WHITE PAPER | CARDIOVASCULAR CENTER OF EXCELLENCE

Your Cardiovascular Clinical Trial Design Was Built for the Regulator. Will It Satisfy the Payer?

Four protocol decisions that serve the regulator and the payer at the same time.

Jaishankar Kutty, Ph.D.
Vice President, Cardiovascular Center of Excellence, RQM+

November 2026

The Paperweight Problem

> **A cleared device that nobody pays for is an expensive paperweight.**

Regulators decide whether a device may be used. Payers decide whether it is meaningfully better than what they already fund, and for whom. The two questions sound like cousins and behave like strangers. The Centers for Medicare & Medicaid Services (CMS) says so in its own notice: authorization by the U.S. Food and Drug Administration (FDA) does not, by itself, entitle a technology to Medicare coverage.[1]

Technically excellent, cleared devices still stall. In our experience, the cause is rarely the engineering. Somewhere in the program, nobody stress-tested the comparator, the endpoints, or the follow-up against the questions a payer would ask. This is a classic evidence design failure, and it is set at protocol lock, long before slow adoption shows up on a sales forecast.

At the RQM+ Cardiovascular Center of Excellence (CV CoE), we see the pattern across structural heart, coronary, electrophysiology, and vascular programs. Four trial design decisions shape both the regulatory outcome and the payer outcome: the indications for use, the comparator, the endpoints and follow-up, and the price of every timeline shortcut. Each can be made once, for both audiences.

Regulators and Payers Read the Same Protocol

Same evidence, different questions

FDA asks whether the device is safe, whether it works, and whether the evidence supports the claim. Payers ask whether it beats the care they already fund, whether the outcomes matter to patients, and whether the economics hold up. For CMS, the formal test is whether an item is reasonable and necessary for the Medicare population, and the agency looks for evidence on that population, on improvement in health outcomes, and on the durability of those outcomes.[1]

	Regulator (FDA)	Payer (CMS)
Core question	Is the device safe and effective for the claimed indication?	Is it reasonable and necessary for Medicare beneficiaries?
Evidence of interest	Safety and effectiveness for the studied population	Health outcomes in the Medicare population, and their durability
Where trials often fall short	Older, multimorbid patients may be excluded to sharpen the signal	Surrogates, weak comparators, and short follow-up

Regulator and payer questions as described in the CMS RAPID notice[1]; the last row reflects our experience.

The Medicare population is the quiet trap. CMS notes that beneficiaries are often older with multiple comorbidities, that approximately 50% of Medicare patients have two or more diseases, and that studies built to win FDA authorization may exclude exactly such patients.[1]

The review bar keeps rising

We see reviewers asking for comparator devices, comparisons across disease states, adaptive designs that defer mortality and morbidity endpoints, and more patient-reported outcomes (PROs). Nothing on this list is purely regulatory. Every protocol decision blends regulatory, clinical, marketing, and business judgment, and the sponsor who treats it as one-dimensional pays for it later.

> **Case file: EVOQUE.** Transcatheter tricuspid valve replacement (TTVR) shows the gap in a single device. EVOQUE's FDA indication is the improvement of health status in patients with symptomatic severe tricuspid regurgitation despite optimal medical therapy. It does not include reducing mortality or heart failure hospitalization, and FDA's summary refers to a planned supplement to the premarket approval (PMA) application to seek a morbidity and mortality indication.[2] Medicare covers TTVR only within coverage with evidence development (CED) under National Coverage Determination (NCD) 20.37, and the CED studies must report primary outcomes of all-cause mortality, hospitalization, or a composite of the two through a minimum of 24 months, with an active comparator.[3] One device, one pivotal trial, two bars: FDA's, which is improved health status, and CMS's, which is mortality or hospitalization through 24 months. At 2 years, the intention-to-treat comparison in the randomized TRISCEND II trial showed no significant difference in all-cause mortality (19.1% vs 25.3%) or in the composite of mortality and heart failure hospitalization (36.0% vs 43.7%), though the trial was not powered for these 2-year comparisons.[4] All five pivotal trials now testing rival valves against EVOQUE (TRINITY, TRIUMPH, PATHFINDER, TRICURE, and TRIVITA) register a 12-month composite of mortality, heart failure hospitalization, and tricuspid valve reintervention as a primary endpoint. In the registrations as of November 10, 2026, only TRIVITA lists outcome assessment at 24 months, for the components of that composite as secondary outcomes. Registrations are summaries, and protocols may go further, but the 24 months that CMS describes is not visible in the other four.[5]

Policy: payer questions are moving upstream

In August 2026, CMS proposed the Regulatory Alignment for Predictable and Immediate Device (RAPID) coverage pathway.[1] RAPID would bring FDA and CMS together at the investigational device exemption (IDE) pre-submission stage. While the pathway is voluntary, it is proposed for Class III Breakthrough-designated devices heading to premarket approval, and for certain Class II Breakthrough devices in FDA's Total Product Life Cycle Advisory Program. The IDE study must enroll Medicare beneficiaries and measure clinical outcomes that FDA and CMS agree are appropriate.[1]

If the data deliver, CMS would post a proposed NCD on the day of FDA authorization and finalize it approximately 90 days later for Class III devices, or 60 days later for Class II devices. National coverage would be limited to the FDA-authorized indications.[1] The public comment period has closed, and RAPID remains a proposal. CMS has also said it would pause new candidates for its earlier Transitional Coverage for Emerging Technologies pathway while RAPID is implemented.[1] The takeaway is plain: Payer questions are moving into protocol design.

> **Regulators and payers read the same protocol. They simply stop at different pages.**

Write the Indications for Use Before You Choose the Pathway

Backward sequencing

Sponsors often choose the quickest regulatory path first and then write the indications for use to fit it. At RQM+ CV CoE, we prefer to start from the clinical condition where the technology is truly differentiated and benefits patients, and to let the pathway follow.

The cost of a broad indication

An extremely broad indication brings more clinical rigor, more post-market requirements, and a different view from CMS and private payers. It sets the evidence requirements and the timeline for everything that follows. My colleague, Deborah Morley, Ph.D., director CV CoE, saw this with a disposable pump head program that arrived with indications pulled in several directions. The sponsor had to decide what to market the device for before the testing and the clinical plan could be tailored.

The payer reads two documents as one

RAPID coverage would be limited to the FDA-authorized indications.[1] The CED guidance expects study populations to reflect the demographic and clinical diversity of the Medicare beneficiaries who are the intended population of the intervention.[6] Between them, the indication and the inclusion criteria decide whom a payer will cover.

The question changes shape by segment. In our experience, structural heart programs enroll older, multimorbid patients, so the trial population needs to look like Medicare patients from the first draft. Coronary programs face a comparator that the field updates faster than a protocol can. In electrophysiology and vascular, the endpoint that matters to the clinician may differ from the one that earns the claim.

> **Choose the destination before you pick the road.**

Choose the Comparator Payers Already Fund

The eleventh-hour trade

We have watched this scene more than once. A trial manager, racing the timeline, waters down the comparator at the eleventh hour. The study succeeds but the payer loses interest because

the comparator was never the standard of care. The net result is that the sponsors earned a monument in the annals of science, and a ruin in the halls of commerce.

Payers compare against what they fund

The CMS CED guidance of August 2024 asks sponsors to justify any design that lacks a contemporaneous comparison group. It describes the most rigorous designs as those that compare the treatment with something else, such as randomization against the current best standard of medical care.[6] Reviewers are moving the same way, as our observation on comparator devices and comparisons across disease states suggests.

Cutlip and Kramer made the value case in 2016. They argued that device trials should test a value-based hypothesis, with patient-reported outcomes as secondary outcomes and cost-effectiveness estimates built into the initial design, and that CMS should agree those design parameters early so that coverage decisions can come sooner.[7]

When a benchmark must do the comparator's job

Several rival TTVR trials pair a randomized cohort against EVOQUE with a single-arm cohort. In all five registrations the single-arm cohort enrolls patients the randomized design leaves out, such as those ineligible for EVOQUE. Such cohorts need an external reference, and TRINITY's registration says its 180-patient single-arm cohort will be tested against a prespecified performance goal.[5] In TRISCEND II, FDA judged 30-day safety in the first 150 randomized patients, the cohort that supported FDA's approval, against a prespecified ceiling of 70% for the major adverse event (MAE) composite (lower is better), a figure derived from surgical tricuspid valve replacement outcomes.[2] The observed rate was 27.4%, and even the upper confidence bound of 36.9% sat more than 30 points below the ceiling. A ceiling that lenient is easy to clear. When a performance goal stands in for a comparator, it deserves the same scrutiny as a comparator. When feasibility forces a weaker comparator, record the payer cost at the moment of the decision. A trade that is written down gets reviewed. A trade that is not written down gets discovered.

> **A comparator that is easy to beat tells the person writing the check very little.**

Set Endpoints and Follow-Up for the Coverage Decision, Too

Endpoints that read like a coverage decision

CMS asks for primary outcomes that matter to patients and caregivers and are clinically meaningful. It accepts a surrogate only when peer-reviewed longitudinal validation studies show that the surrogate predicts those outcomes.[6]

Patient-reported outcomes as shared currency

Lately we are seeing growing weight on quality of life and PROs, especially for wearable and remote devices, where validated instruments and structured collection make the difference. FDA's final guidance on PRO instruments for medical device evaluation, issued in January 2022, stresses fit-for-purpose measures.[8]

Counting belongs to the endpoint

In the structural heart space, we firmly believe that a pacemaker rate quoted without its denominator is a rumor. In FDA's EVOQUE approval document, the same 14 pacemakers equal 14.7% of all patients or 22.6% of patients without a pacemaker or implantable cardioverter-defibrillator at baseline.[2] Published EVOQUE pacemaker figures differ by denominator, event definition, and follow-up clock, so one outcome ends up with several different numbers. The first Tricuspid Valve Academic Research Consortium (TVARC) document already tells the field to exclude patients with a pre-existing pacemaker when calculating new pacemaker rates.[9] A payer cannot compare what a protocol never defined.

Follow-up long enough to show durability

We've approached trial strategies with an adaptive design pattern in which early endpoints are reported first and mortality and morbidity are reported later. We recommend you schedule those later time points so they also answer the payer's durability question. The CED guidance asks for observation long enough to demonstrate the durability of health outcomes.[6]

A coverage-ready endpoint package includes:

- A primary outcome that matters to patients and caregivers
- Validated PRO instruments with structured collection
- Surrogates only where validation studies support them
- Follow-up that reaches durability
- Data elements for resource use and cost offsets

> **An endpoint is a promise. Make sure the payer can cash it.**

Price Every Timeline Shortcut Before You Take It

Daily decisions, late consequences

Every decision a trial manager makes on an ordinary Tuesday carries a commercial consequence that arrives at the eleventh hour. This is why RQM+ scopes those decisions at the start. Shortcuts hide in watered-down comparators, convenient populations, and shortened follow-up. Each saves weeks and can cost a coverage decision.

We ask teams to keep a one-page shortcut register: the trade, the weeks saved, and the payer question it leaves open. If the register looks empty, someone has stopped looking.

Serial planning, the quieter delay

We've frequently noticed sponsors who finish one study before starting the next, and who miss that one study can answer several objectives. An animal study can cover some human factors work. A clinical study can address certain biological safety questions alongside biocompatibility testing. The fastest credible timeline comes from studies designed to answer multiple questions at once.

> **Every shortcut is a loan. The payer collects the interest.**

Coding Opens a Payment Pathway, and Coverage Still Requires Your Data

Reimbursement has three elements: coding, coverage, and payment.[10] A device entering a well-coded area inherits an existing payment pathway. This says nothing yet about coverage for that technology, and coverage often requires the sponsor's own clinical data. The surprise arrives when approval lands and investors expect revenue.

The aortic valve shows how evidence gates coverage. On September 10, 2026, CMS issued its final decision memo revising the national coverage determination for transcatheter aortic valve replacement (TAVR). CED requirements were dropped for symptomatic severe aortic stenosis, and they remain in place for asymptomatic patients, whose coverage is now extended under those requirements.[11]

Scoping coverage at protocol lock removes the surprise. (Related RQM+ reading: Approved, Covered, Adopted: Why Reimbursement Strategy Has to Come First.)

> **A code is a parking spot. Coverage is permission to park.**

Make Each Decision Once, Before Protocol Lock

Use the mechanism available now

FDA's Early Payor Feedback Program (EPFP) lets sponsors obtain payor input on trial design and evidence plans, either in an FDA Q-Submission meeting that payors attend or in a separate meeting.[10] FDA recommends contacting the program when planning the pivotal trial, or sooner.[10]

FDA reports that these interactions have either confirmed the sponsor's approach or led to modified study designs, additional endpoints, altered inclusion and exclusion criteria, added trial sites, and captured health economic and real-world data.[10] As of December 2024, 158 requests had been matched with payors. Participation does not change FDA's review standards or timelines.[10] Parallel Review, in which FDA and CMS review pivotal data concurrently, can follow the EPFP.[10]

RQM+ RQM+

> **Make each decision once. Make it before protocol lock.**

Approval is base camp. The summit is a device that gets adopted, paid for, and scaled.

Five Questions to Ask Before Protocol Lock

Does the indications for use statement reflect where the device is truly differentiated, with a written rationale?

If the rationale is not on paper, the indication was chosen by the pathway. A written rationale also becomes the first page of the payer conversation.

Is the comparator what payers already fund?

Test it against current standard of care and against the CED expectation of a contemporaneous comparison group. If a single-arm cohort is unavoidable, scrutinize the performance goal as hard as a comparator.

Would the endpoints and follow-up support a coverage decision as well as approval?

Check for primary outcomes that matter to patients, validated surrogates and PROs, a defined denominator, and follow-up that reaches durability.

Has each timeline trade-off been priced against its payer impact?

Keep the shortcut register. Every entry names the weeks saved and the payer question left open.

Does the device have a coverage path beyond its codes?

A code opens a payment pathway. Coverage usually depends on your own clinical data, so scope it before the protocol locks.

Approaching Protocol Lock on a Cardiovascular Device?

Jaishankar Kutty, Ph.D., and Deb Morley, Ph.D., of the RQM+ Cardiovascular Center of Excellence build regulatory, clinical, and reimbursement strategy as one plan to help MedTech manufacturers reach commercial success. The Center brings 45+ years of collective cardiovascular regulatory and clinical expertise and has supported more than 40 cardiovascular studies, including ventricular assist devices, structural heart, and transcatheter valve devices. Talk with them before the protocol locks.

> **Let’s make your MedTech program happen.**

References

[1] Centers for Medicare & Medicaid Services. Medicare Program; Regulatory Alignment for Predictable and Immediate Device (RAPID) Coverage Pathway [CMS-3487-NC]. Federal Register, August 11, 2026. https://public-inspection.federalregister.gov/2026-16368.pdf

[2] U.S. Food and Drug Administration. Summary of Safety and Effectiveness Data: EVOQUE Tricuspid Valve Replacement System. PMA P230013. https://www.accessdata.fda.gov/cdrh_docs/pdf23/P230013B.pdf

[3] Centers for Medicare & Medicaid Services. National Coverage Analysis: Transcatheter Tricuspid Valve Replacement (TTVR), CAG-00467N, Decision Memo; and MLN Matters MM14149, National Coverage Determination 20.37 (effective March 19, 2025). https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=314 and https://www.cms.gov/files/document/mm14149-national-coverage-determination-20-37-transcatheter-tricuspid-valve-replacement.pdf

[4] Maxwell, Y.L. Hints of a Mortality Benefit With TTVR at 2 Years: TRISCEND II. TCTMD, April 7, 2026. https://www.tctmd.com/news/hints-mortality-benefit-ttvr-2-years-triscend-ii

[5] ClinicalTrials.gov registrations: TRINITY (NCT07454980), TRIUMPH (NCT07687485), PATHFINDER (NCT07321899), TRICURE US IDE (NCT07528326), TRIVITA (NCT07516444). Accessed November 10, 2026. https://clinicaltrials.gov/study/NCT07454980 and https://clinicaltrials.gov/study/NCT07687485 and https://clinicaltrials.gov/study/NCT07321899 and https://clinicaltrials.gov/study/NCT07528326 and https://clinicaltrials.gov/study/NCT07516444

[6] Centers for Medicare & Medicaid Services. Coverage with Evidence Development Guidance Document. August 7, 2024. https://www.cms.gov/files/document/ced-guidance2024pdf.pdf

[7] Cutlip, D.E., & Kramer, D.B. Value-Based Hypothesis Testing for Cardiac Device Clinical Trials: A Pathway for Accelerated Reimbursement Decisions. Circ Cardiovasc Interv. 2016;9(5):e003627. https://doi.org/10.1161/CIRCINTERVENTIONS.116.003627

[8] U.S. Food and Drug Administration. Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation. Final guidance, January 2022. https://www.fda.gov/media/141565/download

[9] Hahn, R.T., Lawlor, M.K., Davidson, C.J., et al. Tricuspid Valve Academic Research Consortium Definitions for Tricuspid Regurgitation and Trial Endpoints. Eur Heart J. 2023;44(43):4508-4532. https://doi.org/10.1093/eurheartj/ehad653

[10] U.S. Food and Drug Administration. Medical Device Coverage Initiatives: Connecting with Payors via the Payor Communication Task Force. Content current as of June 29, 2026. https://www.fda.gov/about-fda/cdrh-innovation/medical-device-coverage-initiatives-connecting-payors-payor-communication-task-force

[11] Centers for Medicare & Medicaid Services. Transcatheter Aortic Valve Replacement (TAVR), Decision Memo, final NCD. September 10, 2026; and McKeown LA. CMS Finalizes Anticipated Updates to National Coverage of TAVI. TCTMD, September 11, 2026. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=321&ncacaldoctype=all&status=all&sortBy=status&bc=17 and https://www.tctmd.com/news/cms-finalizes-anticipated-updates-national-coverage-tavi