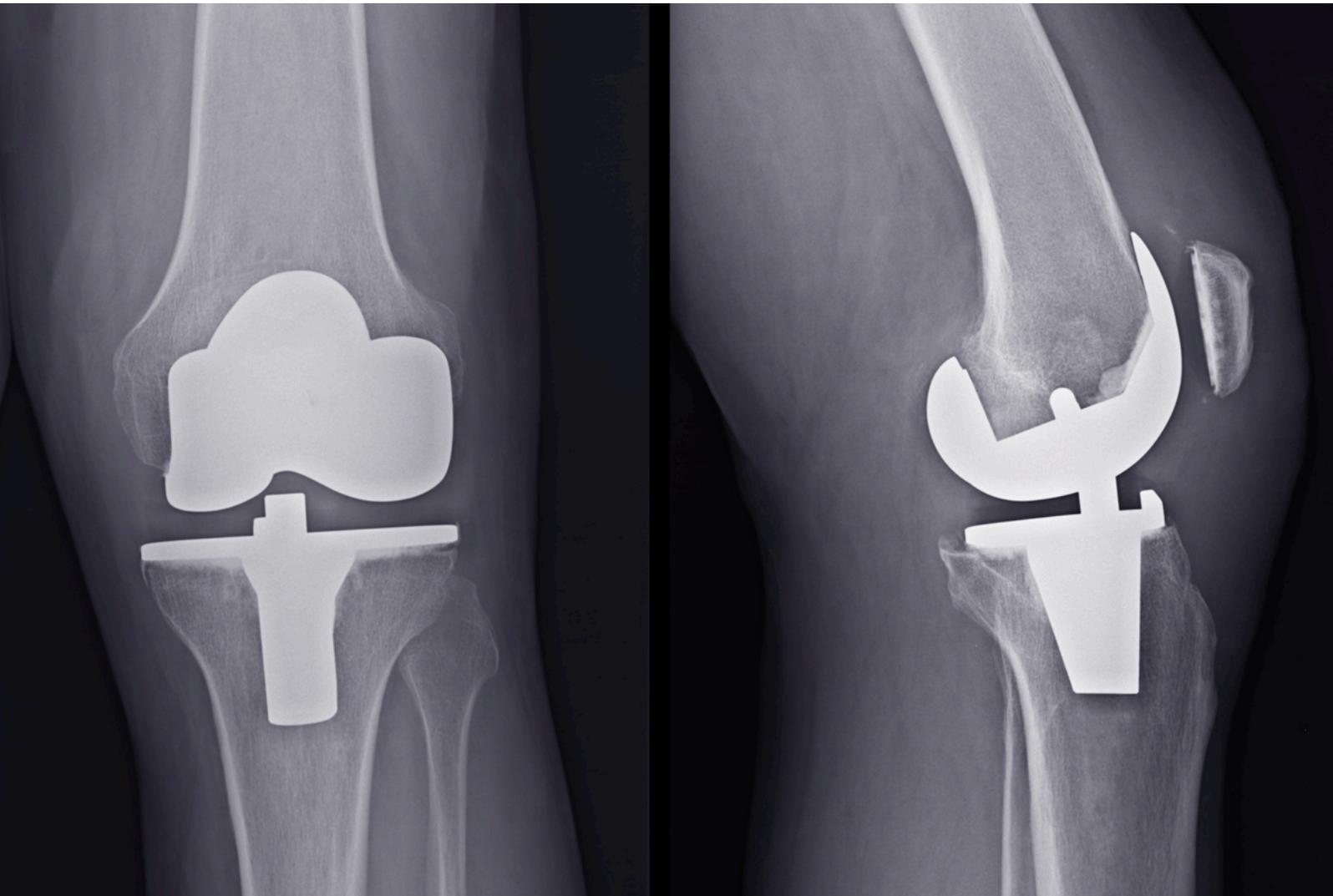


WHITE PAPER

# CIRCLES FOR KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

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# TABLE OF CONTENTS

<b>EXECUTIVE SUMMARY</b>	<b>3</b>
<b>TOTAL KNEE ARTHROPLASTY AND KINEMATIC ALIGNMENT</b>	<b>4</b>
<b>EVIDENCE GAPS IN KINEMATIC ALIGNMENT TKA</b>	<b>8</b>
<b>CIRCLES-BASED REAL WORLD EVIDENCE</b>	<b>10</b>
<b>CIRCLES FOR TKA KINEMATIC ALIGNMENT ISSUES</b>	<b>11</b>
<b>SELECT CIRCLES OBSERVATIONAL PROTOCOLS FOR KA TKA</b>	<b>15</b>
<b>COLLABORATIVE RESEARCH THROUGH CIRCLES</b>	<b>16</b>
<b>CONCLUSION</b>	<b>17</b>
<b>APPENDIX A TABLE: BIG DATA RWE VS. CIRCLES PLATFORM</b>	<b>18</b>
<b>APPENDIX B TABLE: CLINICAL ISSUES IN TKA KINEMATIC ALIGNMENT</b>	<b>20</b>
<b>WORKS CITED</b>	<b>22</b>

Total Knee Arthroplasty (TKA) is a widely performed and effective surgical procedure for end-stage knee arthritis. However, a notable proportion of patients, estimated at 20% to 25%, report persistent dissatisfaction following the procedure, often attributed to the failure to replicate the natural kinematics of the knee.<sup>1</sup> In response to this challenge, Kinematic Alignment (KA) has emerged as an alternative surgical philosophy. Unlike traditional Mechanical Alignment (MA), KA aims to restore the native, pre-arthritic joint lines and rotational axes of a patient's knee, with the objective of promoting a "more natural-feeling knee" and a faster return to function.<sup>2</sup>

Despite the theoretical advantages and promising results observed in some of the literature<sup>5</sup>, the widespread adoption of KA is currently hindered by significant clinical issues and evidence gaps. High-quality randomized controlled trials (RCTs) have not consistently reproduced the favorable outcomes seen in smaller, specialized cohorts. Some meta-analyses, for instance, have found "no clinically important difference" in patient-reported outcomes (PROMs) or range of motion (ROM) when comparing KA to MA.<sup>5</sup>

Furthermore, existing RCTs frequently exhibit a moderate-to-high risk of bias and often provide limited follow-up data, with a mean duration of only 24 months, which is insufficient for assessing long-term implant longevity and revision rates crucial for TKA.<sup>1</sup> Challenges also persist in objectively assessing functional kinematics and soft tissue balance in real-world settings, and in understanding the precise impact of surgeon experience and advanced technologies, such as robotics, on KA outcomes.<sup>1</sup>

The Circles platform offers a transformative solution for generating high-quality Real-World Evidence (RWE) that can directly address these critical gaps. Circles distinguishes itself from conventional "big data" RWE through its robust data integrity, verifiability, and completeness. Data within Circles is sourced directly and verifiably from primary sources, such as physicians, their patients, and laboratories. Each Datapoint is time-stamped, unmanipulated, and collected within transparent, closed Observational Protocols (OPs). This structured approach makes Circles datasets analogous to that of a traditional clinical trial, ensuring adherence to Good Clinical Practice (GCP) principles. This stands in stark contrast to the poor quality, significant gaps, and lack of verifiability often inherent in aggregated "big data" RWE.

By leveraging its unique capabilities, Circles RWE can bridge critical evidence gaps by providing robust, longitudinal data on long-term outcomes, patient satisfaction, and the real-world performance of KA. It can facilitate objective kinematic assessment through the integration of advanced technologies and allow for a detailed analysis of the impact of surgeon variability. Ultimately, this high-integrity RWE can inform the development of evidence-based clinical guidelines and accelerate the responsible adoption of Kinematic Alignment in TKA.



## Overview of TKA and the Historical Context of Mechanical Alignment (MA)

Total Knee Arthroplasty, commonly known as total knee replacement, is a surgical procedure designed to alleviate pain and restore function in patients suffering from severe knee arthritis. During this procedure, the damaged or worn-out components of the knee joint are removed and replaced with artificial implants, or prostheses.<sup>2</sup> For decades, the prevailing surgical philosophy for TKA has been Mechanical Alignment (MA). This traditional approach aims to achieve a "straight" leg by aligning every knee replacement to a neutral Hip-Knee-Ankle (HKA) axis of 0 degrees.<sup>2</sup> This is typically accomplished by performing bone resections perpendicular to the mechanical axis of both the tibia and the distal femur.<sup>5</sup>

The objective of MA is to standardize the limb alignment across all patients, striving for a uniform biomechanical outcome. However, this "one-size-fits-all" approach inherently conflicts with the natural anatomical variability observed in the human population. The HKA axis in healthy individuals naturally ranges from significant varus to neutral to significant valgus.<sup>3</sup> Indeed, a truly neutral alignment is rarely encountered in healthy, non-arthritic knees.<sup>4</sup> Consequently, MA often necessitates forcing a substantial proportion of patients into an alignment that deviates from their individual, pre-arthritic anatomy.

This can lead to alterations in natural limb alignment and may result in "uncorrectable knee instabilities".<sup>4</sup> Such biomechanical compromises are a probable underlying cause for the persistent 20% to 25% patient dissatisfaction reported after TKA<sup>1</sup>, as well as complaints of pain, stiffness, and instability, even when the MA TKA is technically considered successful.<sup>4</sup> This highlights a fundamental limitation of a standardized approach in a biologically diverse patient population.

## Principles of Kinematic Alignment (KA) as a Patient-Specific Approach

Kinematic Alignment (KA) represents a significant paradigm shift in TKA, moving away from the universal alignment of MA towards a customized, patient-specific technique.<sup>2</sup> The core objective of KA is to anatomically position and kinematically align the total knee components to precisely restore the native, pre-arthritic joint lines and rotational axes of an individual patient's knee.<sup>2</sup> This involves replicating the three kinematic axes of the native femur, ensuring the knee moves in a manner more akin to its original biomechanics.<sup>2</sup>

A key characteristic of KA is its "ligament sparing" nature. Rather than relying on soft tissue releases to balance the knee, KA primarily utilizes precise bone cuts to recreate the pre-arthritic knee laxities and compartment forces, thereby avoiding the need to release healthy ligaments.<sup>1</sup> Preoperative planning for KA is notably meticulous, often involving CT scans to generate detailed 3D images of a patient's unique knee anatomy. These images empower surgeons to design a personalized surgical plan, enabling the determination of precise bone cuts and optimal implant sizes before the actual surgery.<sup>2</sup>

During the procedure, the surgeon aims to remove the exact thickness of bone that corresponds to the thickness of the new implant, thereby placing the artificial knee components in the same position as the original native knee.<sup>2</sup> Proponents of KA suggest that this restoration of natural knee motion leads to superior outcomes, including improved knee bending, a faster return to function, and a subjective experience of a "more natural-feeling knee" for patients.<sup>2</sup>

While KA offers a sophisticated biomechanical approach, its successful execution demands a substantially higher level of surgical precision than traditional MA. The reliance on "careful planning" and 3D imaging for "precise bone cuts"<sup>2</sup> underscores a complex surgical workflow that requires millimeter-level accuracy. The principle of removing "the exact same thickness of bone that matches the thickness of the new metal knee"<sup>2</sup> further emphasizes this demand for precision.

This increased technical requirement, particularly for surgeons in the early stages of their learning curve, could introduce variability in outcomes and potentially lead to more intra-operative challenges. The trade-off between the theoretical biomechanical superiority of KA and the practical demands of its surgical execution is a crucial area where real-world data is essential to understand the generalizability and safety of the technique beyond the hands of highly experienced surgeons. This also highlights the potential role of advanced technologies, such as robotic assistance<sup>5</sup>, in achieving the required precision, though these technologies also introduce additional costs, time, and potential risks.<sup>6</sup>

## Current Status of KA Adoption

The adoption of Kinematic Alignment in TKA is currently characterized by an ongoing debate and conflicting evidence regarding its clinical superiority and long-term outcomes. While surgeon case series and case control studies have demonstrated excellent subjective and objective clinical outcomes as well as survivorship for KA TKA with up to 10 years followup<sup>5</sup>, these promising results have not been reproduced in high-quality randomized clinical trials.<sup>5</sup>

Some meta-analyses and randomized control trials indicate that KA may reduce the need for ligament releases and improve functional outcomes without increasing complication rates compared to MA.<sup>1</sup> However, a recent meta-analysis of randomized trials concluded that KA "does not result in clinically important improvements after TKA compared with Mechanical Alignment" in terms of patient-reported outcome measures (PROMs) such as the Oxford Knee Score (OKS), Forgotten Joint Score (FJS), or EuroQol 5-domain instrument VAS score, nor in range of motion (ROM).<sup>6</sup> This meta-analysis specifically noted that the included studies often carried a "moderate-to-high risk of bias".<sup>6</sup>



The prevailing recommendation from this critical meta-analysis is that KA "should not be widely adopted in practice until or unless such advantages have been shown in well-designed RCTs," citing the added costs, time (especially if advanced technologies are used), and potential risks associated with its novelty.<sup>6</sup> This conflicting evidence, where promising results from expert series<sup>5</sup> are not consistently supported by higher-level evidence<sup>6</sup>, creates a significant barrier to the widespread adoption of KA. Clinical guidelines and changes in widespread practice typically necessitate robust, high-quality RCT evidence.

The explicit call for "well-designed RCTs"<sup>6</sup> underscores that the current body of evidence is perceived as insufficient to justify a shift from the established MA. The acknowledged "moderate-to-high risk of bias" in existing RCTs<sup>6</sup> further complicates the situation, suggesting that even the highest-level evidence may be flawed or incomplete. This highlights an urgent need for a new class of evidence — high-quality Real-World Evidence — that can bridge this gap by providing robust, generalizable data without the inherent limitations of traditional "big data" or the resource constraints of long-term, large-scale RCTs.

The discrepancy between the positive outcomes reported by "designer surgeons"<sup>5</sup> and the more tempered findings from meta-analyses<sup>6</sup> suggests that factors beyond the alignment philosophy itself are influential. These likely include the significant impact of surgeon experience and skill<sup>1</sup>, potential patient selection biases in expert centers, or nuances of post-operative care that are not consistently captured in controlled trials.

The fact that KA "adds costs, time... and potential risks"<sup>6</sup> further emphasizes that its benefits must be demonstrably superior to justify these additional burdens in a real-world, cost-conscious healthcare environment. Traditional RCTs, while controlling for many variables, may not fully capture the complexities and variations of real-world surgical practice, including learning curves for new techniques and the diversity of patient populations. This points to a critical role for high-quality RWE to illuminate these real-world variables and their impact on outcomes.

The evolving field of Kinematic Alignment in TKA is marked by several key clinical issues and persistent evidence gaps. These challenges represent crucial areas where the generation of robust, high-quality real-world evidence is most needed to advance understanding and inform clinical practice.

## **Lack of High-Quality, Long-Term Randomized Controlled Trial (RCT) Evidence**

A primary impediment to the widespread acceptance and adoption of KA is the absence of conclusive, high-quality, long-term RCT evidence. While initial "designer surgeon case series" have reported promising outcomes, these results "have not been reproduced in high-quality randomized clinical trials".<sup>5</sup> A meta-analysis of existing RCTs, for instance, concluded that KA "does not result in clinically important benefit" over MA in terms of patient-reported outcomes or range of motion, further noting that the included studies often carried a "moderate-to-high risk of bias".<sup>6</sup>

Many of the studies available on KA are classified as Level III or IV evidence, and critically, they frequently have limited follow-up durations, averaging only 24 months.<sup>1</sup> This short follow-up period is fundamentally inadequate for assessing the long-term outcomes essential for TKA, a procedure where implant longevity is expected to span 15 to 20 years or more.

The distinction between statistical significance and clinical importance is vital in evaluating new surgical techniques. The meta-analysis<sup>6</sup> explicitly differentiates these concepts, setting thresholds for what constitutes a clinically meaningful improvement (e.g., 5 points on the Oxford Knee Score). The finding that KA shows "no clinically important benefit"<sup>6</sup> suggests that even if some studies report a statistically significant difference, patients may not actually perceive a tangible improvement in their daily lives.

This raises questions about the sensitivity of current patient-reported outcome measures (PROMs) to capture the subtle, subjective benefits of a "natural-feeling knee"<sup>2</sup> that KA aims to provide. It also implies that existing RCTs might be missing the true patient-perceived value, or that any benefits are too subtle to be captured by current outcome measures over short follow-up periods.

## **PROMS Variability and Persistent Dissatisfaction Despite Surgical Success**

Despite the technical success of TKA, a significant proportion of patients (20-25%) continue to report postoperative dissatisfaction.<sup>1</sup> This dissatisfaction is often attributed to the failure to replicate the knee's natural kinematics.<sup>1</sup> While Kinematic Alignment is designed to promote a "more natural-feeling knee"<sup>2</sup> and has shown objective improvements in soft tissue balance, these improvements have "not been shown to result in improvements in patient-reported outcomes measures" consistently.<sup>5</sup> This suggests a potential disconnect between objective surgical achievements and the subjective experience of the patient.

The core promise of KA is to deliver a "more natural-feeling knee".<sup>2</sup> The persistent dissatisfaction rate<sup>1</sup> and its link to unnatural kinematics strongly suggest that current, standardized PROMs may not be adequately capturing this subjective "natural feel" or the subtle improvements in knee kinematics that KA aims for.

The observation that objective soft tissue balance improvements from KA do not consistently translate to PROMs<sup>5</sup> further supports this interpretation. This indicates a need for more nuanced, patient-centric outcome measures, potentially including qualitative data or specialized PROMs like the Forgotten Joint Score (FJS) or a direct "Joint perception question"<sup>7</sup>, which specifically probe the patient's awareness and perception of their knee.

## Challenges in Assessing Functional Kinematics and Soft Tissue

Gait analyses have revealed differences in kinematic parameters, such as knee adduction, extension, and external rotation moments, the clinical "relevance of which needs further evaluation".<sup>5</sup> There is a recognized need for advanced technologies, including "robotic- assisted TKA and compartmental pressure sensors," to enhance the understanding of optimal alignment strategies and implant positioning.<sup>5</sup> Furthermore, wearable IMU sensors demonstrate potential for remote monitoring of knee flexion, with the goal of achieving clinical accuracy comparable to in-clinic measurements.<sup>9</sup>

The growing recognition of the importance of objective kinematic data (from gait analysis, pressure sensors, and wearable IMU sensors)<sup>5</sup> is critical for truly understanding the functional implications of KA. However, such data are often collected in isolated research settings or specific trials. The significant challenge lies in integrating this rich, objective biometric data with comprehensive patient-reported outcomes and long-term clinical follow-up in a scalable, real-world context. Traditional "big data" RWE typically lacks this granularity and integration due to its inherent gaps and absence of meaningful longitudinal outcomes data.

## Uncertainty Regarding Long-Term Implant Longevity and Revision Rates

Despite "designer surgeon case series" reporting "excellent... survivorship for KA TKA with up to 10 years follow up," these findings "have not been reproduced in high-quality randomized clinical trials".<sup>5</sup> Many studies on KA suffer from limited follow-up, with a mean of 24 months<sup>1</sup>, which is insufficient to definitively assess the long-term durability, wear characteristics, and revision rates of TKA implants. TKA implants are typically expected to last 15 to 20 years or more. While KA is advocated as a means to prevent "accelerated component wear, and component loosening from uneven load-sharing" often associated with MA<sup>2</sup>, robust long-term evidence supporting this claim is still emerging.

The expected longevity of a TKA implant necessitates very long-term follow-up to accurately assess survivorship and revision rates. Issues such as aseptic loosening or polyethylene wear, which can necessitate revision surgery, often manifest many years post-surgery. RCTs are notoriously difficult and expensive to maintain for such extended durations, creating a significant, unresolved evidence gap for KA.

## Impact of Surgeon Experience and Technique on KA Outcomes

The impact of surgeon experience on KA outcomes is a recognized factor. One study explicitly noted that "only the cohort operated on by experienced surgeons was included due to the limited follow-up of the inexperienced group"<sup>1</sup>, suggesting a dependency on surgeon skill for favorable results. A clinical trial (NCT06709703) is specifically investigating "how long it takes a surgeon to become good at performing a kinematic knee replacement using robotic assistance" and is comparing robotic-assisted KA to traditional manual methods.<sup>7</sup>

The reliance on "experienced surgeons" for positive KA outcomes<sup>1</sup> and the explicit research question about the "learning curve" for robotic-assisted KA<sup>7</sup> underscore a critical challenge for the widespread adoption of this technique. If the benefits of KA are highly dependent on exceptional surgical skill or a prolonged learning period, its generalizability to the broader surgical community is limited. This creates a barrier to broader implementation and raises questions about the consistency of outcomes in diverse clinical settings.

## Investigating Complication Profiles and Ligamentous Management

A foundational principle of KA is its "ligament sparing" nature, aiming to achieve knee balance through precise bone cuts rather than releasing healthy ligaments.<sup>3</sup> Indeed, metaanalyses sometimes suggest that KA reduces the need for ligament releases.<sup>1</sup> However, a clinical trial (NCT06709703) still plans to document the "Need for ligamentous release" (e.g., lateral release, medial release, posterior cruciate ligament release) and the "Need for tibial or femoral recut" during surgery.<sup>7</sup>

The trial also intends to record the incidence of "Unplanned ligament injury" and other intraoperative complications, such as neurovascular damage or intra-operative fractures.<sup>7</sup> The true incidence and patterns of these events in real-world KA practice require comprehensive and systematic capture to fully understand the technique's safety profile and technical demands.

The Circles platform represents a significant advancement in the generation of Real-World Evidence (RWE), offering a novel approach that directly addresses the inherent limitations of conventional "big data" RWE. Its unique design features are specifically engineered to produce high-quality, verifiable, and clinically relevant data, making it an ideal tool for resolving complex clinical questions such as those surrounding Kinematic Alignment in TKA.

## Core Advantages of Circles

### *Data Integrity and Verifiability*

Circle Datasets reflect strong internal integrity and verifiability, as they are sourced directly and transparently from primary origins, including physicians, their patients, and laboratories. This stands in stark contrast to "big data" RWE, which often originates from "multiple, often unidentified and unidentifiable sources" and undergoes manipulation through various "cleansing" and undisclosed algorithms.

Each Datapoint within the Circles platform is time-stamped and not subject to any data manipulation or AI hallucination, thereby ensuring the authenticity and reliability of Circle Datasets comprising such Datapoints. Furthermore, because Circle Datasets are generated within a "closed platform," the entire methodology of data collection and aggregation is "transparent". This transparency allows for a clear understanding of data provenance and processing, mitigating the "garbage in, garbage out" problem that plagues less controlled data sources. For a nuanced field like orthopedic surgery, where subtle differences in alignment or technique can have profound long-term consequences, having verifiable, unmanipulated data is paramount for drawing reliable conclusions and informing clinical practice. This directly counters the "risk-of-bias" concerns frequently cited in existing KA RCTs <sup>6</sup>, elevating RWE to a trustworthy source of evidence.

### *Completeness*

A Circle Dataset comprises well correlated, longitudinal Cases, where all Datapoints are specifically relatable to a Case. This design ensures that the data is comprehensive and interconnected within the context of individual patient journeys. Crucially, each Case captures and integrates relevant clinical data from initial patient enrollment, through clinical diagnoses and interventions, and through completion of long-term patient-reported and/or clinical outcomes surveys. This provides a continuous and complete record of patient information over extended periods.

A major limitation of "big data" RWE is its inherent gaps and the absence of meaningful longitudinal outcomes data. This is particularly problematic for chronic conditions or postsurgical outcomes like TKA, where implant longevity <sup>5</sup> and patient satisfaction evolve over many years.

Circle Datasets comprise well correlated, longitudinal Cases integrating data from initial patient enrollment... through completion of long-term patient-reported and/or clinical outcomes surveys.

This allows researchers to track the entire patient journey, identifying longterm trends, factors influencing success or failure, and the evolution of patient perception over time. This directly addresses the "limited follow-up" issue of current KA studies<sup>1</sup> and provides the temporal depth necessary to assess true implant survivorship and patient adaptation, which is crucial for a procedure with a long expected lifespan.

## *Clinical Relevance*

Each Circle Observational Protocol is prospectively defined by a single anatomical region, pathology, treatment, protocol, and standardized outcomes assessment, ensuring that the collected data is acutely relevant to a particular clinical question. This is supplemented by the association within each OP of applicable medical codes (CPT, ICD, HCPCS, etc.) as well as any other Attributes deemed relevant. The design and underlying processes of Circles are thus closely analogous to those of a traditional clinical trial, greatly enhancing their clinical and regulatory utility.

By defining the scope of data collection with a clear clinical question in mind, Circles ensures that all relevant covariates (e.g., comorbidities, adjunct therapies, often omitted in traditional RWE) are systematically captured. This "clinical trial-like" methodology elevates RWE from descriptive statistics to a powerful tool for comparative effectiveness research and hypothesis testing.

## *Good Clinical Practice Adherence*

Circles inherently help enforce good clinical practice". They can accommodate protocol-specific patient consents, GCP certificate collection, and IRB/MEC support.

# CIRCLES FOR TKA KINEMATIC ALIGNMENT ISSUES

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Circles are well-suited to address the clinical issues and evidence gaps identified in Kinematic Alignment TKA. By generating high-quality RWE, Circles can provide the necessary insights to advance the understanding, validation, and ultimately, the evidence-based adoption of KA.

## **Bridging the Evidence Gap for KA**

The primary challenge for Kinematic Alignment is the persistent lack of high-quality, longterm Randomized Controlled Trial (RCT) evidence.

Existing trials are often inconclusive regarding KA's clinical superiority over Mechanical Alignment and frequently carry a moderate-to-high risk of bias, with limited follow-up durations.<sup>1</sup>

The demand for well-designed RCTs<sup>6</sup> for KA's widespread adoption is valid, but RCTs are inherently resource-intensive, time-consuming, and may not fully capture real-world variability or very long-term outcomes.<sup>1</sup> Circles offers a powerful "hybrid" evidence model. It combines the methodological rigor (GCP adherence, specific OPs, transparent data collection) characteristic of a clinical trial with the scale, real-world applicability, and longitudinal depth of RWE.

This allows for the low-cost, clinically efficient and rapid generation of high-quality evidence on KA's effectiveness and safety in diverse patient populations and surgical settings, thereby accelerating the translation of promising techniques into clinical practice while maintaining scientific integrity. This signifies a move beyond the traditional binary "RCT vs. RWE" debate towards a complementary approach where each methodology contributes its unique strengths.

## Enhancing Understanding of Patient Satisfaction and Functional Outcomes

While KA aims for a "more natural-feeling knee"<sup>2</sup>, objective improvements in soft tissue balance achieved with KA have not consistently translated to improved patient-reported outcomes.<sup>5</sup> Current outcome measures may not fully capture the nuanced subjective patient experience. Traditional PROMs often focus on quantifiable functional limitations, such as the ability to walk or climb stairs.<sup>7</sup> However, the persistent patient dissatisfaction<sup>1</sup> and the core promise of KA — to deliver a "natural-feeling knee"<sup>2</sup> — suggest that success in TKA extends beyond mere functional recovery to a more subjective, experiential quality of life.

Circles Observational Protocols can be designed to include nuanced PROMs, such as the Forgotten Joint Score (FJS) and a "Joint perception question"<sup>7</sup>, or even qualitative data collection methods that specifically probe the subjective "naturalness" and quality of knee motion. This allows for a deeper, more holistic understanding of patient satisfaction beyond standard functional scores.

## Monitoring Long-Term Implant Performance and Revision Rates

Current studies on KA typically have limited long-term follow-up, with a mean of 24 months.<sup>1</sup> This duration is insufficient to definitively assess implant longevity, wear, and revision rates for a procedure where implants are expected to last 15-20 years or more.<sup>5</sup> Uncertainty remains regarding whether KA truly mitigates issues like "accelerated component wear, and component loosening"<sup>2</sup> compared to MA.

Circles can continue to capture longitudinal data for any desired duration. Moreover, they go beyond simply reporting a revision rate by supporting a granular analysis of *why* and *when* revisions occur, and what factors (e.g., patient activity levels, specific implant types, alignment nuances) contribute to them. This level of detailed, long-term data is vital for continuous quality improvement, informing future implant design, and refining surgical techniques.

## Facilitating Objective Kinematic and Soft Tissue Balance Assessment

While KA aims to restore native kinematics, objectively measuring functional kinematics and soft tissue balance in real-world settings remains challenging. There is a recognized need for integrating data from advanced technologies like robotic-assisted TKA, compartmental pressure sensors<sup>5</sup>, and wearable IMU sensors for remote knee flexion monitoring<sup>9</sup>. Circles can capture integrated clinical data throughout the patient journey. Observational Protocols can be designed to include and correlate data streams from these advanced technologies. They can incorporate, for example, intra-operative data (e.g., pressure sensor readings on soft tissue balance, precise bone cut angles from robotic systems<sup>7</sup>) with post-operative objective kinematic data (e.g., knee flexion angles from wearable sensors during daily activities<sup>9</sup>) and patient-reported outcomes.

Circles' ability to integrate diverse "relevant clinical data" positions it as a powerful platform for effectively creating a "digital twin" of the knee for each patient. By combining preoperative 3D imaging data (CT scans for personalized planning<sup>2</sup>), intra-operative data from robotic assistance or pressure sensors<sup>5</sup> on bone cuts, implant positioning, and soft tissue balance<sup>3</sup>, and post-operative kinematic data from wearable sensors<sup>9</sup>, Circles can construct a comprehensive, longitudinal digital record. This enables unprecedented correlation: how accurately was the KA goal achieved surgically? How does that surgical precision translate into actual knee kinematics (e.g., flexion angles, rotational moments) during daily activities? And most importantly, how do these objective kinematic parameters correlate with subjective patient satisfaction, functional recovery, and long-term implant performance?

This level of integrated, multi-modal data is impossible with fragmented "big data" RWE and would be transformative for understanding, optimizing, and validating the biomechanical principles of KA.

## Analyzing Real-World Variability and Best Practices

The impact of surgeon experience on KA outcomes is a recognized factor<sup>1</sup>, and there is observed variability in alignment outcomes.<sup>5</sup> Understanding how KA performs across different surgeons, techniques (e.g., robotic vs. manual), and diverse patient populations in routine practice is crucial for widespread adoption.



Circles' transparent data collection methodology and its ability to collect practitioner credentials<sup>8</sup> enable the systematic study of variability. Specific OPs can be designed to compare outcomes across different surgeon experience levels (e.g., experienced vs. less experienced<sup>1</sup>), different surgical techniques (e.g., robotic-assisted vs. traditional KA<sup>7</sup>), and diverse patient demographics.<sup>7</sup> This allows for robust comparative effectiveness research in a real-world context.

The debate surrounding KA's widespread adoption<sup>6</sup> is partly rooted in concerns about its generalizability beyond highly specialized centers. Circles can play a crucial role in de-risking the broader implementation of KA by providing a robust platform to monitor its real-world performance. By structuring OPs to capture data from a wide range of surgeons (varying experience levels), different institutional settings, and diverse patient populations, Circles can identify the factors that consistently lead to optimal outcomes or increased complications. This granular data allows for the development of evidence-based best practice guidelines, refinement of surgical training protocols, and identification of specific patient profiles that benefit most from KA. This moves beyond anecdotal evidence or limited trial data, providing the practical insights needed for responsible clinical dissemination.

## Investigating Complication Profiles and Ligamentous Management

KA is promoted as a "ligament sparing" technique<sup>3</sup>, aiming to avoid healthy ligament releases.<sup>1</sup> However, a clinical trial (NCT06709703) still plans to note the "Need for ligamentous release" and "Need for tibial or femoral recut" during surgery, as well as the incidence of "Unplanned ligament injury" and other intra-operative complications.<sup>7</sup>

The true incidence of these events in real-world KA practice needs comprehensive capture. Specific Circles OPs can be designed to track intra-operative details, including the precise need for and type of ligamentous release, the frequency of tibial or femoral recuts, and the occurrence of any intra-operative complications.<sup>7</sup> This granular, prospective data collection will provide real-world statistics on the actual incidence of these events, allowing for a robust validation of KA's "ligament sparing" claim and a comprehensive understanding of its safety profile and technical demands.

A foundational principle of KA is its "ligament sparing" nature.<sup>3</sup> However, the inclusion of "Need for ligamentous release" and unplanned ligament injury as outcome measures in a clinical trial<sup>7</sup> suggests that while the intent of KA is ligament sparing, the reality in diverse surgical practices might involve some degree of soft tissue manipulation or unexpected complications.

Circles can provide real-world statistics on how often these intra-operative adjustments or complications occur with KA across different surgeons and patient anatomies.

This data is crucial for validating the theoretical principles of KA against actual surgical practice, understanding the true safety profile, and identifying any discrepancies between ideal technique and real-world application. This allows for continuous refinement of the surgical approach and clearer guidelines for surgeons.

## SELECT CIRCLES OBSERVATIONAL PROTOCOLS FOR KA TKA

Specific Observational Protocols (OPs) can quickly be designed and implemented to target the most pressing unanswered questions in Kinematic Alignment TKA. These OPs should capitalize on Circles' inherent strengths in longitudinal data collection, data integrity, and their capacity for integrating diverse data types. Below are only four examples. The physicianinvestigator can easily identify many more.

### Longitudinal Comparative Effectiveness of KA vs. MA

This large-scale, multi-center OP would focus on capturing long-term patient-reported outcomes, including nuanced questions about "natural feel" and the Forgotten Joint Score (FJS), alongside robust data on implant survivorship (extending beyond 10 years) and revision rates.

The data should be carefully stratified by surgeon experience, patient demographics, and specific implant designs to provide granular insights into performance variations. This would directly address the critical long-term evidence gap that currently exists for KA.<sup>1</sup>

### Impact of Enabling Technologies on KA Outcomes

This OP would systematically compare robotic-assisted KA to manual KA (as in <sup>7</sup>) across several key metrics. These include intra-operative precision (e.g., bone cut accuracy, ligament balance quantified by pressure sensors), the frequency of intra-operative procedures (e.g., need for ligament releases, recuts<sup>7</sup>), complication rates, and post-operative kinematics and PROMs.

Crucially, this OP should also explicitly track the surgeon learning curve for each technique, providing valuable data for training and dissemination.



## Correlation of Objective Kinematics with Patient-Reported Outcomes

This OP would integrate data from wearable sensors<sup>9</sup> or other objective kinematic measurement tools (e.g., gait analysis systems<sup>5</sup>) with detailed patient-reported outcomes, including qualitative data. The goal is to establish clear correlations between objective functional improvements (e.g., range of motion, gait parameters) and subjective patient satisfaction and perceived "naturalness" of the knee. This would help to bridge the current disconnect between objective surgical metrics and subjective patient experience.

## Outcomes of KA in Specific Patient Populations/Deformities

Dedicated OPs could investigate the effectiveness and safety of KA in patients with specific constitutional deformities (e.g., constitutional varus/valgus<sup>3</sup>) or complex patellar tracking issues.<sup>3</sup> Such focused studies would refine patient selection criteria, optimize surgical planning for challenging cases, and provide evidence for tailoring KA to individual patient anatomies.

# COLLABORATIVE RESEARCH THROUGH CIRCLES

By their nature, Circles foster a unique environment highly conducive to collaborative research. They readily facilitate multi-center studies, enabling the collection of data from larger cohorts across diverse clinical settings. This leads to greater statistical power and enhanced generalizability of findings.

This collaborative model can significantly accelerate the accumulation of high-quality RWE, fostering a "learning healthcare system" where clinical practice continually generates data that informs research, and research findings are rapidly translated back into improved practice. This iterative process is particularly important for a dynamic field like orthopedics, which relies heavily on surgical technique, patient-specific factors, and continuous innovation.

The Circles ecosystem can accelerate the accumulation of evidence, effectively transforming the orthopedic community into a "learning healthcare system" where clinical practice continually generates data that informs research, and research findings rapidly translate back into improved practice. This iterative process is crucial for continuous innovation and optimizing patient care in a complex field like TKA.

The ongoing debate surrounding Kinematic Alignment in Total Knee Arthroplasty underscores a critical and unmet need for high-quality, long-term, and clinically relevant evidence to guide its adoption. While KA offers a compelling patient-specific approach with the potential to overcome the limitations of traditional Mechanical Alignment and address patient dissatisfaction, its widespread implementation is currently hampered by inconclusive high-level evidence, insufficient long-term data, and challenges in objectively assessing its realworld performance.

The Circles platform presents a transformative solution to these challenges. It ensures superior data integrity, completeness, and clinical relevance, standing in stark contrast to the inherent limitations of conventional "big data" RWE. By providing a structured environment analogous to traditional clinical trials, enforcing Good Clinical Practice, and facilitating longitudinal data capture, Circles is uniquely positioned to generate the robust evidence necessary to:

- Bridge the existing evidence gap by providing large-scale, long-term data on KA's effectiveness and safety.
- Deepen the understanding of patient satisfaction by capturing nuanced, subjective outcomes.
- Monitor long-term implant performance and revision rates with unprecedented detail.
- Enable objective assessment of kinematics and soft tissue balance through integration with advanced technologies.
- Analyze the impact of surgeon experience and technique variability on outcomes in real-world settings.
- Provide comprehensive data on complication profiles and the true incidence of ligamentous management.

By systematically addressing these key clinical issues, the Circles platform can accelerate the accumulation of trustworthy evidence, inform the development of evidence-based clinical guidelines, and foster a collaborative "learning healthcare system" in orthopedics. This will ultimately enable the responsible and widespread adoption of Kinematic Alignment, leading to improved patient outcomes and a more personalized approach to total knee arthroplasty.

**APPENDIX A TABLE:  
BIG DATA RWE VS. CIRCLES PLATFORM**

QUALITY CRITERION	BIG DATA RWE	CIRCLES
<b>DATA INTEGRITY, VERIFIABILITY</b>	Poor. Derived from multiple, often unidentified sources; manipulated by undisclosed algorithms; impossible to trace datapoints to original sources.	Strong. Sourced directly and verifiably from primary sources (physicians, patients, labs); each datapoint time-stamped and unmanipulated; transparent data collection within a closed platform.
<b>COMPLETENESS</b>	Poor. Typically has gaps, significantly reducing clinical relevance; rarely contains meaningful longitudinal outcomes data.	Strong. Comprised of wellcorrelated, longitudinal Cases; all datapoints relatable to a Case; captures and integrates relevant clinical data from initial enrollment through long-term outcomes.
<b>CLINICAL RELEVANCE</b>	Unknown And Unknowable. Impossible to know circumstances of data collection or by whom; generally impossible to determine IRB involvement or informed patient consents.	Strong. Patented technical platform inherently helps enforce good clinical practice; explicitly provides for collection of GCP certificates, practitioner credentials, and IRB/MEC support.
<b>OWNERSHIP</b>	Often In Dispute. Derives from EMR systems, registries, hospital records, insurance claims; various sources claiming ownership, leading to royalty claims and litigation.	Unambiguous. Data exclusively collected, aggregated, and correlated within a closed, integrated technical platform; ownership unambiguously established in favor of the Circle sponsor, Physicians-Owned Circles Members, and/or RegenMed.

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QUALITY CRITERION	BIG DATA RWE	CIRCLES
<b>COST AND BURDEN</b>	High. Expensive for vendors (licensing, manipulation algorithms); substantial time and resource burdens on physicians and patients creating primary data (EMR entries, insurance claims).	Low. Technical platform designed to generate high-quality datasets at much lower cost than traditional clinical trials; supported by services ensuring minimal burden for clinicians and patients.
<b>FINANCIAL BENEFIT</b>	Inequitable. Healthcare data analytics market worth billions, but data sources (physicians, patients) receive nothing of that value.	Equitable. Physicians-Owned Circles return up to 85% of licensing value to POC Members; datasets represent significant and increasing balance sheet equity for POC Members.
<b>REPORTING CAPABILITIES</b>	Limited, Extra Charges. Limited by dataset constraints; most vendors impose separate charges for various reports.	Robust, Included. Any Circles Question can be queried against any outcomes assessment, allowing many dozens of specific reports to be generated and compared; no additional charge to Physicians-Owned Circles Members for such reports.



**APPENDIX B TABLE:  
CLINICAL ISSUES IN TKA KINEMATIC ALIGNMENT**

Key Clinical Issue in KA TKA Current Evidence	Current Evidence Gap/Challenge	How Circles RWE Addresses This
<p><b>Lack of High-Quality, LongTerm RCT Evidence</b></p>	<p>Inconclusive RCTs, often with moderate-to-high risk of bias and limited follow-up (mean 24 months), failing to show clinically important benefits or long-term outcomes.</p>	<p>Circles provides "clinical trialanalogous" RWE with strong data integrity and longitudinal cases, enabling large-scale, longterm data collection in real-world settings to complement and extend RCT findings.</p>
<p><b>Variability in Patient Satisfaction &amp; Functional Outcomes</b></p>	<p>Significant patient dissatisfaction (20-25%) persists, attributed to unnatural kinematics; objective improvements not consistently translating to improved PROMs; standard PROMs may not capture "natural feel."</p>	<p>Circles captures comprehensive, long-term patient-reported outcomes (including nuanced PROMs like FJS and "Joint perception questions") within specific OPs, allowing for a deeper understanding of subjective patient experience and "experiential outcomes."</p>
<p><b>Uncertainty Regarding LongTerm Implant Performance &amp; Revision Rates</b></p>	<p>Limited long-term follow-up (mean 24 months) insufficient for assessing implant longevity (15-20+ years), wear, and revision rates; unvalidated claims about preventing accelerated wear/loosening.</p>	<p>Circles' inherent design for "longitudinal Cases" and "longterm patient-reported and/or clinical outcomes surveys" enables continuous tracking of implant survivorship, wear patterns, and precise revision rates over extended periods in real-world settings.</p>



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<p><b>Challenges in Objective Kinematic &amp; Soft Tissue Balance Assessment</b></p>	<p>Difficulty in objectively measuring functional kinematics and soft tissue balance in realworld settings; need for integrating data from advanced technologies (robotics, pressure sensors, wearables) with patient outcomes.</p>	<p>Circles' capacity for "integrated clinical data" within "specific Observational Protocols" allows for the correlation of intraoperative data (robotics, pressure sensors) with post-operative objective kinematics (wearable sensors) and patient-reported outcomes, creating a "digital twin" of the knee.</p>
<p><b>Impact of Surgeon Experience &amp; Technique on Outcomes</b></p>	<p>Reliance on "experienced surgeons" for positive outcomes; uncertainty about learning curve for new techniques (e.g., roboticassisted KA) and generalizability across diverse surgical practices.</p>	<p>Circles' transparent data collection and ability to capture practitioner credentials enable systematic study of outcomes across different surgeon experience levels and techniques (robotic vs. manual), providing data on learning curves and best practices.</p>
<p><b>Complication Profiles &amp; Ligamentous Management</b></p>	<p>While KA is "ligament sparing," real-world incidence of ligamentous releases, recuts, and unplanned intra-operative complications needs comprehensive capture and validation against theoretical principles.</p>	<p>Circles' integrated clinical data capture within specific OPs allows for documentation of intra-operative details, including the need for ligamentous releases, recuts, and the occurrence of any complications, providing real-world statistics on safety and technical demands.</p>



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