Use Case

Building Regulatory-Grade Synthetic Control Arms with Real-World Data / Evidence (RWD/E)

Enrolling enough participants in clinical trials can be a time-consuming and difficult process. This not only delays bringing new treatments to market but also limits patient access. Synthetic Control Arms (SCAs) utilize real-world data (RWD/E) to create robust control arms, bypassing the need for traditional enrollment and accelerating the development of new therapies. This document showcases Maxis Clinical Sciences' (MCS) RWE services in building regulatory-grade SCAs, presenting a use case scenario that demonstrates our expertise and our methodological approach in addressing enrollment challenges, ethical concerns, and regulatory requirements in a biopharmaceutical company's development of a novel cancer therapy.

Section	Details
Background	Synthetic control arms (SCAs) are derived from carefully curated and analyzed real-world data sources, serving as comparator arms in clinical trials. Regulatory agencies like the FDA and EMA have provided guidance on using RWD/E for this purpose, emphasizing the importance of data quality, relevance, and robust statistical methodologies to ensure validity and reliability.
Use Case Scenario	A biopharmaceutical company is developing a novel targeted therapy for non-small cell lung cancer (NSCLC). In their pivotal phase 3 clinical trial, they plan to compare the efficacy and safety of their investigational drug against the current standard of care treatment. To address challenges in enrolling patients into the control arm and to expand access to the investigational therapy, the sponsor explores using RWD/E to create an SCA.
MCS' Methodological Approach	1. **Data Acquisition and Integration:** MCS collaborates with the biopharmaceutical company to access and integrate high-quality, relevant real-world data (RWD) from sources such as electronic health records (EHRs), cancer registries, patient databases, and medical claims data. Our team employs rigorous data quality checks and curation processes to ensure the integrity and usability of the data. 2. **Target Population Identification:** Our analytics experts identify a target population from the RWD sources that closely matches the planned phase 3 study population's baseline characteristics (e.g., demographics, disease stage, comorbidities) and treatment patterns for the current standard of care therapy. 3. **Propensity Score Matching:** We apply propensity score matching techniques to create a synthetic control arm (SCA) from the curated RWD. This would involve identifying a cohort of patients who are statistically similar to the planned trial population, except for the exposure to the investigational drug, ensuring comparability between the SCA and the treatment arm. 4. **Handling Missing Data:** Our team uses advanced imputation techniques to handle missing data, if any, a common issue with RWD to handle missing data, if any, a common issue with RWD, ensuring the robustness and reliability of the synthetic control arm. 5. **Analysis and Reporting:** Our statisticians conduct rigorous analyses,

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	including techniques like inverse probability weighting, sensitivity analyses, and causal inference modeling, to assess the comparability of the SCA to the planned trial population and mitigate potential biases. We prepare a comprehensive regulatory-grade report detailing the methodologies, results, and evidence supporting the use of the RWD-based SCA as a comparator arm for the phase 3 trial. This report is suitable for regulatory submission and review.
Potential Benefits of using MCS' approach	• **Reduced Costs:** Using an RWD/E-derived SCA can significantly reduce the need for enrolling patients into the control arm, thereby accelerating trial timelines and reducing associated costs. • **Expanded Patient Access:** With an SCA, a larger proportion of the trial population can be assigned to the investigational therapy arm, expanding access to the potential new treatment. • **Increased Statistical Power:** By using an SCA, more patients can be assigned to the investigational therapy arm. This can increase the statistical power of the study and the reliability of the trial results. • **Improved Generalizability:** RWD often captures a more diverse and representative patient population than traditional clinical trials, improving the generalizability and real-world relevance of the trial results. **Ethical Considerations:** Fewer patients are exposed to potentially less effective or more toxic standard treatments when using an SCA.
Regulatory Considerations	Regulatory agencies emphasize the need for robust methodologies, data quality checks, and transparent reporting to ensure the validity and reliability of RWD-based SCAs for regulatory submissions. MCS stays up-to-date with the latest guidelines and documents from regulatory agencies that support the use of RWD/E and SCAs, to ensure compliance at every stage.
MCS Perspectives	MCS can contribute to defining the regulatory landscape for the use of RWD/E in clinical trials by: • **Engaging with regulatory agencies:** MCS can actively collaborate with regulatory bodies like the FDA and EMA to provide insights, participate in developing guidance, and contribute to the evolving regulatory framework for RWD/E-based synthetic control arms. • **Publishing research:** MCS can publish research findings, case studies, and methodological advancements in the field of RWD/E-based synthetic control arms, furthering the understanding and adoption of this approach. • **Developing best practices:** Through its extensive experience and expertise, MCS can establish and disseminate best practices for the ethical, scientifically rigorous, and compliant use of RWD/E in building synthetic control arms for regulatory submissions.
Additional Considerations	• While the use of RWD/E-derived synthetic control arms is gaining acceptance, regulatory agencies continue to refine their guidance and expectations. MCS can help sponsors navigate this evolving regulatory landscape and ensure compliance with the latest standards. • Data quality and representativeness are crucial for the validity and reliability of RWD-based synthetic control arms. MCS has robust data quality management processes and statistical expertise to ensure the RWD used is fit for purpose and appropriately addresses potential biases and confounding factors.

Conclusion

Maxis Clinical Sciences can help stakeholders in Clinical Research / Clinical Trials Studies (Sponsors, CROs, Research teams, Regulatory experts, or Study investigators) or Healthcare Decision-making (Payers, HTA agencies, or Patient advocacy groups), tap into the benefits of RWD/E, creating synthetic control arms that accelerate clinical and drug development timelines, broaden patient access, and enhance the reliability of clinical trial data.

If you have any questions or would like to learn more about our methodological approach and how we can support your specific needs, please don't hesitate to connect with us. We'd be delighted to discuss our services in further detail and explore how we can collaborate to drive innovation in clinical research and healthcare decision-making.

Contact us at info@maxisclinical.com or via our website contact form – Make an appointment.