

Managing uncertainty in decision-making of common congenital cardiac defects

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Abstract

Decision-making in congenital cardiac care, although sometimes appearing simple, may prove challenging due to lack of data, uncertainty about outcomes, underlying heuristics, and potential biases in how we reach decisions. We report on the decision-making complexities and uncertainty in management of five commonly encountered congenital cardiac problems: indications for and timing of treatment of subaortic stenosis, closure or observation of small ventricular septal defects, management of new-onset aortic regurgitation in ventricular septal defect, management of anomalous aortic origin of a coronary artery in an asymptomatic patient, and indications for operating on a single anomalously draining pulmonary vein. The strategy underpinning each lesion and the indications for and against intervention are outlined. Areas of uncertainty are clearly delineated. Even in the presence of “simple” congenital cardiac lesions, uncertainty exists in decision-making. Awareness and acceptance of uncertainty is first required to facilitate efforts at mitigation. Strategies to circumvent uncertainty in these scenarios include greater availability of evidence-based medicine, larger datasets, standardised clinical assessment and management protocols, and potentially the incorporation of artificial intelligence into the decision-making process.

How we make decisions in medicine is rarely simple and often confounded by lack of data, conflicting data, and consequent lack of certainty in what represents the best management strategy.¹ The impact of uncertainty in clinical decision-making in medicine has become an important topic of study for both practitioners and patients.^{2–9} We often work in a culture within which admission of uncertainty is anathema.⁹ Indeed, the need for certainty may undervalue the iterative complex nature of decision-making in providing bespoke patient-centric care.⁹ In this article, we examine how we manage “simple” congenital cardiac lesions, the decision-making for which can become quite complex when one analyses the rationale or indications for intervention. In the behavioural economics arena, hidden traps or pitfalls in decision-making have been recognised as far back as the 1990s,¹⁰ and only recently have we questioned the relevance of this challenge in paediatric cardiac care.¹¹

Although decision-making in the business world may have significant implications, making the wrong medical decision, be it within the catheterisation laboratory, surgical suite or, indeed, in the multidisciplinary Joint Cardiac Surgery and Cardiology conference beforehand, may cost the patient his or her life. Hence, the stakes within paediatric cardiac care are exceedingly high. Research over several decades has revealed how people use underlying subconscious routines in order to cope with complex decision-making tasks. Within paediatric cardiac care, the best management plan may not be clear because of the frequently limited evidence base to inform decision-making. Furthermore, several recent studies have highlighted the impact of cognitive

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biases within paediatric cardiology and surgery,¹² the cardiac catheterisation laboratory,^{13–14} the ICU,¹⁵ and even as a framework for decision-making about donor organs in cardiac transplantation, which complicates the process of decision-making still further.¹⁶

Role of heuristics in decision-making

Heuristics is a term used to define unconscious routines that each of us use to cope with the complexity inherent in decision-making. These cognitive shortcuts usually help us to make correct decisions, but they occasionally cause cognitive biases that influence our decision-making. The danger of heuristics is often related to their unexplored impact and magnitude of effect in the medical field. Kahneman, in his seminal book *Thinking Fast and Slow*, describes the two decision-making processes we employ.¹⁷

- System 1 thought is rapid, instinctual, and emotional, often on impulse, and is part of the fight or flight response.
- System 2 thought is slower, more deliberate, and logical.

The research questions addressed in this current manuscript investigate which areas of uncertainty surround decision-making for each of the five common congenital cardiac conditions outlined.

Approach to decision-making in specific congenital cardiac lesions

This paper reviews the indications for and against surgical intervention, and areas of uncertainty, for each of five common clinical congenital cardiac scenarios outlined below:

1. Subaortic stenosis – Who does not need an operation?
2. Damned if you do, damned if you don't – What are the life-long implications of closing, or not closing, a small ventricular septal defect?
3. Ventricular septal defect with new-onset aortic regurgitation – Shoot on sight or keep your powder dry?
4. Surgery for asymptomatic anomalous aortic origin of a coronary artery – Is the juice worth the squeeze?
5. Should we operate on a single anomalously draining pulmonary vein?

The Heart University webinar “*Contemporary Questions in Congenital Heart Disease: ‘Simple’ congenital heart disease: not so simple after all?*” was a good example of sharing the knowledge of evidence-based medicine in borderline cases, where we have no robust evidence to guide us (Link to Webinar Recordings). Each of these topics is very different, but they are unified by the somewhat nebulous nature of the data that support decision-making. Discussion focused around available evidence from relevant cohort studies. The presentations and discussions held during this webinar serve the basis for our review.

1. “Subaortic stenosis – who does not need an operation?”

Discrete subvalvar or subaortic stenosis refers to localised obstruction of the left ventricular outflow tract. The incidence is estimated at 9 per 100,000 live births, with a male predominance of approximately 2:1.¹⁸ Discrete subaortic stenosis may occur in isolation or in association with other forms of CHD, with approximately 30% co-occurring with a ventricular septal defect.¹⁸ The most common form involves a thick fibromuscular ridge located at variable

distance proximal to the aortic valve. Alternatively, the obstruction may be due to muscular extension related to the anterolateral papillary muscle, septal hypertrophy, accessory tissue related to the mitral valve, or a combination thereof. The typical fibromuscular subaortic ridge is a proliferative disorder, involving the left ventricular outflow tract with a variable distance between the obstructive lesion and the attachments of the aortic valvar leaflets to the ventriculoarterial junction. Histologically, the obstructive tissue is comprised of fibroblasts, myocytes, collagen, and elastic fibres. Typically, the anatomic substrate is present at birth, but haemodynamically significant obstruction is rare in early infancy. More commonly, it tends to develop during the first decade of life, with an average age of clinical presentation around the age of 5 years. It is common for physicians caring for these patients to notice echocardiographic abnormalities of the left ventricular outflow tract in the first months of life, often prior to the development of clinical manifestations or a significant pressure gradient. Examples of such abnormalities include steep angulation between the long axis of the left ventricle and the proximal ascending aorta, and increased distance between the hinge points of the aortic and mitral leaflets manifesting as elongation of the intervalvar fibrosa, or aortic-mitral fibrous curtain.²⁵

Pickard et al. studied 155 children following resection of subaortic stenosis, with a median postoperative follow-up time of 10.9 years (range 2.5–27 years).¹⁹ Despite excellent survival rates in the first 15 years postoperatively, there was a decrease in survival starting in the third decade of life. Furthermore, there was a significant recurrence rate of up to 12% requiring reoperation within 5 to 10 years after the first operation.¹⁹ However, not all patients with discrete subaortic stenosis progress in severity and need intervention. While approximately two-thirds of patients had a progressive disease, the remaining had no significant progression.²⁰

Infants and children with evolving subaortic stenosis can present a dilemma regarding the timing and indications for intervention. Although some authors advocate for transcatheter interventions to provide relief of subaortic obstruction, surgery is the preferred approach in most centres.²¹ Given that approximately one in three patients with a subaortic ridge will not experience progressive worsening of their left ventricular outflow tract obstruction, it is helpful to identify those patients who will not experience progressive worsening, and, conversely, those with progressive disease. Bezold et al. reported that the initial gradient by Doppler echocardiography at the time of presentation was independently predictive of the need for future surgery. The greater the initial gradient, the higher the likelihood of having progressive disease requiring surgical intervention. In addition, the odds of progressive obstruction were 58-fold higher if the patient had extension of the subaortic ridge onto the base of the anterior mitral leaflet, indicating the circumferential nature of the lesion.²² Furthermore, the closer the lesion was to the aortic valvar leaflets, the more likely it was to be progressive. The inverse also proved true in predicting lack of progression. There has been additional focus on the occurrence of aortic regurgitation as an indication for surgery in patients with subaortic stenosis. Aortic valvar intervention before the subaortic stenosis surgery for concomitant aortic valvar stenosis was shown to portend high risk for development of significant aortic regurgitation requiring subsequent intervention on the aortic valve.^{19,23} It is clearly better to resect a subaortic membrane prior to the development of an indication for repair or replacement of the aortic valve.

Pediatric cardiologists often face a decision regarding expectant observation or referral for surgical intervention in patients with

Table 1. Indications for subaortic stenosis resection. The following guidelines apply to children and young adults with discrete subaortic stenosis as the dominant obstructive lesion in the left ventricular outflow tract. These guidelines do not apply to patients with hypertrophic cardiomyopathy, unrepaired interrupted aortic arch, non-restrictive ventricular septal defect, unrepaired atrioventricular septal defect, complex segmental cardiovascular anatomy, or functionally univentricular circulation.

	Surgical intervention (≥2 criteria)	Uncertainty	Continued observation
Doppler maximum instantaneous gradient*	≥60 mmHg	50–59 mmHg	<50 mmHg
Doppler mean gradient*	≥40	35–39 mmHg	<35 mmHg
Peak-to-peak gradient by catheterisation	≥40	35–39 mmHg	<35 mmHg
Left ventricular systolic pressure	≥140 mmg	130–139 mmHg	<130 mmHg
Left ventricular end-diastolic pressure	≥12	10–12 mmHg	<10 mmHg
Left ventricular mass index z-score	>2.0	1.8–2.0	<1.8
Aortic regurgitation**	>Mild	Mild	None-trivial
Cardiac-relatable symptoms***	Present	Ambiguous	None

*Doppler signal obtained either from the subxiphoid, apical, or suprasternal notch windows without angle correction; optimise signal-to-noise to near full suppression of background signal (noise); measure solid/consistent signal – avoid spurious signals at peak velocities.

**Criteria for aortic regurgitation based on regurgitation fraction evaluated either by Doppler²⁶ or by MRI: non-trivial = ≤5%; Mild = >5 to ≤20%; moderate = 21–40%; severe = >40%.

***Cardiac symptoms include exercise intolerance documented by an exercise stress test (<2 SD below age and gender norms); exercise-associated chest pain; exercise-associated syncope; or high-grade ventricular ectopy.

— Recommended references.^{19–34}

subaortic stenosis. Criteria for expectant observation typically include (1) an initial left ventricular outflow tract peak Doppler gradient less than 20 mm Hg not exceeding 40 mm Hg during follow-up; (2) absence of a circumferential subaortic lesion with no extension of the obstructing tissue onto the base of the anterior mitral leaflet; (3) longer distance between the obstructive ridge and aortic valve (>5–6 mm/body surface area^{0.5}); (4) no more than mild aortic regurgitation; (5) no left ventricular hypertrophy; (6) no evidence of impaired diastolic function; (7) no cardiac-related symptoms that cannot be otherwise explained; and (8) no other indications for surgery.²⁴ Older age at presentation (usually after age 5 years) is associated with slower disease progression.

Echocardiography is the primary diagnostic modality to define the anatomy and the physiology of discrete subaortic stenosis.³⁴ When transthoracic imaging is not clear, transoesophageal echocardiography provides definitive imaging in the majority of cases. Cardiac MRI is an additional tool for evaluation of the anatomy and allows measurements of aortic regurgitation fraction and assessment of the presence or absence of left ventricular diffuse myocardial fibrosis. CT is reserved for exceptional cases, such as in patients with pacemakers. Cardiac catheterisation can be used for haemodynamic evaluation in select patients with unclear clinical and non-invasive data to aid decision-making regarding surgical intervention versus expectant follow-up. Table 1 summarises criteria for expectant observation, surgical intervention, and where uncertainty requires further evaluation. Again, it is clearly better to resect a subaortic membrane prior to the development of an indication for repair or replacement of the aortic valve.

2. Damned if you do, damned if you don't – what are the lifelong implications of closing, or not closing, a small ventricular septal defect?

Usually, it is a clear-cut decision to close a haemodynamically significant ventricular septal defect. However, according to Norwegian and Danish population studies, only 5 to 8% of small ventricular septal defects have clear criteria to be closed.³⁵ The decision has to be made for the remaining 92–95% of patients

with ventricular septal defect. Uncertainty of how to proceed in a borderline case may prompt differences of opinion between clinicians. Furthermore, the potential for small perimembranous ventricular septal defects to close, even into the third decade of life, juxtaposed with the small but real risk of postoperative heart block, adds to the potential uncertainty of optimal management.

During the Heart University webinar, a 5-year-old child was discussed with a small ventricular septal defect, Qp/Qs = 1.4:1, left-to-right shunt with Doppler restrictive flow pattern of 5 m/second, no progression to closure, no aortic regurgitation nor valvar prolapse, and no symptoms of heart failure. The first question usually asked is:

- “What are the life-long implications of closing or not closing a small VSD?”

In a large national study of children with ventricular septal defects, approximately 92% of defects were not surgically addressed.³⁵

- “What is the potential burden on the ventricular function, pulmonary vascular resistance, and risk for developing aortic regurgitation in this population?”
- “What happens to the heart after 50 years with a small VSD?”

There are data showing no significant changes in the left heart parameters between small persistent ventricular septal defect, a small ventricular septal defect which closes, and a control group of patients. However, there are some changes in the right heart parameters between these groups. A cohort of patients with small ventricular septal defects compared to a control group demonstrated increased right atrial volume (25 ± 8 versus 18 ± 5 ml/m²), slightly decreased right ventricular systolic function (right ventricular fractional area change 40 ± 7 versus 48 ± 7 %), slightly dilated pulmonary artery (25 ± 5 versus 21 ± 1 mm), more tricuspid regurgitation, larger right ventricular outflow tract dimensions, lower isovolumetric acceleration and systolic velocities during exercise, as well as decreased VO₂ max (26 ± 6 versus 34 ± 9 ml/kg/m²) in the small ventricular septal defect cohort.³⁶

Eckerström et al. found that older patients with a surgically corrected ventricular septal defect display reduced dynamic pulmonary function, increased airway resistance in the small airways, and reduced diffusion capacity compared with healthy age- and gender-matched controls.³⁶ A separate small ventricular septal defect cohort without surgical intervention was reported in the same study to have very similar right heart parameters compared with the closed small ventricular septal defect group. The oxygen uptake during exercise was ~20% lower in both the closed and not closed small ventricular septal defect groups compared with controls.³⁷

Furthermore, the current surgical results are not comparable to those performed five decades ago, when the average closure was performed around 6 years of age. In the current era, the timing of closure and operative techniques, as well as surgical skills, have improved tremendously. Hence, it is difficult to compare between the two eras, as well as compare patients with large ventricular septal defects experiencing significant volume overload for a short period of time to patients with small ventricular septal defects experiencing a small volume overload over a longer period. Maagaard et al. compared 20-year-old patients who had a persistent small ventricular septal defect or who had their small ventricular septal defect surgically closed before 2 years of age with controls. MRI showed no difference in the left heart parameters. However, the right ventricular end-diastolic volume was significantly higher in patients with open as well as surgically closed small ventricular septal defects compared with controls (105 ± 17 in patients with open ventricular septal defects versus 102 ± 20 in patients with surgically closed ventricular septal defects versus 88 ± 13 ml/m² in controls); they also demonstrated significantly greater myocardial trabeculation.³⁸ Eckerström et al. compared young patients with small unrepaired ventricular septal defect aged 27 ± 6 years with controls, demonstrating at rest there was no difference in terms of pulmonary function testing. However, when the cardiorespiratory system is stressed, the patients with small ventricular septal defects tended to have lower forced expiratory volume in one second, lower peak expiratory flow, showed tendencies towards lower forced vital capacity and increased airway resistance, as well as a lower oxygen uptake, minute ventilation, and respiratory rate, which may be early signs of parenchymal dysfunction and restrictive airway disease.³⁹ There have been reports that older patients with surgically closed ventricular septal defects demonstrate poorer exercise capacity than healthy peers and younger surgically closed ventricular septal defect peers, as well as patients with unrepaired ventricular septal defects. Exercise capacity was 29% lower in older patients with surgically closed ventricular septal defects than in healthy peers, whereas younger patients with surgically closed ventricular septal defects demonstrated 18% lower capacity compared with healthy peers. Older patients with unrepaired ventricular septal defects reached 21% lower exercise capacity, while younger patients with unrepaired ventricular septal defects previously demonstrated 17% lower oxygen uptake than healthy peers.⁴⁰ Lastly, the impaired peak exercise capacity is found to be related with lower self-estimated physical health.⁴¹

In conclusion, the vast majority of patients with small ventricular septal defects have haemodynamic changes predominantly involving the right side of the heart, compromised exercise capacity, reduced right ventricular myocardial contractility, and slightly reduced lung function. The cohort with small ventricular septal defects have a small volume overload for a long time, whereas the cohort with surgically closed large ventricular septal defects have been exposed to a short period of high-volume overload.

Changes in pulmonary vasculature and increasing afterload might be involved in the pathogenesis of these changes. So, there appears to be little difference in cardiopulmonary function between those with a large ventricular septal defect who underwent closure and those who were left with an unrepaired small ventricular septal defect. Although treatment is clear for the 5–8% of patients with haemodynamically significant ventricular septal defects, some uncertainty remains in the optimal treatment of the remaining 92–95% of patients. As Eleanor Roosevelt said: “Do what you feel in your heart to be right – for you’ll be criticised anyway. You’ll be damned if you do and damned if you don’t.”

3. Ventricular septal defect with new-onset aortic regurgitation – shoot on sight or keep your powder dry?

Aortic valvar regurgitation is mostly associated with doubly committed juxta-arterial ventricular septal defect in association with right coronary leaflet prolapse (Figure 1), so that aortic regurgitation is five times more likely in the presence of a doubly committed juxta-arterial ventricular septal defect (Figure 2) in comparison with a perimembranous ventricular septal defect.^{42–44} The landmark paper by Tatsuno et al. described the aortic valvar prolapse into the ventricular septal defect due to the lack of anatomical support of the valve and the secondary haemodynamic effects, which actually produce prolapse of the valve into the ventricular septal defect. When fluid flows across the constricted ventricular septal defect, the adjacent pressure drops – this phenomenon is referred to as the Venturi effect. The left-to-right shunt of blood through the ventricular septal defect during the early systolic phase pulls the anatomically unsupported aortic valve into the defect. In diastole, the closed valve is subject to intra-aortic pressure, causing the free margin of the prolapsed leaflet to hang down, to gradually become elongated, and finally to separate from the free margin of the other two leaflets, and thus become incompetent.⁴⁵ Other possible pathogenic mechanisms have been proposed including partial fusion between the zone of apposition between two leaflets⁴⁴ and loss of continuity of the media between the wall of the aorta and the hinge line of the valvar leaflet.⁴⁶ Given these possible pathogenic mechanisms, the aortic valvar regurgitation resulting from an underlying ventricular septal defect is an acquired condition.

In patients with a large ventricular septal defect causing heart failure, aortic regurgitation is uncommon, as opposed to patients with a restrictive ventricular septal defect, when moderate to severe aortic regurgitation may develop. Although both scenarios require surgical repair of the ventricular septal defect with or without valvoplasty, the question is:

- “Should we close a restrictive VSD with new-onset trivial to mild aortic regurgitation?”

The guidelines do not give a straight answer to this common question. In order to answer this question, we have to evaluate multiple factors including the type of ventricular septal defect, the size of the shunt, and the valvar substrate (Table 2).

Lun et al. reported that, of the 139 asymptomatic patients with a doubly committed ventricular septal defect managed conservatively, 102 (73%) developed aortic leaflet prolapse and 78% of whom (80 of 102) developed aortic regurgitation. The prevalence of aortic leaflet prolapse and aortic regurgitation at 10 years was 64 and 45%, respectively. All patients with aortic leaflet prolapse had a defect size of ≥ 5 mm. Lun et al. concluded that the doubly committed ventricular septal defect of ≥ 5 mm should be closed



Figure 1. Transthoracic two-dimensional echocardiography from the parasternal long-axis view showing prolapse of the right coronary cusp (white arrows).

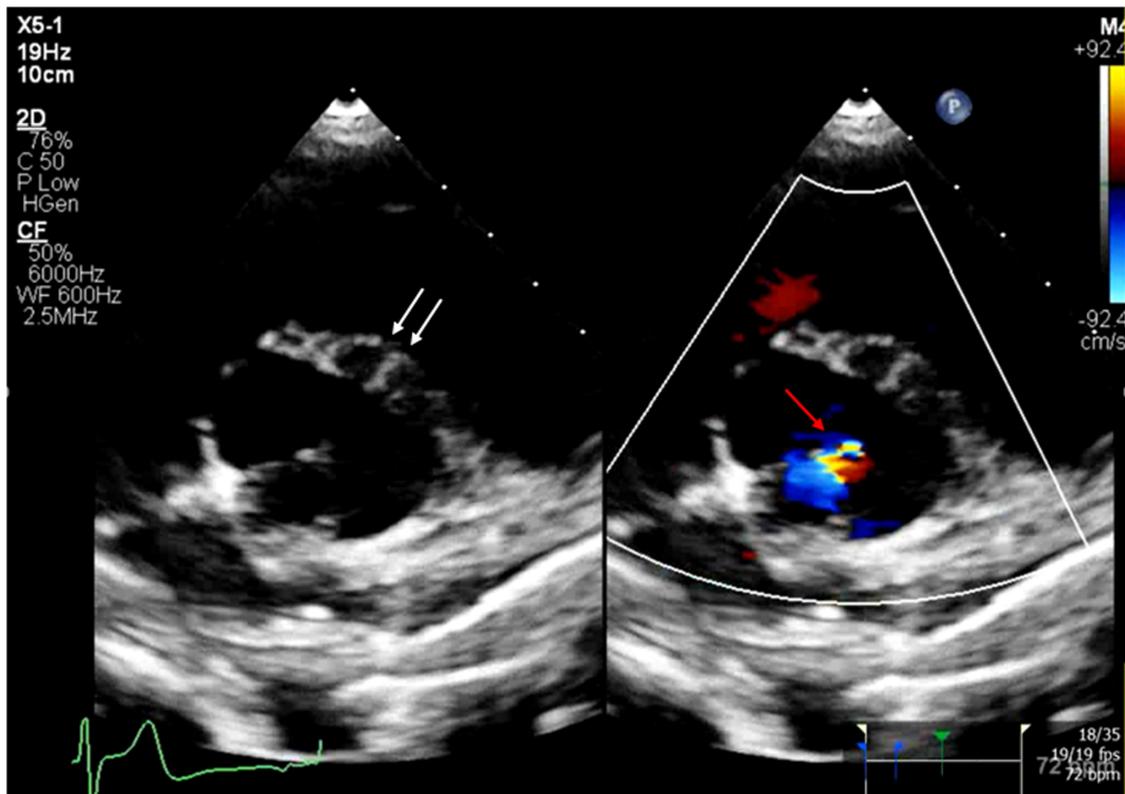


Figure 2. Transthoracic two-dimensional echocardiographic (left) and colour flow mapping assessment (right) from the parasternal short-axis view showing prolapse of the right coronary cusp (white arrows) and aortic regurgitation (red arrow), respectively.

as early as possible to prevent aortic leaflet prolapse and aortic regurgitation, while asymptomatic patients with small defects <5 mm could be managed conservatively.⁴⁷ One might underestimate the true defect size by only measuring the effective shunt size by

colour Doppler when there is prolapse of an aortic valvar leaflet into the defect. It is important to use two-dimensional echocardiography to define the real margins of the true ventricular septal defect without superimposed colour flow mapping. Other factors

Table 2. Indications for surgery in children with ventricular septal defect and aortic regurgitation.

	Type of defect	True defect size	Left-to-right shunt†	Clinical evidence of heart failure	Leaflet prolapse	Severity of AR
Surgery indicated	Any type	Large	Large	Present	Any degree	Any degree
	Any type	Moderate to large	Small	Absent	Any degree	Moderate to severe
	Doubly committed or outlet	Moderate to large	Small	Absent	Moderate to severe RCL prolapse	Any degree
	Perimembranous	Moderate to large	Small	Absent	Moderate to severe RCL and NCL prolapse	Mild to severe
Surgery not indicated	Any type	Small	Small	Absent	Nil	Trivial
	Any type	Small	Small	Absent	Mild	Trivial
	Any type	Small	Nil	Absent	Mild	Trivial
Uncertain and requires regular reassessment	Any type	Small	Small	Absent	Mild	Mild
	Any type	Moderate to large	Small	Absent	Mild	Trivial to mild
	Any type	Moderate to large	Nil	Absent	Moderate prolapse ± SOV aneurysm	Trivial
	Perimembranous	Moderate to large	Small	Absent	Moderate to severe RCL and NCL prolapse	Trivial
	Perimembranous	Moderate to large	Nil	Absent	Mild RCL and/or NCL prolapse	Trivial to mild

†The magnitude left-right shunt may be small or absent even in the presence of sizable VSDs due to coverage by the prolapsed coronary leaflet(s). Abbreviations: AR, aortic regurgitation; NCL, non-coronary leaflet; RCL, right coronary leaflet; SOV, sinus of Valsalva; VSD, ventricular septal defect.

to consider are the magnitude of the left-to-right shunt and to ensure the absence of pulmonary hypertension. The degree of leaflet distortion differs from mild to severe, a difference which impacts the decision of ventricular septal defect closure. Significant aortic leaflet prolapse is commonly associated with more severe aortic regurgitation. And, it is clearly better to close the ventricular septal defect prior to the development of an indication for repair or replacement of the aortic valve.

Preoperative leaflet prolapse has an important bearing on post-operative progression of aortic regurgitation. In a study of 135 patients who underwent ventricular septal defect closure, none of the 39 patients with mild to moderate aortic leaflet prolapse in the preoperative period were shown to have significant aortic regurgitation postoperatively.⁴⁸ Tomita et al. proposed two metrics to predict progression of aortic regurgitation:

- A right coronary leaflet deformity index of ≥ 0.3 or right coronary leaflet imbalance index of ≥ 1.3 was associated with moderate aortic regurgitation or rupture of a sinus of Valsalva aneurysm.⁴⁹
- The same group of investigators further reported that non-coronary leaflet prolapse, in addition to the right coronary leaflet prolapse in patients with perimembranous ventricular septal defect, significantly increased the risk of developing significant aortic regurgitation.⁵⁰

Characterizing the number of leaflet involvement is also an important factor. Another substrate for the aortic regurgitation in perimembranous ventricular septal defect is overriding of the aortic root over the crest of the ventricular septum. This feature is defined

as a shift in the aortic leaflet hinge point, medial to the central plane of the ventricular septum. Visualization from a five-chamber view and subcostal coronal view may be more useful than the parasternal long-axis view in this regard.⁵¹

It is important to consider whether we can afford to wait when we see new onset of mild aortic regurgitation. One group found that progression of aortic regurgitation after surgical repair of various types of outlet ventricular septal defects were similar, with a less-than-moderate degree of aortic insufficiency preoperatively rarely progressing after ventricular septal defect repair.⁵² Cheung et al., reporting on three decades of follow-up after surgical closure of doubly committed ventricular septal defects, revealed that aortic regurgitation is common and may progress even after surgical repair of the defect.⁵³ They additionally reported that the severity of preoperative aortic regurgitation is the most significant predictor of its persistence and progression after surgical closure of doubly committed ventricular septal defects. So, should you shoot on sight or keep your powder dry? We should not just concentrate on the new onset of aortic regurgitation when making decisions. Philosophically, the proponents of shoot on sight might suggest that the benefits for the many outweigh the imposition of a potentially unnecessary operation on the few, but this is not really supported by the currently available data. The downside of keeping our powder dry while the patient has less than moderate aortic regurgitation seems small. Consequently, we should rather concentrate on the following features:

- the location of the defect,
- the true defect size,
- the magnitude of the shunt,

- the severity of leaflet prolapse,
- the involvement of not only the right coronary leaflet but also the non-coronary leaflet in the setting of a perimembranous ventricular septal defect, and
- an understanding for other abnormal valvar substrates.

Nonetheless, if we choose to keep our powder dry, we have to monitor the progress of aortic valvar prolapse and aortic regurgitation and evaluate the development of a sinus of valsalva aneurysm. Again, it is clearly better to close the ventricular septal defect prior to the development of an indication for repair or replacement of the aortic valve.

4. Surgery for asymptomatic anomalous aortic origin of the coronary artery: is the juice worth the squeeze?

Anomalous aortic origin of a coronary artery is a rare congenital cardiac lesion, which occurs when one or both coronary arteries arise from an abnormal position on the aorta. It is the second leading cause of sudden cardiac arrest in otherwise healthy young individuals, commonly during or after vigorous physical exercise. In most cases, the anomalous coronary artery arises from one of the other two sinuses of valsalva; however, it can also arise from above the sinotubular junction. The primary conundrum is that we still do not know which asymptomatic lesions require surgery to prevent subsequent ischaemia and sudden cardiac arrest or, in the absence of "perfect" operative outcomes, what the risk/benefit of surgical intervention is for the asymptomatic individual who seeks our advice. The difficulty in decision-making is compounded by the anatomic heterogeneity. The anomalous vessel affected can be the right coronary artery, left main coronary artery, left anterior descending coronary artery, circumflex coronary artery, or any combination. The origin can be high, stenotic, or slit-like, and the course of the vessel can be inter-arterial, intraconal, retroaortic, prepulmonic, retrocardiac, and all can potentially occur with a concomitant intramural course of varying lengths.

While the estimated prevalence ranges from 0.01 to 2% of the population, the actual number of patients with this lesion remains unclear because of lack of general population screening.⁵⁴ The majority of patients are asymptomatic and are found incidentally. While it is clear that patients presenting with ischaemia or sudden cardiac arrest require exercise restriction until surgical repair, those patients diagnosed incidentally are more challenging to manage, especially given the heterogeneity of their coronary lesion. For this cohort, it is unclear when the risk/benefit favours surgical intervention over the risk of ischaemia and sudden cardiac arrest. Historically, the high-risk variant was believed to be patients with an intramural and/or inter-arterial course, who generally underwent surgery even when asymptomatic. However, more recently, the Congenital Heart Surgeons' Society found several other anatomical variants to be associated with ischaemia, including⁵⁵:

- anomalous aortic origin of the left coronary artery, especially those with an intramural course,
- a high orifice, and
- a slit-like orifice.

In anomalous aortic origin of the right coronary artery, a longer intramural course was associated with ischaemia. Anomalous right coronary artery was present in 20 of 49 patients (41%) with ischaemia and 6 of 18 (33%) who experienced sudden cardiac arrest.

Despite several published guidelines and/or protocols, there is a lack of higher quality or level A evidence regarding the management of patients with anomalous aortic origin of a coronary artery.⁵⁶ These guidelines and/or protocols include:

- the expert consensus guidelines published in *Journal of Thoracic and Cardiovascular Surgery*,⁵⁷
- guidelines from the *American College of Cardiology / American Heart Association Guideline for the Management of Adults with Congenital Heart Disease*,⁵⁸ and
- the algorithm for patient management from Texas Children's Hospital.⁵⁹

What is clear from the guidelines is the following: patients with anomalous aortic origin of a coronary artery, irrespective of variant, with clear signs and/or symptoms of ischaemia (e.g., syncope not vasovagal in nature, ST changes, elevated cardiac enzymes, and arrhythmias), or sudden cardiac arrest, require activity restriction until they undergo repair.⁵⁷⁻⁵⁹

It is not currently believed that all patients with anomalous aortic origin of the left coronary artery should undergo surgery (Table 3). Currently, repair for these patients without ischaemia has a Class IIa recommendation from the guidelines, while inter-arterial anomalous aortic origin of the left coronary artery origin was a Class I recommendation on the expert consensus guidelines. While previously a diagnosis alone would be an indication for repair without any further testing, this strategy is no longer deemed appropriate. It is now recommended that all patients, regardless of their anatomy, undergo cross-sectional imaging, in addition to anatomic and physiological evaluation.⁵⁸ This evaluation is important to understand what defects are present preoperatively in order to have an appropriate baseline to compare with postoperative tests. Of note, physiological evaluation may be avoided where patients have presented with a sudden event in order to avoid further insults. Additionally, exercise restriction should no longer be an indefinite management strategy, unless patients decline surgery or cannot undergo surgery for alternative reasons.⁵⁹ Exercise restriction should primarily be used to manage patients while awaiting surgery.⁵⁹

An important concept to question is:

- "Whether an inter-arterial course is invariably a major cause of ischaemia?"

One study reported 95% (467/490) of patients with available data of ischaemia had an inter-arterial course. If this was the primary cause of ischaemia, then surely it would suggest that almost all such patients be considered high risk. However, what the study found was the association of an intramural course with ischaemia. Since the inter-arterial course is less likely to be the primary culprit, pulmonary artery translocation should only be considered as an adjunct procedure. It is the intramural course that requires elimination, in addition to any ostial narrowing.⁵⁷ In addition, similar to patients with anomalous aortic origin of the right coronary artery, it is felt that patients without any evidence of ischaemia with anomalous aortic origin of the left coronary artery should no longer be immediately put forth for surgery without thorough investigation. Surgery is now a Class IIb recommendation (as is conservative management) and requires careful discussion of patient factors including participation in competitive sports.⁵⁸

Table 3. Key concepts that have evolved pertaining to AAOCA patients.. Reproduced with permission from Anusha Jegatheeswaran MD, PhD, FRCS.

PREVIOUS	CURRENT
<i>Anatomy</i>	
<ul style="list-style-type: none"> • AAORCA is benign. 	<ul style="list-style-type: none"> • An important proportion of patients with AAORCA experience ischaemia and SCA.⁵⁵
<ul style="list-style-type: none"> • An inter-arterial course is the primary reason for ischaemia. 	<ul style="list-style-type: none"> • An intramural course is associated with ischaemia.⁵⁵
<i>Diagnosis and preoperative management</i>	
<ul style="list-style-type: none"> • Patients diagnosed with AAOLCA do not require any further evaluation prior to surgery. 	<ul style="list-style-type: none"> • Asymptomatic patients with AAOLCA require full investigation.⁵⁵
<ul style="list-style-type: none"> • Echocardiography is an adequate form of imaging. 	<ul style="list-style-type: none"> • Coronary anatomy should be confirmed using CCT or MRI.⁵⁵
<ul style="list-style-type: none"> • Patients can be left indefinitely exercise restricted. 	<ul style="list-style-type: none"> • Patients should not be exercise restricted indefinitely. Exercise restriction should primarily be used as a temporary measure while awaiting surgery, or in circumstances where surgery is declined or not possible for various reasons.⁵⁹
<i>Surgery</i>	
<ul style="list-style-type: none"> • AAOCA repair is a low-risk procedure. 	<ul style="list-style-type: none"> • The rate of surgical adverse events is not insignificant and is higher in those with preoperative ischaemia, AAOLCA, those undergoing repair strategies other than unroofing, and those undergoing unroofing with commissural manipulation.⁶⁰
<ul style="list-style-type: none"> • Pulmonary artery translocation is an adequate repair. 	<ul style="list-style-type: none"> • Pulmonary artery translocation should only be used as an adjunct procedure.⁵⁷
<ul style="list-style-type: none"> • An inter-arterial course, as opposed to an intramural course, is associated with ischaemia. 	<ul style="list-style-type: none"> • It is important to eliminate any intramural course.^{57,61}
<ul style="list-style-type: none"> • Unroofing with commissural takedown is a straightforward surgical strategy. 	<ul style="list-style-type: none"> • Unroofing requiring commissural takedown is associated with \geq mild aortic regurgitation.⁵⁸ Strategies which do not necessitate commissural takedown such as reimplantation, neo-ostial creation, and aortocoronary window creation may avoid the risk of aortic insufficiency.⁶⁰
<i>Postoperative management</i>	
<ul style="list-style-type: none"> • Once patients have surgery, they are no longer at risk of ischaemia/SCA and do not require long-term cardiac follow-up. 	<ul style="list-style-type: none"> • Patients require annual follow-up with Cardiology, including exercise stress testing with imaging at 3 months to be cleared for participation in activity.⁵⁷ If the patient presented with SCA, they should be restricted from participation in high level athletics for 12 months.⁵⁷ • They should also have MRI at 6 months, when possible, for the evaluation of their anatomy.⁵⁷ • Patients should be treated with low-dose aspirin indefinitely based on the expert consensus guidelines, and at least for 3 months based on the Texas protocol.^{57,59}

AAOCA = anomalous aortic origin of a coronary artery; AAOLCA = anomalous aortic origin of a left main coronary artery; AAORCA = anomalous aortic origin of a right coronary artery; CCT = coronary computed tomography; SCA = sudden cardiac arrest.

Although surgical repair was previously believed to be relatively benign, with the benefit of eliminating the risk of sudden cardiac arrest or death, recent studies highlight potential risks. The Congenital Heart Surgeons' Society recently evaluated 395 patients from 45 institutions with a median follow-up of 2.8 years.⁶⁰ In addition to primary repair, predominantly performed with unroofing (87 and 26% of repairs occurring with commissural manipulation), 13 patients had 15 coronary-related reoperations. Overall, 7–13% of patients developed surgical adverse events. The definition of surgical adverse events included:

- reoperations (3%),
- new mild or moderate aortic regurgitation (8 or 2%),
- new abnormal ejection fraction (2%),

- new positive postoperative ischaemia test at any time or at last evaluation (4 or 2%), and
- death within 30 days (1%–4 patients, 1 presented in extremis, 2 asymptomatic, and 1 symptomatic).

This study also found that new mild or worse postoperative aortic regurgitation was associated with commissural manipulation, suggesting that strategies to avoid commissural takedown may decrease the risk of developing aortic regurgitation.

This study also highlighted failure to follow established guidelines following surgery, including the need for follow-up evaluations. After surgery, in addition to having follow-up with cardiology at 7–10 days, and at 4–6 weeks with an electrocardiogram and echocardiography, it is recommended that patients

undergo exercise stress testing with imaging for activity clearance at 3 months. Only then should patients resume competitive athletics (12 months if the patient presented with aborted sudden cardiac arrest). In addition, at 6 months, patients should again have a follow-up electrocardiogram and MRI where available. Over the long term, patients should be seen annually by their cardiologist with electrocardiogram, echocardiogram, and exercise stress test every 1–3 years based on activity level and annually if involved in high-level recreational or competitive sports, with nuclear perfusion/stress echocardiogram/Holter if new symptoms should develop. Finally, it should be noted that the expert consensus guidelines recommend indefinite treatment with baby aspirin, something that often seems to be forgotten.⁵⁷

5. When should we operate for isolated anomalous pulmonary venous connection?

Partial anomalous pulmonary venous connection is a rare congenital anomaly noted in 0.4–0.7% of autopsies.^{62–64} In patients with Turner syndrome, the incidence has been reported as high as approximately 20–25%.^{65–66} With the advent of newer imaging modalities, the diagnosis can now be made non-invasively with echocardiography, ventilation perfusion scan, CT, and MRI.

Partial anomalous pulmonary venous connection can involve one or more right- or left-sided pulmonary veins draining to the right atrium, coronary sinus, or systemic veins. Scimitar syndrome refers to hypoplasia of the right lung along with anomalous right pulmonary vein draining into the inferior caval vein. The most common form of partial anomalous pulmonary venous connection is a right-sided pulmonary vein draining to the superior caval vein, followed by right-sided pulmonary vein draining to the right atrium, and then anomalous left pulmonary vein draining to the left brachiocephalic vein.^{63,67} Each pulmonary vein contributes about 20–25% of the total pulmonary venous blood flow, and when less than half of the pulmonary venous return is anomalous, cardiac decompensation is unlikely and most patients remain asymptomatic. Patients with all but one anomalously draining pulmonary vein would exhibit similar physiology and clinical presentation as those with total anomalous pulmonary venous return.^{64,65,68}

Partial anomalous pulmonary venous connection gives rise to right ventricular volume overload due to increased pulmonary blood flow with recirculation of oxygenated blood through the lungs. The physiologic impact of partial anomalous pulmonary venous connection correlates with multiple factors⁷⁸:

- the number of pulmonary veins involved,
- the amount of lung tissue they drain,
- the compliance of the receiving chambers,
- the relative resistance of the involved vascular beds, and
- the presence and severity of obstruction to pulmonary arterial blood flow.

With stable pulmonary vascular resistance, blood flow tends to be greater in the anomalous draining pulmonary veins in view of the greater right-sided ventricular compliance. The magnitude of the left-to-right shunt is affected by the number and location of pulmonary lobe or lobes drained by the anomalous pulmonary vein, body position, and level of activity. At rest and in the upright position, pulmonary blood flow is preferentially distributed to the middle and lower lobes; however, in the supine position and during exertion, the pulmonary blood flow is redistributed to the upper lobes.⁶⁸

Many patients with isolated partial anomalous pulmonary venous drainage escape diagnosis until adulthood, as they are typically asymptomatic, especially if less than 50% of the pulmonary venous return is draining anomalously. Symptoms in childhood may include:

- poor weight gain,
- recurrent respiratory infections,
- cyanosis, and
- dyspnoea.

In adulthood, and depending on the magnitude of the left-to-right shunting, symptoms may include:

- dyspnoea,
- decreased exercise tolerance,
- palpitations associated with atrial arrhythmias, and
- symptoms of right-sided heart failure and pulmonary hypertension.

The diagnosis of partial anomalous pulmonary venous connection may be picked up incidentally on chest imaging, and the diagnosis should be sought if unexplained enlargement of the right cardiac chambers is noted in the absence of an atrial septal defect or right-sided valvar disease. A detailed comprehensive transthoracic echocardiogram should be performed, attempting to delineate all the pulmonary veins from parasternal, apical, subcostal, and suprasternal windows. Dilated caval veins, coronary sinus, or other systemic veins may be clues for the diagnosis. However, it may be missed in patients, especially with suboptimal acoustic windows, on transthoracic echocardiography, and additional imaging with transoesophageal echocardiography, MRI, CT, or cardiac catheterisation may be required. MRI, unlike CT, does not provide ionising radiation but has longer acquisition time. Moreover, MRI quantifies right-sided volumes and function, assesses the haemodynamic consequences of the anomalous pulmonary venous connection (i.e., shunt fraction), and provides excellent spatial orientation and delineation of the pulmonary veins. Cardiac catheterisation can be considered for the following reasons⁶⁶:

- haemodynamic assessment to gauge the presence and severity of pulmonary hypertension,
- complement anatomic delineation of the defect, and
- preoperative coronary angiography.

Indications for surgical intervention in isolated cases of partial anomalous pulmonary venous connection are not as clearly defined compared to other "simple" shunt lesions. Table 4 lists indications for surgical intervention; nevertheless, management decisions need to be individualised in the context of an evaluation by the multidisciplinary team. According to the 2018 guidelines, surgical repair can be considered in asymptomatic adults with:

- right ventricular volume overload,
- net left-to-right shunt sufficiently large to cause physiological sequelae with Qp:Qs >1.5:1,
- pulmonary pressures less than 50% systemic, and
- pulmonary vascular resistance less than 1/3 systemic.

According to the 2020 *European Society of Cardiology Guidelines*, surgical intervention would follow similar indications for

Table 4. Suggested management of isolated partial anomalous pulmonary venous return.

Number of anomalous pulmonary veins	Is repair Indicated?	Testing and follow-up
One	Unlikely	Periodic follow-up in the congenital clinic to serially assess the right-sided cardiac chambers, estimated pulmonary pressures, and screen for atrial arrhythmias.
Two or more	Likely – especially if associated volume overload of right cardiac chambers, significant shunt fraction, Qp/Qs >1.5:1 (CMR/catheterisation), and development of pulmonary hypertension (pulmonary pressures less than 50% systemic and pulmonary vascular resistance less than one third systemic)	Regular follow-up in the congenital clinic with periodic echocardiography and tomographic imaging to delineate pulmonary venous drainage before and after repair, assess right ventricular and valvar status, and estimate pulmonary pressures and any residual shunt. Periodic rhythm monitoring to screen for dysrhythmias would be prudent.

intervention in isolated atrial septal defect, although surgical complexity, technical suitability, and operative risk must be weighed against the benefits.^{68–71} Surgical intervention should be pursued in a tertiary care centre by cardiac surgeons with expertise in congenital heart surgery. Moreover, surgical repair has low morbidity and mortality, with noted reduction in right ventricular size, decreased right ventricular systolic pressure, decreased tricuspid valvar regurgitation, and improved NYHA classification postoperatively.^{72–73} The rate of surgical complications is low but includes the risks of pulmonary vein stenosis at the anastomotic site, arrhythmias, caval vein obstruction, and residual shunts.^{74–76}

Discussion

Although there is an increasing evidence base to support decision-making in specific areas of congenital cardiac care, the extraordinary progress made in our field has not been, and current decision-making cannot be, based on data from large multi-centre randomised clinical trials. Although we seek evidence-based medicine to direct our decisions, especially in the setting of randomised control trials in large adult datasets, the smaller population of CHD patients we look after does not always afford us this privilege. Randomised clinical trials are relatively rare among the CHD population,^{77–79} and often, even well-conducted studies may have conflicting findings, which adds further to uncertainty^{80–82} or alternative strategies to treatment.^{24,31} This paper attempts to address common clinical conundrums in congenital cardiac lesions where there are areas of uncertainty whether intervention is needed.

It is beyond the scope of this article to challenge the "assumed robustness" of the randomised clinical trial, which are beset by issues of scalability to the general population of patients because of a variety of factors, including:

- patient selection,
- ethnic and gender inequity,
- variable genetic substrate,
- inappropriate trial design, or
- even academic malpractice.

Nevertheless, even if the evidence base in our field could be bolstered, uncertainty is unavoidable. Our patients often have unique characteristics that challenge clinicians to balance the consistency in which they apply the limited evidence against the uniqueness of the patient in front of them.⁸³ Furthermore, deciding on invasive intervention is highly context-dependent,⁸⁴ where clinicians must integrate multiple competing outcomes of interest, including:

- the potential benefit of intervention versus its inherent risk, and
- the early risks of intervention versus the difficult-to-predict downstream consequences of living with uncorrected, or corrected, pathology.

As the outcomes of interest are often interdependent, the result cannot be predicted with any certainty, consistent with the truly complex nature of the decision. As a result, clinicians must wrestle with the inherent uncertainty germane to many of their management decisions⁸⁵ and must adopt an adaptive approach to learning from past cases, as repeating the same management strategies in similar circumstances does not guarantee similar results.⁸⁶

Uncertainty in clinical medicine has always been present, but only recently greater attention has been brought to this challenge in our practice.^{2–9} Physicians, although rational individuals, often work in a culture with a deep-rooted unwillingness to acknowledge and accept uncertainty.⁹ As cardiologists and surgeons, we do not like to admit to uncertainty, but it remains a fundamental component of many of the decisions we face on a daily basis in managing our patients. We often focus on transforming the grey-scale narrative of a patient into a black-and-white paradigm with definitive diagnosis and optimal treatment.⁹ Simpkin et al. pointed out that this need for certainty oversimplifies the iterative evolutionary nature of clinical reasoning and represents the antithesis of patient-centric care.⁹ Clinicians may avoid admission of uncertainty and avoid ambiguous decision for fear of judgement by colleagues.⁸⁷ Gerrity et al. reported a wide variation in comfort with uncertainty for clinicians, which was influenced by gender, duration of practice, and degree of specialisation.³ Heuristics and biases have been well recognised as having an impact on decision-making under such conditions of uncertainty. We often see this impact on decision-making with confirmation bias, the anchoring effect, availability, and representativeness biases.¹¹

Several potential solutions exist to managing comfort with uncertainty, including different qualitative and quantitative methods.⁷ Quantitative methods, including decision trees, Monte Carlo simulation, and Markov chain analysis, are complex and based on probability estimates.⁸⁸ Evidence-based medicine has been promoted as a more appropriate instrument, as it combines the expertise of physicians and the best available evidence.⁸⁹ Several centres have developed standardised clinical assessment and management protocols that clarify pathways for the management of common congenital cardiac conditions such as syncope.⁹⁰ Big data analysis, particularly in our field, may aid in removing human factors in the interpretation of data obtained in the ever-increasing number of registries and databases that exist. The implementation of machine

learning and artificial intelligence into the clinical decision-making process, not usurping but assisting the clinician, may also assist us in managing specific areas of uncertainty.¹⁴ Notwithstanding the aforementioned frailties of worshipping at the altar of the randomised clinical trial, their use in guiding progress and decision-making in CHDs is practically and numerically challenging. Instead, we are poised better than some specialities, because of the phenotypic and genotypic data stored in our many registries and databases, to be the poster child of patient-specific "precision medicine" based on deep analytics of merged datasets, an approach that has the capacity to overcome many of the problems we have discussed.

While we await solutions, perhaps the most important solution to managing comfort with uncertainty lies in the education and the training of clinicians. Such complex skills training should be based on real-life tasks (cf. the cases described in this article) that deliberately allow for uncertainty in the decision-making process.⁹¹ Rather than viewing uncertainty as a weakness on behalf of the decision-maker, it should be acknowledged as a cognitive "cue" that might have a positive impact on learning how to manage uncertainty.⁹² Feelings of discomfort with uncertainty should trigger learners to

- scrutinise possible sources of uncertainty,
- ask for help from their supervisor or others, and
- step back to monitor their progress and plan actions that might decrease or help to accept uncertainty.

Learners must understand that uncertainty is an integral part of complex decision-making and discomfort with uncertainty might act as a cue that helps to self-regulate their learning process in such a way that cognitive strategies for managing uncertainty are developed.

Trainers must create a psychologically safe learning environment in which uncertainty is accepted as a normal aspect of complex decision-making. First, situations may exist where trainers recognise that their trainees experience uncertainty, for example, because they are pausing, hesitating, or slowing down.⁹³ In such situations, trainers may start a dialogue with their trainees and explain how they maintain safety when dealing with uncertainty themselves (i.e., how they build confidence when dealing with complex problems); thus, acting as role models that do not neglect uncertainty but use it as a cue for self-regulating performance and learning. Alternatively, there might be learning situations where trainees do not experience uncertainty in the decision-making process, but the trainers do. Then, the trainers may point out cues that are missed by the trainee and help them understand why their feeling of certainty is misplaced. Most important in the trainer–trainee dialogue is that uncertainty is accepted as a valuable cue in the teaching–learning process.

In conclusion, even "simple" congenital cardiac lesions pose challenges in decision-making, and uncertainty is an inevitable component to their management. Increased awareness of the prevalence of uncertainty in clinical decision-making is the first step in addressing this problem. Exciting potential solutions include:

- larger datasets,
- multi-centre collaboration,
- standardised care pathways, and
- incorporation of artificial intelligence.

While further research into managing uncertainty in CHD is warranted, we have reviewed the process of utilising the available

evidence, in combination with recognising uncertainty, in guiding clinical decision-making in common clinical conundrums that present within the field of CHD. Decision-making in congenital cardiology remains an art as well as a science.

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