REASONS TO NOT IGNORE THIS PAPER

#1: CLINICAL TRIALS CAN MAKE OR BREAK YOUR DEVICE. ARMED WITH OUR EXPERTISE, IT'S LESS 'BREAK' AND MORE 'BREAKTHROUGH.

#2: WHEN IT COMES TO CLINICAL TRIALS, DON'T GAMBLE, READ OUR WHITEPAPER AND LEARN HOW TO ACE THE APPROVAL AND ACCESS GAME EVERY TIME.

WHITE PAPER

Trials That Pay: Designing Clinical Studies to Optimize Reimbursement and Market Access

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RQM+ Evolving MedTech

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EXECUTIVE SUMMARY

Designing Clinical Studies to Optimize Reimbursement and Market Access

The optimal clinical study design ensures not only regulatory compliance but also generates high-quality, valid data[1] essential for securing favorable reimbursement and market access in the United States and European Union (EU). A well-designed trial mitigates risks of bias, maintains internal and external validity, and delivers statistically robust results that can be confidently applied to real-world settings. In contrast, poor study design may lead to insufficient statistical power, unclear endpoints, and irrelevant outcomes, causing regulatory delays, increased costs, and missed market opportunities. Most critically, it can undermine the case for reimbursement, making it difficult to demonstrate the device's value to key stakeholders such as physicians, patients, and payers.

This white paper presents real-world case studies involving medical technology, demonstrating how thoughtful study design has led to successful trial outcomes. We also explore the limitations of alternative designs and their regulatory and reimbursement consequences in both the US and EU.

REGULATORS ARE LIKE YOUR IN-LAWS: THEY WANT EVERYTHING PERFECT. WE CAN SHOW YOU HOW TO IMPRESS THEM WITHOUT BREAKING THE BANK.

Additionally, we showcase how **RQM+** serves as a strategic partner, guiding manufacturers through the complexities of clinical trial design, and execution, ensuring trials are optimized not just for regulatory approval, but also for reimbursement success, long-term market access and post-market evidence generation. At **RQM+**, we are committed to a capital-efficient approach in generating the high-quality evidence needed to meet both regulatory and reimbursement standards, maximizing value while minimizing unnecessary costs.

INTRODUCTION

The Critical Impact of Study Design on MedTech Success

In medical technology clinical trials, study design is not merely a regulatory requirement, it is a strategic decision that influences the entire product lifecycle. Valid trial designs, ensuring both internal validity (freedom from bias) and external validity (applicability to real-world populations)[1], are critical not only for securing regulatory approval but also for paving the way to reimbursement. Clinical evidence that meets the rigorous demands of regulators must also satisfy payers, who control access to healthcare markets. Importantly, there are typically more payers than regulators, each with unique "requirements" for reimbursement.

CLINICAL TRIALS & REIMBURSEMENT: LIKE TRYING TO FOLLOW A RECIPE FROM A COOKING SHOW. IT LOOKS EASY ON TV, BUT IN REALITY, YOU NEED THE RIGHT GUIDE TO AVOID A KITCHEN DISASTER.

OUR EXPERTISE IS YOUR FOOLPROOF RECIPE FOR SUCCESS.

At **RQM+**, we design trials that optimize data collection to meet both regulatory and reimbursement requirements, ensuring efficient alignment between the evidence generated and the specific needs of each market. Our approach balances time-to-market goals, reimbursement potential, sustainable market share opportunities, and healthcare impact to maximize the value and accessibility of innovations. Each trial is tailored to address payer expectations, intended marketing claims, and global market dynamics, enabling manufacturers to demonstrate not only the clinical value of their innovations but also their economic impact. The right study design doesn't just accelerate time-to-market; it lays the foundation for sustainable commercial success and broad patient access.

In the following sections, we will present and critique study design choices with a focus on sustainability in medical device development (section 1), provide some handy hints used by RQM+ to refine study designs (section 2), and conclude with our strategic approach for medtech innovation, aligned with your market access strategy (section 3).

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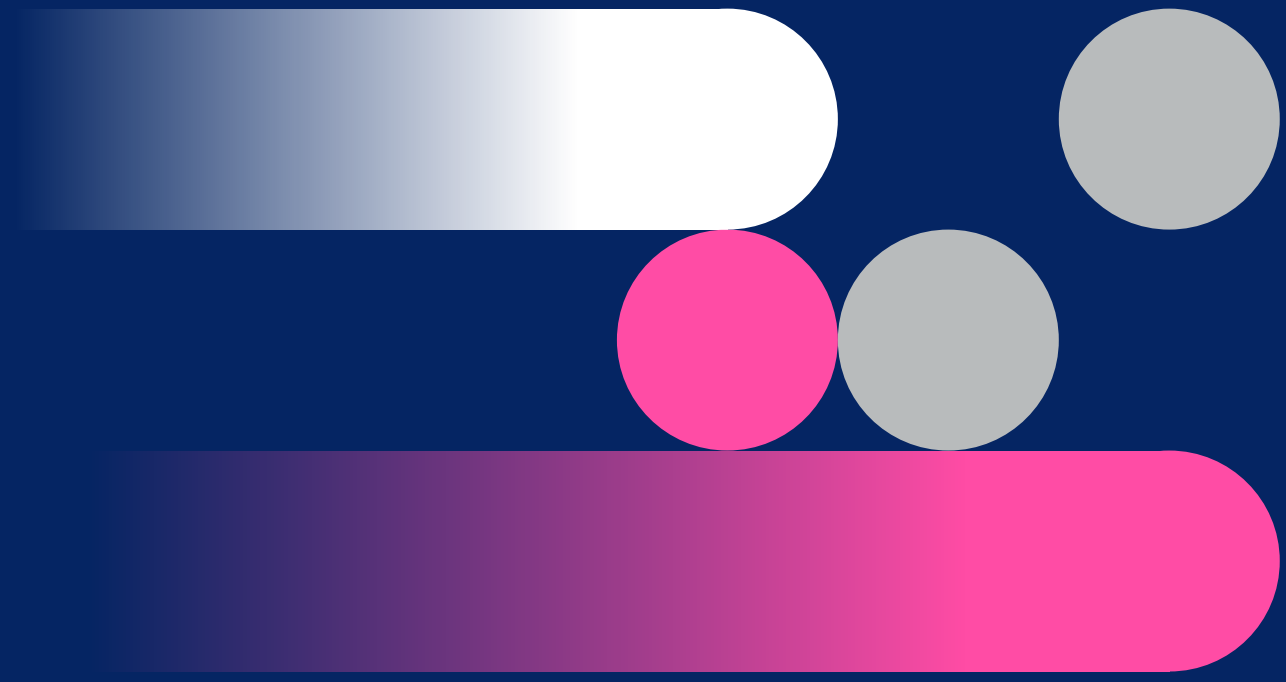
Evolving MedTech

DISCUSSION SECTION 1

Case Studies in Clinical Trial Design that Accelerated Market Access and Facilitated Reimbursement



CASE STUDY 01

Superiority Randomized Controlled Trial (RCT) Trial for the Watchman Left Atrial Appendage Closure Device

Context

WHY DID THE WATCHMAN DEVICE CROSS THE ROAD?

TO BEAT WARFARIN AT ITS OWN GAME AND REDUCE BLEEDING RISKS!

The Watchman Left Atrial Appendage Closure (LAAC) device was developed as an alternative to long-term anticoagulation therapy for patients with non-valvular atrial fibrillation (AF) at risk of stroke. The device aimed to reduce stroke risk while minimizing bleeding complications associated with warfarin, the standard treatment. To validate its clinical and economic value, a superiority trial was conducted, designed to demonstrate that the Watchman device not only matched warfarin's efficacy in stroke prevention but outperformed it in reducing major bleeding events, a significant factor for patients on anticoagulants. In other words, the trial had to show superiority because warfarin was significantly less expensive than the Watchman device.

Study Design

A superiority trial was chosen over other design types to directly compare the Watchman device against warfarin. The trial's objective was to show that the device not only prevented stroke effectively but also offered a clear advantage in reducing major bleeding risks, addressing a key limitation of anticoagulation therapy. Ensuring internal validity was critical, with stringent controls and randomization to reduce bias and confounding variables, enhancing the trial's power and reliability[2].

Outcome

The trial demonstrated that the Watchman device was non-inferior to warfarin for preventing stroke and systemic embolism, and superior in reducing hemorrhagic stroke and major bleeding events. These results were crucial in securing FDA approval and supporting reimbursement, especially for high-risk patients contraindicated for long-term warfarin use. The strong internal validity of the trial made the results highly credible, aiding both regulatory and payer acceptance.

A SUPERIORITY TRIAL ISN'T JUST PROVING YOUR DEVICE WORKS; IT'S DECLARING WAR ON MEDIOCRITY.

Reimbursement Impact

US: The superiority data from the Watchman trial was essential in securing coverage from both Medicare and private insurers. CMS places high value on strong evidence when considering alternatives to well-established therapies like anticoagulants. Coverage under NCD 20.34 applies specifically to patients with non-valvular atrial fibrillation who cannot tolerate long-term anticoagulants, making it an option only where the risk-benefit profile is appropriate for those contraindicated for anticoagulation therapy. This focused, broad coverage under both Medicare and Medicare Advantage not only accelerated market adoption but also expanded access for patients in need across various care settings[3,4].

EU: In Europe, HTA bodies like NICE and HAS don't directly offer reimbursement, but their evaluations of the device's cost-effectiveness for high-risk patients shape reimbursement decisions. Favorable assessments by these bodies have led to the Watchman being recommended for reimbursement by national health systems in the UK and France[5]. By demonstrating clear clinical superiority over warfarin, the Watchman gained acceptance across multiple markets, supported by solid cost-effectiveness data.

Alternative Design and Implications

Non-Inferiority Trial

While a non-inferiority trial could have shown the Watchman was as effective as warfarin, it wouldn't have provided the superiority data needed to prove the device's clear advantages in reducing bleeding risks, which was crucial for regulatory and payer acceptance (who look for clear, incremental benefits).

Regulatory and Reimbursement Implications

Without superiority data, the device may have struggled to gain approval and reimbursement due to insufficient proof of its clinical benefits over warfarin. The trial's strong internal validity ensured that the findings were robust, giving both regulators and payers confidence in the device's benefits.

Cost Implications

Superiority trials require larger investments but provide stronger evidence, accelerating regulatory approval and reimbursement, leading to quicker market adoption. In this case, the larger investment yielded quicker market access, which likely helped recoup trial costs more swiftly due to earlier adoption.

CASE STUDY 02

Non-Inferiority RCT for the PARTNER 2 Trial (Transcatheter Aortic Valve Replacement)

Context

The PARTNER 2 trial was a landmark study evaluating the use of **TAVR** using the Edwards SAPIEN XT valve in intermediate-risk patients with severe aortic stenosis, comparing it to traditional surgical aortic valve replacement (SAVR). The trial's aim was to demonstrate that TAVR could serve as a viable alternative for patients at intermediate surgical risk, as it had already been established for high-risk patients. This comparison was crucial in addressing both clinical effectiveness and the economic sustainability of the TAVR procedure for broader patient groups[6].

TAVR VS. SAVR: IT'S LIKE COMPARING A SPORTS CAR TO A SEDAN. BOTH GET YOU THERE, BUT ONE DOES IT WITH A LOT MORE STYLE AND LESS RECOVERY TIME.

Study Design

Non-Inferiority Trial

A non-inferiority randomized controlled trial (RCT) was chosen to compare TAVR and SAVR because it provided the highest level of evidence while focusing on showing that TAVR was at least as effective as SAVR, without setting an unrealistic bar for superiority. This design was selected to address internal validity by ensuring that any differences in outcomes could be attributed to the intervention itself, minimizing confounding factors and biases. In terms of external validity, the diverse patient population and real-world clinical setting ensured that results could be generalizable to a broader population of intermediate risk patients[6].

Outcome

The trial successfully demonstrated that TAVR was non-inferior to SAVR in terms of key outcomes like mortality and stroke rates at two years. Furthermore, TAVR showed significant advantages in terms of recovery time and patient quality of life, leading to lower long-term healthcare costs and improvements in quality-adjusted life years (QALY). These findings provided a compelling case for TAVR as a standard alternative to SAVR, particularly for intermediate-risk patients. The strong internal and external validity of the trial ensured that results could be confidently applied to wider clinical practice, reinforcing the economic and clinical value of TAVR for reimbursement[6,7,8,9].

Reimbursement Impact

US: For high-risk interventions like TAVR, both Medicare and private insurers require robust RCT data to support reimbursement. The PARTNER 2 trial provided sufficient evidence for CMS to expand reimbursement coverage from high-risk to intermediate-risk patients, increasing access to the procedure. Moreover, the improved QALY finding was important towards securing reimbursement, as TAVR became the preferred treatment option for many intermediate-risk patients from both a clinical and economic standpoint[7,8,9].

EU: Positive evaluations from Health Technology Assessment (HTA) bodies like NICE (UK) and HAS (France) based on the PARTNER 2 trial influenced reimbursement decisions across Europe. While HTA bodies do not directly provide reimbursement, their cost-effectiveness assessments guide national health systems in adopting TAVR as an alternative to surgery. Favorable assessments from these bodies led to the inclusion of TAVR in national reimbursement schemes, making it accessible to more intermediate-risk patients across the EU[10].

Alternative Design and Implications

Superiority Trial

A superiority trial would require the valve to outperform surgery, setting an unnecessarily high bar. Additionally, the cost implications of conducting a superiority trial, with its larger patient numbers and longer follow-up, would have delayed market entry and increased financial burdens without clear added benefit. A single-arm study lacks a comparator, weakening the case for reimbursement.

Other Designs

A single-arm study or observational study designs would lack a comparator, weakening the study's ability to convince regulators and payers of the device's clinical and economic benefits. Cohort or case-control studies, while potentially faster, introduce bias and confounding factors that would make it harder to secure robust RCT-level evidence required for reimbursement in high-risk procedures like TAVR.

Regulatory and Reimbursement Implications

Regulatory bodies and payers typically require RCT data for high-risk interventions like TAVR. However, while RCTs are often essential for demonstrating equivalence or non-inferiority to established procedures like SAVR, in some cases, achieving this level of evidence may not be feasible. A well-planned trial design must carefully consider multiple factors such as diversity, patient risk profiles, study feasibility, and data requirements (among others) for each specific market. Therefore, it's critical to have the experience in designing trials that navigate these complex considerations, towards optimizing the evidence generated to meet both regulatory standards and the cost-effectiveness demands of payers, especially in cost-sensitive markets like the EU where reimbursement could otherwise be delayed or rejected.

Cost Implications

While a superiority trial would have increased costs due to larger patient numbers and longer follow-up, a single-arm or observational study might have lowered upfront costs but would likely have led to additional trials and further regulatory delays, ultimately increasing long-term costs. The non-inferiority trial struck a balance, providing the strongest evidence needed for rapid approval and reimbursement while maintaining cost-efficiency.

CASE STUDY 03

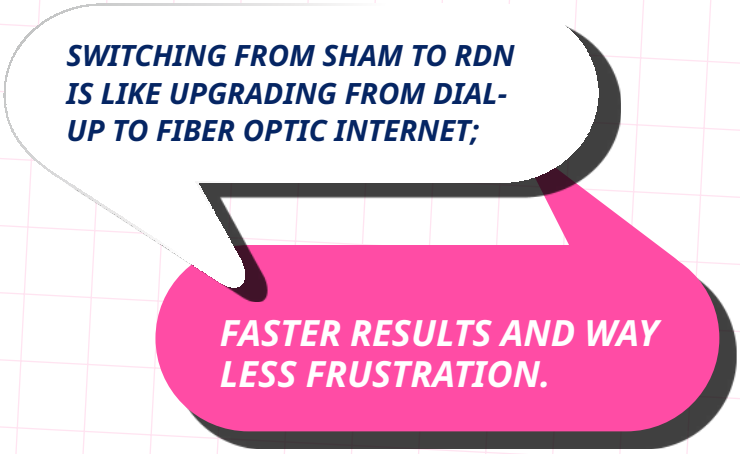
Crossover Randomized Controlled Trial RADIANCE-HTN TRIO Trial for Renal Denervation in Resistant Hypertension

Context

The RADIANCE-HTN TRIO trial assessed ultrasound-based renal denervation (RDN) in patients with resistant hypertension who remained hypertensive despite multiple medications. The trial's aim was to compare the effectiveness of RDN against a sham procedure, a necessary step given the high placebo effect commonly seen in hypertension trials. By targeting a population of patients who had exhausted medication options, the study focused on validating RDN as a treatment solution for this challenging cohort[11].

Study Design

A crossover randomized controlled trial was chosen to enhance the study's internal validity and precision. By allowing participants in the sham group to cross over to the RDN group after two months, the design minimized variability between groups, allowing for within-subject comparisons. This approach reduced potential confounding factors and strengthened the trial's statistical power, providing more robust and reliable evidence to support reimbursement applications[11].



Outcome

The trial demonstrated that RDN significantly reduced daytime ambulatory systolic blood pressure (SBP) by 8 mm Hg compared to a 3 mm Hg reduction in the sham group after two months. The safety profile was strong, with no significant differences in adverse events between the groups. The results provided a clear and valid demonstration of the treatment's effectiveness, which is crucial for both regulatory approval and reimbursement by healthcare payers.

Reimbursement Impact

US: The significant blood pressure reduction achieved in the RADIANCE-HTN TRIO trial provided compelling evidence for CMS and private insurers to consider reimbursement for RDN, particularly in patients with resistant hypertension. Recently, both Medtronic's Symplicity Spyral and Recor Medical's Paradise ultrasound RDN systems have since been granted transitional pass-through (TPT) payment status by CMS under the Medicare outpatient prospective payment system. This TPT status is a significant advancement, as it provides additional reimbursement for hospitals to adopt these systems, supporting the financial viability of RDN procedures and promoting wider access to the technology for eligible patients[11,12,13,14a]. Previously, both the Paradise ultrasound RDN and Medtronic's Symplicity Spyral systems were eligible for payment under the New Technology Add-On Payment (NTAP) program, offering financial incentives to hospitals using them[14b].

EU: The Paradise RDN system has received CE Mark approval, allowing it to be marketed in Europe. In our understanding, HTA bodies like NICE and HAS are still assessing renal denervation, and the trial data from RADIANCE-HTN TRIO will be key in influencing future reimbursement decisions. Meanwhile, this device is being evaluated through the Global Paradise System (GPS) Registry, which collects long-term real-world data in the US, EU and UK. Along with the data from the crossover-RCT, this registry is crucial for ongoing reimbursement discussions with HTA bodies like NICE and HAS since their evaluations will pave the way for national health systems to consider reimbursing RDN technologies across the EU[15].

Alternative Design and Implications

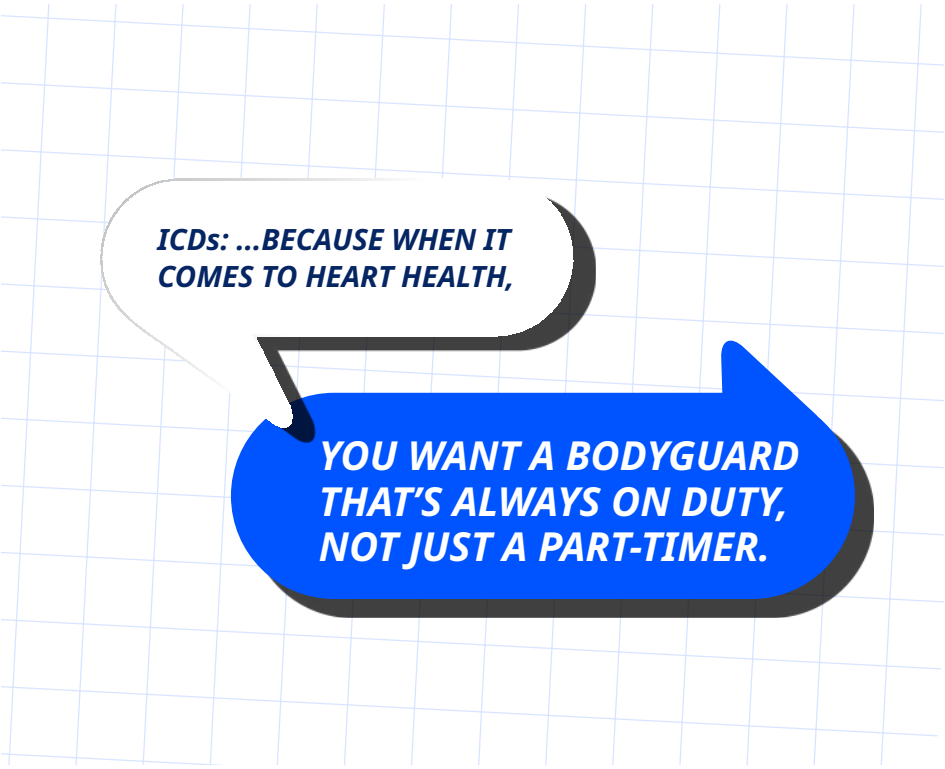
Parallel-Group Design	A parallel-group design would have required more participants and increased variability between the groups, potentially reducing the study's statistical power. This would have made it harder to demonstrate the treatment's effectiveness and obtain rapid regulatory and reimbursement approvals.
Single-Arm Study	A single-arm study would lack a comparator group, severely weakening the case for reimbursement as the placebo effect is strong in hypertension studies. The crossover design was thus critical in enhancing internal validity by allowing within-patient comparisons.
Regulatory and Reimbursement Implications	Regulatory bodies prefer the more robust data provided by crossover designs, particularly for treatments like RDN where placebo effects are considerable. Strong efficacy data makes the case for reimbursement in both the US and Europe.
Cost Implications	The crossover design reduced the number of patients required, thereby improving cost efficiency and accelerating the trial timeline. This helped bring RDN to the market faster while potentially reducing long-term healthcare costs for patients with resistant hypertension.

CASE STUDY 04

Cohort Study on Long-Term Outcomes of Implantable Cardioverter Defibrillators (ICDs)

Context

The MADIT-II trial evaluated the long-term effectiveness of ICDs for the primary prevention of sudden cardiac death in patients with a history of myocardial infarction and reduced left ventricular ejection fraction. Unlike a randomized controlled trial, this study used a prospective cohort design to follow patients who received ICDs based on established clinical indications, assessing their real-world outcomes over time. The cohort study focused on generating evidence under real-world conditions, which is valuable for reimbursement decisions where long-term outcomes are key[16,17].



Study Design

A prospective cohort study was chosen to observe the real-world performance of ICDs over time in a clinical setting. Patients were not randomized; instead, they were treated based on established guidelines, allowing the researchers to track the natural course of their outcomes. This design facilitated the collection of real-world data on ICD effectiveness in typical practice settings, enhancing external validity by reflecting broader patient populations than those typically included in controlled trials[16,17].

Outcome

The study showed that ICD therapy significantly reduced mortality rates in high-risk patients and decreased the frequency of sudden cardiac death, reinforcing the device's role in primary prevention. Despite potential biases introduced by the lack of randomization, the large sample size and real-world relevance of the results supported the trial's findings, making the case for expanded ICD use and reimbursement.

Reimbursement Impact

US: Large cohort studies like MADIT-II are often used by CMS and private insurers in the absence of RCT data. The real-world evidence generated by the trial was critical in expanding CMS coverage for ICDs in high-risk patients, eliminating the need for prior electrophysiologic testing and broadening access for Medicare beneficiaries[18].

EU: HTA bodies like NICE and HAS incorporated the MADIT-II trial data into their evaluations, recommending ICDs for primary prevention in patients with reduced ejection fraction. This resulted in widespread reimbursement across the EU, ensuring high-risk patients have access to this lifesaving technology[19,20].

Alternative Design and Implications

Randomized Controlled Trial (RCT)	An RCT could have provided stronger internal validity by controlling for confounding factors through randomization. However, the cohort study design allowed researchers to observe a larger, more diverse population under real-world conditions, reflecting typical clinical practice more closely.
Regulatory and Reimbursement Implications	While RCT data is often preferred for high-risk interventions, cohort studies like MADIT-II are still influential in supporting reimbursement decisions when they provide robust, long-term data on device performance. The lack of randomization does introduce potential biases, but the large sample size and real-world relevance often offset these concerns.
Cost Implications	Cohort studies tend to be less expensive and faster to conduct than RCTs, as they do not require the same level of randomization and control. The MADIT-II study allowed for quicker access to real-world data, which supported timely decisions on ICD use and reimbursement.

CASE STUDY 05

Post-Market Surveillance Study of the Medtronic Micra Transcatheter Pacing System (TPS)

Context

The Medtronic Micra TPS is a leadless pacemaker that was subject to a post-market surveillance study to evaluate its long-term safety and performance in real-world settings. As a leadless system, it offers advantages in reducing complications associated with traditional pacemakers. The post-market study was designed to assess real-world safety and efficacy data for patients already using the device, following FDA approval.

Study Design

A retrospective cohort study was selected for this post-market surveillance phase, gathering real-world data (RWD) from patients implanted with the Micra TPS. This design was ideal for collecting data on safety and efficacy in real-world use, enabling researchers to identify rare complications that might not have been observed during pre-market studies[21].

Outcome

The study confirmed the long-term safety and performance of the Micra TPS, with rare but identifiable complications emerging from real-world use. The retrospective cohort design allowed for the timely collection of these data points, reinforcing the device's safety profile and providing critical insights for both regulators and payers as they consider ongoing reimbursement and coverage decisions.

THE MICRA TPS IS LIKE THE NINJA OF PACEMAKERS: SMALL, STEALTHY, AND GETS THE JOB DONE WITHOUT A TRACE

Reimbursement Impact

US: CMS approved coverage for the Micra TPS under its Coverage with Evidence Development (CED) program following FDA approval[22]. The long-term safety and effectiveness data gathered through this post-approval study reinforced its reimbursement status, particularly as CMS increasingly values real world evidence (RWE).

EU: NICE and HAS evaluated the Micra TPS positively, based on its clinical effectiveness and reduced complication rates compared to traditional pacemakers[23]. This paved the way for reimbursement across key EU markets, with the NHS and French health systems adopting the device for leadless pacing technology.

Alternative Design and Implications

RCT	An RCT would be impractical in a post-market setting, as the device is already approved. Post-market studies typically rely on observational data like those collected in this retrospective cohort design to track real-world outcomes and maintain market access. Please note that whilst confirmatory clinical investigations can be conducted, most post-market studies are typically observational in nature.
Regulatory and Reimbursement Implications	A cohort study is sufficient for post-market surveillance and ongoing reimbursement. An RCT would be redundant and unnecessary.
Cost Implications	A cohort study is cost-effective for post-market data collection. An RCT at this stage would add unnecessary expenses without additional regulatory or reimbursement benefits.

CASE STUDY 06

Diagnostic Accuracy Study for iRhythm's Zio Patch (Wearable ECG Monitor)

Context

The Zio Patch by iRhythm is a wearable electrocardiogram (ECG) monitor designed for detecting arrhythmias over extended periods. Given its innovative approach compared to the traditional Holter monitor, a diagnostic accuracy study was conducted to assess its ability to detect arrhythmias with superior sensitivity and specificity. This study was essential not only for regulatory approval but also for securing reimbursement, as diagnostic accuracy is key for both payers and regulators in evaluating new diagnostic devices[24].

THE ZIO PATCH: DETECTING ARRHYTHMIAS LIKE A DETECTIVE ON A STAKEOUT, ALWAYS WATCHING, NEVER MISSING A BEAT.

Study Design

A diagnostic accuracy study was selected to compare the Zio Patch's performance against the gold-standard Holter monitor, focusing on the device's sensitivity (its ability to detect arrhythmias) and specificity (its accuracy in avoiding false positives). This design ensured that the study was centered on the core metrics important for diagnostic tools and met the strict validity criteria needed to demonstrate the Zio Patch's superiority in clinical practice. Unlike RCTs or cohort studies, which would have been impractical and irrelevant for measuring diagnostic performance, the diagnostic accuracy study provided targeted, efficient, and conclusive data[24].

Outcome

The Zio Patch demonstrated superior diagnostic accuracy, detecting more arrhythmias with higher sensitivity and specificity compared to the Holter monitor. This led to its rapid adoption in clinical settings, with healthcare providers favoring the Zio Patch for long-term monitoring of patients at risk of arrhythmias. The findings were critical in securing regulatory approval and supporting reimbursement applications, particularly as the data showed clear advantages over the established diagnostic standard.

Reimbursement Impact

US: CMS and private insurers rely on diagnostic accuracy studies to assess devices like the Zio Patch. The strong evidence of the device's accuracy in detecting arrhythmias has facilitated coverage under Medicare Part B, using specific Current Procedural Terminology (CPT) codes based on the monitoring duration[25]. Unlike traditional Holter monitors, the Zio Patch measures arrhythmias in a significantly shorter time frame, necessitating new codes to account for its unique application and use case. New technologies often require custom CPT codes that align with their distinct functionalities and monitoring durations, as in this case. Processes within the American Medical Association, CPT and CMS can expedite the creation and approval of such codes, which, if leveraged appropriately, can help accelerate the reimbursement timeline. These tailored codes ensure that healthcare providers can adopt the Zio Patch without financial barriers, contributing substantially to its market success and wider acceptance in clinical practice.

EU: NICE and HAS require clear diagnostic accuracy data to evaluate devices for reimbursement. NICE, issued guidance endorsing the Zio Patch for arrhythmia detection, citing its advantages over standard Holter monitors, which has facilitated reimbursement across the NHS and encouraged broader adoption in other EU markets[26]. The device's ability to provide better long-term monitoring supported payer decisions, as it was seen to reduce the need for additional testing and hospital visits.

Alternative Design and Implications

RCT or Cohort Study

These designs would not focus on diagnostic accuracy and would be unnecessary for a diagnostic device where the primary concern is sensitivity and specificity. Diagnostic accuracy studies are optimized to measure sensitivity and specificity, making them the most appropriate choice for evaluating a device like the Zio Patch. RCTs or cohort studies, while useful for interventional studies, would have increased costs unnecessarily without delivering useful insights for diagnostic performance.

Regulatory and Reimbursement Implications

Diagnostic accuracy studies are required by both regulatory bodies and payers for diagnostic devices. Alternative designs would fail to meet reimbursement criteria in both the US and EU.

Cost Implications

The diagnostic accuracy study proved to be the most cost-effective approach for assessing the Zio Patch. It provided clear and actionable data without the need for larger, more complex trials. Conducting an RCT or cohort study would have increased costs and delayed market entry without offering additional value for reimbursement purposes. This study demonstrated the economic efficiency of choosing a targeted diagnostic trial for regulatory approval and payer acceptance.

CASE STUDY 07

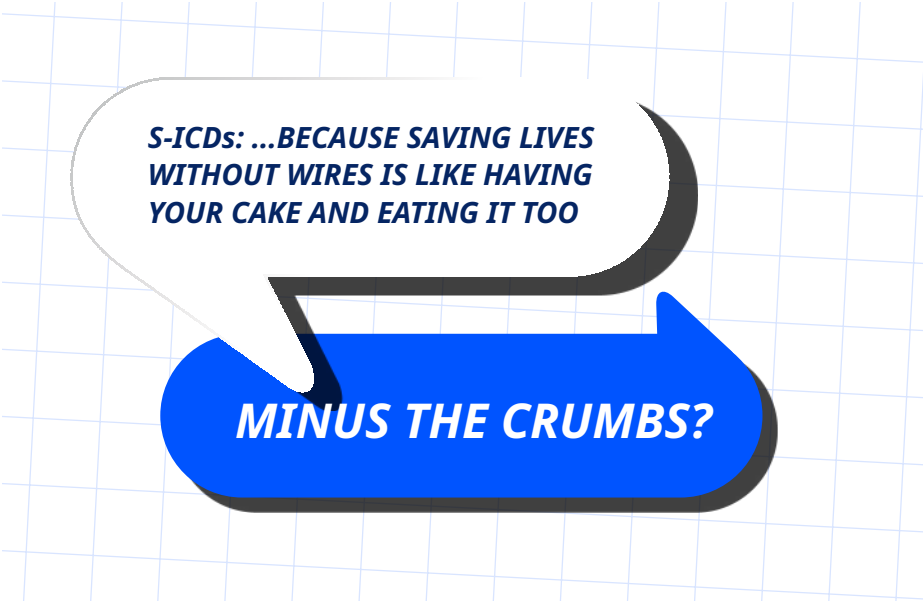
Registry Studies for Subcutaneous ICDs (S-ICD)

Context

The S-ICD was developed to reduce the risks associated with traditional ICDs by eliminating the need for intravascular leads, which are linked to complications. To assess the long-term safety, efficacy, and real-world performance of the S-ICD, multiple registry studies, including the EMBLEM S-ICD Registry and the EFFORTLESS Study, were established[27]. These studies aimed to provide comprehensive data on the device's effectiveness in preventing sudden cardiac death and assess its impact on patient outcomes, which would be crucial for securing reimbursement.

Study Designs

- **EMBLEM S-ICD Registry:** This was a multi-national, prospective registry collecting data from patients who had been implanted with the S-ICD. The registry focused on long-term safety and effectiveness, monitoring patients for several years after implantation. By including a diverse patient population, the study ensured that its findings were widely applicable, thereby enhancing external validity.



- **EFFORTLESS Study:** This study was one of the largest post-market studies on the S-ICD, enrolling approximately 985 patients. The study assessed outcomes over a five-year period, aiming to confirm the device's low complication rates and effectiveness in preventing sudden cardiac death. As an RWE study, EFFORTLESS provided the kind of long-term safety data necessary for continued market access and reimbursement.

Outcome

Both registry studies demonstrated the long-term safety and effectiveness of the S-ICD, confirming its effectiveness in preventing sudden cardiac death with low complication rates. These results were crucial for obtaining and maintaining reimbursement, as both regulators and payers increasingly look to RWE to support their decisions. The studies reinforced the device's clinical value in real-world use, which is often a key factor in reimbursement decisions.

Reimbursement Impact

US: The positive outcomes from the registry studies were instrumental in gaining broad acceptance of the S-ICD among US insurers. Data showing low complication rates and effective outcomes played a critical role in securing reimbursement from both Medicare and private payers. This use of RWE aligned with recent FDA guidance, which encourages payers to consider RWE in their reimbursement decisions. Notably, how devices are "actually" used in real-world settings is key to reimbursement, as payers often assess the practical utility of a device in everyday clinical practice. There are examples of products that, despite showing promising outcomes, were not covered due to limited or inappropriate use in practice. The strong, real-world usage data from the S-ICD registries ensured the device would meet payer expectations, securing widespread coverage and enabling greater patient access to this safer alternative to traditional ICDs[30,31].

EU: NICE and HAS have incorporated data from the registry in their evaluations of the S-ICD's cost-effectiveness and clinical value. While these HTA bodies do not directly grant reimbursement, their positive assessments have facilitated reimbursement decisions across European national health systems, making the device more accessible to eligible patients[32].

Alternative Design and Implications

RCT or Cohort Study

While an RCT could provide stronger internal validity, the registry study was advantageous in gathering RWE that RCTs may not capture effectively, particularly for long-term outcomes and patient adherence. The data from these registries were critical in demonstrating how the S-ICD performed outside of controlled clinical trials, which is exactly the type of evidence payers look for in making reimbursement decisions.

Regulatory and Reimbursement Implications

The FDA recognized the importance of RWE in monitoring the performance of medical devices post-market. The data from the registry study facilitated ongoing discussions about the regulatory pathways for future devices, emphasizing the need for adaptable frameworks to include RWE. By leveraging the data from these registries, the S-ICD secured both regulatory approval and reimbursement in various regions.

Cost Implications

Utilizing existing registry data minimized the costs associated with conducting new trials while still providing high-quality evidence to support reimbursement. This approach demonstrated a cost-effective method of gathering necessary data for regulatory approval and continued market access.

CASE STUDY 08

Prospective Cohort Studies for Galleri Cancer Screening *in vitro* diagnostic (IVD)

Context

Galleri was developed as a multi-cancer early detection screening tool. To assess the long-term safety, effectiveness, and real-world performance of the Galleri test, multiple clinical studies were conducted and are in progress including prospective studies, observational and interventional studies, and real-world evidence[33]. Studies include both cohort and randomized control trials. These studies aimed to provide comprehensive data on the test's effectiveness in early cancer detection across multiple different cancers, and optimize reimbursement pathways available for the test, specifically in the US and UK. Of note for the Galleri test is that it is available to patients in the US as a laboratory developed test (LDT), and as such, was not subject to FDA regulatory review. It is important to note that generally, LDTs are less likely to be covered by payers because of the nature of the test; only one (or a few) laboratories are performing the test and there is less evidence available as to testing procedures and reliability of the validation.

Study Designs

- **PATHFINDER:** This was a prospective, interventional, multi-center study in which over 6,600 participants were enrolled. The study contained two cohorts: an elevated risk group based on health history comprised 70% of the participants, and a non-elevated risk group comprised the other 30%. The study measured participant outcomes based on number and type of tests required for diagnostic follow up of the results. Positive predictive value (PPV), negative predictive value (NPV), and specificity were calculated based on results[34]. Results for this study were published in the Lancet[35].

MULTI-CANCER DETECTION SCREENING IS LIKE A SUPERHERO CATCHING CANCER EARLY WITH X-RAY VISION.

- **The Circulating Cell-free Genome Atlas Study (CCGA):** This is a prospective, multi-center, observational study with collection of de-identified biospecimens and clinical data from at least 15,000 participants from clinical networks in the United States and Canada. The study will enroll approximately 10,500 cancer participants (CANCER arm) and approximately 4,500 representative participants without a clinical diagnosis of cancer (NON-CANCER arm)[36].

- **STRIVE:** Prospective, multi-center, observational cohort study to validate the assay for early detection of breast cancer and other invasive cancers including hematologic malignancies. The study collected samples from patients within 28 days or receiving a screening mammogram and included enrollment of over 99,000 patients[37].

- **SUMMIT:** This is a prospective, observational, cohort study to clinically validate a blood test for early detection of multiple cancer types and deliver low dose CT screening for lung cancer to an at-risk population. This study is based in London with enrollment of over 13,000 participants. This study is ongoing[38].

- **NHS GALLERI TRIAL:** This is a multi-center randomized control trial that will enroll approximately 140,000 participants aged 50-77years in the UK. The study will be used to demonstrate if using the Galleri blood test alongside existing cancer screening can help in early cancer detection. The primary endpoint of the trial is an absolute reduction in the number of late stage (stage 3 and 4) cancers diagnosed, and cancer-specific mortality will also be analyzed after five years of follow up. This study is ongoing[39].

- **REFLECTION TRIAL:** This is a multi-center, prospective, non-interventional, cohort study that will enroll approximately 17,000 individuals who have opted to be screened with Galleri®, a blood-based, multi-cancer early detection (MCED) test in routine clinical settings. The purpose of the study is to understand the real-world experience of Galleri® in clinical settings. This study is ongoing[40].

- **PATHFINDER 2:** This is a prospective, multi-center interventional study of the GRAIL multi-cancer early detection (MCED) test with return of test results for participants enrolled through healthcare systems in North America. The purpose of this study is to evaluate the safety and performance of the GRAIL MCED test in a population of individuals who are eligible for guideline-recommended cancer screening. This study is ongoing[41].

- **GALLERI IN THE MEDICARE POPULATION:** This is a multi-center comparative prospective cohort study is designed to assess the real-world clinical impact, including safety and test performance, of Galleri®, a blood-based multi-cancer early detection (MCED) test. The study will seek to enroll approximately 20% of the study participants from under-represented minority populations (e.g., racial / ethnic minority groups, socioeconomically disadvantaged populations, rural populations). This study is ongoing[42].

Outcome

Clinical trials for Galleri are still ongoing in most cases but initial studies demonstrated feasibility of the device. However, it is not clear if sufficient evidence exists for FDA clearance, or whether clear clinical utility has been demonstrated. In addition, these studies (overall) had low diversity, for example, although ~92% of participants of the PATHFINDER trial were white, effectiveness was not fully proven even in the majority white population.

Reimbursement Impact

US: The decision to offer Galleri as an LDT, rather than undergoing FDA review and approval through the PMA process has implications for reimbursement in the US. While LDTs are able to receive reimbursement codes through CMS, some payer benefit designs require FDA approval or clearance for reimbursement. Tests may be given “investigation or experimental” without “FDA Approval”. Currently the Galleri test is being offered as a patient pay model. It is clear that the ongoing clinical trials are targeted for gaining access to CMS reimbursement (e.g. the “GALLERI IN THE MEDICARE POPULATION” study). Similarly, private payers are also concerned with performance across diverse populations. These studies are likely necessitated by the lack of diversity included in the initial studies.

UK: The test is currently not available in the EU and no EU centric clinical trials are currently listed on their website. However, there has been a focus on the UK including two clinical trials specifically targeting patients in the UK, one of which is a collaboration with the UK National Health Services (NHS). The NHS Galleri Trial is critical for a sustainable reimbursement model in the UK as it will be used to determine if the test is fit for use in the national cancer screening program.

Alternative Design and Implications

Study to support FDA PMA and/or IVDR certificate

Studies conducted with regulatory approval in mind could have changed the trajectory of this test and shortened the reimbursement pathway as regulatory approvals support clinical utility and efficacy for the test. Investors and startups often focus on early and fast return on investment (ROI), which is facilitated by an LDT pathway, but overall ROI could benefit from more burdensome regulatory pathways.

Regulatory and Reimbursement Implications

Use of the LDT pathway is beneficial for the Galleri test in that it is faster to market and can begin to see returns on the high cost development and clinical trials that were completed without waiting for PMA approval by FDA. However, this pathway has become more uncertain with the introduction of FDAs LDT Final Rule[43], wherein laboratory developed tests must come into compliance with FDA regulations over the next four years. Even without the LDT final rule, the company may want to pursue FDA approval, but since the FDA requirements were not designed in from the beginning, it is possible that indications or test design would need to change in order to comply with FDA regulations and expectations for IVDs. For example, diversity action plans could have been utilized to ensure appropriate participant diversity and negating the need for the "Galleri in the Medicare Population" study. These changes could also impact reimbursement for the test. For example, understanding the use of the test in diverse populations supports clinicians in appropriate use of the test. Demonstration that the test is more (or less) beneficial for certain parts of the population is valuable information for payers to determine the appropriate prior authorization and medical policy.

Cost Implications

Robust clinical data within target populations with the appropriate indications has large implications for payers within the US healthcare system. Indeed, this is likely why the test is not currently reimbursed by CMS, and why subsequent studies have been started to bridge this gap and support further reimbursement. Using a patient payer model has benefits in that there is no third party (e.g. CMS or private payers) involved in the transaction, making it more straightforward, but it also limits the patients willing to go through the testing due to the high patient cost ($949).

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DISCUSSION SECTION 2

Typical Pitfalls in Clinical Trial Design and Execution

From the previous section it is clear that designing and executing clinical trials for medical technologies is complex, and even experienced manufacturers face challenges that can lead to costly delays or missed market opportunities. Here are some of the most common pitfalls that can undermine trial success.

A CLINICAL TRIAL WITHOUT A SOLID DESIGN IS JUST EXPENSIVE GUESSING.

1. Misalignment with Regulatory and Reimbursement Requirements

One of the most frequent issues is failing to align trial designs with the specific demands of both regulatory bodies and payers, especially across global markets.

Regulatory Oversights

Focusing too narrowly on clinical efficacy without considering all regulatory expectations (FDA, Notified Bodies, Expert Panels, EMA, etc.) can result in additional data requests, significantly delaying approvals.

PROACTIVE SOLUTION

Engage early with regulators and HTA bodies to understand evolving guidelines and expectations, ensuring all necessary endpoints are addressed. RQM+ facilitates these early consultations, avoiding costly reworks later.

Reimbursement Gaps

Trials that focus only on efficacy often miss the critical cost-effectiveness data needed by payers like Medicare and HTA bodies (e.g., NICE, HAS).

PROACTIVE SOLUTION

Integrate economic endpoints (for e.g., cost-effectiveness) as well as other reimbursement concerns, such as length of stay (LOS), additive cost or substitutionary, and both short- and long-term outcomes early to demonstrate the device's value to payers. RQM+ helps manufacturers include these measures, ensuring both regulatory approval and payer acceptance.

SKIPPING REIMBURSEMENT PLANNING IS LIKE BUILDING A ROCKET AND FORGETTING THE FUEL. GOOD LUCK GETTING OFF THE GROUND.

2. Suboptimal Site Selection and Patient Recruitment

Inefficient site selection and recruitment strategies can lead to significant delays and affect data quality, often negatively impacting approval timelines and market access.

Poor Site Performance

Low-performing sites may struggle with recruitment, causing protocol deviations and delays.

PROACTIVE SOLUTION

Conduct thorough site feasibility assessments. RQM+ uses data-driven insights to select high-performing sites, ensuring that recruitment goals are met on time.

Lack of Diverse Populations

Failing to include diverse populations may lead to challenges in regulatory approval, as agencies require data from underrepresented groups to ensure the device's safety and efficacy across demographics.

PROACTIVE SOLUTION

Tailor recruitment strategies to target underrepresented populations, ensuring trials meet diversity expectations from global regulators. RQM+ implements inclusive recruitment strategies, reducing this risk.

EVERY DELAY IN YOUR TRIAL ISN'T JUST TIME LOST; IT'S A COMPETITOR'S GAIN.

RECRUITING THE WRONG PARTICIPANTS IS LIKE CASTING A FISH TO PLAY A BIRD. IT'S NEVER GOING TO FLY

3. Inflexibility in Trial Design

Sticking to rigid, traditional trial designs can limit the potential for adaptive responses to emerging data, wasting time and resources.

Failure to Adapt

Static trial designs that do not allow for adjustments based on interim results can slow down time-to-market and fail to capitalize on early findings.

PROACTIVE SOLUTION

RQM+ recommends adaptive trial designs that allow for modifications as new data emerges, reducing the trial duration and cost while improving the chances of success. Also, consider the sequential parallel comparison design (SPCD) which is a two-stage design recommended for trials with a possibly high placebo response.

4. Underutilization of RWE

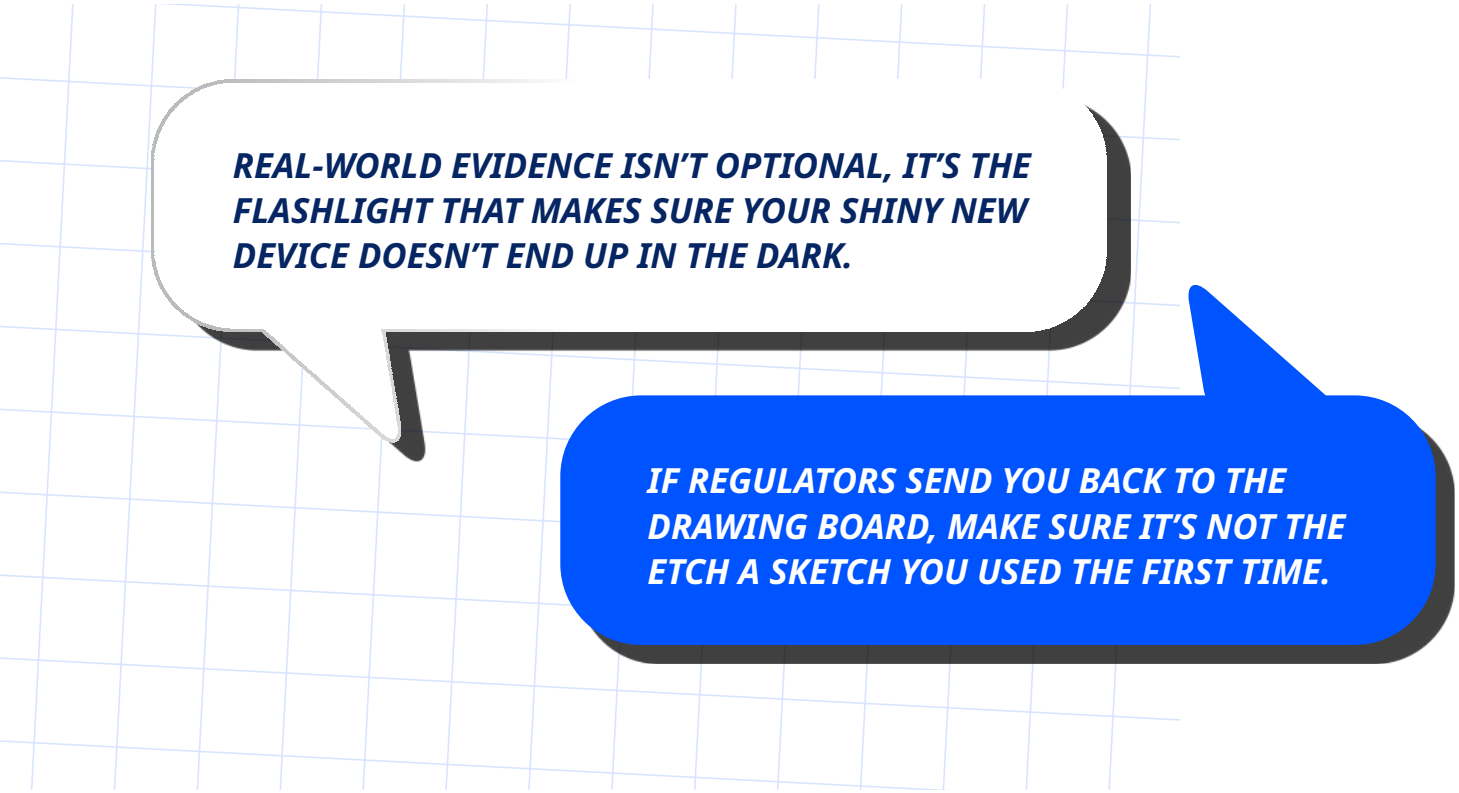
As regulatory authorities and payers increasingly value RWE, manufacturers must leverage it to strengthen both regulatory and reimbursement submissions.

Missed Opportunities with RWE

Without incorporating RWE, manufacturers miss an opportunity to demonstrate long-term safety and effectiveness, limiting the chances of reimbursement success. While RWE can get tricky, it can be used in treatment value modeling to drive decision-making when looking at indication sequencing, to cite an example.

PROACTIVE SOLUTION

RQM+ integrates RWE from registries, patient data, and post-market surveillance to bolster both regulatory submissions and reimbursement applications.



5. Lack of Comprehensive Post-Market Planning

Failing to plan for post-market surveillance can lead to compliance issues or loss of market access, especially under stringent regulations like the EU MDR.

Regulatory Non-Compliance

Without robust post-market surveillance, manufacturers risk delayed detection of safety issues, emerging risks, and negative trends, which could lead to product recalls or market withdrawal. Effective risk management and design control are key to preventing such actions.

PROACTIVE SOLUTION

RQM+ develops comprehensive post-market surveillance strategies that align with global regulatory requirements, ensuring continued compliance and patient safety.

Missed Reimbursement Opportunities

Lack of post-market real-world data limits the ability to demonstrate ongoing cost-effectiveness, reducing chances of expanding reimbursement.

PROACTIVE SOLUTION

RQM+ ensures continuous RWE collection to support sustained reimbursement and expand market share.

Why Do Manufacturers Need RQM+ As A Strategic Partner?

These pitfalls underscore the complexity of clinical trial design and execution. Partnering with **RQM+** ensures that manufacturers avoid these challenges, achieving timely regulatory approval and successful reimbursement outcomes. Our end-to-end support helps manufacturers design, execute, and monitor trials that meet both clinical and market needs, positioning their devices for long-term success.

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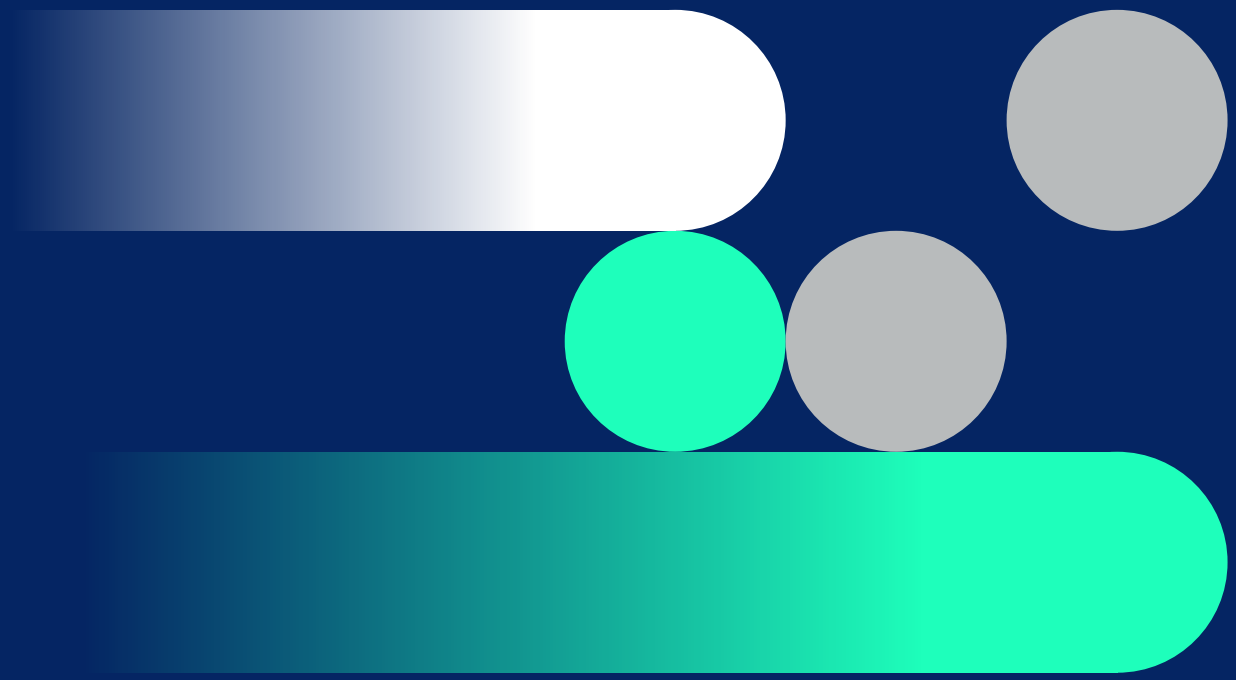
DISCUSSION SECTION 3

RQM+’s Strategic Approach to Clinical Trial Design and Execution

At **RQM+**, we provide tailored, comprehensive clinical trial solutions for MedTech manufacturers, aligning study designs with regulatory, reimbursement, and market access requirements. Our approach ensures trials generate high-quality data for regulatory approval while enhancing the device’s value proposition for patients, physicians and payers.



1. Early Engagement for Optimal Study Design

Strategic trial design is the foundation of success. At **RQM+**, we engage early in the product development process to craft trial designs that meet not only regulatory expectations but also market and reimbursement goals.

Regulatory-Centric Design

We tailor trial designs to meet global regulatory expectations, including the FDA, Notified Bodies (and Expert Panels), EMA, and HTA agencies, ensuring maximum chances of approval and market success.

Customized Clinical Strategies

We collaborate closely with manufacturers to develop trial designs that reflect the clinical realities of the device, account for market dynamics, and support a robust reimbursement landscape. Every trial is designed with the patient, end-user and manufacturer in mind, ensuring that data supports the device's clinical and commercial success. RQM+ aims to target all potential reimbursement-regulatory coordination to optimize capital efficiency.

2. Tailored Trial Execution

RQM+ provides bespoke trial execution strategies that balance the need for high-quality, actionable data with operational efficiency. Our experts, best-practice methods and streamlined procedures ensure that trials run smoothly, meet recruitment goals, and generate real-world, representative data.

Optimized Recruitment and Site Selection

Data-driven site selection and recruitment strategies ensure trials reach diverse patient populations, producing representative data that meets regulatory and payer expectations.

Real-Time Monitoring

Advanced electronic data capture (EDC) systems and real-time tracking allow us to make timely, informed decisions, improving efficiency and data quality.

Risk-Based Monitoring (RBM)

Focusing on high-risk areas of trials, our RBM approach ensures patient safety and data accuracy while reducing costs traditionally associated with full-scale monitoring.

Adaptive Trial Designs

We implement flexible trial designs that adjust sample sizes, endpoints, or stratification based on interim data, allowing trials to evolve as new information emerges without compromising integrity and constantly optimizing reimbursement opportunities.

TRIAL DESIGNS THAT CAN'T ADAPT ARE LIKE DINOSAURS, GREAT IN THEORY, EXTINCT IN PRACTICE.

3. Focus on Patient Diversity

Diversity in clinical trials is more than just a regulatory requirement, it is essential for generating results that are reflective of real-world patient populations. Furthermore, diversity is a reimbursement requirement. Coverage by CMS during clinical trials, investigation device exemption trials (IDEs), requires demonstration of inclusion of diversity in the Medicare population, gender, ethnic, disabilities, etc. **RQM+** prioritizes patient diversity from the outset, ensuring trials are designed to produce inclusive data.

Inclusive Recruitment Strategies

We implement strategies that actively recruit underrepresented populations, utilizing digital outreach platforms, community health initiatives, and partnerships with diverse clinical sites. This approach helps manufacturers meet global regulatory diversity requirements while gathering comprehensive data that reflects the full spectrum of patients who will benefit from the device.

Diversity-Centric Protocols

RQM+ ensures that trial protocols are designed to address the specific needs of diverse populations. From age and gender differences to genetic, racial, ethnic and socio-economic factors, our approach ensures that clinical outcomes are relevant to all demographics.

IGNORING DIVERSITY IN TRIALS IS LIKE BUILDING A BRIDGE FOR ONLY HALF THE POPULATION: DANGEROUS, SHORT-SIGHTED, AND DESTINED TO FAIL.

4. Integrated Regulatory and Reimbursement Expertise

Navigating the complex regulatory and reimbursement landscapes requires deep expertise, understanding of the latest trends and strategic foresight. RQM+ integrates regulatory compliance with reimbursement planning to ensure your device's success from development to market access.

Global Regulatory Compliance from Day One

We guide manufacturers through the complexities of global regulatory environments, ensuring that trial protocols align with international standards, accelerating approvals.

Reimbursement-Driven Outcomes

Trials are designed to collect the data payers need, such as demonstrating cost-effectiveness and long-term value, ensuring a strong case for reimbursement.

Streamlining Global Market Access

By aligning trial data with the requirements of key regulatory authorities, we minimize the need for additional studies or region-specific modifications, speeding up time to market.

5. Post-Market Surveillance and RWE

The clinical trial journey doesn't end at approval. Long-term success requires continued monitoring and post-market surveillance. **RQM+** offers comprehensive post-market surveillance services to ensure continued compliance, support reimbursement, and maintain market access.

Continuous Monitoring

Our post-market surveillance programs are designed to meet the rigorous global regulatory requirements including the EU MDR. By generating RWE through patient registries, claims data, and electronic health records (EHRs), we ensure ongoing compliance and support for reimbursement decisions.

RWE Collection

Leveraging real-world data is critical to validating a device's long-term performance and ensuring it continues to meet safety and effectiveness standards. RQM+ enables manufacturers to collect and analyze RWE, which supports both ongoing regulatory compliance and payer evaluations for sustained reimbursement. For example, RWE was crucial in the FDA's decision to approve the Micra leadless pacemaker based on post-market data showing lower complications compared to traditional pacemakers.

NOT PLANNING FOR POST-MARKET SURVEILLANCE IS LIKE SETTING SAIL WITHOUT A COMPASS. YOU'RE JUST HOPING FOR THE BEST WHILE HEADING FOR DISASTER.

CONCLUSION

RQM+, Driving Clinical Excellence, Fast Market Access, and Reimbursement Success

In today's competitive and highly regulated medical device landscape, success hinges on more than just innovation; it requires strategic, well-executed clinical trials that align with regulatory requirements, secure reimbursement, and demonstrate real-world value. The right study design not only accelerates market entry but also ensures your device is positioned for long-term success, meeting the needs of healthcare providers, patients and payers.

RQM+ stands out as a trusted partner with a deep understanding of the complex intersection between regulatory approval, clinical evidence, and payer expectations. From early engagement through post-market surveillance, we offer tailored, end-to-end clinical trial solutions that de-risk the process and maximize outcomes. Our expertise in designing trials that meet the highest standards of quality, patient safety, and efficiency ensures that your device not only reaches the market but thrives there.

EVERY DOLLAR WASTED ON A POORLY PLANNED TRIAL IS A DOLLAR NOT SPENT ON SAVING LIVES.

By choosing **RQM+**, you gain more than a CRO, you gain a strategic partner dedicated to helping you navigate the most challenging aspects of medical device development, turning clinical trials into catalysts for success. With our proven track record and comprehensive approach, we ensure that every clinical trial you conduct is not just a regulatory requirement but a powerful asset that accelerates approval, drives reimbursement, and positions your device for lasting impact in the global healthcare market.

Let's work together to turn your innovations into market leaders, faster, smarter, and with greater impact.

Takeaway Recommendations for Manufacturers

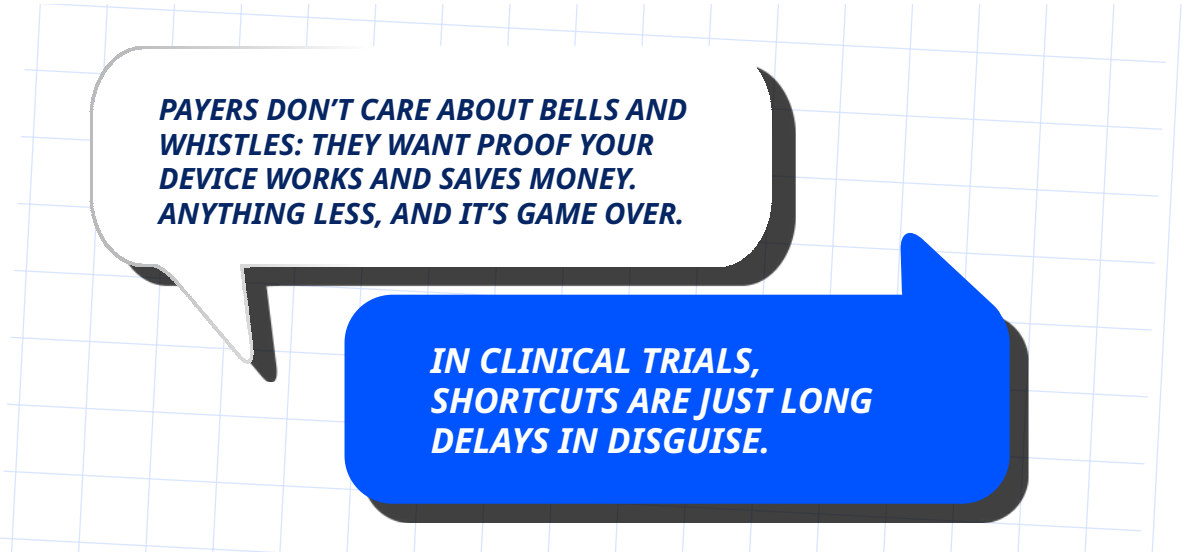
Bringing medical technology to market requires more than groundbreaking innovation, it demands clinical evidence that not only meets regulatory requirements but also convinces patients and payers of the device's long-term value. To ensure clinical trials drive both **regulatory approval** and **reimbursement success**, manufacturers must adopt a proactive and strategic approach. Here's how:

1. Engage Early with a CRO to Optimize Study Design

Starting early with a **CRO** like **RQM+** can drastically shape the success of your clinical trials. Collaborating during the early product development phase ensures that your study design aligns with regulatory and commercial goals right from the start. The right design avoids costly mid-trial adjustments, reduces delays, and produces data that meets the expectations of global regulators and payers.

ACTIONABLE TIP

Begin engaging your CRO during the concept phase to map out a strategy that aligns clinical objectives with real-world applicability, maximizing regulatory approval and market access.



2. Prioritize a Custom, Patient-Centric Approach

Not all clinical trials should be treated the same. Tailoring your trial design to the unique characteristics of your device and patient population is key to success. A **patient-centric approach** focused on usability, satisfaction, and diversity makes your trial more appealing to regulators and payers while ensuring that data better reflects real-world conditions.

ACTIONABLE TIP

Ensure your trial includes diverse demographic groups, aligning with global regulatory diversity requirements. This not only enhances the robustness of your data but also improves the device's marketability.

3. Plan for Reimbursement as Part of Your Clinical Strategy: *No Margin, No Mission!*

Regulatory approval is only half the battle. To help patients effectively, a device must be both accessible to patients and financially sustainable, making profitability essential to delivering meaningful healthcare solutions. To ensure market access, plan with the end goal in mind. In other words, your clinical trial must also generate data that speaks to payers, showing **cost-effectiveness** and **clinical value.** Aligning trial outcomes with reimbursement requirements, such as **Medicare** in the US or **HTA bodies** in the EU, is essential to ensure that your device not only gets approved but also reimbursed.

ACTIONABLE TIP

Integrate economic endpoints that demonstrate healthcare savings, better patient outcomes, and long-term performance to solidify your reimbursement case.

4. Leverage RWE for Post-Market Success

Post-market surveillance is critical for maintaining regulatory approval and securing ongoing reimbursement. **RWE** provides valuable insights into the long-term safety, performance, and cost-effectiveness of your device, critical factors for keeping payer support and ensuring continued market competitiveness.

ACTIONABLE TIP

Implement a strong post-market surveillance plan to collect real-world data on device performance and cost-effectiveness, ensuring sustained market presence and payer support.

5. Stay Agile with Adaptive Trial Designs

Adaptive trial designs allow manufacturers to adjust sample sizes, endpoints, or criteria based on interim results, making the trial process more efficient and responsive. This flexibility can shorten timelines, reduce costs, and focus the trial on what's working, thereby increasing the likelihood of success.

ACTIONABLE TIP

Use interim data analysis to adjust trial parameters, optimize outcomes, and potentially avoid the need for additional studies. Adaptation can be a game-changer in fast-paced, competitive markets.

6. Consider Global Market Requirements from the Outset

If your goal is to expand into multiple markets, it's crucial to design clinical trials that align with the varying requirements of global regulators. By doing so, you can avoid duplication of trials and expedite market entry in multiple regions.

ACTIONABLE TIP

Work with your CRO to harmonize clinical trial designs with the regulatory requirements of key global markets (US, EU, Asia-Pacific) from day one. This proactive approach ensures a smoother, more efficient global launch.

Prepare for Success from Day One!

By following these recommendations and partnering with a strategic CRO like **RQM+**, manufacturers can mitigate risks, enhance trial outcomes, and dramatically improve their chances of regulatory and reimbursement success. Strategic, well-planned clinical trials are more than just a regulatory checkbox; they are a vital component in ensuring your device's market success and patient impact.

BIOGRAPHY

Jaishankar Kutty

Leads regulatory and clinical strategy within the Trials Services Business Unit and across the RQM+ organization. His extensive background includes key strategic and operational roles in cardiovascular product development. Previously, as a clinical team leader (and lead reviewer) at BSI, he was instrumental in reviewing and CE marking numerous innovative structural heart devices under both MDR and MDD regulations. At RQM+, Jaishankar applies his unique EU notified body expertise and extensive product development industry experience to craft effective clinical and regulatory strategies. His responsibilities encompass designing clinical studies, conducting and analyzing retrospective data, performing biological safety evaluations, ensuring stringent compliance, and facilitating interactions with regulatory authorities to reinforce the evidentiary foundations for medical devices.

BIOGRAPHY

Margot Borgel

Margot Borgel is an expert in the technical and regulatory requirements of in vitro diagnostics (IVDs) and laboratory developed tests (LDTs) with over 10 years of experience in both the US and EU markets. She helps RQM+ clients meet regulatory requirements for IVDs and LDTs through strategic regulatory support and guidance throughout the entire product lifecycle. She also performs regulatory intelligence activities at RQM+ to ensure compliance to the ever-changing IVD regulatory landscape. Margot holds a BSc and Ph.D. in Chemistry and has IVD experience within the industry as well as with a notified body. A strategic thinker and collaborator, she has an extensive scientific background in assay development, IVD manufacturing, process improvement, regulatory requirements, and quality management systems. She is a subject matter expert for performance evaluation and clinical requirements, international standards, and guidance documents for IVDs and LDTs. She has held roles within an IVD manufacturer in R&D, Scientific Affairs/Product Transfer, and Senior Manager of Manufacturing. Prior to joining RQM+ she was a part of the BSI Notified Body acting as a Technical Specialist on the IVD team. Margot is passionate about supporting companies looking for market access of their innovative test systems and IVDs and takes on every project as if family was on the other side of the diagnostic.

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