNBAR-MASTERSON, C., WYPIJ, D., BELLINGER, D. C., RAPPAPORT, L. A., BAKER, A. L., JONAS, R. A. & NEWBURGER, J. W. 2001. General health status of children with D-transposition of the great arteries after the arterial switch operation. *Circulation,* 104, I-138-I-142.

EISER, C. & MORSE, R. 2001. A review of measures of quality of life for children with chronic illness. *Archives of disease in childhood,* 84, 205-211.

ERNST, M. M., MARINO, B. S., CASSEDY, A., PIAZZA-WAGGONER, C., FRANKLIN, R. C., BROWN, K. & WRAY, J. 2018. Biopsychosocial Predictors of Quality of Life Outcomes in Pediatric Congenital Heart Disease. *Pediatr Cardiol,* 39, 79-88.

FAYED, N., AVERY, L., DAVIS, A. M., STREINER, D. L., FERRO, M., ROSENBAUM, P., CUNNINGHAM, C., LACH, L., BOYLE, M. & RONEN, G. M. 2019. Parent proxy discrepancy groups of quality of life in childhood epilepsy. *Value in Health,* 22, 822-828.

FIELD, J., HOLMES, M. M. & NEWELL, D. 2019. PROMs data: Can it be used to make decisions for individual patients? A narrative review. *Patient related outcome measures,* 10, 233.

FRANICH-RAY, C., BRIGHT, M. A., ANDERSON, V., NORTHAM, E., COCHRANE, A., MENAHEM, S. & JORDAN, B. 2013. Trauma reactions in mothers and fathers after their infant's cardiac surgery. *Journal of pediatric psychology,* 38, 494-505.

GANTT, L. T. 1992. Growing up heartsick: the experiences of young women with congenital heart disease. *Health care for women international,* 13**,** 241-248.

GAYNOR, J. W., STOPP, C., WYPIJ, D., ANDROPOULOS, D. B., ATALLAH, J., ATZ, A. M., BECA, J., DONOFRIO, M. T., DUNCAN, K., GHANAYEM, N. S., GOLDBERG, C. S., HÖVELS-GÜRICH, H., ICHIDA, F., JACOBS, J. P., JUSTO, R., LATAL, B., LI, J. S., MAHLE, W. T., MCQUILLEN, P. S., MENON, S. C., PEMBERTON, V. L., PIKE, N. A., PIZARRO, C., SHEKERDEMIAN, L. S., SYNNES, A., WILLIAMS, I., BELLINGER, D. C., NEWBURGER, J. W. & FOR THE INTERNATIONAL CARDIAC COLLABORATIVE ON NEURODEVELOPMENT, I. 2015. Neurodevelopmental Outcomes After Cardiac Surgery in Infancy. *Pediatrics,* 135**,** 816-825.

HUISENGA, D., LA BASTIDE-VAN GEMERT, S., VAN BERGEN, A., SWEENEY, J. & HADDERS-ALGRA, M. 2020. Developmental outcomes after early surgery for complex congenital heart disease: A systematic review and meta-analysis. *Developmental Medicine & Child Neurology*.

JACKSON, J. L., TIERNEY, K., DANIELS, C. J. & VANNATTA, K. 2015. Disease knowledge, perceived risk, and health behavior engagement among adolescents and adults with congenital heart disease. *Heart & Lung,* 44**,** 39-44.

JANSSENS, A., GOOSSENS, E., LUYCKX, K., BUDTS, W., GEWILLIG, M., MOONS, P. & INVESTIGATORS, I.-D. 2016. Exploring the relationship between disease-related knowledge and health risk behaviours in young people with congenital heart disease. *European Journal of Cardiovascular Nursing,* 15**,** 231-240.

KOLAITIS, G. A., MEENTKEN, M. G. & UTENS, E. M. 2017. Mental health problems in parents of children with congenital heart disease. *Frontiers in pediatrics,* 5**,** 102.

KOOT, H. & WALLANDER, J. 2014. *Quality of life in child and adolescent illness: Concepts, methods and findings*, Routledge.

LAN, S.-F., MU, P.-F. & HSIEH, K.-S. 2007. Maternal experiences making a decision about heart surgery for their young children with congenital heart disease. *Journal of Clinical Nursing,* 16**,** 2323-2330.

LAPIN, B. R., HONOMICHL, R. D., THOMPSON, N. R., ROSE, S., SUGANO, D., UDEH, B. & KATZAN, I. L. 2019. Association Between Patient Experience With Patient-Reported Outcome Measurements and Overall Satisfaction With Care in Neurology. *Value in Health,* 22**,** 555-563.

LATAL, B., HELFRICHT, S., FISCHER, J. E., BAUERSFELD, U. & LANDOLT, M. A. 2009. Psychological adjustment and quality of life in children and adolescents following open-heart surgery for congenital heart disease: a systematic review. *BMC Pediatrics,* 9**,** 6-6.

LEE, S., KIM, S. & CHOI, J. Y. 2014. Coping and resilience of adolescents with congenital heart disease. *Journal of Cardiovascular Nursing,* 29**,** 340-346.

LOTTO, R., JONES, I., SEATON, S. E., DHANNAPUNENI, R., GUERRERO, R. & LOTTO, A. 2019a. Congenital Cardiac Surgery and Parental Perception of Risk: A Quantitative Analysis. *World J Pediatr Congenit Heart Surg,* 10**,** 669-677.

LOTTO, R., SMITH, L. K. & ARMSTRONG, N. 2018. Diagnosis of a severe congenital anomaly: A qualitative analysis of parental decision making and the implications for healthcare encounters. *Health Expectations,* 21**,** 678-684.

LOTTO, R. R., JONES, I. D., GUERRERO, R., DHANNAPUNENI, R. & LOTTO, A. A. 2019b. Congenital cardiac surgery and parental perception of risk: a qualitative study. *Cardiology in the Young,* 29**,** 1361-1367.

LUNT, D., BRIFFA, T., BRIFFA, N. K. & RAMSAY, J. 2003. Physical activity levels of adolescents with congenital heart disease. *Australian Journal of Physiotherapy,* 49**,** 43-50.

MAJNEMER, A., LIMPEROPOULOS, C., SHEVELL, M., ROHLICEK, C., ROSENBLATT, B. & TCHERVENKOV, C. 2008. Developmental and functional outcomes at school entry in children with congenital heart defects. *The Journal of pediatrics,* 153**,** 55-60. e1.

MAKRINIOTI, H., BUSH, A. & GRIFFITHS, C. 2020. What are patient-reported outcomes and why they are important: improving studies of preschool wheeze. *Archives of Disease in Childhood-Education and Practice,* 105**,** 185-188.

MALINA, R. M. 2001. Physical activity and fitness: pathways from childhood to adulthood. *American Journal of Human Biology: The Official Journal of the Human Biology Association,* 13**,** 162-172.

MARINO, B. S., TOMLINSON, R. S., DROTAR, D., CLAYBON, E. S., AGUIRRE, A., ITTENBACH, R., WELKOM, J. S., HELFAER, M. A., WERNOVSKY, G. & SHEA, J. A. 2009. Quality-of-life concerns differ among patients, parents, and medical providers in children and adolescents with congenital and acquired heart disease. *Pediatrics,* 123**,** e708-e715.

MARTIN, G. R. & JONAS, R. A. 2018. Surgery for congenital heart disease: improvements in outcomes. *American journal of perinatology,* 35**,** 557-560.

MASSIN, M. M., HÖVELS-GÜRICH, H. & SEGHAYE, M.-C. 2007. Atherosclerosis lifestyle risk factors in children with congenital heart disease. *European Journal of Cardiovascular Prevention & Rehabilitation,* 14**,** 349-351.

MATZA, L. S., SWENSEN, A. R., FLOOD, E. M., SECNIK, K. & LEIDY, N. K. 2004. Assessment of health-related quality of life in children: a review of conceptual, methodological, and regulatory issues. *Value in health,* 7**,** 79-92.

MCMAHON, E. & CHANG, Y.-S. 2020. From surviving to thriving-parental experiences of hospitalised infants with congenital heart disease undergoing cardiac surgery: A qualitative synthesis. *Journal of pediatric nursing,* 51**,** 32-41.

MCMURRAY, R., KENDALL, L., PARSONS, J., QUIRK, J., VELDTMAN, G., LEWIN, R. & SLOPER, P. 2001. A life less ordinary: growing up and coping with congenital heart disease. *Coronary Health Care,* 5**,** 51-57.

MOOLA, F., MCCRINDLE, B. W. & LONGMUIR, P. E. 2009. Physical activity participation in youth with surgically corrected congenital heart disease: devising guidelines so Johnny can participate. *Paediatrics & child health,* 14**,** 167-170.

MOONS, P., VAN DEYK, K., BUDTS, W. & DE GEEST, S. 2004. Caliber of quality-of-life assessments in congenital heart disease: a plea for more conceptual and methodological rigor. *Archives of pediatrics & adolescent medicine,* 158**,** 1062-1069.

MUSSATTO, K. & TWEDDELL, J. 2005. Quality of life following surgery for congenital cardiac malformations in neonates and infants. *Cardiology in the Young,* 15**,** 174.

MUSSATTO, K. A., HOFFMANN, R. G., HOFFMAN, G. M., TWEDDELL, J. S., BEAR, L., CAO, Y. & BROSIG, C. 2014. Risk and prevalence of developmental delay in young children with congenital heart disease. *Pediatrics,* 133**,** e570-e577.

NELSON, E., EFTIMOVSKA, E., LIND, C., HAGER, A., WASSON, J. & LINDBLAD, S. 2015. Patient reported outcome measures in practice. BMJ, 350, g7818.

NICOR, N. I. F. C. O. R.-. 2017. *National Congenital Heart Disease Audit Report* [Online]. Available: https://www.nicor.org.uk/wp-content/uploads/2018/08/09729-UCL-Congenital-Report-2013-16-UPDATES-JULY-2018-v1.pdf [Accessed 10-11 2018].

REID, G. J., WEBB, G. D., MCCRINDLE, B. W., IRVINE, M. J. & SIU, S. C. 2008. Health behaviors among adolescents and young adults with congenital heart disease. *Congenital heart disease,* 3**,** 16-25.

SILVA, G. V. D., MORAES, D. E. B., KONSTANTYNER, T. & LEITE, H. P. 2020. [Social support and quality of life of families with children with congenital heart disease]. *Cien Saude Colet,* 25**,** 3153-3162.

SJOSTROM-STRAND, A. & TERP, K. 2017. Parents' Experiences of Having a Baby With a Congenital Heart Defect and the Child's Heart Surgery. *Comprehensive child and adolescent nursing***,** 1-14.

SLUYS, K. P., LANNGE, M., ISELIUS, L. & ERIKSSON, L. E. 2015. Six years beyond pediatric trauma: child and parental ratings of children's health-related quality of life in relation to parental mental health. *Quality of Life Research,* 24**,** 2689-2699.

SNOOKES, S. H., GUNN, J. K., ELDRIDGE, B. J., DONATH, S. M., HUNT, R. W., GALEA, M. P. & SHEKERDEMIAN, L. 2010. A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. *Pediatrics,* 125**,** e818-e827.

SPECTOR, L. G., MENK, J. S., KNIGHT, J. H., MCCRACKEN, C., THOMAS, A. S., VINOCUR, J. M., OSTER, M. E., ST LOUIS, J. D., MOLLER, J. H. & KOCHILAS, L. 2018. Trends in long-term mortality after congenital heart surgery. *Journal of the American College of Cardiology,* 71**,** 2434-2446.

STERKEN, C., LEMIERE, J., VANHOREBEEK, I., VAN DEN BERGHE, G. & MESOTTEN, D. 2015. Neurocognition after paediatric heart surgery: a systematic review and meta-analysis. *Open heart,* 2.

TAKKEN, T., HULZEBOS, H., BLANK, A., TACKEN, M., HELDERS, P. & STRENGERS, J. 2007a. Exercise prescription for patients with a Fontan circulation: current evidence and future directions. *Netherlands Heart Journal,* 15**,** 142-147.

TAKKEN, T., TACKEN, M. H., BLANK, A. C., HULZEBOS, E. H., STRENGERS, J. L. & HELDERS, P. J. 2007b. Exercise limitation in patients with Fontan circulation: a review. *Journal of Cardiovascular Medicine,* 8**,** 775-781.

THIYAGARAJAN, A., BAGAVANDAS, M. & KOSALRAM, K. 2019. Assessing the role of family well-being on the quality of life of Indian children with thalassemia. *BMC pediatrics,* 19**,** 1-6.

UTENS, E. M., VERSLUIS-DEN BIEMAN, H. J., VERHULST, F. C., WITSENBURG, M., BOGERS, A. J. & HESS, J. 2000. Psychological distress and styles of coping in parents of children awaiting elective cardiac surgery. *Cardiology in the Young,* 10**,** 239-244.

UZARK, K., VONBARGEN-MAZZA, P. & MESSITER, E. 1989. Health education needs of adolescents with congenital heart disease. *Journal of Pediatric Health Care,* 3**,** 137-143.

VAN VELTHOVEN, M. H., ATHERTON, H. & POWELL, J. 2018. A cross sectional survey of the UK public to understand use of online ratings and reviews of health services. *Patient Education and Counseling,* 101**,** 1690-1696.

VOSS, C., DUNCOMBE, S. L., DEAN, P. H., DE SOUZA, A. M. & HARRIS, K. C. 2017. Physical activity and sedentary behavior in children with congenital heart disease. *Journal of the American Heart Association,* 6**,** e004665.

WEI, H., ROSCIGNO, C. I., HANSON, C. C. & SWANSON, K. M. 2015. Families of children with congenital heart disease: A literature review. *Heart & Lung: The Journal Of Critical Care,* 44**,** 494-511.

WILLIAMS, B. 1994. Patient satisfaction: a valid concept? *Soc Sci Med,* 38**,** 509-16.

WOOLF-KING, S. E., ARNOLD, E., WEISS, S. & TEITEL, D. 2018. “There's no acknowledgement of what this does to people”: A qualitative exploration of mental health among parents of children with critical congenital heart defects. *Journal of clinical nursing*.

WRAY, J. & SENSKY, T. 2004. Psychological functioning in parents of children undergoing elective cardiac surgery. *Cardiology in the Young,* 14**,** 131-139.