

Depression in adults with congenital heart disease-public health challenge in a rapidly expanding new patient population

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Abstract

There is a growing population of adults with congenital heart disease (CHD) due to improved survival beyond childhood. It has been suggested that adults with CHD may be at increased risk for mental health problems, particularly depression. The reported incidence of depression in CHD varies from 9% to 30%. This review examines the evidence for a higher depression rate in CHD vs general population. Possible explanations are offered from a variety of disease models, ranging from brain injury to the psychoanalytical approach. Risk factors for an abnormal emotional adjustment and depression include early exposure to stress from illness and medical interventions in infancy, separation from the parents during hospitalizations and brain organic syndromes. Later in life, patients often have to cope with physical limitations. Recent improvements in care may be protective. Current patients may benefit from an earlier age at first surgical intervention, fewer reoperations and inclusion to the mainstream schooling, among other factors. At this point, there is little systematic knowledge about evidence-based therapeutic interventions for depression in adults with CHD. Health care providers of patients with CHD should be aware of mental health challenges and may take a more proactive approach to identifying patients at risk for depression.

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Key words: Congenital heart disease; Cardiopulmonary bypass; Depression; Outcomes research

Core tip: More and more adults with congenital heart disease (CHD) survive to adulthood. Having survived grave illness in infancy, these patients appear to be at increased risk for mental health problems as adults. This review specifically examines the relationship of CHD and depression. Risk factors and protective strategies are explored. There still is little knowledge on specific treatment for depression in the growing patient population of adults with CHD. When health care providers are aware of depression in adults with CHD this may improve access to appropriate care.

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INTRODUCTION

Adults with congenital heart defects are a growing population since the results of open heart surgery in children constantly improve. At the same time, this growing number may be at risk for psychiatric problems, particularly depression. An increased incidence of depression in adults with congenital heart disease (CHD) was first suggested by studies conducted in Boston^[1,2]. The first study included 29 adults with CHD from a medical follow up clinic at Massachusetts General Hospital^[1]. It identified major depression in 4 (14%) and dysthymic disorder in 11 more (38%) of these patients using DSM-III-R crite-

ria^[1]. Another early study used a structured interview in addition to a questionnaire in 22 different adult survivors of CHD^[2]. Here, 27% of the patients fulfilled DSM-IV criteria for depression. Remarkably, neither the cardiology care providers nor the patients themselves had voiced concerns prior to the testing.

Since then a number of population-based studies from multiple cultural backgrounds have raised similar concerns. Eslami *et al*^[3] found increased problems with anxiety but depressive symptoms were similar to matched control population in 347 Swedish adults with CHD. In another Swedish cohort of 1274 patients (with a mean age of 33 years) 29.8% of the participants self-reported symptoms of anxiety or depression^[4]. In Portugal, Freitas *et al*^[5] documented a 21.8% lifetime prevalence of psychopathology in a cohort of 110 CHD patients. A Korean study examined 210 Korean 19 years old males of military draft age to 300 controls and found an increased incidence of psychological abnormalities^[6]. Among 119 Australian adolescents with CHD, 9% were positive on a screening test for depression; anxiety was even more prevalent^[7].

The impact of physical symptoms on quality of life and depression is somewhat unclear: One study in 53 patients with Fontan for single ventricle hearts also found an increased incidence of depressive symptoms^[8]. In a German study 8.6% of 767 patients with CHD (median age 26 years old) exhibited depressive symptoms when they presented for a formal exercise stress test^[3]. The authors concluded that the effect of physical limitations on quality of life was relatively smaller than that of depression, highlighting the complex interactions between physical and psychological well being^[9].

Pediatric follow up studies using parental observations also indicate an increased risk of mental health problems in CHD patients^[10,11]. In a Dutch study, parents completed a child-behavior checklist for a cohort of 125 children aged 10-16 years old from a single surgical center^[10]. The incidence of emotional and behavioral problems in CHD patients was increased. Behavior problems were more common in patients who had more hospital admissions and operations^[10]. A follow-up study on 430 Norwegian children with CHD had the same conclusion. In this study, boys with CHD had a greater incidence of behavioral problems than girls but both groups were higher than expected^[11]. Another study utilized the "Mood and Feelings Questionnaire" in 58 children awaiting heart or heart and lung transplantation including 32 children with CHD^[12]. Patients and parents were interrogated. In this population, depression scores were higher than reference values before and after transplant. Pre-transplant, 21% of all children with CHD scored in the abnormal range; however, children with other diagnosis like cardiomyopathy or cystic fibrosis fared even worse. Parent and child scores on depression agreed to some degree but the correlation coefficient was relatively low at $R = 0.5$. These studies offer good evidence that adults with CHD are at higher risk for depression than the general population. This has now affected treatment guidelines for

adults with CHD^[13,14]. At this point, however, there are still more studies focusing on children with CHD than on adults^[13].

In general, the co-morbidity of medical illness and depression is well described^[14]. For instance, several studies in adults have focused on the relationship of depression and coronary artery heart disease^[15]. Depression appears to be a risk factor for the manifestation of coronary artery disease^[15]. It is also more prevalent in patients after heart attacks^[15]. In a large study, 39% of all patients with acute myocardial infarction (MI) had criteria for depression (ENRICHD)^[14]. Moreover, MI patients with depression have less favorable outcomes in terms of morbidity and survival. Significant differences persisted 5 years after the event when compared to controls without depressive symptoms^[14].

Can treatment of depression make a difference? The ENRICHD trial randomly assigned 1238 MI patients to a 6-mo period of cognitive therapy. Both these patients and a matching control group of MI patients had access to antidepressant medication^[15]. The study did not find a benefit for the psychotherapy group with regards to event-free-survival but symptoms improved. On post-hoc analysis, there was a survival benefit for those MI patients on serotonin re-uptake inhibitory drugs (with or without psychotherapy).

In light of the experience in coronary artery disease, it would seem important to aggressively address and treat depression in adults with CHD. However, this area appears to be largely unexplored: There were no randomized controlled trials on psychological interventions in adolescents and adults with CHD based on a Cochrane review from 2003^[16].

This problem has another important aspect. Depression is a silent epidemic^[17,18]. When it comes to unrecognized mental health issues, the situation of patients with heart disease may not be so different from the general population. Disability due to depression has a similar incidence as coronary artery disease and cancer^[18], yet it is more hidden from the public eye, perhaps due to the stigma still associated with mental illness. Epidemiological studies suggest a lifetime prevalence of 16.2% for major depressive disorder with a 1-year-prevalence of 6.6% in the general population in the United States^[19]. The prevalence of severe mental disorders (of about 7%) appears to be stable over 2 decades^[19]. Even after diagnosis, only about half of all patients receive treatment^[20]. These are the findings of the National Co-morbidity Survey which included adults from 18 and 54 years of age^[19].

Under-diagnosed, under-treated and still a shameful illness-depression poses a major public health challenge for the general population. Are adults with CHD at a higher risk than the general population?

ADULTS WITH CHD-A GROWING POPULATION AT RISK FOR DEPRESSION?

CHD affects about 0.8% of all live-born infants, based

Table 1 Selected quality of life indicators in adult congenital heart disease

Study	n	Exercise tolerance ¹	Health Self-assessment	Unemployed	Site
Nieminen <i>et al</i> ^[27]	2896	97% good	77% good	Not increased	Finland
Crossland <i>et al</i> ^[28]	299	N/A	N/A	33%, increased	United Kingdom
Lane <i>et al</i> ^[29]	276	Diminished	Diminished	Increased	United Kingdom
Moons <i>et al</i> ^[30]	629	95% < class 3	Good	6.7%	Belgium
Jefferies <i>et al</i> ^[31]	32	Diminished	Diminished	47%, increased	KY, United States
Kamphuis <i>et al</i> ^[32]	156	N/A	N/A	36%, increased	Holland

¹New York Heart Association Classification. N/A: Not assessed.

on the data of the Baltimore-Washington Infant study^[20]. About half of these children require a surgical or catheter intervention to survive beyond infancy. Palliative heart operations started in 1944^[21]. The development of the heart-lung machine by Gibbons in the early 1950s opened the era of open-heart surgery^[21]. It is estimated, that 10% of all patients with complex congenital heart defects born in the era from 1940-1959 were still alive in the year 2000 compared to 50% from the surgical era 1960-1979 and 80% of those infants with CHD born in the 1980s^[22]. Children with significant CHD requiring surgery now have an estimated 85% chance to survive to age 16 years old^[23]. The overall surgical mortality for CHD most recently had fallen to about 5% with further improvements expected^[24].

As a result of this progress, the adult CHD population is growing rapidly. For the first time, there are more adults than children with CHD in the United States. Therefore, several working groups have tried to address the medical needs of these adult survivors of what once used to be a pediatric illness, including mental health needs^[13,24-26].

Mental health is related to the economic and social circumstances of the population. How do adults with CHD fare in this regard? Several outcome studies from different countries have addressed these issues. Table 1 gives an overview. Overall, adults with CHD tend to have lower employment rates, less exercise tolerance and a lower self-assessment of good health than population average.

Nevertheless, most patients with CHD appear to enjoy a good quality of life as adults^[27-32]. In a detailed quality of life study from Belgium, 514 adults with CHD were compared to a matched control group from the general population at a median age of 23 years^[33]. Employment was similar in this sample but the highest educational achievement and marriage rate were slightly lower than controls. There also was a (statistically insignificant) trend to fewer children in patients. The most striking difference, however, was that patients stood out for their different values: These adults with CHD ranked "financial means and material well-being" as less important to their well-being than their healthy peers. A recent population study in Finland found similar results^[27]. The investigators evaluated 2896 adults with CHD using a self-report from a standardized questionnaire^[27]. The response rate was high at 76% of the national adult CHD population. The Finish patients were older than the group from Belgium with a mean age of 33 years (ranging from 15 to 59

years). Their employment and marriage (or cohabitation) rates were similar to the general population. However, both men and women with CHD were less likely to have children than controls^[27].

Another study based on quality of life questionnaires conducted in the United Kingdom found significantly diminished scores compared to population normative data in adults with CHD, including "emotional role"^[29]. It is unclear whether patients with palliated heart disease and cyanosis as adults fare worse. In the study by Lane *et al*^[29] the subgroup of patients with cyanotic heart disease scored worse than those with acyanotic defects. In contrast, Moons *et al*^[30] found similar quality of life in cyanotic and acyanotic patients. Even in this study, cyanotic patients perceived the severity of their disease as higher those with acyanotic defects but this did not seem to affect their overall quality of life^[30]. The severity of disease had an influence on the perceived quality of life but there was only a weak correlation. In Moons's study, 95.8% of the 628 patients had an ability index above class 3, defined as being able to work and bear children. This is similar to the findings in the study from Munich, Germany, comparing objective exercise tolerance on formal stress test with quality of life scores in 767 patients^[11]. In contrast to these favorable results, unemployment among the patients was high in Kentucky^[31]. Nevertheless, even here, 66% of adults were married and social support was deemed "good" in 91% by the patients themselves.

In summary, several studies found increased unemployment and indicators of a diminished quality of life in adult survivors of CHD (Table 1). Yet other studies present evidence that the majority of patients can attain a high level of functioning under the right circumstances. There is potential for a normal or near normal quality of life. Therefore, it is an important public health goal to assist this rapidly growing population to realize their full potential and to achieve the highest possible degree of independence. Mental health issues are an important component of this process as it will empower the patients to find their own solutions in a challenging environment where they may face disadvantages at the work place.

EPIDEMIOLOGY OF DEPRESSION IN ADULTS WITH CHD

Several investigators have studied depression in adults with CHD but the design of the studies varied mak-

ing a direct comparison between studies difficult^[1-9]. Some studies contract a cohort of patients operated at a single surgical center while others used a sample of convenience from an outpatient clinic. Methods applied included standardized questionnaires and interviews where the controls were taken from normative data or matched controls. Some studies indicate an increased risk for adults with CHD while others found a similar profile as in the comparison group as will be discussed in more detail below. The conflicting results of different studies may be related to the heterogeneity of the methodology used.

Studies supporting a higher risk for depression in adult CHD

As mentioned in the introduction, two small studies from Boston found diagnostic criteria for depression in about one third of adults attending a CHD outpatient clinic^[1,2]. Both studies concluded that these patients may have a higher risk for depression than the general population. As an important limitation, both studies had small sample sizes with 22 and 29 participants, respectively. In addition, there may have been selection bias due to the recruitment from an outpatient clinic.

According to a recent Canadian study, patients attending specialized follow-up clinics at tertiary care centers represent only about half of all adults with complex CHD (47%)^[34]. In this national survey, 27% of patients with complex heart defects simply had no further cardiologist visits after age 18 years old^[32]. The others took their follow up care to a non-specialist^[32]. Recruiting patients in a specialized follow-up setting could therefore lead to the wrong conclusion. It is conceivable that the more symptomatic patients prefer specialist care and would also be more likely to be referred back to a specialist if they went to see another doctor because of the obvious complexity of their medical needs. The severity of the illness appears to impact on the patient's quality of life to a degree that is somewhat disputed^[8,9,30]. Patients in a tertiary care center outpatient clinic may therefore represent a group with higher risk factors than the average adult with CHD.

However, the relationship between the type of heart defect and quality of life is not straight-forward^[29,30]. One would expect that patients who had successful surgery ("surgically cured") should also consider themselves as fully functional in their self-perception. Lane *et al*^[29] assessed the quality of life of 276 patients with CHD, including 68 with "surgically cured" disease. This "surgically cured" group had diminished scores for "role-emotional" with 70 compared to the population normative value of 83, a significant difference. The 18 patients with cyanotic heart disease in this study had an even lower score than the acyanotic control group of patients. All other patients including those with inoperable disease scored similar to normal population^[29]. In the Korean cohort of 19 years old males there were no differences between patients with and without history of open heart surgery although both groups differed from the controls^[6].

These findings illustrate the difficulty of detecting mental health issues in adults with CHD as they are not a homogeneous group. The experience appears to vary in relationship to the underlying diagnosis and severity of the illness. However, the relationship may be complicated as highlighted by the fact that in Lane *et al*^[29] found abnormal "quality of life" scores in patients who were considered "surgically cured" with little physical impairment and low probability of further complications.

More recently, van Rijen studied a cohort of 362 adults with CHD from a single surgical center^[35]. At follow-up, patients were 20-46 years old. Most patients were well adjusted or in some aspects even better adjusted than age-matched normal controls. However, the investigators identified sub-groups of patients at higher risk for depression. These risk factors included female sex, low exercise capacity, more physician-ordered restrictions, worse self-perception of scars (as opposed to physician assessment of the appearance of scars), early hospitalizations and the number of re-operations^[35]. In addition, patients with 2 common diagnoses, ventricular septal defect and complete transposition of the great arteries, also had a significantly higher risk of emotional mal-adjustment.

In summary, there are several studies pointing to an increased risk of depression in adults with CHD. However, this finding may not be true across the spectrum of all congenital heart defects but only for specific sub-groups including: (1) cyanotic heart disease; (2) ventricular septal defect; and (3) complete transposition of the great arteries. However, all studies were relatively small and there are no large-scale or population-based studies addressing this issue.

Studies contradicting a higher risk for depression in adult CHD

Some studies suggest that adults with CHD are at similar risk for mental health problems as the general population or even, in some aspects, better adjusted than others^[36,37]. Cox *et al*^[37] compared 87 patients from a hospital-based adult CHD outpatient clinic to a control group of 45 patients attending the orthopedic outpatient department at the same institution using a questionnaire approach. In this study, CHD patients had similar Hospital Anxiety and Depression Scale (HADS) scores as orthopedic patients; 36% of the cardiac patients and 51% of the orthopedic patients scored higher than 11, a difference that did not reach statistical significance. On the "General Health Questionnaire 30", cardiac patients perceived themselves as healthier than their orthopedic patient control group. The investigators concluded that psychopathology was less prevalent than expected in the adult CHD group. However, this result may have been influenced by the low response rates and the unusual characteristics of the control group. In a large United States study, the National Comorbidity Survey, 29% of the general population had evidence of mental disorders of any kind^[20]. While a direct comparison would not be valid, the rate of 36% abnormal results on the HADS questionnaire in adults with

CHD certainly does not seem to be particularly low.

van Rijen *et al*^[36] performed a very detailed psychological follow-up evaluation of a cohort of 363 consecutive patients operated at the Thoraxcenter Rotterdam in the Netherlands in the years between 1968 and 1980. After the initial study, patients were studied again following a 10 year interval using the Heart Patients Psychological Questionnaire and a number of other tools^[38]. The response rate was high, 90.7% of the patient treated at that institution. The reference group was carefully chosen and consisted of 1742 Dutch citizens who completed the “Short Form-36 health survey”, based on an unrelated study published in 1998. Compared to this reference population, adults with CHD generally scored lower for physical functioning; however, the difference was small with 90.3 *vs* 93.1 on a scale from 0 to 100 for patients and controls^[36]. Patients reported more bodily pain. Nevertheless, the subjective perception of health was similar in the patients and in the reference population. For “social functioning”, “general mental health” and “limitations of role due to emotional problems” adults with CHD rated themselves higher than the reference population^[38]. The self-assessment of emotional health suggested that these patients functioned better than the population average.

However, even in this Dutch study, comparison of the earlier findings with the follow up study ten years later revealed an increase in “displeasure (negative moods and emotions)” based on the Heart Patients Psychological Questionnaire. This score for “displeasure” was reportedly at the lower limit of the scoring range. Overall, older women reported a decrease in their well-being as they grew older while men improved.

So both the study by Cox *et al*^[37] and the Dutch study support that adults with CHD are emotionally well adjusted when compared to controls but on closer examination this statement only holds true when some special considerations are taken into account^[38]. The Dutch investigators from Rotterdam identified certain subgroups at higher risk, including those with early hospitalizations and re-operations, as mentioned above. Moreover, they discovered that young women with CHD, particularly those between 20 and 27 years of age, were significantly more likely to express symptoms of depression than the reference population. This was the result of a related study in which the same investigators analyzed 252 patients aged 20-32 years old from the same center. Women with CHD had abnormal results on the “Young Adult Self Report”, confirmed by the “Young Adult Behavior Checklist” which was completed by parents and partners^[33]. The 28-32 years old counterparts did better while still at slightly higher risk for anxiety and depression than control.

Overcompensation and denial may influence patient’s self-reported symptoms. In the study from Rotterdam, patient responses were compared to the assessment of parents and partners which suggested more problems than self-report^[38,39]. The scores based on the responses of family members were more abnormal as those reported by the patients themselves.

It is difficult to reconcile all the findings. It is pos-

sible that there truly could be regional differences or, as discussed above, selection bias due to overrepresentation of symptomatic adults with CHD in specialty outpatient clinics at tertiary care centers.

Depression in the families of patients with CHD

Closely related to the question of depression in adult with CHD is the mental health and incidence of depression in their parents^[40-43]. A Swedish study found an increased incidence of depression in parents of children with CHD among 1092 members of the Swedish Heart Child Foundation^[40]. They were parents to 691 children with heart defects^[40]. The 2 control groups consisted of 293 parents of 162 healthy children and 112 parents of 74 children with other disease in a cross-sectional study using questionnaires. In all 3 groups, mothers had higher scores than fathers. Parents of children with CHD, older and unemployed parents were more likely to be depressed. Overall, 18% of the parents of children with congenital heart defects had abnormal scores for depression, nearly twice as many as in the control group with health children and ill children (10% in both groups)^[40].

Another study assessed the parents of 75 children before and one year after open heart surgery^[41]. Indicators of “psychological distress” were present in 63% of the mothers before surgery with a decrease to 25% at follow up^[41]. Again fathers were less distressed than mothers with abnormal scores in 48% preoperatively and 17% at follow-up, compared to 13% fathers of healthy children. Prenatal diagnosis of CHD also impacts parental mental health^[42].

When confronted with CHD, parents appear to be at high risk for depression. Yet, it is unclear how depression in the parents will affect their children, the CHD patients. One study from Leuven, Belgium, suggested that a more controlling parenting style may negatively impact the psychological well-being of children with CHD^[43]. Overall, this question seems to be under-studied.

ETIOLOGICAL CONSIDERATIONS FOR DEPRESSION IN CHD PATIENTS

Are there any psychological or medical reasons why patients with CHD would be at increased risk for depression? The theoretical foundation of psychotherapy is still characterized by pluralism with a number of competing schools of thought coexisting at the same time. As a consequence, there are several disease models for depression (Table 2). Yet it appears that when it comes to risk factors for depression and CHD, the case can be made regardless of the disease model (Table 2).

Psychoanalytical model

In 1917, Freud S^[44] published his basic idea of the pathogenesis of depression in a short essay entitled “Trauer und Melancholie”, mourning and melancholia. According to Freud, the self-tormenting and low self-regard characteristic of depression are possible only because

Table 2 Risk factors for depression in congenital heart disease and theoretical model

Disease model	Risk factor in congenital heart disease patients
Psychoanalytical model (Freud S)	Psychological trauma in oral phase) due to illness, hospitalizations and separation from parents.
Attachment theory (Bowlby)	Separation from parents. Parent's subconscious fear of bonding with a sick child that may not live long?
Biological model: Neurotransmitter imbalance	High stress during a vulnerable phase of development permanently alters physiological stress response.
Biological model: Brain organic cause	Cerebral insults secondary to heart disease and open-heart surgery.
Learning theory	"Learned helplessness" due to chain of adverse life-events, perceived or real lack of control during illness and hospitalizations, and socio-economic disadvantages.

the patient displaced a love-object taken from him (or her) early in life into his own self in a pathological manner. During depression, patients really wish to punish the source of their earlier frustration but instead redirect the destructive impulse against their own self, as internalization. The lost object could be a nurturing parent who disappears during a hospitalization. Freud also observed that depressed patients often refuse oral gratification from food. Depression has since been linked to a trauma in the oral phase, the earliest stage of psychological development in early infancy according to the Freudian school.

Freud's observation still stands that difficult life experiences during infancy (and particularly early parental loss) are associated with depression^[45]. The studies of van Rijen *et al*^[35] have demonstrated a higher risk for depression and emotional problems in patients with ventricular septal defects and complete transposition of the great arteries, two defects that require repair in early infancy with all the necessary hospital admissions and separation from the parents. Utens *et al*^[10] also showed a link between early hospitalizations and behavior problems in children with CHD.

Insecure attachment due to separation in infancy

According to Bowlby, difficult adult relationships and depression derive from the infant's difficulty in forming a strong bond to his or her parents, resulting in an insecure attachment. In a large survey in 879 college students, poor quality of the relationship with the parents was associated with the incidence of depression, based on self-report data^[45]. Among the respondents, 26% had been verbally, physically and sexually abused as children, and this subgroup had more depression than others. Differences were primarily related to the lower quality parental relationships in the group with childhood abuse rather than to the abuse itself. A Canadian study analyzed depressive symptoms in college students with a similar approach and also confirmed the close relationship between the quality of the primary attachment to the parents and

depression^[46]. It is conceivable that illness and hospital admissions and operations in early childhood with the separation of parents and children at times hinder a secure attachment.

Biological model: Altered neurotransmitter pathways, stress and cerebral insults

It is now widely accepted that depression is associated with a neuro-transmitter imbalance in the brain and that it may improve if the cerebral metabolism is normalized as a result of pharmacotherapy^[18]. Animal experimental data show that stressful life events in early life (for instance repeated short separations from the mother animal) result in an activation of the hypothalamic-pituitary-cortical axis with permanent alterations of the stress response in the exposed animals^[47]. Investigators also showed loss of volume of the hippocampus area of the brain, a part of the limbic system that is involved in the serotonin pathways^[47]. This biological model therefore provides a potential explanation for the link between early life stress and adult depression^[48].

Agid *et al*^[49] proposed a disease model where adverse life events in infancy make the individual more vulnerable for an abnormal stress response later in life when they are again confronted with challenges; depending on the presence or absence of genetic predisposition, the mal-adaptive psychological response may then take the form of post-traumatic stress disorder, depression or schizophrenia, with female sex as a modulating factor. Applied to CHD, the infant would become more vulnerable to depression when exposed to the stress of separation from the parents during hospitalization. In addition, these infants experience physical stress from pain related to blood draws, intravenous access and from the operation itself. Their cries may go unanswered creating the experience of an unresponsive environment. According to the animal research these repetitive stress events could alter the patient's stress response permanently. These abnormal patterns can surface when the patient is again confronted with adverse life events during adult life. The fact that adults with multiple hospitalizations, hospital admissions early in life and re-operations appear to have more depression would support this model indirectly.

Another important argument for a possible anatomic basis for depression in adults with CHD derives from recent neuroimaging studies on the brains of infants before and after open-heart surgery. In the Boston Cardiac Arrest Trial, there was a 15% incidence of abnormal brain scans in a group of children operated during the newborn period for transposition of the great arteries early on with higher rates in the subgroup presenting for follow up brain magnetic resonance imaging at age 16^[50-52]. Two more recent studies also obtained magnetic resonance imaging of the brain not only after but also before open heart surgery^[53,54]. They found an even higher incidence of cerebral insults pre- and post-open heart surgery during infancy: In the first study, the incidence

Table 3 Improvements in the treatment of children with congenital heart disease

Previously	In the current era
Difficult diagnosis-invasive testing	Noninvasive diagnosis by ultrasound
Presentation in critical condition	Earlier diagnosis, newborn intensive care
Emergency surgery or interventions	Emergency treatment rare
Long hospitalizations for weight gain	Neonatal surgery and short hospital stays
Limited visiting hours for parents	Parents involved in hospital care
Medical focus	Child life teams and psycho-social support
High surgical mortality and morbidity	Improved surgical mortality and morbidity
Admissions for infections	New immunization, improved antimicrobial treatment
Re-operation	More catheter interventions, shorter admissions
Limited rehabilitation options	Early intervention programs
Special education placement	Integration in the main-stream
Limited opportunities for peer support	Self-help groups, internet resources

of abnormal brain scans was 28% before surgery and in the second study 24% with an increase to 67% on post-operative follow up^[51-53].

Children with CHD appear to have multiple organic reasons to be at risk for depression. They live through high stress situations in the context of their hospitalizations and heart operations. Some patients even experienced resuscitation events. Stressors like this in early infancy may permanently alter the physiological stress response of the individual. In addition, a significant proportion of CHD patients suffer cerebral insults secondary to their disease and also in the peri-operative period^[50-53].

Yet, the exact relationship of these brain injuries for patient behavior and emotional adjustment remain murky as the presence of magnetic resonance imaging abnormalities didn't predict behavior problems in the Boston Cardiac arrest trial^[51].

Learning theory and environmental risk factors

Depression can also be conceived as “learned helplessness”-in experiments, an animal loses the initiative to escape or fight and becomes passive when repeatedly exposed to an unalterable stress situation^[48]. A small infant could argue perceive medical and surgical treatment in a similar way. As an aggravating factor, patients may feel more helpless because of their physical appearance and self-image^[55]. Their higher unemployment rates (Table 1) and greater physical limitations may also contribute to a sense of being helpless^[38,39].

Are adults with CHD at risk for depression?

The life experience associated with open-heart surgery in early childhood entails multiple risk factors for later emotional mal-adjustment. Despite these risk factors, studies indicate that many adults with CHD are well adjusted with good problem solving skills^[38]. In addition, it even appears that things get better as they age: Their “social isolation” decreased during follow up based on the Rotterdam study^[38]. However, there the good outcome in the Dutch and German experience may not be representative for the universal experience as studies from other countries now indicate a significant increase in depressive symptoms in diverse populations^[1-9].

PREVENTIVE STRATEGIES AND PROTECTIVE FACTORS

Preventive factors and resilience

Despite the risk for mental health problems, the real story of depression in adults with CHD may be their resilience-the ability to remain fully functional in the face of adversity^[55,56]. The parents of patients with CHD may experience more psychological distress than the patients themselves although this review didn't find any study using direct comparison^[40-42]. While risk factors are present overall outcomes appear to be good. The topic of specific protective factors in children with CHD appears to be largely unexplored at this time.

Finally, it is important to remember that today's adults with CHD grew up in an era where hospital visiting hours were shorter and mortality rates were higher (Table 3). Because of the harsher conditions in the past, it may well be that the current adult survivors of CHD represent a selection of only the most resilient individuals. In a study by Wray *et al*^[57] children who perceived themselves as more “weak” or “miserable” before surgery were less likely to survive. Today's adults with CHD are these survivors. However, the same investigators did not see a difference of the psychological profile of survivors and patients with adverse outcomes in a second, smaller study on 32 children with CHD awaiting heart or heart-and-lung transplantation; the psychological profile of the 18 surviving children were similar to those who died in the context of cardiac transplantation^[12].

Differences of current and previous treatment

Table 3 summarizes some important changes implemented in recent years that are likely to improve the psychological outcome of children with CHD. Many changes were introduced because of better insight into the psychological and developmental needs of sick children. It would be an important goal to build on that and improve primary prevention of mental health issues in these patients. Secondary prevention would consist of early identification and improved access to treatment for depression in adult survivors of CHD.

SUMMARY AND CONCLUSION

There is an increasing population of adults with CHD. Most of these patients could potentially be fully functional in society. CHD impacts on risk factors for depression in multiple ways. Whether depression in adults with CHD is increased or just under-diagnosed and under-treated-it is an issue for these patients. Cardiac diagnosis, medical history and patient sex appear to affect the relative risk of depression, particularly early hospitalizations and re-operations. Little is known about protective factors and the personality profiles of the higher functioning survivors and their parents. Systematic studies on treatment of depression in adult CHD are lacking.

In conclusion, it appears to be an important public health goal to increase the awareness of adults with CHD and their medical caretakers for the significant incidence of depression in this patient population. While the exact incidence of depression in the adult CHD population is unknown, it is clear that these patients potentially benefit from routine mental health screening.

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