Acute endocarditis cannot be viewed as an ideal setting for recellularization by regular recipient cells. The open matrix may even allow for bacterial invasion, thereby prompting infiltration of immune competent cells and inflammatory cascades leading to early calcification. We, therefore, do not recommend the use of decellularized matrices in the setting of acute endocarditis, even though the endocarditis susceptibility of DAH at this point appears low.

The ARISE investigators strongly agree with the editorial comments made by Dr Bando proposing late outcome studies on DAH.⁶ In fact, prospective long-term follow-up is part of both investigator-initiated European-wide trials on fresh decellularized allografts for pulmonary and aortic valve replacement^{7,8} to answer the question of whether such homografts are really superior, or just fashion.⁹

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References

1. Helder RK, Kouchoukos NT, Zehr K, Dearani JA, Maleszewski JJ, Leduc C, et al. Late durability of decellularized allografts for aortic valve replacement: a word of caution. *J Thorac Cardiovasc Surg.* 2016;152:1197-9.
2. Sarathchandra P, Smolenski RT, Yuen AH, Chester AH, Goldstein S, Heacock AE, et al. Impact of γ -irradiation on extracellular matrix of porcine pulmonary valves. *J Surg Res.* 2012;176:376-85.
3. Tudorache I, Horke A, Cebotari S, Sarikouch S, Boethig D, Breymann T, et al. Decellularized aortic homografts for aortic valve and aorta ascendens replacement. *Eur J Cardiothorac Surg.* 2016;50:89-97.
4. Sarikouch S, Horke A, Tudorache I, Beerbaum P, Westhoff-Bleck M, Boethig D, et al. Decellularized fresh homografts for pulmonary valve replacement: a decade of clinical experience. *Eur J Cardiothorac Surg.* 2016;50:281-9.
5. Horke A. Decellularization of aortic valves: only time will tell. *Eur J Cardiothorac Surg.* 2016;49:707-8.
6. Bando K. A proposal for prospective late outcome analysis of decellularized aortic valves. *J Thorac Cardiovasc Surg.* 2016;152:1202-3.
7. Aortic Replacement Using Individualised Regenerative Allografts. ARISE home page. Available at: <http://www.arise-clinicaltrial.eu>. Accessed February 27, 2017.
8. European Clinical Study for the Application of Regenerative Heart Valves. ES-POIR home page. Available at: <http://www.espoir-clinicaltrial.eu>. Accessed February 27, 2017.
9. d'Udekem Y. Decellularized homografts: in fashion or really superior? *Eur J Cardiothorac Surg.* 2016;50:291-2.

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FINDING THE NEXT GOOD THING

Reply to the Editor:

Cardiovascular surgeons continue to innovate materials. Artificial vascular grafts such as polytetrafluoroethylene and Dacron have a long history of “adequacy” with acknowledged limits. Bioprosthetic grafts have offered a dense forest of options. Current efforts include cryopreserved homografts, bovine jugular grafts (some with bioprosthetic valves), harvested umbilical vein, and various types of decellularized vascular grafts. Each has potential advantages. Tissue-engineered approaches are starting to show promise. With that many options, it is obvious there is not a perfect choice. In this

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issue of the *Journal*, Drs Sarikouch and Havirich, and the European-based Aortic Valve Replacement using Individualized Regenerative Allografts (ARISE) investigators respond to the cautionary note that Helder and colleagues¹ wrote this fall.

The “numbers” in different series are relatively clear and in conflict. Helder and colleagues’ data¹ are prominent for 3 key observations. Their decellularized approach was compared with a more traditional cryopreserved aortic homograft in adolescents and young adults. As with virtually every material, the early results (3-5 years) were outstanding. As the experience gets extended 7 to 8 years, there was a rapid decline in conduit function. Finally, they rapidly published interpretable life tables with clear and widening confidence intervals, accepting a borderline *P* value as a cautionary note.

The ARISE group responds largely with a beautiful picture of an 8-year-old valve in a child and some solid but relatively follow-up limited published data on their approach in both the aortic² and pulmonary positions.³ The smaller aortic experience has a mean follow-up of 2 years and single patient follow-up curves that mostly end at 4 years. With this, they have an approximately 17% reoperation rate at 5 years. This report certainly is not convincing that this is superior technology. The pulmonary experience is both larger and more gratifying. With a mean follow-up of 4.6 years and some with a follow-up of 10 years (longer in the comparison groups), the ARISE decellularized group had the best outcomes, nearly reaching the threshold with a *P* value of .06. With 86% of patients not requiring a catheter or surgical intervention, this is certainly reason for cautious optimism.

My concern when reading this and viewing the admittedly beautiful images of an 8-year-old graft is how to help us all decide whether any approach is superior.

The editorialists for these articles have started this discussion. Martin Elliot discussed these ideas at a Robert Gross lecture at Boston Children’s Hospital last spring and then expanded those thoughts in a Gresham lecture worth reviewing (<https://www.gresham.ac.uk/lectures-and->

[events/seeing-through-the-lies-innovation-and-the-need-for-transparency](#)). His proposals amplify the intent of the new Food and Drug Administration rules regarding clinical trials.⁴ Together they give a road map for how to think about any novel material, drug, or approach. That road map includes the following:

1. Establish uniform guideposts for evaluation. In this scenario, establish guideposts for valve stenosis and regurgitation that all groups will use.
2. Rapidly move those with the greatest financial (or academic) stake in the procedure further from control and eventually away from controlling the data and analysis.
3. Be prepared to share data early; with uniform guideposts, this will enable effective comparison between approaches. This is becoming required.

When something new moves into the marketplace (cars, arts, or medical devices), we make rapid judgments. We need to remember that classics and masterpieces continue to look fantastic over time, whereas many other cars, pieces of art, and medical innovations end up not aging well. The continuing challenge is deciding early when you have a future masterpiece (and making comparison shopping simple!).

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References

1. Helder MRK, Kouchoukos NT, Zehr K, Dearani JA, Maleszewski JJ, Leduc C, et al. Late durability of decellularized allografts for aortic valve replacement: a word of caution. *J Thorac Cardiovasc Surg*. 2016;152:1197-9.
2. Tudorache I, Horke A, Cebotari S, Sarikouch S, Boethig D, Breyman T, et al. Decellularized aortic homografts for aortic valve and aorta ascendens replacement. *Eur J Cardiothorac Surg*. 2016;50:89-97.
3. Sarikouch S, Horke A, Tudorache I, Beerbaum P, Westhoff-Bleck M, Boethig D, et al. Decellularized fresh homografts for pulmonary valve replacement: a decade of clinical experience. *Eur J Cardiothorac Surg*. 2016;50:281-90.
4. Zarin DA, Tse T, Williams RJ, Carr S. Trial reporting in ClinicalTrials.gov—the final rule. *N Engl J Med*. 2016;375:1998-2004.

<http://dx.doi.org/10.1016/j.jtcvs.2017.02.030>