When appropriate, and with cautious attention to inherent limitations, TSA can complement available statistical models and help clinicians critically appraise the available data when considering applications to clinical practice.

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Commentary: Seeing the faces in Rubin's vase

Jacquelyn Quin, MD, MPH

As surgeons increasingly turn to the published literature to guide clinical practice, Chan and Harky¹ provide a timely tutorial on analyzing meta-analysis data using trial sequential analysis (TSA). TSA is essentially the same statistical methodology as interim analysis, which allows investigators in clinical trials to analyze data as it accumulates in “real time” rather than having to wait for a final accounting of all anticipated results.^{2,3} The authors showcase TSA using a recently published meta-analysis by Woldendorp and colleagues on subclinical valve thrombosis (SCVT), stroke, and different antithrombotic strategies in patients who underwent transcatheter valve insertion.⁴ Using the 12 studies from the original publication, the investigators reconfigure the data from forest plots into TSA diagrams. Although the information is essentially the same, a distinctly new perspective

Rubin's vase: a vase with embedded faces.

CENTRAL MESSAGE

Surgeons should be familiar with the principles and caveats of trial sequential analysis, an emerging statistical methodology that offers a unique view of meta-analysis data.

emerges. With TSA, one can visualize the contribution of each individual study, added over time, in the march toward a finite answer.

In the case of the association of SCVT with stroke, the TSA diagram presented in the didactic suggests we ponder this question no further; the statistical significance boundary, set to query whether SCVT was associated with at least a 100% increase in stroke compared with normal leaflet motion, was crossed several studies ago. Additional investigation is unlikely to alter conclusions. However, investigators interested in differences between antithrombotic regimens of dual- versus single-antiplatelet therapy can see that, for a relative risk reduction (RRR) of 20%, the strength of the currently available data renders this question

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FIGURE 1. Rubin's vase: the portrait of a vase that shows the silhouettes of 2 opposing faces in its outline.

unanswerable at the present time—and possibly for a long time coming.

However, lest we rush to celebrate a vehicle that we hope will drive us to definite solutions for these and other pressing clinical questions—or perhaps discourage us from even starting the journey, Chan and Harky caution us on some of the potential pitfalls of using TSA. As illustrated in their tutorial, a major caveat in applying this statistical methodology is the vital importance of a carefully considered effect size, or RRR. Chosen inappropriately, the RRR has the

undesirable potential to erroneously render a conclusion unattainable or to offer conclusions that are definite but meaningless. Also, as with all methodologies that examine data from 30,000 feet above, granularity is lost and can only be restored by the clinician. After all, understanding the data is only half the task; the bigger challenge lies in understanding how such information pertains to the individual patient.

With increasing use of TSA on the horizon,⁵⁻⁷ will we wake one day to find the familiar and comfortable forest plots extinct and replaced by this new aesthetic? Doubtful. Even so, TSA is sure to become a strong complement to currently used methods of analyzing data. It helps us to see the faces in Rubin's vase (Figure 1)⁸ and, in doing so, achieve a fuller understanding of the portrait.

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