Neurodevelopmental Outcomes in Children With Congenital Heart Disease: Evaluation and Management : A Scientific Statement From the American Heart Association

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AHA Scientific Statement

Neurodevelopmental Outcomes in Children With Congenital Heart Disease: Evaluation and Management

A Scientific Statement From the American Heart Association

This statement has been approved by the American Academy of Pediatrics.

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Background—The goal of this statement was to review the available literature on surveillance, screening, evaluation, and management strategies and put forward a scientific statement that would comprehensively review the literature and create recommendations to optimize neurodevelopmental outcome in the pediatric congenital heart disease (CHD) population.

Methods and Results—A writing group appointed by the American Heart Association and American Academy of Pediatrics reviewed the available literature addressing developmental disorder and disability and developmental delay in the CHD population, with specific attention given to surveillance, screening, evaluation, and management strategies. MEDLINE and Google Scholar database searches from 1966 to 2011 were performed for English-language articles cross-referencing CHD with pertinent search terms. The reference lists of identified articles were also searched. The American College of Cardiology/American Heart Association classification of recommendations and levels of evidence for practice guidelines were used. A management algorithm was devised that stratified children with CHD on the basis of established risk factors. For those deemed to be at high risk for developmental disorder or disabilities or for developmental delay, formal, periodic developmental and medical evaluations are recommended. A CHD algorithm for surveillance, screening, evaluation, reevaluation, and management of developmental disorder or disability has been constructed to serve as a supplement to the 2006 American Academy of Pediatrics statement on developmental surveillance and screening. The proposed algorithm is designed to be carried out within the context of the medical home. This scientific statement is meant for medical providers within the medical home who care for patients with CHD.

Conclusions—Children with CHD are at increased risk of developmental disorder or disabilities or developmental delay. Periodic developmental surveillance, screening, evaluation, and reevaluation throughout childhood may enhance identification of significant deficits, allowing for appropriate therapies and education to enhance later academic, behavioral, psychosocial, and adaptive functioning. **(*Circulation*. 2012;126:1143-1172.)**

Key Words: AHA Scientific Statements ■ cardiopulmonary bypass ■ heart defects, congenital ■ heart diseases, follow-up studies, brain ■ pediatrics

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Over the past several decades, new surgical techniques and advances in cardiopulmonary bypass (CPB), intensive care, cardiac catheterization, noninvasive imaging, and medical therapies have significantly lowered mortality rates for children and adolescents with complex congenital heart disease (CHD).[1,2] Survivors are at risk for neurodevelopmental morbidity caused by both biological and environmental risk factors. Biological risk factors include underlying syndromes or genetic/developmental disorders, the circulatory abnormalities specific to the heart defect, and the medical and surgical therapies required. Biological risk factors are modified by environmental risk and protective factors at home, school, and work. With increased survival rates, the focus of clinical research in the pediatric cardiac population has paralleled this population shift and transitioned from short-term surgical survival to the assessment of long-term morbidity. Among pediatric patients with complex CHD, there is a distinctive pattern of neurodevelopmental and behavioral impairment characterized by mild cognitive impairment, impaired social interaction, and impairments in core communication skills, including pragmatic language, as well as inattention, impulsive behavior, and impaired executive func-

tion.[3–5] Many school-aged survivors of infant cardiac surgery require habilitative services, including tutoring, special education, and physical, occupational, and speech therapy.[6,7] The neurodevelopmental and psychosocial morbidity related to CHD and its treatment often limit ultimate educational achievements, employability, lifelong earnings, insurability, and quality of life (QOL) for many patients.[7–14] A significant proportion of patients with complex CHD may need specialized services into adulthood.[12,13] Incorporation of a new stratification method and clinical algorithm may result in increased surveillance, screening, evaluation, diagnosis, and management of developmental disorders or disabilities (DDs) in the complex CHD population and consequent improvement in neurodevelopmental and behavioral outcomes in this high-risk population. With early identification of DDs and developmental delays, children have the best chance to reach their full potential.

Despite the well-documented presence of DD in the CHD population,[5,15–17] no practice guidelines for the evaluation and management of these impairments currently exist. Because the developmental surveillance and screening regimen currently used during routine pediatric care is not designed to prioritize children at known risk for DD, CHD patients may be delayed in referral for evaluation and early intervention. In addition, uncertainty about which care providers should be responsible for overseeing the management of these DDs can also hinder optimal and efficient care. This statement will review the factors underlying the increased risk for DD in the CHD population, recommend a CHD algorithm for DD that incorporates risk stratification, review age-based management of CHD patients, and discuss the impact of DD on QOL for the CHD population. Through review and synthesis of the current body of knowledge, the present statement seeks to provide a new framework for the surveillance, screening, evaluation, and management of DDs in the pediatric CHD population. Recommendations are evidence based and derived from published data. MEDLINE and Google Scholar database searches from 1966 to 2011 were conducted for English-language articles cross-referencing CHD with pertinent search terms (ie, attention deficit hyperactivity disorder, autism spectrum disorders, brain injury, behavioral issues, cardiopulmonary resuscitation, developmental disorder, developmental disability, developmental delay, developmental screening, fine and gross motor abnormalities, genetic disorder or syndrome, heart transplantation, mechanical support, microcephaly, neurodevelopment, neurodevelopmental outcome, periventricular leukomalacia, prematurity, prolonged hospitalization, psychological issues, psychosocial abnormalities, quality of life, seizures, stroke, transition, and adult CHD). The reference lists of identified articles were also searched. Published abstracts from major pediatric scientific meetings in 2010 and 2011 were also reviewed. Classification of recommendations and level of evidence were assigned to each recommendation per the manual for American College of Cardiology (ACC)/American Heart Association (AHA) guideline writing committees ("Methodologies and Policies From the ACC/AHA Task Force on Practice Guidelines," section 4: writing recommendations). The ACC/AHA guidelines grading schema based on level of evidence and class of recommendation (Table 1) were used.[18] The level of evidence classification combines an objective description of the existence and the types of studies that support the recommendation and expert consensus, according to 1 of the following 3 categories:

1. Level of Evidence A: Recommendation based on evidence from multiple randomized trials or meta-analyses.
2. Level of Evidence B: Recommendation based on evidence from a single randomized trial or nonrandomized studies.
3. Level of Evidence C: Recommendation based on expert opinion, case studies, or standards of care.

1. Note Regarding Language

For consistency, this statement uses terminology in accord with the 2006 American Academy of Pediatrics (AAP) policy statement on developmental surveillance and screening policy for the general pediatric population.[19] Developmental "disorder" and "disability" (DD) are used equivalently within the context of this document and refer to the existence of a neurocognitive or neurobehavioral limitation or abnormality, psychosocial maladjustment, or physical limitation.[19] In contrast, "development delay" is used to denote that a child's developmental maturation or "mental and/or physical skills are not consistent with the typical time frame."[19] Surveillance, screening, and evaluation have distinct meanings and are defined as follows: (1) *Surveillance*—"the process of recognizing children who may be at risk for developmental delay"; (2) *screening*—"the use of standardized tools to identify and refine the risk" recognized from surveillance; and (3) *evaluation*—"a complex process aimed at identifying specific developmental disorders or disabilities that are affecting a child."[19] The term *medical home* is per the 2002, 2005, and 2006 AAP policy statements and is "the optimal setting for family-centered care coordination."[19–21]

2. Patients With CHD Have Increased Risk for DD

2.1. CHD Prevalence and Patient Survival

The prevalence of CHD is estimated to be 9 per 1000 live births,[22,23] with 3 per 1000 requiring catheter-based or surgical intervention early in life.[24] An estimated 85% of children diagnosed with CHD will survive into adulthood,[25] yielding between 1.0 and 2.9 million adult survivors with CHD.[26] Survival rates vary by disease complexity: Long-term survival (>20 years) rates for children are estimated to be 95% for simple CHD (eg, isolated semilunar valve disease, atrial and ventricular septal defects), 90% for moderate-severity CHD (eg, coarctation of the aorta, atrioventricular septal defect, ventricular septal defect with comorbidities, tetralogy of Fallot [TOF]), and 80% for CHD of great complexity (eg, single ventricle, truncus arteriosus, complex transposition of the great arteries [TGA]).[27] Although specific types of complex CHD (eg, hypoplastic left heart syndrome) may have lower survival rates, overall survival rates have increased for even the most complex palliated defects.[1] For those with complex CHD, adults are now believed to outnumber children.[28,29]

Table 1. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT: CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test: COR III: No benefit — Not Helpful; COR III: Harm — Excess Cost w/o Benefit or Harmful Treatment: No Proven Benefit; Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

2.2. Prevalence of DD in the CHD Population

The prevalence and severity of DD and developmental delay increases with the complexity of CHD[30] and is associated with several genetic syndromes[31–38] (Figure 1; Table 2). Recent studies have shown that children with complex CHD have a significantly increased risk for DD in the areas of intelligence,[15–17,47,48] academic achievement,[5,16,17,48,49] language (development, expressive and receptive),[5,15,16,48,50,51] visual construction and perception,[5,16,49,52–55] attention,[5,6,16,49,51,56] executive functioning,[51,57] fine motor skills,[15,48,49,51,52] gross motor skills,[5,15,48,50,58,59] and psychosocial maladjustment (internalizing and externalizing problems).[60–65]

3. Risk Categories and a CHD Algorithm for DD

Given the prevalence of DD in specific subpopulations of complex CHD and in patients with CHD and certain comorbidities, this statement proposes specific low- and high-risk groups (Table 3) for DD to facilitate early evaluation, diagnosis, and intervention that may improve developmental outcome. In addition, a CHD algorithm for surveillance, screening, evaluation and management of DD was developed (Figure 2A and 2B) to complement the general algorithm from the AAP 2006 policy statement entitled, "Identifying Infants and Young Children with

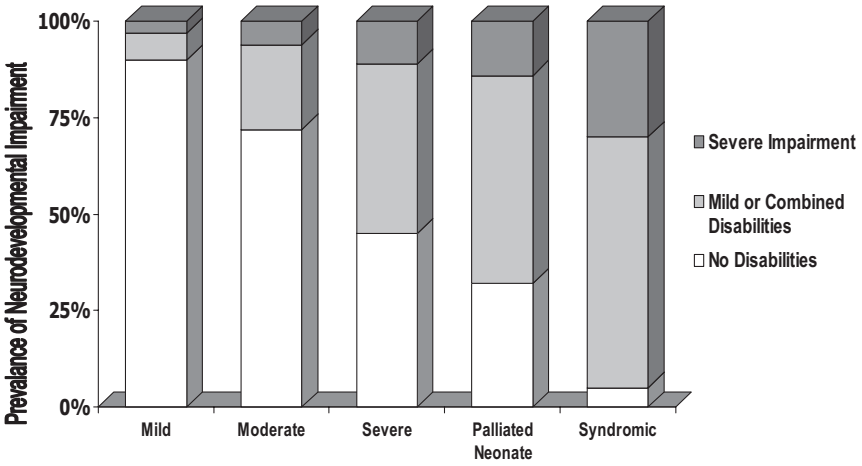

Figure 1. Prevalence of neurodevelopmental impairment in the population with congenital heart disease (CHD). Schematic representation of developmental disorders or disabilities (DDs) in children with CHD. Children with milder forms of CHD (eg, atrial septal defect or ventricular septal defect, isolated semilunar valve disease) have a low incidence of DDs. Increasingly complex forms of moderate 2-ventricle CHD (eg, coarctation of the aorta, complex semilunar valve disease, atrioventricular septal defect, ventricular septal defect with comorbidities, tetralogy of Fallot, total anomalous pulmonary venous connection) are associated with increasing numbers of children with DDs, and in severe 2-ventricle or palliated single-ventricle CHD (eg, transposition of the great arteries, truncus arteriosus, interrupted aortic arch, tetralogy of Fallot/pulmonary atresia with major aortopulmonary collateral arteries, pulmonary atresia with intact ventricular septum, hypoplastic left heart syndrome, tricuspid atresia), only the minority of children are completely normal in all respects. CHD associated with genetic disorders or syndromes (eg, Down syndrome, 22q11 deletion, Noonan syndrome, Williams syndrome) and multiple congenital anomalies (eg, CHARGE syndrome) are nearly always associated with DDs. Adapted from Wernovsky[39] with permission of the publisher. Copyright © 2006, Cambridge University Press.

Developmental Disorders in the Medical Home: An Algorithm for Developmental Surveillance and Screening."[19]

3.1. Medical Home Visit of a Patient With CHD

3.1.1. The Medical Home

Much of the focus of the pediatric cardiology and cardiac surgery community centers on optimizing high-acuity, hospital-based care for children with CHD; however, important long-term care issues for this population include neurodevelopmental surveillance, screening, evaluation, and management. To achieve the best care for this population, a coordinated care model is needed. The US Department of Health and Human Services' *Healthy People 2010* goals and objectives state that "all children with special health care

Table 2. Common Genetic Syndromes Associated With CHD and Developmental Disorder or Disability

Syndrome	Common Genetic Cause*	% With CHD	Common Lesions*	Developmental Disorder or Disability
Alagille	*JAG1* gene mutation or deletion	85	PPS, TOF	IQ varies between normal and moderate intellectual disability
CHARGE	*CHD7* gene mutation or deletion	>50	TOF, IAA, TA, PDA, VSD, ASD	Intellectual disability in almost all cases[38]
Down	Trisomy 21	40	AVSD, VSD, TOF, PDA	Median IQ <50[31,32]
Deletion 22q11	22q11.2 microdeletion	60	IAA, TOF, TA	Mean IQ 70–80[33,34]; ADHD[40,41]
Jacobsen	11q23 deletion	65	HLHS	Intellectual disability in 97% of cases[37]
Noonan	*PTPN11* gene mutation; *SOS1, RAF1, KRAS, or NRAS* gene mutations (less common)	>50	PVS, ASD, HCM	Mean IQ 84[42–44]
Turner	Monosomy of chromosome X	30	BAV, CoA	Mean IQ 90[35,36]
VACTERL	Unknown	75	VSD, ASD, PDA, TGA	Majority with normal IQ but majority with DD caused by multiple congenital anomalies; malformations
Williams	Microdeletion 7q11.23	60	SVAS, PPS	Mean IQ 56[44a]; visual-spatial impairments[45]; hypotonia/hypertonia[46]

CHD indicates congenital heart disease; PPS, peripheral pulmonary stenosis; TOF, tetralogy of Fallot; IQ, intelligence quotient; CHARGE, Coloboma of the eye, Central nervous system anomalies, Heart defects, Atresia of the choanae, Retardation of growth and/or development, Genital and/or urinary defects, Ear anomalies and/or deafness; IAA, interrupted aortic arch; TA, truncus arteriosus; PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, atrial septal defect; AVSD, atrioventricular septal defect; ADHD, attention deficit hyperactivity disorder; HLHS, hypoplastic left heart syndrome; PVS, pulmonary valve stenosis; HCM, hypertrophic cardiomyopathy; BAV, bicuspid aortic valve; CoA, coarctation of aorta; VACTERL, Vertebral anomalies, Anal atresia, Cardiovascular anomalies, Tracheoesophageal fistula, Esophageal atresia, Renal/kidney and/or Radial anomaly, Limb defects; TGA, transposition of the great arteries; DD, developmental disorder or disability; and SVAS, supravalvar aortic stenosis.

*Common genetic causes and common lesions for syndromes are available from OMIM (http://www.ncbi.nlm.nih.gov/omim; accessed October 2011).

Table 3. Categories of Pediatric CHD Patients at High Risk for Developmental Disorders or Disabilities

1. Neonates or infants requiring open heart surgery (cyanotic and acyanotic types), for example, HLHS, IAA, PA/IVS, TA, TAPVC, TGA, TOF, tricuspid atresia.
2. Children with other cyanotic heart lesions not requiring open heart surgery during the neonatal or infant period, for example, TOF with PA and MAPCA(s), TOF with shunt without use of CPB, Ebstein anomaly.
3. Any combination of CHD and the following comorbidities:
   - 3.1. Prematurity (<37 wk)
   - 3.2. Developmental delay recognized in infancy
   - 3.3. Suspected genetic abnormality or syndrome associated with DD
   - 3.4. History of mechanical support (ECMO or VAD use)
   - 3.5. Heart transplantation
   - 3.6. Cardiopulmonary resuscitation at any point
   - 3.7. Prolonged hospitalization (postoperative LOS >2-wk in the hospital)
   - 3.8. Perioperative seizures related to CHD surgery
   - 3.9. Significant abnormalities on neuroimaging or microcephaly*
4. Other conditions determined at the discretion of the medical home providers

CHD indicates congenital heart disease; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; PA/IVS, pulmonary atresia with intact ventricular septum; TA, truncus arteriosus; TAPVC, total anomalous pulmonary venous connection; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; PA, pulmonary atresia; MAPCA, major aortopulmonary collateral arteries; CPB, cardiopulmonary bypass; DD, developmental disorder or disability; ECMO, extracorporeal membrane oxygenation; VAD, ventricular assist device; and LOS, length of stay.

*Normative data by sex, including percentiles and *z* scores, are available from the World Health Organization (www.who.int/childgrowth; accessed February 2010).

needs will receive regular ongoing comprehensive care within a medical home,"[19–21] and multiple federal programs require that all children have access to an ongoing source of health care.[66]

3.1.2. Medical Home: Individualized Approach

The recommendations provided within this statement should be used to guide development of individualized follow-up plans for each patient on the basis of that patient's particular risk for late complications. A number of critical factors are likely to influence the approach for supportive interventions and therapies for children with CHD who have ongoing developmental concerns. For example, proximity to highly specialized pediatric care or familial work constraints that necessitate "after-hours" services may mean that 2 children with similar developmental concerns would need to receive support services using 2 separate, tailored approaches. Individualized plans should be developed through shared partnership and comanagement, which may include the primary care provider (eg, general pediatrician, family practitioner, nurse practitioner) and/or subspecialists (eg, pediatric cardiologist, pediatric neurologist, developmental pediatrician, psychologist, or other pediatric developmental specialist), the child, and the family, to coordinate and implement a specific care plan as an organized team.

3.1.3. Medical Home: Collaboration

An important component of the medical home is the acknowledgement of the need for consultation and appropriate referral to pediatric medical subspecialists and surgical specialists. Recently, focused neurodevelopmental follow-up clinics for children with complex CHD have been created at several pediatric cardiac centers in North America. These clinics have tremendous expertise in the identification of DDs and developmental delay through multidisciplinary teams, which may include a developmental pediatrician, pediatric psychologist, and neurologist, as well as important consultative services such as nutrition, special education or school intervention, speech and language therapy, and physical or occupational therapy. Children with CHD lesions of moderate or great complexity require lifelong care, initially by a pediatric cardiologist and later by an adult CHD specialist or cardiologist familiar with CHD.[13] It is therefore important that the primary, subspecialty, and surgical pediatric medical care providers collaborate to establish shared management plans in partnership with the child and family and to formulate a clear articulation of each other's role. Medical home providers should also interact with early intervention programs, schools, early childhood education, child care programs, and other public and private community agencies to be certain that the special needs of the child and family are addressed through the medical home.

3.1.4. Medical Home: Comprehensive Record

One of the other key elements of the medical home is the maintenance of an accessible, comprehensive, central record that contains all pertinent information about the child. It is incumbent on the pediatric cardiologist, cardiothoracic surgeon, hospitalist, and other health professionals involved in the acute care of a child with CHD to provide a comprehensive report of hospital-based care. The record should include relevant neuroimaging results, genetic testing, speech and feeding evaluations, and a projected plan of surgical care so that the medical home practitioners may better plan future care. This record should also include relevant educational records whenever possible. In addition, it is recommended that the primary care physician caring for the child with CHD within the medical home also maintain a comprehensive outpatient record (with notes on surveillance, screening and evaluation results, therapeutic and educational services, feeding issues, growth parameters, and immunizations).

Because many care centers are either using or transitioning to electronic health records, this format is recommended to facilitate the maintenance and accessibility of the comprehensive record. Although there are no standard formats for the electronic health record, accessibility and portability are critically important. This is especially important for adolescent and adult CHD patients, who will need to take their information with them as they transition through various medical providers during their adult years.

3.2. Risk Stratification

Inclusion of a risk-stratification step is a deviation from the original algorithm in the 2006 AAP statement on developmental surveillance and screening for the general pediatric population and classifies patients with CHD into low- and high-risk categories for DD. The incorporation of a risk-stratification schema specific to the CHD population is

intended to strengthen surveillance and screening for patients with CHD and to prioritize predisposed individuals for evaluation. Although many treatment- and patient-specific factors contribute to the increased risk for DD, certain categories of pediatric patients with CHD are at higher risk for DD (Table 3). More specifically, neonates or infants requiring open heart surgery (cyanotic and acyanotic types), children with other cyanotic heart lesions not requiring open heart surgery during the neonatal or infant period, and patients with CHD accompanied by certain comorbidities are all at increased risk for DDs. Even if a CHD patient is categorized as low risk for DD, continued surveillance is critical because the level of risk can change over time. This systematic assessment for risk should be comanaged by the primary care physician and the pediatric subspecialists within the medical home.

3.2.1. Neonates or Infants Requiring Open Heart Surgery (Cyanotic and Acyanotic Types)

In children with CHD, altered cerebral blood flow with impaired cerebral oxygen delivery, both in utero[67] and after birth,[68] may impact subsequent brain development. Recent studies have shown that in utero brain development is delayed in children with some types of complex CHD; thus, the brain is less mature and more vulnerable at birth than suggested by gestational age.[69] The fetal and neonatal periods are a critical time for brain growth and maturation, myelination, and development of neural networks. Altered cerebral blood flow and brain immaturity during these sensitive developmental periods may lead to increased risk of DD and susceptibility to injury.[70,71]

In addition, underlying CHD complexity often necessitates cardiac surgery during early infancy, and the morbidities that often accompany these medical, surgical, or catheter-based interventions may affect neurodevelopmental outcome. Research demonstrating the increased neurodevelopmental risk for children with CHD was predominantly performed in patients with single-ventricle CHD (eg, hypoplastic left heart syndrome) requiring Fontan palliation or in patients with complex biventricular CHD (eg, TGA, TOF) who had undergone surgical repair as a neonate or infant. Children who have undergone Fontan operations generally have lower intelligence quotient (IQ) scores than control populations.[16,17] Children diagnosed with TGA who have undergone the arterial switch operation using either CPB with deep hypothermic circulatory arrest (DHCA) or low-flow CPB are at increased risk for DD in the areas of intelligence,[5,15] academic achievement,[5] executive functioning,[5] language,[5,15,50] and fine and gross motor skills.[5,15,50] Evaluation of patients with TOF who have undergone surgical repair has shown increased risk for psychosocial maladjustment (internalizing and externalizing problems)[60] and decreases in intelligence (IQ),[48] academic achievement,[48] language (expressive and receptive),[48] gross motor function,[48] oral and speech motor control functions,[72] and attention (executive control).[56]

Methods of vital organ support during infant heart surgery, including CPB and DHCA, may result in cerebral macroemboli and microemboli to the central nervous system[30,73] or a period of global cerebral ischemia[74–76] and thereby contribute to observed DDs. These central nervous system events may contribute to the presence of acute arterial ischemic strokes or cerebral venous sinus thromboses or to the increased prevalence of periventricular leukomalacia in neonates and children after surgery for CHD.[77–79] In addition, for newborns with complex CHD who underwent cardiac surgery during the neonatal period or early infancy, subsequent operations with CPB during infancy are associated with decreased mental and psychomotor developmental indices at 1 year of age.[80]

3.2.2. Children With Other Cyanotic Heart Lesions Not Requiring Open Heart Surgery During the Neonatal or Infant Period

Children with cyanotic CHD who do not undergo neonatal or infant surgery (eg, TOF with shunt placement without the use of CPB, TOF with pulmonary atresia and major aortopulmonary collateral arteries, Ebstein anomaly) may avoid some of the inherent risks associated with open heart surgery. However, these patients may still be at higher risk of DD because of chronic hypoxemia caused by their underlying CHD or because of palliative or reparative surgeries that they may undergo later in childhood.[30]

3.2.3. CHD With Comorbidities

3.2.3.1. Prematurity and/or Developmental Delay Recognized in Infancy

In addition to the delay in brain maturation that is found in some CHD infants born at term, some infants with CHD incur the additional risk associated with premature birth. Premature infants (<37 weeks), especially those born weighing <1500 g, are at increased risk for developmental delay.[81–83] Lower birth weight and gestational age are also associated with DD in the complex CHD population.[80,84,85] A recent study showed that late-preterm infants without CHD had the same risk for DD as very preterm infants without CHD and were at a significant risk for requiring early intervention services at a corrected age of 12 months when the study corrected for neonatal comorbidities.[86] Another study that looked at the general population found that healthy late-preterm infants (34–36 weeks) compared with healthy term infants (≥37 weeks) had a greater risk for developmental delay and school-related problems through the first 5 years of life.[87] Two recent studies have shown that delivery of neonates with critical CHD before 39 weeks' gestation is associated with greater mortality and morbidity rates and greater resource use at progressively earlier gestational ages.[88,89] These data suggest that heightened developmental screening and evaluation may be valuable in CHD patients who are premature, including late-preterm infants born at 34 to 36 weeks' gestation.[69,90]

3.2.3.2. Genetic Abnormality or Syndrome Associated With DD

Genetic disorders or syndromes may be found in up to 30% of pediatric patients with CHD.[80] Down syndrome and other aneuploidies, Williams syndrome, Noonan syndrome, CHARGE syndrome, VACTERL association, and deletion 22q11 syndrome (also known as DiGeorge and velocardiofacial syndromes) are all genetic anomalies that have a high rate of CHD and are associated with DD (Table 2).[91,92] In general, developmental status after surgery for a variety of CHD lesions is worse for children with genetic syndromes than for those without a diagnosed syndrome.[84,85,93–95] In addition,

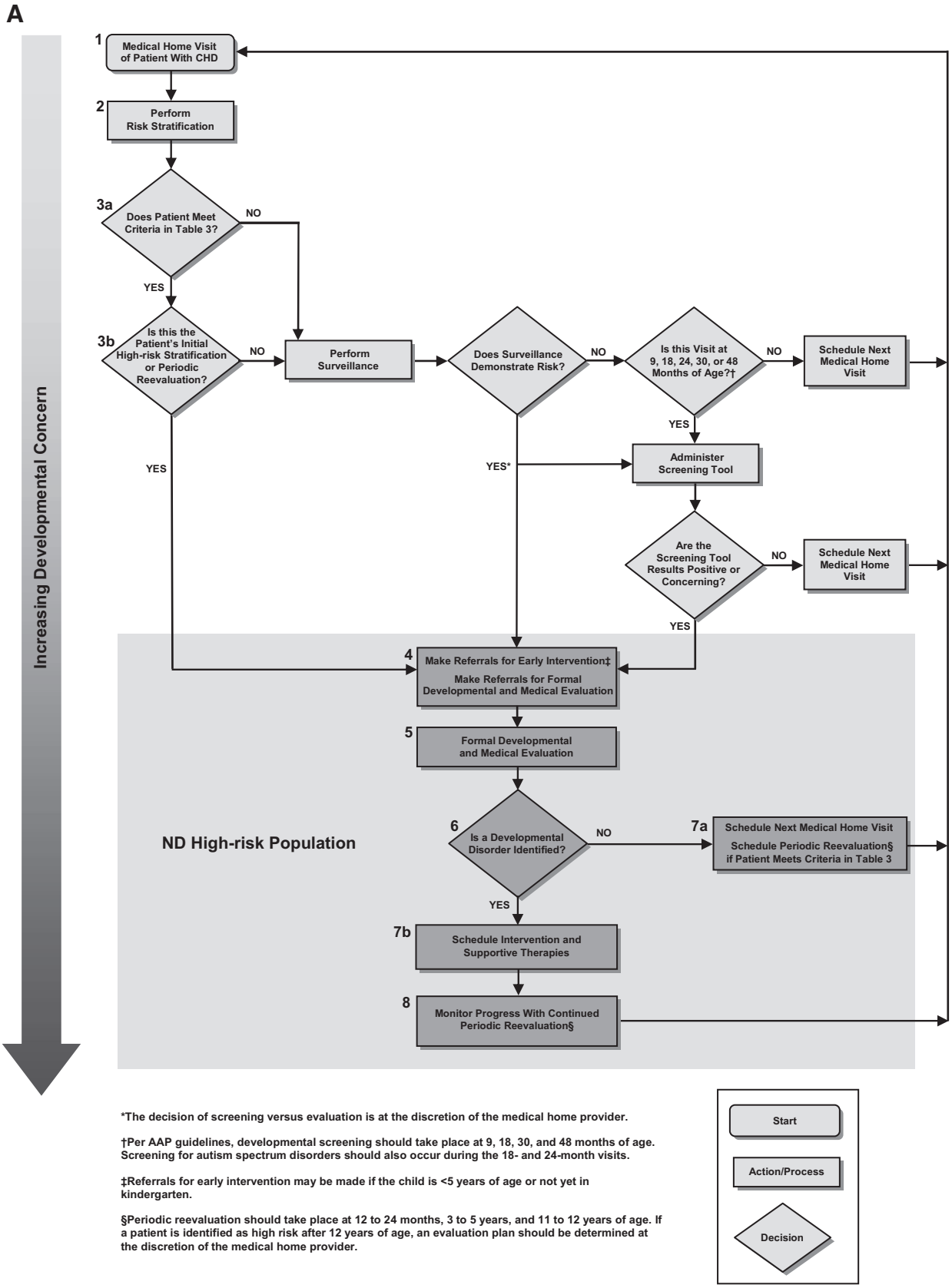

Figure 2. A, Congenital heart disease (CHD) algorithm for surveillance, screening, evaluation, and management of developmental disorders and disabilities. ND indicates neurodevelopmental; AAP, American Academy of Pediatrics.

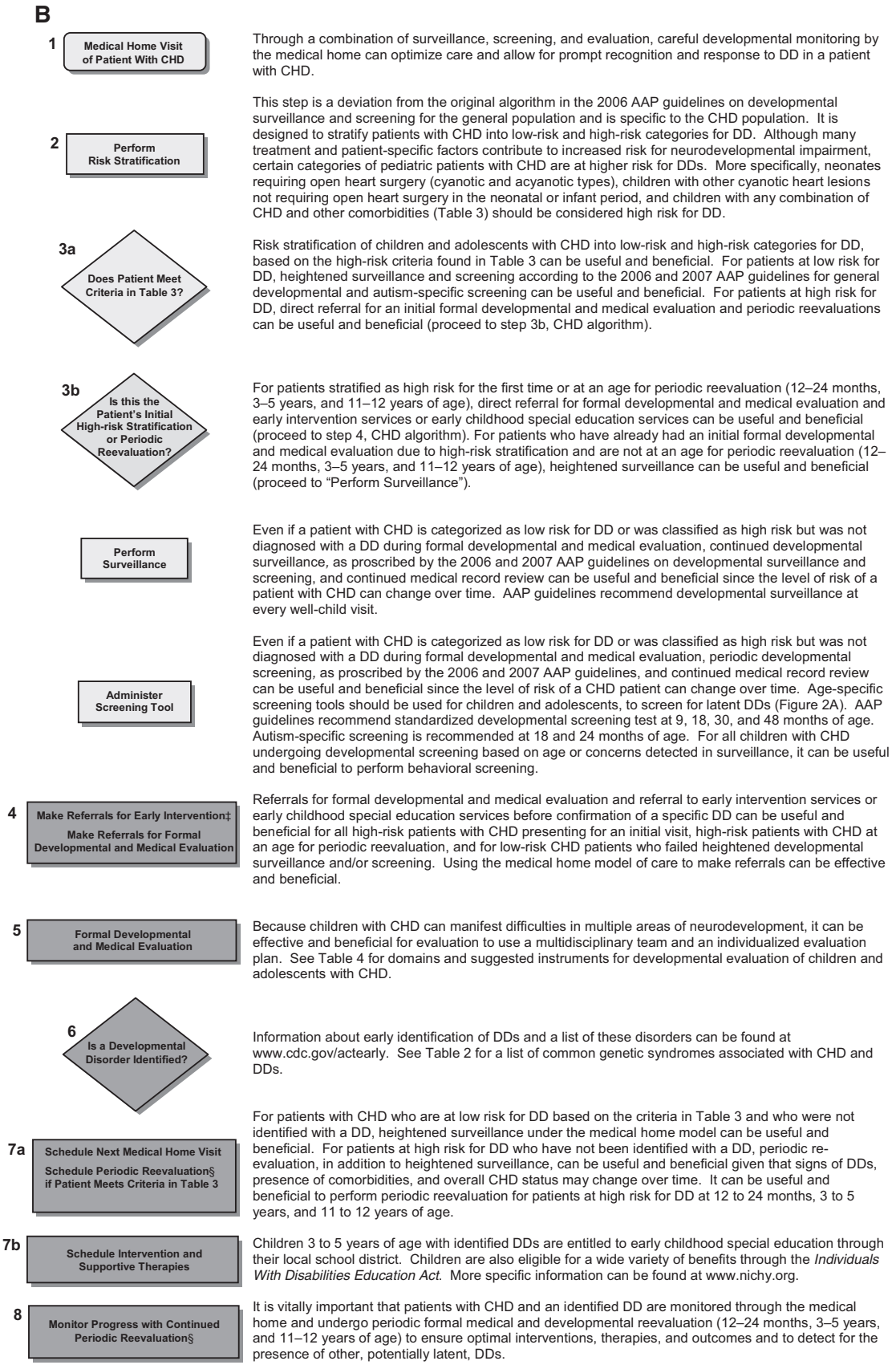

Figure 2 (Continued). B, Description of congenital heart disease algorithm for surveillance, screening, evaluation, and management of developmental disorders and disabilities. AAP indicates American Academy of Pediatrics, CHD, congential heart disease; DD, developmental disorder or disability.

gene-environment interactions involving susceptibility genes in multiple biological systems (eg, inflammatory and oxidative pathways, coagulation cascades, response to hypoxia/ischemia) may lead to poor outcomes by exacerbating central nervous system injury after cardiac surgery.[96] Polymorphisms of the apolipoprotein E gene (*APOE*) and the environmental factors associated with CHD and cardiac surgery are an example of a gene-environment interaction. APOE-containing lipoproteins are the primary lipid transport vehicles in the central nervous system and are thought to be important for neuronal repair.[97–99] A longitudinal study of a single cohort of pediatric patients with CHD found that the *APOE* ε2 allele had a negative impact on neurodevelopmental outcome after pediatric cardiac surgery.[3,84,100] Because neurodevelopmental outcome is highly and independently associated with the presence of an underlying syndrome or genetic abnormality,[92] early diagnosis is key to establishing a neurological and cognitive prognosis and to directing the patient and their family with regard to early intervention.

3.2.3.3. Mechanical Support or Heart Transplantation

Patients who require mechanical support (eg, extracorporeal membrane oxygenation and ventricular assist device) or heart transplantation are also at risk for DD.[101–113] Neurological events (eg, thromboembolism, hemorrhage) may occur when patients are placed on extracorporeal membrane oxygenation or ventricular assist devices with or without subsequent heart transplantation.[102,104,107,109] Developmental delays and disabilities after heart transplantation include delays in motor development, speech/language acquisition, and abstract reasoning/goal-directed behaviors[110] and impairments in IQ,[111] expressive language,[111] visual-motor skills,[111] fine motor skills,[111] psychosocial functioning,[112] and psychomotor scores.[113]

3.2.3.4. Cardiopulmonary Resuscitation

Patients with CHD who require cardiopulmonary resuscitation generally undergo a period of decreased cerebral perfusion or hypoxemia that may result in permanent neurological injury or predispose them to subsequent DD.[114,115]

3.2.3.5. Prolonged Hospitalization

Prolonged hospital length of stay is associated with worse neurodevelopmental outcome and may be a surrogate for the effect of medical complexity on neurodevelopmental function.[80,116] When adjusted for perioperative and sociodemographic variables, longer postoperative cardiac intensive care unit length of stay and hospital length of stay (>2 weeks) were each associated with poorer late cognitive function in 8-year-old children with TGA who had undergone the arterial switch procedure during the neonatal period; patients in the longest quartile of cardiac intensive care unit length of stay had an average IQ that was 7.2 points (almost one-half standard deviation) lower than those in the shortest quartile.[116]

3.2.3.6. Perioperative Seizures Related to CHD Surgery

Seizures are a common manifestation of acquired neurological injury in children in the acute postoperative period after cardiac surgery.[15,50,117–120] Perioperative seizures may be associated with particular CHD anatomies, aortic arch obstruction, and genetic conditions, as well as use of DHCA and prolonged DHCA time.[117,119,121] Newburger et al[117] showed that clinical seizures within 7 days after heart surgery were more common in infants whose repair was performed with a predominant DHCA strategy (11.5%) versus with predominant low-flow CPB (1.2%). In the same cohort, seizures seen by electroencephalography within 48 hours of surgery were also more frequent in the DHCA group (25.7% versus 12.9%).[117] When the cohort reached age 16 years, seizure in the postoperative period was the medical variable most consistently related to adverse neurodevelopmental outcome.[122] However, Clancy et al,[120] in another large, single-center study, showed that neonates and infants who underwent CPB had no clinically apparent seizures and a similar incidence of electroencephalogram-detected perioperative seizures (11.5%) with or without DHCA within 48 hours after surgery. Reports vary on whether perioperative seizures predict lower neurodevelopmental outcome when evaluated at 1 year of age[50,118,123]; however, these differences may be related to center-specific resources and management strategies or era effect. Perioperative seizures have been linked to an increased risk for worse neurodevelopmental outcome and neurological abnormalities in preschool-aged children.[15,50]

3.2.3.7. Significant Abnormalities on Neuroimaging or Microcephaly

There appears to be an association between CHD and structural brain abnormalities or microcephaly that may contribute to neurological impairments and developmental delay.[30,124,125] Alterations in cerebral blood flow have been noted in fetuses with complex CHD.[67,126,127] Several studies have noted that third-trimester fetuses diagnosed with CHD had impaired volumetric brain growth.[128,129] Notably, a study that assessed brain maturation by magnetic resonance imaging (MRI) in a cohort of full-term neonates with CHD after birth revealed an average brain maturation of only 35 weeks' gestation.[69] Newborns with complex CHD who require a palliative or reparative surgical procedure as a neonate or infant have a prevalence of microcephaly that varies from 8% to 33%, depending on the specific lesion,[68,70,125,130,131] and half will have abnormal neurobehavioral findings (hypotonia, hypertonia, jitteriness, motor asymmetries, and absent suck) before any cardiothoracic surgical intervention.[70] Low brain maturity scores have been shown to be associated with a higher risk of acquired brain injury in newborns with CHD.[132] Chen et al[79] found that the incidence of stroke on brain MRI in infants who had undergone an operation with CPB for CHD was 10%; however, most strokes were clinically silent and would not have been detected in the short-term without the use of neuroimaging. Another study found that the incidence of periventricular leukomalacia in neonates with CHD increased from 16% before surgery to 48% after surgery.[77] Abnormalities on neuroimaging, including stroke and periventricular leukomalacia, have been shown to be associated with DD.[77] The identification of significant structural lesions or acquired brain injury, such as stroke or higher grades of periventricular leukomalacia, may be an indication for more formal developmental evaluation.

3.3. Does the Patient With CHD Meet the Criteria for the Neurodevelopmental High-Risk Category?

Patients with CHD present with a spectrum of neurodevelopmental risk from low to high. This risk is not based solely on

disease severity, because some patients with less complex CHD may be deemed high risk. The present statement recommends that children and adolescents with CHD be stratified into low-risk and high-risk categories for DD or developmental delay based on the high-risk criteria found in Table 3. Patients at low risk should be screened according to the 2006 and 2007 AAP guidelines for general developmental and autism-specific surveillance and screening.[19,133] High-risk patients should be referred directly for formal developmental and medical evaluations (Figure 2). Because different types of DDs become apparent during certain developmental periods, all patients must be monitored throughout childhood and adolescence and evaluated with age-specific tools for latent DDs (Table 4). Through this combination of surveillance, screening, evaluation, and reevaluation, careful developmental monitoring by the medical home providers can optimize care and allow for prompt recognition and response to DD or developmental delay.

3.3.1. Perform Surveillance

Surveillance should be performed in all children with CHD. The prompt and accurate recognition of DD is one purpose of the medical home and a key element of comprehensive care for children. The AAP has advocated this objective through policy statements that emphasize several important components of developmental surveillance, including its incorporation into every well-child preventive care visit.[19,133,138,139] The combination of surveillance and formal screening, as discussed below (Administer Screening Tool), is intended to achieve the earliest identification and treatment of DD and related conditions. Although the 2006 AAP policy statement on developmental surveillance and screening is designed for the general population, children with CHD require heightened surveillance, including systematic risk stratification (Table 3) for early identification of developmental problems. Surveillance involves the following critical elements.

3.3.1.1. Elicit and Attend to the Parents' Concerns

Responses obtained through posing questions to parents or caregivers regarding their concerns about their child's development can be a powerful predictor of developmental problems.[140] Similarly, concerns expressed by the parents of a child with CHD should be evaluated and triaged appropriately, because these discussions may provide important information beyond the data obtained by formal screening.

3.3.1.2. Maintain a Developmental History

The traditional inquiry around developmental milestones allows medical home providers to recognize delays, disorders, or other developmental problems in a child. However, a developmental history is also useful for tracking the progress of children receiving therapies for known developmental concerns and for monitoring of latent problems. It is important to use appropriate developmental milestones for each child (eg, trisomy 21 milestones for a child identified with that syndrome, rather than general milestones).

3.3.1.3. Make Accurate and Informed Observations of the Child

Observation of a child's development by the medical home providers during all medical home visits remains an important part of overall surveillance.

3.3.1.4. Identify the Presence of Risk and Protective Factors

CHD itself is a significant risk factor for developmental problems. Specific risk factors may be identified through past medical history, perioperative course, and presence of a known genetic or neurological disorder. Additional risk factors may include parental guilt relative to causation of birth defect, attachment issues, fear of the child dying, stress related to surgeries, and parental competence with regard to feeding issues. However, the influence of noncardiac risk and protective factors (eg, environmental, demographic, and familial) should also be considered. Risk factors may be balanced by protective factors in the environment or family. For example, higher socioeconomic status may be a particularly important predictor, potentially having a greater impact than many clinical or operative factors on neurodevelopmental outcome. Socioeconomic status has been shown to have a positive correlation with IQ and academic achievement in pediatric patients with CHD.[48,80,92,141]

3.3.1.5. Document the Process and Findings

Creation of a formal developmental record is recommended to allow families, caregivers, and other medical home providers to better understand a patient's suspected or diagnosed DD or developmental delay and alter care management appropriately (eg, arranging for specific follow-up visits or additional evaluations as indicated).[142]

3.3.2. Screening Versus Evaluation

When a developmental concern is identified through surveillance, the medical home provider should either screen the child for confirmation of the developmental delay using standardized developmental screening tools or directly refer the child for formal developmental evaluation (Figure 2). The decision between screening and evaluation is made at the discretion of the medical home providers, who will balance the individual needs of the child with the specific resources locally available.

Formal developmental evaluation is composed of more detailed testing that typically requires specially trained medical or developmental professionals and standardized instruments of greater length and depth. The aim of evaluation is for identification of the specific DD affecting the child and his or her appropriate management (as discussed in Formal Developmental and Medical Evaluation). On recognition of a significant developmental delay or DD by evaluation, a child should be referred for early intervention services, including special early childhood instruction or education and developmental therapies such as motor or speech-language therapies (as discussed in Schedule Intervention and Supportive Therapies).

3.3.3. Administer Screening Tool

A formal algorithm on developmental surveillance and screening in the general population was published in the 2006 AAP policy statement and the 2008 *Bright Futures* guidelines.[19,143] Screening tools should be administered to children with CHD who are undergoing age-recommended screening and to children with CHD for whom DD or developmental delay is suspected on the basis of surveillance. Formal, standardized developmental screening tools are recommended to be adminis-

Table 4. Domains and Suggested Instruments for Developmental Evaluation of Children and Adolescents With CHD

Age-Specific Measurement		
Age	Evaluation Component	Examples
Infant (birth to 1 y)	Developmental history Growth Feeding history Neuromotor examination Audiologic examination	
Toddler (1 to 3.5 y)	Standardized developmental measure	• Bayley Scales of Infant Development–III[4] • Mullen Scales of Early Learning[134]
	Behavior parent report	• Child Behavior Checklist[135] • Brief Infant-Toddler Social Emotional Assessment[115]
Preschooler (3.5 to 5 y)	Standardized developmental measure	• Differential Ability Scale[64] • Stanford-Binet 5th Edition[136] • Wechsler Preschool and Primary Scale of Intelligence[63]
	Speech-language evaluation (if impairment noted)	
	Behavior parent report	• Behavior Assessment System for Children[137] • Child Behavior Checklist[135]
Child and adolescent (6 to 18 y)	Intelligence	• WISC-IV*
	Academic achievement	• WIAT-III* • WJ-III* • WRAT-IV*
	Language	• CELF-IV* • EVT* • NEPSY-II* • PPVT* • WJ-III*
	Visual construction and perception	• NEPSY-II* • ROCF* • VMI* • VMI Supplemental–Visual Perception*
	Attention	• CPT-II* • NEPSY-II*
	Processing speed	• CPT-II*
	Memory	• CMS* • NEPSY-II* • WRAML-II2*
	Executive functioning	• BRIEF† • D-KEFS* • NEPSY-II* • ROCF* • Tower of London* • Wisconsin Card Sorting Test2*
	Fine motor skills	• BOT-2* • Grooved Peg Board* • NEPSY-II* • PDMS-II* • SIB-R‡ • Vineland-II‡ • VMI Supplemental–Motor Coordination2*
	Gross motor skills	• BOT-2* • PDMS-II* • SIB-R‡ • Vineland-II‡

(*Continued*)

Table 4. Continued

Age-Specific Measurement		
Age	Evaluation Component	Examples
	Presence of ADHD	• ADHD-IV‡ • CBCL‡ • YSR§ • CRS-R‡§ • DISC-IV*‡
	Behavioral functioning	• BASC-21,2 • CBCL‡ • YSR§ • DABS‡
	Adaptive functioning	• SIB-R‡ • Vineland-II‡

All instruments listed have been used previously for evaluation in children and adolescents with CHD.

CHD indicates congenital heart disease; WISC, Wechsler Intelligence Scale for Children; WIAT, Wechsler Individual Achievement Test; WJ, Woodcock Johnson; WRAT, Wide Range Achievement Test; CELF, Clinical Evaluation of Language Fundamentals; EVT, Expressive Vocabulary Test; NEPSY, Neuropsychological Assessment; PPVT, Peabody Picture Vocabulary Test; ROCF, Rey-Osterrieth Complex Figure Test; VMI, Visual-Motor Integration; CPT, Conners' Continuous Performance Test; CMS, Children's Memory Scale; WRAML, Wide Range Assessment of Memory and Learning; BRIEF, Behavior Rating Inventory of Executive Function; D-KEFS, Delis-Kaplan Executive Function System; BOT, Bruininks-Oseretsky Test of Motor Proficiency; PDMS, Peabody Developmental Motor Scales; SIB-R, Scales of Independent Behavior-Revised; ADHD, Attention Deficit/Hyperactivity Disorder Rating Scale; CBCL, Child Behavior Checklist; YSR, Youth Self-Report; CRS-R, Conners' Rating Scale-Revised; DISC, Diagnostic Interview Schedule for Children; BASC, Basic Assessment System for Children; and DABS, Diagnostic Adaptive Behavior Scale.

*Self-report or direct testing of patient.

†Parent-proxy report only for children (5–10 years of age); parent-proxy (BRIEF) and self-report for adolescents (BRIEF-SR, 11–18 years of age).

‡Proxy report (parent or teacher).

§Adolescent report only (11–18 y of age).

tered at the 9-, 18-, 30-, and 48-month visits. A 48-month screening visit is being recommended by the present statement on the basis of the school-readiness 4-year-old visit recommended by the 2006 AAP statement and the ongoing developmental risks seen in children with CHD.[19] Autism-specific screening is recommended at 18 and 24 months of age.[19,133,139] Both of these AAP developmental screening statements recommend specific screening tools. Acceptable screening tests with good psychometric properties for practical use in the pediatric office are available for review through several sources.[19,144–146] These tests are reliable, valid, sensitive, and specific for the identification of developmental delay and typically require only a brief time for completion and scoring.[147] Current screening tests are of 2 types: (1) Parental questionnaires about the child's development and (2) patient screening tests that involve direct testing of a patient by a trained child health professional.[19,146,147] Parental questionnaires can often be completed by the parent before the visit or in the office waiting room. Specific information on screening for behavioral and psychosocial issues, autism spectrum disorders, and fine and gross motor skills is delineated below.

3.3.3.1. Behavioral and Psychosocial Issues

Concerns have arisen about the behavioral or mental health outcome of children with complex CHD.[4,6,68,69,71–73,81,140–142] These behavioral and psychosocial issues have been noted in children and adolescents with 2-ventricle CHD (eg, TGA, ventricular septal defect [VSD], and TOF), as well as single-ventricle CHD (eg, hypoplastic left heart syndrome).[4,60,61,63,64,134,136] The prevalence of "internalizing" problems (ie, anxiety, depression, withdrawal, somatization) and "externalizing" problems (ie, attention, aggression) are similar and range from approximately 15% to 25% by parent report in the CHD population.[4,60,64,122,134] In a cohort of CHD patients who had undergone atrial septal defect or VSD closure, arterial switch operation for TGA, and balloon-dilation valvuloplasty for pulmonary stenosis, parents perceived increased levels of behavioral and emotional problems (eg, somatic, social, attention, and internalizing problems).[136] In measures of functional health status of children 10 to 18 years of age who have undergone the Fontan procedure, parents have reported problems in behavior, mental health, and self-esteem.[63] Similarly, children with CHD 7 to 14 years of age who underwent surgery during the neonatal or infant period for TGA, TOF, or VSD have reduced school performance and total competence, as well as increased prevalence of internalizing, externalizing, social, and behavioral problems.[60,64] In addition, those with TGA or TOF have an increased risk of attention dysfunction.[6,56,64,73] Considering the widespread prevalence across the various CHD physiologies, one needs to consider heightened surveillance, screening, and evaluation for behavioral problems in all children with CHD. Parents and patients may be hesitant to mention these problems during routine clinical follow-up. Therefore, it can be useful and beneficial for medical home providers to directly question them for concerns about these issues.

During the process of surveillance, behavior should be monitored at every medical home visit from infancy through adolescence through risk factor analysis, history gathering, and observation. For all children with CHD undergoing developmental screening based on age (9, 18, 24, 30, and 48 months) or concerns detected in surveillance (early childhood through adolescence), it can be useful and beneficial to perform behav-

ioral screening. Screening for both developmental and behavioral skills at the 30- and 48-month visits is especially important, because this can serve in the early identification of the symptoms associated with common learning and behavior disorders seen during school age, including learning disabilities and attention deficit hyperactivity disorder (ADHD).

The behavior screening tests most useful in the pediatric setting are parent-completed questionnaires. Appropriate measures are age specific and are outlined in the 2010 AAP Task Force on Mental Health, "Enhancing Pediatric Mental Health Care."[137] Examples include using the Ages and Stages Questionnaire–Social Emotional[148] at the 9-, 18-, 24-, or 30-month visit and the Brief Infant-Toddler Social and Emotional Assessment[149] at the 18- and 30-month visits. The Pediatric Symptom Checklist[150] and the Strengths and Difficulties Questionnaire[151] are well suited for screening from 48 months of age through adolescence. In addition, the Vanderbilt Attention Deficit Hyperactivity Disorder Rating Scales may be used from 6 years of age and older to screen for ADHD, related behavior disorders (oppositional defiant disorder, conduct disorder, and anxiety and depression symptoms), and general academic and behavioral performance.[152] As with developmental surveillance and screening, further comprehensive behavioral or mental health evaluation as prescribed by the medical home providers can be useful and beneficial for children with CHD who show behavioral concerns on surveillance or screening.[153]

Routine screening for psychosocial adjustment problems by primary care practitioners is likely adequate for the majority of adolescents with CHD. For those with identified or suspected problems, however, more formal psychological evaluation may be warranted. There are multiple, well-established, psychometrically sound instruments used to evaluate psychosocial function in adolescents that allow comparison to healthy normative samples.[154,155] Use of multiple informants, including the adolescents themselves, parents, and teachers, provides a more comprehensive evaluation of the adolescent's psychosocial and mental health. Those adolescents with behavior or mental health concerns identified by screening should be referred for further evaluation by an appropriate behavioral or mental health specialist, with ongoing monitoring by the pediatric healthcare provider in the primary care medical home. The 2010 AAP statement on mental health guidelines for pediatric office–based mental health care[153] may serve as an appropriate guide for addressing screening and evaluation for behavioral and mental health disorders issues in adolescents with CHD.

3.3.3.2. Autism Spectrum Disorders

Autism spectrum disorders describe a group of developmental disabilities in which people have problems with socialization, communication, and repetitive and unusual behaviors.[156] Early signs of autism spectrum disorders may present as global developmental delays, and early detection is instrumental to improve prognosis.[139,157] These lifelong disorders include autistic disorder, Asperger disorder, and "pervasive developmental disorder, not otherwise specified."[156] In 2009, the Centers for Disease Control and Prevention reported an estimated prevalence of autism spectrum disorders of 9 per 1000 or 1 per 110 in children 8 years of age.[158]

A number of recent studies have suggested that children with CHD may be at increased risk for communication impairment,[54,111] decreased social competence,[159] and autism spectrum disorders[160–162] compared with the estimated prevalence for the general population. Bellinger[159] studied children with TGA and noted social impairments, including the inability to "read" other people ("theory of mind" domain). The prevalence of autism spectrum disorders in children with deletion 22q11 syndrome has been estimated at between 20% and 40%.[160,163] A slightly increased risk for autism spectrum disorders has been noted in children with congenital malformations compared with children who were born without congenital anomalies.[161,162] All children should be screened for autism spectrum disorders; however, heightened surveillance and screening for autism spectrum disorders in children with CHD is reasonable given that preliminary studies suggest increased risk. In accordance with current guidelines from the AAP, screening for autism should occur at 18 and 24 months at the child's regular well-child care visits.[133] Older children should be screened for behavioral and social concerns at their yearly preventive care medical home visit.[133] At any time, additional screening should be performed if a medical home provider is concerned that the child might be exhibiting symptoms of autism spectrum disorders.[133] Children who fail autism spectrum disorders screening should be referred for a specific diagnostic evaluation for autism spectrum disorders.[139]

3.3.3.3. Fine and Gross Motor Skills

Fine and gross motor functioning are critical to overall physical functioning and, depending on the severity of the motor impairments, may affect psychosocial function as well. The majority of studies investigating motor outcomes after surgery in children with complex CHD have revealed some degree of persistent impairment in fine or gross motor function[164–166]; however, results have varied depending on the measures used to evaluate motor function and age at time of evaluation.

Among children undergoing open heart surgery with CPB, 42% exhibited delays in gross or fine motor skills at a mean age of 19 months as measured by the Peabody Developmental Motor Scales.[167] When these children were reevaluated at 5 years of age, motor delay persisted: 49% had gross motor delays, and 39% had fine motor delays. Despite the prevalence of their motor impairments, severe disability was uncommon.[165] Gross and fine motor delay occurred more often in children undergoing palliative procedures, whereas fine motor delays were also associated with DHCA time, microcephaly, and number of hospitalizations.[165]

In a study of school-aged children who underwent surgical intervention for complex CHD within the first year of life, 42.5% had motor problems compared with 7% of age-matched healthy control subjects.[166] The risk of having any degree of motor difficulty was 6 times greater than that of healthy control subjects, and the risk of severe motor impairment was 11 times greater than for control subjects.[166] More than half of all children who experienced an arterial ischemic

stroke in the perioperative period had persistent sensory or motor impairments, with hemiparesis being the most common finding.[78]

These studies suggest that some degree of fine or gross motor impairment is common in survivors with complex CHD. Screening for fine and gross motor skill impairments in children with complex CHD should follow the current AAP guidelines[19] for the general pediatric population or be at the discretion of the medical care provider. For children with motor abnormalities detected by developmental screening, referral for formal neurodevelopmental evaluation, early intervention, and physical or occupational therapy can be useful and beneficial.[19]

3.4. Make Referrals for Early Intervention and Formal Developmental and Medical Evaluation

The *Individuals With Disabilities Education Act* mandates that every state provide early identification programs for infants and toddlers with developmental delays, established medical conditions, and biological risk factors that are highly associated with DD. Early intervention services (birth to 3 years of age) and early childhood special education services (3–5 years of age) are aimed at improving short- and long-term outcomes for children who are at risk for DDs, including but not limited to motor, cognitive, language, and social problems.[168] The National Dissemination Center for Children with Disabilities provides state-specific resources for families of children identified with a disability or delay (www.nichcy.org). Insurance coverage for testing varies for individual patients based on their specific insurance coverage.

For all high-risk patients with CHD and low-risk patients with CHD who failed developmental screening, referrals for early intervention services (as discussed in Schedule Intervention and Supportive Therapies) and formal developmental and medical evaluation before confirmation of a specific developmental diagnosis can be useful and beneficial. A triaging mechanism based on categories of risk for DD (low versus high risk) is shown in Figure 2. The primary medical home provider should refer all high-risk patients with CHD and low-risk patients with CHD who failed developmental screening to a developmental pediatrician, pediatric neurologist, pediatric psychologist, and/or geneticist, depending on the specific evaluations deemed necessary. Primary medical home providers should also consider referral of children with CHD, genetic syndromes, and developmental delay to early intervention so that children can receive services. The Centers for Disease Control and Prevention's "Learn the Signs, Act Early" campaign provides parents with educational materials on developmental milestones and early warning signs of delay (www.cdc.gov/actearly).

3.5. Formal Developmental and Medical Evaluation

3.5.1. Individualized Approach

Because children with complex CHD can manifest difficulties in multiple areas of neurodevelopment, developmental and medical evaluations require a multidisciplinary team. To best address the individual needs of the child, the composition of the evaluation team should be tailored according to the results of the baseline evaluation. Although the available qualified specialists will vary on the basis of local resources, the evaluation team will typically include pediatric healthcare providers with neurodevelopmental expertise in genetics, neurology, developmental pediatrics, and behavioral and neuropsychology, as well as related developmental professionals in fields such as speech language pathology, physical therapy, and occupational therapy. The next few sections focus specifically on genetic evaluation, structural brain imaging, and age-specific domains and instruments of the neurodevelopmental evaluation.

3.5.2. Genetic Evaluation

3.5.2.1. Early Identification

Prenatal diagnosis of CHD is common,[169] and genetic evaluation and counseling are often incorporated into prenatal counseling for fetuses with CHD. Depending on the type of lesion, associated findings, and parent preference, an amniocentesis or chorionic villus sampling may be performed to assess for a specific genetic diagnosis. Additionally, chromosome analysis with further testing, such as fluorescence in situ hybridization (FISH) or multiplex ligation-dependent probe amplification analysis for 22q11.2 microdeletion, may be used prenatally in fetuses with conotruncal anomalies (interrupted aortic arch, truncus arteriosus, TOF, VSD [conoventricular, conoseptal hypoplasia, and malalignment types] with aortic arch anomaly, or isolated aortic arch anomaly).[91,170]

General recommendations for genetic testing in children with CHD can be found in a 2007 AHA scientific statement endorsed by the AAP.[91] The approach to genetic testing after birth varies among centers, reflecting both the rapidly changing genetic testing options and the available expertise. In most centers, children with heart defects and concern for a possible genetic syndrome will undergo chromosome-based analysis. When aneuploidy is suspected, routine chromosome analysis should be performed with or without rapid FISH. In other cases of suspected genetic syndromes, chromosome microarray is increasingly becoming the test of choice given its comprehensive nature and increased diagnostic yield.[171] FISH testing for 22q11.2 microdeletion is suggested for all newborns and infants with conotruncal anomalies (interrupted aortic arch, truncus arteriosus, TOF, VSD [conoventricular, conoseptal hypoplasia, and malalignment types] with aortic arch anomaly, isolated aortic arch anomaly, or discontinuous pulmonary arteries) before surgical intervention, regardless of whether these children have facial dysmorphisms or other laboratory findings suggestive of the disorder. In addition, any child, adolescent, or adult with interrupted aortic arch, truncus arteriosus, TOF, VSD, or aortic arch anomaly not previously tested for deletion 22q11 syndrome should be tested for 22q11.2 microdeletion. Children with a 22q11.2 microdeletion should be referred to a geneticist for parent testing and counseling and for management.[172]

According to the 2007 AHA scientific statement on genetic testing in children with CHD, "genetic consultation is recommended in the presence of intellectual disability, multiple congenital anomalies, or facial dysmorphia or if the standard karyotype is normal despite the clinical suspicion of a genetic

abnormality."[91] In addition, genetic consultation should be considered in patients with CHD who have a DD or developmental delay, hypotonia, failure to thrive (not related to CHD), or microcephaly. Appropriate assessment of other organ system structural anomalies may include head ultrasound, brain computed tomography (CT) scan or MRI, and abdominal and renal ultrasound. A formal genetic consultation will allow for assessment of potential teratogens, recurrence risk for family planning (parents), potential associated problems in other individuals within the family, informed transition to adult care (reproductive concerns for the proband), and determination of whether additional genetic testing is required. Early identification of genetic conditions is valuable in counseling families about expected neurodevelopmental outcomes, as well as for planning for special services such as feeding and speech therapy and physical and occupational therapy.

3.5.2.2. Latent and Subtle Phenotypes

Genetic conditions commonly associated with CHD are most often recognized by their characteristic and distinctive phenotypes, including gross aneuploidy syndromes such as trisomy 21, 18, and 13 and Turner syndrome (Table 2). However, even among aneuploidies, the phenotypic features may be subtle, in some cases caused by mosaicism.[173] The diagnosis of Turner syndrome is often missed in the newborn period and should be considered in females with left-sided heart lesions as varied as bicuspid aortic valve, mitral stenosis, subaortic stenosis, aortic stenosis, coarctation of the aorta, partial anomalous pulmonary venous connection, and hypoplastic left heart syndrome.[173]

More than 750 genetic syndromes[174] are associated with CHD, of which only a small number are reliably detected by routine chromosome analysis.[21,22] The phenotypic features of many genetic syndromes are often not apparent during the newborn period. A recent study suggested that when children with CHD were reevaluated by a geneticist at 1 year of age, >10% of subjects were newly diagnosed with genetic disorders, most of which are associated with developmental delay.[80] Thus, diagnosis of genetic conditions is sometimes delayed by failure to recognize the possibility of a syndrome not caused by abnormal chromosome number (aneuploidy) or by failure to obtain relatively simple and cost-effective disease-specific genetic testing.

3.5.2.3. Specialized or Advanced Analyses

Even with the addition of FISH analysis for deletion 22q11 syndrome and Williams syndrome, standard cytogenetic testing may detect or confirm the diagnosis in only a fraction of children thought to have a genetic syndrome. As stated previously, the use of microarray technology is becoming more prevalent and may play an earlier or more widespread role in the diagnosis of genetic disorders in the future. Microarray detects all aneuploidies, including mosaicism (syndromes testable by FISH), as well as rare submicroscopic chromosomal deletions, duplications, and complex rearrangements (copy number variations), thus identifying many other genomic disorders that have not been detectable previously with standard techniques. Patients with CHD and DD may be diagnosed with genetic syndromes by microarray despite having "normal" findings on standard genetic evaluations. However, many genetic syndromes with CHD are caused by mutations in single genes rather than submicroscopic chromosomal deletions or duplications. These syndromes, such as Noonan syndrome, Alagille syndrome, or CHARGE syndrome, will not be detected by microarray and require direct testing of the causative gene rather than a chromosome-based approach.[42] Finally, in genetic syndromes for which the molecular basis has not yet been identified, a diagnosis is based on clinical features, some of which may not become apparent until later in childhood. When there is high suspicion for a genetic disorder, referral to a geneticist for evaluation and genetic testing is recommended.

3.5.3. Structural Brain Imaging

Before any complex neonatal cardiac surgery is undertaken, many centers obtain a head ultrasound on the basis of clinical history (eg, shock, severe hypoxia), specific neurological symptomatology, microcephaly, or other major noncardiac congenital anomalies. Preoperative head ultrasound is intended to identify major structural anomalies of the brain or intracranial hemorrhage that may worsen with the anticoagulation required for CPB. In some cases, additional neuroimaging with CT or MRI may be obtained to further delineate detected structural anomalies or brain injury that may influence the decision to proceed with surgery or the timing of surgery.

If a seizure is detected after cardiac surgery, careful evaluation and treatment are required. A pediatric neurology consultation is generally recommended. Under the guidance of a pediatric neurologist, basic evaluation should include an electroencephalogram and neuroimaging with CT. The initial head CT scan performed after a seizure episode or other acute neurological symptom allows for detection of hemorrhage or gross structural abnormalities. However, early ischemic stroke[175] or white matter injury[176] may be missed on head CT, because perioperative strokes in this population may be clinically silent.[79] Therefore, further imaging with MRI should be obtained as soon as clinically feasible.[177]

Although MRI has been used to measure and differentiate the neurological impact of various surgical strategies on the brain,[77,178,179] the indications for brain MRI for the asymptomatic child with CHD are poorly defined given the unclear prognostic value of abnormal findings and the lack of a consensus on the need for treatment of asymptomatic periventricular leukomalacia. When magnetic resonance techniques (MRI, diffusion tensor imaging, and spectroscopy) are used before and after cardiac surgery, full-term newborns with complex CHD will frequently demonstrate white matter abnormalities similar to those of premature infants.[77,180] However, performance of serial MRIs by 1 group has demonstrated that unlike the white matter lesions found in premature infants, the white matter lesions of infants after cardiac surgery may no longer be detectable by routine MRI within months of the original findings.[77] These results suggest that more sensitive imaging techniques may be required to visualize white matter injury in patients with CHD after resolution of the acute injury.[181] Studies evaluating the longer-term predictive validity of perioperative brain MRI in

the pediatric CHD population have not yet been reported. Because the significance of early evidence of periventricular leukomalacia remains undetermined in infants with CHD, one cannot conclude that the predictive value of MRI that has been substantiated in the very low-birth-weight population[182,183] applies equally to the CHD population. At present, a postoperative MRI in neonates with CHD is not routinely performed at most centers. However, brain MRI may be a useful clinical adjunct in individual patients, as determined by clinicians on a case-by-case basis, for the diagnosis and management of possible contributors to DDs.

3.5.4. Age-Specific Neurodevelopmental Evaluation: Domains and Instruments

The use of age-specific standardized measures for evaluation is recommended. These measures provide the practitioner with information about the child's functioning and enable the identification of deficits with known prevalence in the CHD population. Structured follow-up programs that focus on children who are at high risk for DD or exclusively on those with heart defects may be considered to optimize neurodevelopmental outcome. In all cases, evaluation needs to be paired with parent education and referral for any needed intervention. For infants, toddlers, preschoolers, school-aged children, and adolescents, the recommended domains for evaluation and appropriate instruments differ by age (Table 4). Table 4 provides examples of evaluation instruments that have been used in children and adolescents with CHD. Other instruments recommended for evaluation of children and adolescents are available in the AAP guidelines on developmental surveillance and screening[19,133] and mental health care.[137,153]

3.5.4.1. Infant/Toddler/Preschooler

Formal evaluation during infancy and early childhood (birth to 1 year of age, 1–3.5 years of age, and 3.5–5 years of age) may enhance early recognition of DD or developmental delays. Standardized measures for formal evaluation of infants, toddlers, and preschoolers are available and may be beneficial when used in conjunction with medical assessment of neurodevelopmental status. Inclusion of a developmental pediatrician, pediatric neurologist, and/or pediatric psychologist on the evaluation team is recommended. The medical home provider may also consider collaboration with local early intervention personnel.

3.5.4.1.1. Infant: Birth to 1 Year of Age. During the first year of life, all aspects of the development of an infant with CHD should be followed closely by the child's primary medical home provider. Formal evaluation should include the following:

1. *Developmental history:* Systematic comparison of the infant's developmental history to appropriate milestones. Any sign of developmental regression, as opposed to delay or impairment, should also warrant prompt investigation.
2. *Growth measurement:* Height, weight, body mass index, and head circumference.
3. *Feeding:* A thorough review of feeding, because feeding difficulties are common in children with CHD.
4. *Neuromotor examination:* Evaluation of passive and active muscle tone, primitive and deep tendon reflexes, sensory status (general hearing and vision), and quality of gross motor skills.
5. *Audiologic examination:* If there is suspicion of hearing loss, if the infant has undergone surgery since the neonatal audiologic examination, or if there is no record of a neonatal audiologic examination.
6. *Parent-child observation:* Clinical observation of interaction may aid in determining patient social interaction and language skills, parental stress, and its impact.

In addition, standardized measures as deemed appropriate by the developmental specialist should be performed.[139,140]

3.5.4.1.2. Toddlers and Preschoolers: 1 to 5 Years of Age. For toddlers and preschoolers with CHD, there are several developmental domains to monitor: Cognitive, gross motor, fine motor, communication (including speech, expressive language, receptive language, and pragmatics), adaptive skills, and social and behavioral interactions. There should be close surveillance for symptoms of autism spectrum disorders. The use of standardized measures designed for toddlers and preschoolers will typically provide standardized scores in cognition, language (receptive and expressive) and motor skills (fine and gross).[184] Table 4 has age-specific measures. For children who demonstrate impairments in speech and language, a formal evaluation by a speech and language pathologist is recommended. A parental report of a child's behavior is also recommended to detect behavioral problems and delays in social competence.

Evaluation of the preschool child with appropriate standardized scales is recommended before the child begins kindergarten (ages 3.5–5 years). Evaluation at this time optimizes identification and planning of additional educational supports and services before the child's entry into the educational system.

Unrecognized sensorineural hearing loss may impair normal language development and result in school or behavioral problems. Any child presenting with language delays should be considered for hearing testing. Children who have genetic syndromes (eg, CHARGE syndrome and 22q11 deletion syndrome) or have undergone extracorporeal membrane oxygenation therapy are at a higher risk for sensorineural hearing loss.[172,185,186] This hearing loss may be subtle or not appreciated during the newborn period or at 1 year of life. Children who have undergone extracorporeal membrane oxygenation may be at risk for progressive or delayed onset hearing loss.[187,188]

3.5.4.2. Child/Adolescent

Recent studies in children with complex CHD have suggested that DD may impact behavior and social cognition and may not be recognized until the child reaches school age or adolescence.[4,41,43,159] It is therefore critical to continue with systematic surveillance, screening, and evaluation in these age groups. For school-aged children and adolescents, measurement of IQ alone is not sufficient to provide an accurate and comprehensive understanding of a patient's functioning in these areas. Follow-up studies of children with complex CHD have identified multiple areas in which their mean

scores are lower than those of children in the general population, including fine and gross motor skills, visual construction and perception, attention, and executive functioning.[189] An evaluation must therefore encompass all the major domains of neuropsychological functioning, including intelligence, academic achievement, language, visual construction and perception, attention, processing speed, memory, executive functioning, and fine motor skills. In addition, evaluation of gross motor skills, the presence of ADHD, and issues related to behavioral and adaptive functioning can be useful and beneficial. However, evaluation should not be limited to these suspected areas, because a particular child may not present with a typical pattern of impairments or may have neuropsychological impairments or predispositions unrelated to CHD (ie, caused by prematurity or another medical condition) that may exacerbate his or her CHD-related morbidities. The mechanisms underlying the neurodevelopmental vulnerabilities of children with complex CHD are not understood to the degree that would permit prediction of the precise areas of weaknesses that would be expected in a particular child. Thorough evaluation and creation of a neurodevelopmental profile of a child or adolescent can be useful and beneficial in the development of an individualized management plan that builds on the child's particular strengths to mitigate the weaknesses.

For school-aged children and adolescents, DDs may become more apparent during times of transition when the complexity and types of developmental tasks required of the child increase. Difficulties arise as the complexity of the educational curriculum progressively increases, and it can be useful and beneficial to monitor the transitions between the following developmental and educational stages: (1) Acquisition of basic academic skills (ie, learning to read) typically occurs during the first grade (6–7 years of age); (2) application of basic academic skills to learn new material (ie, reading to learn) is usually required of children during the middle years of elementary school (8–10 years of age); and (3) acquisition and independent implementation of higher-order planning and organizational skills are needed for success as children enter and progress through middle school (11–14 years of age) and high school (15–18 years of age). Reevaluation for patients with CHD at high risk for DD may be useful and beneficial, because a child or adolescent who successfully managed an early transition may not be as successful managing a later transition.

During middle school (11–14 years of age) and high school (15–18 years of age), evaluations are important not only to track existing issues but also to detect presentation of new problems. Unlike younger children, older children (>10 years of age) with CHD have an increased risk for overall, internalizing, and externalizing behavioral problems.[62,65,136]

Adolescence is a critical time for identification of any preexisting or emerging impairments so that appropriate structure and supports may be implemented to maximize their potential through transition to adulthood. Further concerns that these young adults may face are addressed in the Transition to Adulthood section.

Age-appropriate instruments for evaluation of the aforementioned domains (neuropsychological, gross motor skills, presence of ADHD, and behavioral and adaptive functioning) are delineated in Table 4. Given the increased psychological maturity of adolescents, self-report can be useful and beneficial alone or in conjunction with parent and/or teacher report to identify neurodevelopmental concerns.

3.6. Is a Developmental Disorder Identified?

For some children, formal developmental evaluation will result in the diagnosis of a DD. Diagnoses are made with multiple sources of information and knowledge of a child's functioning in various settings. Information about the DD, including description, recommendations for intervention, and expected long-term outcome, may be beneficial to patients and families. Plans for patient management, including interventions and periodic reevaluation, should be discussed.

3.7. Schedule Periodic Reevaluation in Patients With CHD Deemed at High Risk for DD

All children with CHD should be followed up in the medical home for ongoing monitoring. Heightened surveillance in the medical home can be useful and beneficial for patients with CHD who are at low risk for DD based on the criteria in Table 3 who have not been identified with a DD. Because signs of DDs, presence of comorbidities, and overall CHD status can change over time, periodic reevaluation can also be beneficial in patients with CHD deemed at high risk for DD who have not been identified with a DD or developmental delay. Periodic reevaluation for CHD patients at high risk for DD or developmental delay should take place at 12 to 24 months, 3 to 5 years, and 11 to 12 years of age. Plans for scheduled reevaluations should be discussed with the family.

3.8. Schedule Intervention and Supportive Therapies

For those children with significant DDs or developmental delay, treatment services can be obtained through early intervention and special education programs in the United States. If a patient is determined to be eligible as a result of testing and a multidisciplinary team meeting, families will be offered services in the areas in which a child is delayed or disabled. Eligibility criteria for services differ from state to state. Details of state-specific requirements can be found at the National Dissemination Center for Children with Disabilities at www.nichcy.org. Infants to children 3 years of age who exhibit or are at risk for impairments are evaluated in their natural environment in 5 areas (social, communication, cognitive, gross and fine motor, and adaptive functioning), and interventions are scheduled, if required. Some infants or young children with CHD who are in the high-risk neurodevelopmental group may be referred to early intervention even before hospital discharge to implement timely provision of developmental support services. Children 3 to 5 years of age with significant developmental delay or disabilities are entitled to early childhood special education through their local school district.[190] For children >5 years of age, special educational supports and supportive therapies may be arranged through their local school district and medical home provider.

3.9. Monitor Progress With Continued Periodic Reevaluation in Patients With CHD With Identified DD

It is vitally important that patients with CHD with an identified DD or developmental delay be monitored through the medical home and undergo periodic formal medical and developmental reevaluation (12–24 months, 3–5 years, and 11–12 years of age) to ensure optimal interventions, therapies, and outcomes and to look for the presence of other potential latent DDs or developmental delays.

4. Management of DD in School-Aged Children and Adolescents With CHD

The presence of CHD has an impact on the everyday life of a significant number of children, adolescents, and families.[39,191,192] DDs of school-aged children may manifest themselves as developmental, academic, or behavioral issues, whereas DDs in adolescents may manifest themselves as psychosocial, behavioral, or social issues. In both school-aged children and adolescents with CHD, impairments in school and social competence, as well as behavioral problems and depression, have been noted.[64,65,135,191,193,194] Early recognition and subsequent management of these issues in children and adolescents with CHD may facilitate functional adaptation to overcome the perceived or diagnosed concerns.

4.1. School-Aged Child Developmental, Academic, and Behavioral Issues

DDs, academic difficulties, behavioral abnormalities, and psychosocial problems are some of the most prevalent and important consequences of pediatric heart conditions.[6,39,192] In a cohort of children with TGA who underwent a neonatal arterial switch operation, 55% had DDs or developmental delay at a mean age of 10.5 years compared with 26% at a mean 5.4 years of age, with the noted increase in prevalence mainly caused by the increased recognition of neurological abnormalities with fine and gross motor impairment.[64] Although most children with complex CHD have intelligence (IQ) within the normal range, school-aged children with CHD have a higher incidence of problems with visual-spatial or visual motor integration, executive functioning, academic difficulties, inattention, and hyperactivity, even after successful cardiac surgical correction or palliation.[54,56,59,141,195–197] In addition, low emotional, social, and school functioning was found in 23% of children 8 to 12 years of age with CHD.[192] In the 16-year follow-up of those children with TGA who underwent arterial switch operation who participated in the Boston Circulatory Arrest Trial, 65% received remedial academic or behavioral services.[122]

Learning disabilities, behavioral problems, and ADHD may result in persistent academic difficulties that potentially may have negative lifelong consequences, as discussed in Transition to Adulthood. Early neuropsychological evaluation for school-aged children who have concerning surveillance or screening results or who are at high risk for DD can be useful and beneficial for the identification of interventions that may help to optimize school performance. It may be beneficial for medical home providers to collaborate with education personnel in securing resources for the school-aged patient with complex CHD, because children with complex CHD are more likely to use special education services than the general population.[6,195] It may be beneficial and useful to have education specialists/school intervention personnel partner with medical home providers to assist the family with presentation of the formal medical and developmental evaluation to school personnel to maximize school support. At present, there are professional and cultural barriers and logistical challenges to collaboration. There are ongoing efforts by the AAP and other professional groups to improve these potential collaborations. A meta-analysis of studies on cognitive and psychological functioning revealed that children with complex CHD would benefit from interventions that specifically target visual-spatial abilities.[62] Interventions might include occupational therapy that specifically focuses on problems with writing skills or potentially an assistive technology evaluation for children who have difficulties writing quickly or reading what they write. Potential accommodations include using a computer and allowing more time to take tests. Further efforts are needed to identify the best approaches to remediation; however, an individualized plan can be formulated after a thorough evaluation of how the child learns.

4.1.1. Attention Deficit and ADHD

Recent studies suggest that compared with the general population, ADHD (inattentive type and combined type) may be more prevalent in children with a wide range of CHD, including but not limited to single-ventricle malformations, d-TGA, and total anomalous pulmonary venous connection.[6,16,49,56] Increased prevalence rates ranging from 40% to 50% have been described by several groups.[6,16,49,56,73,198] Children with ADHD are at high risk for injuries, poor academic performance, and social difficulties such as peer rejection.[199,200] Individuals with ADHD attain lower occupational status than peers and are at increased risk for developing problems with substance use and antisocial behavior.[200] Treatment of ADHD is essential to optimize the child's functioning and to prevent long-term consequences.[201] Optimal diagnosis and management of ADHD are achieved with multimodal interventions that can include pharmacotherapy, behavioral therapy, and psychoeducational interventions as recommended by the AAP.[202] Refer to the AAP Task Force on Mental Health Guidelines[137,153] and the AAP and AHA guidelines related to evaluation and monitoring of children who have CHD and ADHD.[203]

4.2. Adolescent Psychosocial, Behavioral, and Social Issues

Healthy developmental progress and psychosocial adjustment are critical to adolescents with chronic health conditions, because poor psychosocial adjustment may impinge on their successful transition from adolescence to adulthood (Transition to Adulthood). Adolescents with CHD must cope not only with the normative transitions of adolescence but also with developing an

appropriate sense of self, autonomy and independence from their parents, and self-management of their condition within the context of their illness.[204] The best approach to adolescent psychosocial adjustment, behavioral problems, and social issues is enhanced prevention through early childhood surveillance and detection, counseling, and management strategies that target normalization, social skills development, healthy self-perception, and planning for transition to adolescence and adulthood. Measurement of QOL, psychosocial and behavioral functioning, and patient and parental perceptions of and responses to a child's CHD can be useful and beneficial when included in routine follow-up of children and adolescents with CHD.

4.2.1. Psychosocial Adjustment

The added burden of chronic illness in adolescents with CHD places them at increased risk for mental health or social problems.[136,198,205,206] Self-perceived impaired psychosocial functioning is found in 18.6% of adolescents 13 to 18 years of age with CHD.[192] In a large multicenter cohort of 537 Fontan patients 6 to 18 years of age, parent responses on the Child Health Questionnaire (CHQ-PF50) indicated rates of problems with anxiety, depression, and behavior that were significantly greater, by 50% to 8-fold, than in the general population.[198] Successful adjustment is reflected in behaviors and perceptions that are age appropriate, normative, healthy, and follow a trajectory toward positive, autonomous adult functioning.[207] Adjustment to the stress of chronic illness is a complicated, multifactorial process and involves a highly subjective, personal interpretation of the impact of disease on one's life, which makes the self-reported perspective of the individual adolescent uniquely important. That the severity of disease does not predictably correlate with psychosocial outcomes[192,208] reflects the complexity of this process.

Tactics to foster healthy psychosocial adjustment include (1) encouraging normal life experiences, (2) improving coping and adaptive abilities, (3) helping children to empower themselves, (4) expanding social support networks, (5) addressing parent-identified needs, and (6) coordinating multidisciplinary care services.[209] The AAP has set a goal for advancement of behavioral and mental health competencies, as well as new strategies for education, for pediatric primary care clinicians to reduce mental health and substance abuse problems in the pediatric population.[210] Anticipatory guidance, health promotion, surveillance, and intervention when needed can help to prevent mental health problems associated with the typical transitions of adolescence.[143]

4.2.2. Behavior

Behavior has commonly been used as a measure of psychosocial adjustment in adolescents with chronic health conditions. Multiple studies have identified an increased incidence of behavioral problems in adolescents with heart disease.[16,53,56,64,211–216] Research has identified internalizing problems, particularly social withdrawal, anxiety, somatic complaints, and depressive symptoms, to be more common in older children with pediatric heart disease than in the general population.[62,64,135,198,211,213,214] Externalizing problems, most commonly attention deficits, and hyperactivity have also been identified in adolescents: however, these appear to be more prevalent in younger children with heart disease.[6,55,65,198] Anxiety and depression are forms of internalizing behavior problems that have been identified in subjects with pediatric heart disease.[135,217–222] The presence of these symptoms has been shown to directly impact health-related QOL.[48,64] These potential behavioral issues, especially anxiety, depression, social withdrawal, and attention deficits or hyperactivity, should be managed through the medical home.

4.3. Adaptive Functioning

Adaptive behavior is an age-related construct that reflects learned skills in conceptual, practical, and social arenas that are necessary for function in everyday life. Because of their underlying disease, its treatment, and related morbidities, children and adolescents with CHD may have increased difficulties acquiring these skills, often in the areas of daily living, social interaction and communication, and community living. Adaptation processes that have been found to influence child adjustment in the setting of childhood chronic illness include child self-esteem, expectations, beliefs about health locus of control, and coping skills.[223] Self-esteem is derived from perceptions of competence in areas of life considered important.[224] Notably, maternal perceptions have been found to be an important predictor of a child's emotional adjustment.[225–227]

Adaptation in children and adolescents with CHD can be fostered by helping them to develop improved perceptions of competence in areas they deem important or by helping them to reduce the level of importance assigned to areas in which their competence is hindered, such as daily living, social, communication, and community living skills. Therefore, a partnership among families, educational personnel, and medical caregivers may be useful and beneficial in recognition and management of problems and to maximize adaptive functioning. Involvement of developmental specialists and provision of adequate psychological, social, or rehabilitative supports will ultimately improve functional adaptation and enhance the health and well-being of a patient and family.[164]

4.3.1. Activities of Daily Living

Functional limitations in activities of daily living have resulted in reports of lower health-related QOL in children with heart disease.[208,228] Physical limitations, including activity restrictions, have also been associated with poorer self-concept and more behavioral problems.[229] It may be useful and beneficial for restrictions on physical and social activity to be reviewed. Counseling families to avoid overprotection and unnecessary restriction of a child or adolescent with CHD may be an important intervention.[192,208]

4.3.2. Social and Communication Skills

Social skill development and the ability to foster meaningful relationships with others are important developmental tasks of childhood and adolescence. The presence of strong social ability and skills for coping with stress are protective factors in fostering psychosocial health.[230] Impairments in social cognition,[231] reflected as limitations in skills needed to

interpret the thinking and actions of others, as well as limited awareness of one's own internal state, have been identified in children with complex CHD.[40,41,43,159] These difficulties in perceptual abilities may result in actions that are perceived as inappropriate behavior or poor communication skills and can limit a child or adolescent's ability to form healthy relationships.

4.3.3. Community Living Skills

Poor adjustment in the areas of vocation, social and domestic environment, and psychological distress has been identified in young adults with CHD.[232] Overprotective parenting and uncertainties about long-term prognosis may result in missed critical adolescent milestones that focus on development of autonomy in these important areas. Developmental immaturity and poor understanding of their illness may make adolescents with heart disease vulnerable to engaging in risk-taking behaviors such as substance abuse or sexual activity in an effort to feel similar to their peer group.[204]

5. Transition to Adulthood

An increasing number of patients with CHD are surviving to adulthood.[13,27] The development of an adequate model of transition to adult care is a key initiative and has been addressed in detail in recent AHA and ACC policy statements.[233,234] In addition, transition within the medical home should follow the recommendations found in the 2011 clinical report, "Supporting the Health Care Transition From Adolescence to Adulthood in the Medical Home," which has been endorsed by the AAP, American Academy of Family Physicians, and the American College of Physicians.[235] Patients with complex cardiac disease are more likely to have social functioning issues because of their increased risk for severe neurocognitive impairment.[8] For adults with CHD, particular attention is being given to their marital status, employment, insurability, educational achievement, and level of physical activity.[7,9,236,237] Vocational planning early in adolescence may be beneficial so that appropriate educational options can be pursued long before the patient enters the work force.[12]

5.1. Psychiatric Disorders and Self-Management

The prevalence of comorbid psychiatric disorders is 3 to 4 times higher among adults with neurocognitive impairment than in the general population.[10,11] In 1 cohort of 280 patients with CHD evaluated at a mean age of 32 years, 50% met diagnostic criteria for at least 1 mood or anxiety disorder.[238] Therefore, careful review of depression or anxiety symptoms and their potential overlap with symptoms of medical illness or medication side effects must be part of the clinical evaluation. However, social adjustment and patient-perceived health status are more predictive of depression and anxiety than medical variables.[11] Difficulties in these areas are related to factors that include impaired peer relationships, family overprotection, and delayed progression into independent adulthood.[8,10] Many adults with CHD struggle to assume greater independence and control over their health care and lifestyle and can have gaps in their knowledge about their disease, treatment, and prevention of complications.[239]

5.2. Impact of CHD on QOL During Transition to Adulthood

The overall QOL for adults with CHD is reduced compared with the general population.[9,240–244] Adult CHD patients often have reduced health status, exercise tolerance, and psychosocial impairments that diminish their QOL.[9,240–244] As these patients mature and transition their care to adult CHD programs, it is important that the patients, their families, and their future care providers are given the resources to address the neurodevelopmental, psychosocial, self-management, educational, and employment issues that impact their lives.[14] Future research should focus on neurocognitive sequelae, psychosocial functioning, and coping strategies of these patients in addition to the influence of ongoing medical variables on their QOL.

6. Impact of DD on QOL for Children With CHD

Although self-reported QOL related to physical health, psychosocial health, social functioning, and school functioning for children with CHD is reduced compared with healthy children,[192,208,245,246] few studies have investigated the impact of neurodevelopmental outcome on QOL in the pediatric CHD population. For children with d-TGA, Dunbar-Masterson et al[195] found that lower full-scale IQ (intelligence) and lower performance in reading and math (academic achievement) were associated with lower parent-reported psychosocial QOL scores at 8 years of age. Williams et al[58] found that children with Fontan palliation for hypoplastic left heart syndrome displayed significant delays in communication and motor skills and lower parent-reported psychosocial QOL scores. Of note, both of these studies used a generic QOL instrument to measure psychosocial QOL, which may not be as sensitive or accurate as a disease-specific instrument.[144] In addition, neither study measured patient-perceived QOL or specifically assessed the association between neuropsychological impairments and patient-perceived QOL. Parent-reported and self-reported QOL are both important, because perception of QOL differs between patients and parents.[192,247]

QOL research in children with CHD has been further advanced with the development of the cardiac-specific module of the PedsQL (Pediatric Quality of Life Inventory)[248,249] and the cardiac-specific Congenital Heart Adolescent and Teenager Questionnaire,[250] ConQol,[251] and Pediatric Cardiac Quality of Life Inventory.[252] The cardiac-specific module of the PedsQL includes a cognitive problems subscale and a communication subscale.[249,253] Using the PedsQL cardiac-specific module, Uzark and colleagues[192] found that children with severe cardiovascular disease have lower parent-reported and self-reported QOL scores on the cognitive problems subscale and lower parent-reported QOL scores on the communications subscale than children with less severe cardiovascular disease. Recently, Marino et al[57] demonstrated that worse executive functioning, gross motor ability, and

mood (presence of anxiety and depression) significantly predicted lower Pediatric Cardiac Quality of Life Inventory score after controlling for patient demographics and important clinical covariates. Executive functioning, gross motor ability, and mood accounted for up to 50% of the variance in patient- and parent-reported QOL scores. These factors appear to be key drivers of QOL in survivors with complex CHD and may be targets for future intervention.[57]

Further research is needed to discover links between specific aspects of neurodevelopmental outcome and QOL to identify DDs that may be improved through intervention. By characterizing the relationship between disease complexity, neurodevelopmental morbidity, and QOL, physicians and caregivers will be able to change the medical care delivery system to significantly improve the lives of children with CHD and ensure their future success.

7. Conclusions

Surveillance, screening, evaluation, and reevaluation of DD and developmental delays in the pediatric CHD population are essential steps to obtain appropriate interventions to maximize these children's potential overall development, QOL, and opportunity to become productive, responsible adults. As the population of pediatric and adult patients with CHD increases, risk stratification may be beneficial in efficiently promoting early recognition of neurodevelopmental morbidities and implementation of supportive therapies. Heightened and ongoing surveillance and screening are important for all pediatric patients with CHD. For those classified as being at high risk for DD, initial and periodic reevaluation will serve to monitor the impact of potential DDs. Further research on the efficacy of interventions and refinement of the criteria for high risk are needed to optimize preventive and interventional strategies for DDs in children with CHD. Finally, it is imperative that funding and reimbursement mechanisms be identified to appropriately cover the time and effort committed by pediatric healthcare providers with neurodevelopmental expertise and related developmental professionals.

8. Recommendations

1. **The medical home model of care may be effective and beneficial in the management of patients with chronic conditions such as CHD (*Class IIa; Level of Evidence B*).**
2. **Existing AAP guidelines for surveillance, screening, evaluation, and intervention should be adhered to, with the following additions for patients with CHD:**
   a. **The following groups should be considered at high risk for DD (*Class I; Level of Evidence A*):**
      (1) **Neonates or infants requiring open heart surgery (cyanotic and acyanotic types)**
      (2) **Children with other cyanotic heart lesions not requiring open heart surgery in the neonatal or infant period**
      (3) **Children with any combination of CHD and other comorbidities (Table 3)**
      (4) **Other conditions determined at the discretion of the medical home providers**
   b. **Risk stratification of patients with CHD into low- and high-risk categories for DD at every medical home visit can be useful and beneficial (*Class IIa; Level of Evidence C*).**
   c. **Behavioral screening of patients with CHD undergoing developmental screening based on age (9, 18, 30, 48 months) or concerns detected in surveillance (early childhood through adolescence) can be useful and beneficial (*Class IIa; Level of Evidence C*).**
3. **For patients with CHD stratified as being at high risk for DD, the following strategies can be useful and beneficial:**
   a. **Referral to formal developmental and medical evaluation can be useful and beneficial (*Class IIa; Level of Evidence C*).**
   b. **Referral to early intervention services or early childhood special education services before confirmation of a specific developmental diagnosis can be useful and beneficial (*Class IIa; Level of Evidence B*).**
   c. **Periodic reevaluations for DDs and developmental delays at 12 to 24 months, 3 to 5 years, and 11 to 12 years of age can be useful and beneficial (*Class IIa; Level of Evidence C*).**
   d. **Referral of young adults for higher education and/or vocational counseling can be useful and beneficial (*Class IIa; Level of Evidence C*).**

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Appendix. Abbreviations Used in This Scientific Statement

AAA	aortic arch anomaly
AAP	American Academy of Pediatrics
AHA	American Heart Association
ACC	American College of Cardiology
ADHD	attention deficit hyperactivity disorder
APOE	apolipoprotein E
CHD	congenital heart disease
CPB	cardiopulmonary bypass
CT	computed tomography
DD	developmental disorder or disability
DHCA	deep hypothermic circulatory arrest
FISH	fluorescence in situ hybridization
IQ	intelligence quotient
MRI	magnetic resonance imaging
QOL	quality of life
TGA	transposition of the great arteries
TOF	tetralogy of Fallot
VSD	ventricular septal defect

Disclosures

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Paul H. Lipkin	Kennedy Krieger Institute	None	None	None	None	None	Bristol-Myers Squibb*; InfaCare Pharmaceutical Corp*	None
Kathleen A. Mussatto	Children's Hospital of Wisconsin	None	None	None	None	None	None	None
Jane W. Newburger	Boston Children's Hospital	None	None	None	None	None	Bristol-Myers Squibb*	None
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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Michael Dowling	University of Texas Southwestern Medical Center	Doris Duke Charitable Foundation*	None	None	None	None	None	None
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Patricia O'Brien	Boston Children's Hospital	None	None	None	None	None	None	None

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*Significant.

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