RegenMed

WHITE PAPER

CIRCLE DATASETS FOR THE VISCOSUPPLEMENTS MARKET

WITH A FOCUS ON KNEE OSTEOARTHRITIS

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EXECUTIVE SUMMARY

The overall healthcare sector stands at a precipice, characterized by a fundamental disconnect between the delivery of care and the verification of its value. This forces stakeholders -- regulators, payers, and providers -- to rely on secondary data or "data exhaust" (billing codes and administrative claims) to guess at clinical efficacy. Nowhere is this gap more palpable than in the management of knee osteoarthritis (KOA), a condition plagued by subjective endpoints, high placebo response rates in clinical trials, and contentious reimbursement debates surrounding viscosupplementation.

By shifting the operational paradigm from a volume-based service model to a "schema-on-capture" data generation engine, providers have the potential to mint "deterministic ground truth".

This paper suggests illustrative clinical questions required to validate this transition, analyzes the market forces driving the value of such data, and provides a detailed financial valuation of the real-world evidence (RWE) datasets that could be generated by practitioners. By bridging the verification gap, providers treating KOA can transition from commoditized procedures to sovereign generators of regulatory-grade evidence, earning license fees significantly higher than paid for standard electronic medical record (EMR) datasets.

THE GLOBAL VISCOSUPPLEMENTATION MARKET

The global viscosupplementation market is a mature yet evolving sector, fundamentally driven by the demographic inevitability of an aging global population and the rising prevalence of osteoarthritis. It acts as a critical bridge therapy between conservative management (NSAIDs, physical therapy) and invasive surgical intervention (Total Knee Arthroplasty - TKA).

Market Dimensions and Trajectory

The market for intra-articular hyaluronic acid (HA) alone is substantial, with valuations ranging between $1.6 B and U$4.7 B in 2024, depending on market definition (global vs. regional inclusions). Projections suggest a steady compound annual growth rate (CAGR) of

approximately 9% through 2032-2034. This growth is underpinned by the "graying" of the population; estimates indicate that by 2030, one in six people globally will be aged 60 or over , a demographic that correlates strongly with the 43% prevalence of osteoarthritis in populations aged 65 and above.

Despite this growth, the market faces significant headwinds in the form of reimbursement pressure and clinical skepticism. The "twin sins" of payer behavior -- overpaying for low-value care while denying high-value innovation -- are rampant. Payers often categorize viscosupplementation as a "lifestyle" procedure or question its long-term efficacy compared to corticosteroids or total knee arthroplasty (TKA), leading to stringent medical necessity criteria. Commercial payers frequently implement "step therapy" or "fail first" policies, requiring patients to demonstrate failure of corticosteroids and conservative care before authorizing HA injections.

Competitive Landscape and Product Segmentation

The market is dominated by a few key incumbents controlling the majority of market share through established brand loyalty and contracting leverage. The competitive dynamics are shaped by product formulation (molecular weight, cross-linking) and injection regimen (single vs. multi-injection).

A critical trend in this landscape is the shift toward single-injection formulations (e.g., Synvisc-One, Monovisc, Durolane), which now account for the largest revenue share (over 47%). This shift is driven by patient convenience and the reduction of office visits. However, multi-injection regimens (3-5 shots) like GenVisc 850 remain relevant for specific payer formularies and clinical preferences where volume and repeated contact with the patient are prioritized. The multi-injection market allows for closer patient monitoring but faces higher scrutiny regarding "unnecessary" facility utilization.

The "GenVisc 850" Strategy and Regulatory Nuance

GenVisc 850 is manufactured by OrthogenRx (acquired by Avanos Medical in 2021 for $160 million). GenVisc 850's approval was a regulatory landmark: it was approved as a Class III medical device via a PMA (Premarket Approval) pathway that demonstrated "indistinguishable" physical, chemical, and clinical performance to Supartz FX. This

regulatory nuance is critical: GenVisc 850 is essentially a "bio-equivalent" to Supartz, positioned as a cost-effective alternative. It is indicated for patients who have failed conservative non-pharmacologic therapy and simple analgesics.

The approval relied on a Bayesian network meta-analysis demonstrating non-inferiority to Supartz and superiority to saline. This "equivalence" strategy allows GenVisc 850 to piggyback on the extensive safety data of Supartz while offering a potentially lower acquisition cost, creating a margin opportunity for providers. However, its 5-injection regimen requires patients to commit to a 5-week treatment course, a factor that aligns with a high-touch, frequent-visit business model but also invites payer audits regarding the necessity of multiple facility fees.

The Clinical Controversy: AAOS vs. The Real World

The market exists in a state of tension with clinical guidelines. The American Academy of Orthopaedic Surgeons (AAOS) has historically recommended *against* the use of viscosupplementation for knee osteoarthritis, citing a lack of statistically significant improvement in pain and function compared to placebo. The 2013 guideline was a "strong recommendation against", while the updated 2021 guideline softened this slightly but still found "statistically significant improvements" were not always "clinically important".

This stance is controversial and conflicts with guidelines from other bodies (e.g., the American College of Rheumatology, which conditionally recommends it) and the real-world experience of many clinicians who observe tangible benefits in specific patient subgroups. The AAOS position is largely based on meta-analyses of randomized controlled trials (RCTs) that aggregate heterogeneous patient populations. Critics argue that these trials often include late-stage OA patients who are poor candidates for HA, thereby diluting the efficacy signal.

ILLUSTRATIVE CLINICAL QUESTIONS

The "Precision Hypothesis"

Does fluoroscopy-confirmed intra-articular delivery of GenVisc 850 result in superior "Time to Total Knee Arthroplasty" compared to blind injection controls?

- **Rationale:** The current literature is mixed. While some studies suggest image guidance improves accuracy (96-100% vs. 70-80% for blind), the correlation with long-term *clinical* outcomes (pain reduction, delay of surgery) is less robustly established. Blind injections often miss the joint space, delivering expensive HA into the fat pad where it provides no benefit.
- **Circle Datasets** can utilize "schema-on-capture" to tag every injection record with its corresponding fluoroscopic image (the "ground truth"). By linking this to long-term claims data or patient-reported outcomes (PROs), the provider can definitively establish whether "hitting the target" matters. This requires a rigorous definition of "success" in the metadata of the image itself.
- **Market Value:** Demonstrating that *verified* delivery delays TKA by 1-2 years would have immense economic value to payers (Medicare/commercial). Studies show delaying TKA can save significant healthcare costs. A delay of TKA by 2 years shifts significant cost into the future, a key metric for payer actuarial models.

The "Responder Phenotype"

Can multimodal "schema-on-capture" data (biomarkers, radiographic severity, patient demographics) identify a specific phenotype of "super-responders" to GenVisc 850?

- **Rationale:** Viscosupplementation fails in many patients, driving the negative AAOS recommendations. However, it works profoundly well for some. Current "secondary data" (claims) lacks the granularity to explain *why*. Is it the KL grade? The inflammatory state of the synovium? The BMI?

- **A Circle Dataset Observational Protocol** can be designed to collect:
    - **Baseline Radiographic Metrics:** Kellgren-Lawrence (KL) grade, Joint Space Width (JSW) measured digitally.
    - **Synovial Biomarkers:** Since aspiration is often performed prior to injection to remove effusion, the provider has access to synovial fluid (SF). Analyzing SF for inflammatory markers (IL-6, MMP-3, VEGF) could predict response. High levels of IL-6 or MMP-3 might indicate an inflammatory phenotype less responsive to HA alone, or more responsive to specific cross-linked formulations.
    - **Patient Phenotype:** BMI, activity level, mechanical alignment.
- **Market Value:** A validated algorithm that predicts *who* will respond to HA injections would be a "Holy Grail" for payers (eliminating waste) and the manufacturer (securing the formulary for responders). This moves risk from "probabilistic" (it might work) to "deterministic" (it will work for *this* patient).

"Placebo Minimization" Protocol and Synthetic Control Arm

Does the rigorous protocol of fluoroscopy-guided injection create a "ritual of care" that maximizes therapeutic benefit, and can we disentangle the physiologic effect of HA from the placebo response to create a Synthetic Control Arm?

- **Rationale:** The placebo response in OA trials is massive (up to 75% of pain reduction), often masking the true effect of drugs and leading to Phase 3 failures. The "ritual" of 5 weekly visits, imaging, and interaction contributes to this.
- **Circle Datasets** can capture high-frequency longitudinal data and correlate it with the *verified* technical success of the injection. This can create a "synthetic control arm" of Standard of Care (SOC). This dataset characterizes the "background noise" of OA treatment in a high-fidelity way.
- **Market Value:** This can be the most valuable asset of a physician contributing to a Circle Dataset. Pharma companies developing Disease-Modifying Osteoarthritis

Drugs (DMOADs) struggle to recruit patients and often fail trials due to high placebo rates. An imaging-verified, longitudinally tracked "Standard of Care" control arm allows them to compare their new drug against a known, high-quality benchmark without recruiting hundreds of placebo patients.

VALUE OF VARIOUS REAL-WORLD EVIDENCE DATASETS

Following is a range of potential Circle Datasets value generated by a large KOA provider group utilizing viscosupplements. It reflects the movement from low-value pricing of "Data Exhaust" (claims data) to the premium pricing of "Regulatory-Grade" evidence.

The Valuation Hierarchy

Healthcare data is not a commodity; it is a tiered asset class. The value is determined by the **Veracity** (truthfulness) and **Completeness** of the record.

Data Tier	Definition	Content	Typical Price/ Record	Provider Group Potential
Tier 3: Data Exhaust	Raw claims, billing codes, unverified EMR scraps. High "Inference Gap".	ICD-10, CPT codes, limited demographics. No outcomes.	**$50 - $150**	**Current State (Low Value)**
Tier 2: Curated Clinical Data	Structured EMR data, chart abstraction, longitudinal tracking.	Structured notes, labs, some PROs. (e.g., CorEvitas model).	**$500 - $1,500**	**Immediate Target**
Tier 1: Deterministic	**Schema-on-Capture**, Imaging-	**Fluoroscopic Image (Proof)** + Outcomes + Biomarkers +	**$2,500 - $8,500+**	**Future State (High Value)**

Ground Truth	Confirmed, "Verified Delivery", outcomes-linked.	Longitudinal tracking.		

Valuation Methodology 1: Comparable Transactions

To triangulate the value, we look at market precedents for high-quality clinical data platforms:

- **CorEvitas (Autoimmune/Registry):** Acquired by Thermo Fisher for $912.5M. CorEvitas manages registries with ~100,000 longitudinally followed patients across autoimmune and inflammatory conditions.
    - *Implied Value:* $912.5M / 100,000 patients = ~$9,125 per longitudinal patient record (enterprise value). Even discounting for the service component and multiple datasets per patient, the value of a high-fidelity, longitudinal record is substantial.
- **Flatiron Health (Oncology):** Acquired by Roche for $1.9B - $2.1B. Flatiron's value lay in its ability to normalize unstructured oncology notes into structured "regulatory-grade" data, effectively creating external control arms for cancer trials.
    - *Insight:* The premium was paid for veracity and depth—the ability to answer questions (like tumor progression) that claims data could not.
- **23andMe / GSK:** $300M investment for access to genetic database of ~5 million customers.
    - *Implied Value:* ~$60 per record. This is lower because the data is largely patient-reported, unverified clinically, and lacks deep longitudinal phenotypic context compared to a clinical registry.

Application to Large Provider Group:

If the provider group has treated 60,000 patients with 700,000 injections, and can structure this data to meet "regulatory-grade" standards through Circle Datasets, the valuation shifts from the "23andMe" tier ($60/record) toward the "CorEvitas" tier ($9,000+/record enterprise value).

Valuation Methodology 2: Cost-Avoidance (The Synthetic Control Arm)

The "Synthetic Control Arm" (SCA) model values data based on what it saves a pharmaceutical buyer.

- **The Cost of Trials:** Pharmaceutical companies spend $41,000 to $113,000 per patient in Phase 3 clinical trials. Recruiting patients for OA trials is notoriously difficult due to high screen failure rates (up to 73%) caused by strict inclusion criteria (e.g., specific KL grades, pain scores).
- **The Savings:** If a pharma company needs a control arm of 100 patients receiving Standard of Care (HA injection), they would typically spend ~$5,000,000 (100 * $50k) to recruit and manage them.
- **Provider Group Value Proposition:** The provider group can generate a "virtual" control arm of 100 matched patients from its database. These patients have *verified* injections (images) and longitudinal outcomes.
- **Pricing:** Charging $10,000 per record for a high-fidelity, imaging-verified SCA record represents an 80% discount to the pharma company's internal cost of generating that data manually ($50k). This is a compelling "buy vs. build" arbitrage.

The "Fee-for-Veracity" Price Tag

Reasonable estimates for Circle Datasets generated by a large KOA provider group can be calculated as follows:

1. The "Verified Delivery" Dataset (Level 1 Asset)

- *Content:* Patient demographics + Fluoroscopic Image (Proof of Delivery) + Brand of HA used (GenVisc 850).
- *Use Case:* Post-market surveillance (FDA 522 orders), implant safety monitoring, basic utilization trends.
- *Estimated License Fee:* $250 - $400 per record per year.

2. The "Longitudinal Responder" Dataset (Level 2 Asset)

- *Content:* Verified Delivery + Longitudinal PROs (WOMAC/KOOS scores at 3, 6, 12 months) + TKA status (survival analysis).
- *Use Case:* HEOR (Health Economics and Outcomes Research) for payer negotiations, value-based contracting, comparative effectiveness research.
- *Estimated License Fee:* $1,200 - $2,500 per record.

3. The "Deterministic Ground Truth" / Synthetic Control Arm (Level 3 Asset)

- *Content:* Schema-on-Capture fully enforced. Verified Delivery + Radiographic grading (JSW) + Synovial Biomarkers (if collected) + High-frequency PROs + matched control variables.
- *Use Case:* Regulatory submission (FDA), Synthetic Control Arm for Phase 2/3 DMOAD trials.
- *Estimated License Fee:* $5,000 - $8,500 per record**.**

Total Potential Revenue Impact: If the provider group matches the data fidelity of a registry like CorEvitas for just 10% of a 60,000 patient volume (6,000 records) at Level 2 pricing ($1,500):

- 6,000 records * $1,500 = $9,000,000 in pure data licensing revenue.
- At Level 3 (SCA) pricing for a smaller cohort of 1,000 “perfect” records: 1,000 * $8,500 = $8,500,000.

FROM "DATA SWAMPS" TO "SCHEMA-ON-CAPTURE"

To realize this valuation, the provider group must move from "marketing fluff" to "industrial precision".

Implementing Schema-on-Capture

It must define the data architecture *before* the patient walks in. This means:

- **Standardized Imaging Metadata:** Fluoroscopy images must not just be saved; they must be tagged with metadata (e.g., injection angle, contrast dispersion grade, needle placement verified") at the moment of capture.
- **Structured PROs:** Moving beyond "how do you feel?" to standardized, digitizable instruments (KOOS-JR, WOMAC) collected at rigid intervals via automated platforms (e.g., tablets in the waiting room, text links).
- **Biomarker Integration:** Standardizing the collection of synovial fluid during aspiration for biomarker analysis (IL-6, MMPs) to fuel the "responder phenotype" model.
- **Identity Resolution:** Using tokenization to link the provider group records with external claims data (to track TKA events that happen elsewhere) without violating HIPAA. This allows the provider group to know if their patient had surgery at a competitor's hospital 2 years later.

The "Settlement Layer" Integration

The provider group should position itself not just as a clinic, but as a node in the RegenMed "Settlement Layer". By proving outcomes (e.g., "Patient X received GenVisc 850, verified by image Y, and did not require TKA for 3 years"), the provider group can engage in Value-Based Contracts with payers.

- *Proposal:* "We will take risk. If our fluoroscopy-guided injection fails to delay TKA by

12 months, we rebate the cost. If it succeeds, we share in the savings."

Addressing the "Sovereignty" of the Physician

The RegenMed model emphasizes "Scientific Sovereignty". The provider group physicians are currently on a "hamster wheel" of procedure volume, which can lead to legal/regulatory issues, as well as costly physician turnover.

- *The Shift:* Incentivize physicians not just on *doing* the injection, but on *capturing the high-fidelity data*.
- *The Dividend:* A portion of the data licensing revenue flows back to the practice/physicians in an ethical manner (since the physician is unaware of eventual licensees, and unaware of ultimate measured outcomes.) This creates alignment: the physician ensures the data is perfect because the data is the product.

CONCLUSION

The "Inference Gap" in osteoarthritis—the inability to distinguish effective treatment from placebo or poor delivery—is a billion-dollar problem for the industry. Knee OA provider groups are uniquely positioned to solve it by implementing clinically reasonable practice-of-medicine hypotheses.

However, operating this model without the "data rail" can expose them to regulatory risks. Without such an approach, the clinical model may look like "churning." In contrast, a data-based model looks like "scientific rigor". By structuring its clinical data for "schema-on-capture", the provider group can unlock substantial data revenue, validate its clinical approach, and move from a defensive regulatory posture to a sovereign, value-based market position. The transition is not just financial; it is existential—moving from a provider of services to an architect of truth.

TABLE 1: KEY VISCOSUPPLEMENTATION PLAYERS AND PRODUCTS

Manufacturer	Product	Regimen	Type	Market Position
Sanofi	Synvisc-One	1-shot	Cross-linked Hylan G-F 20	Market Leader (US). High brand recognition.
Sanofi	Synvisc	3-shot	Cross-linked Hylan G-F 20	Legacy standard.
Anika / DePuy Synthes	Monovisc	1-shot	High MW Hyaluronan	Strong challenger in single-shot space.
Anika / DePuy Synthes	Orthovisc	3-4 shot	High MW Hyaluronan	High purity, non-avian.
Bioventus	Durolane	1-shot	NASHA (Non-Animal Stabilized)	Growing share, emphasizes longevity.
Bioventus	Gelsyn-3	3-shot	Sodium Hyaluronate	Positioned as a cost-effective 3-shot option.
Seikagaku	Supartz FX	5-shot	Sodium Hyaluronate	The "Gold Standard" for safety/efficacy comparisons.
Fidia Farmaceutici	Hymovis	2-shot	Viscoelastic Hydrogel	Niche "high elasticity" positioning.
Fidia Farmaceutici	Hyalgan	5-shot	Sodium Hyaluronate	One of the earliest products; established safety profile.

OrthogenRx (Avanos)	**GenVisc 850**	**5-shot**	**Sodium Hyaluronate**	**"Bio-equivalent" to Supartz. Cost-effective strategy.**
OrthogenRx (Avanos)	TriVisc	3-shot	Sodium Hyaluronate	Same formulation as GenVisc, different regimen.

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