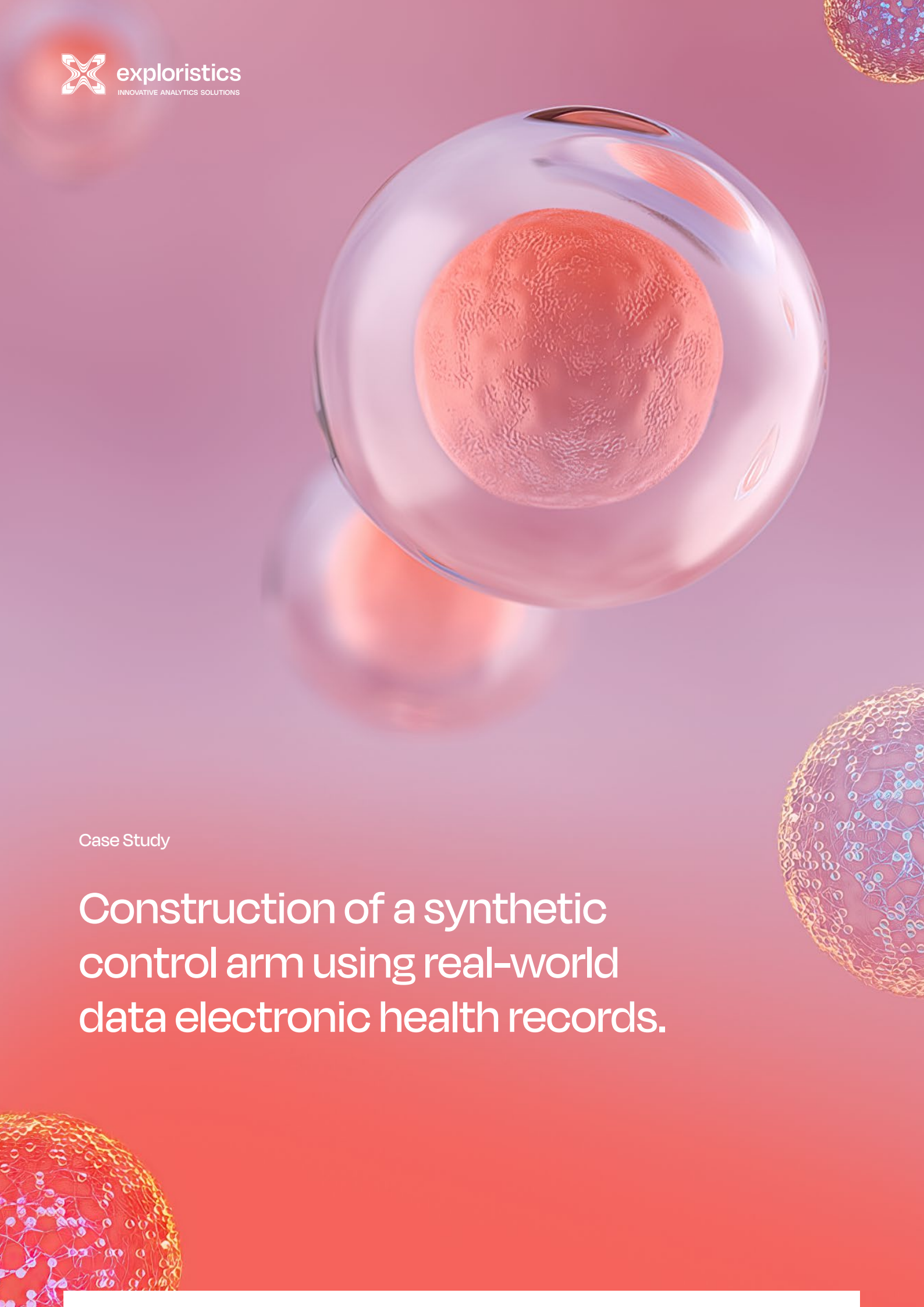
exploristics
INNOVATIVE ANALYTICS SOLUTIONS



Case Study

Construction of a synthetic control arm using real-world data electronic health records.

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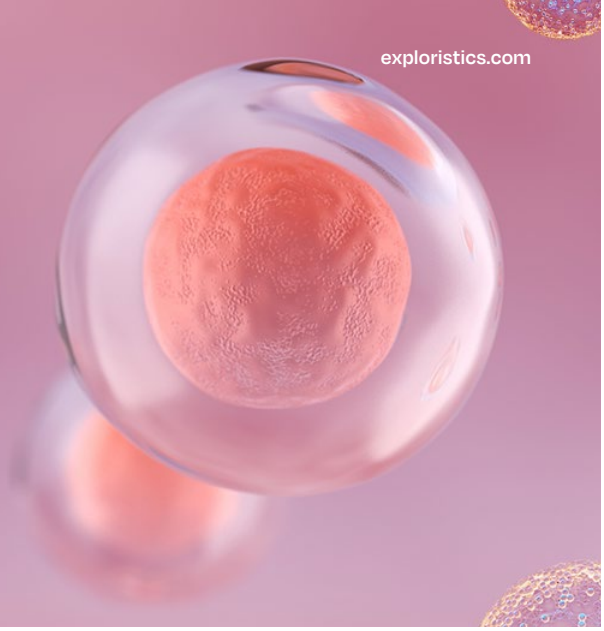

The **Data Science team** provide **advanced analytics** using proprietary **algorithms, tools, machine learning** and **predictive modelling approaches** to extract insights and synthesize evidence that can be used to inform the assumptions, strategy, and direction of any clinical trial program.

The Challenge

A biotechnology company was investigating a newly developed technology which aimed to enable radiotherapy to kill more tumour cells while minimizing the effects on healthy tissue. They had access to an extensive database of real-world healthcare data and wanted to generate evidence in support of the development of a synthetic control arm for their clinical program in a specific oncology subpopulation, with specific prerequisites for prior treatment regime and disease severity. The company wished to consider if they could use real-world data (RWD) in a synthetic control arm to replace enrolling patients.

Why Synthetic Control Arms?

There is a growing demand for the use of real-world data to support regulatory approval in contexts where a randomised control trial would not be feasible, especially when the use of a placebo would inhibit participant recruitment and retention. By eliminating the need to enrol control participants, synthetic control arms can increase efficiency, reduce trial costs, and accelerate much needed drugs to market.

The Approach

The Data Science team conducted a structured review and evaluation of the data which included data synthesis, data wrangling and analysis to identify patients derived from the database who aligned with the inclusion and exclusion criteria and baseline characteristics of patients taking part in a clinical trial.

The key objectives were to:

- Characterise the available real-world data including key outcomes in subgroups.
- Assess the utility and strategy for a synthetic control group.

Characterisation of real-world data

The RWD registry contained thousands of entries for the main oncology disease area, however the synthetic control arm required a cohort with specific eligibility criteria including matching to:

- Clinical trial timelines
- A treatment regimen of named radiotherapy and chemotherapy in a specific order
- Specific location of disease
- Disease severity

Therefore, the search was filtered using these criteria and a RWD cohort was constructed using the method outlined in Figure 1:

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Disease Overview
Gain an understanding of the disease.

Data Collection
Apply the same selection criteria as the population in the single arm trial to identify a random sample of eligible de-identified patient data sets from the RWD registry.

Data Integrity
Ensure data integrity by selecting patients from the RWD registry without prior knowledge of patient outcomes in the single arm trial.

Data Quality
Assess data completeness and carry out logic checks on data variables to ensure selected patient data sets are suitable.

Patient Matching
Produce summary statistics of patient baseline and diagnosis characteristics to ensure they fall within a reasonable range to patients in the single arm trial.

Outcomes
Analyse and report survival outcomes and response rates to provide a comparative analysis of progression.

Figure 1. Methodology for generating a RWD cohort.

Feasibility of constructing a synthetic control arm

Once a RWD cohort had been constructed, the following process (Figure 2) was employed in assessing the feasibility of a synthetic control arm for clinical development and clinical trial optimisation:

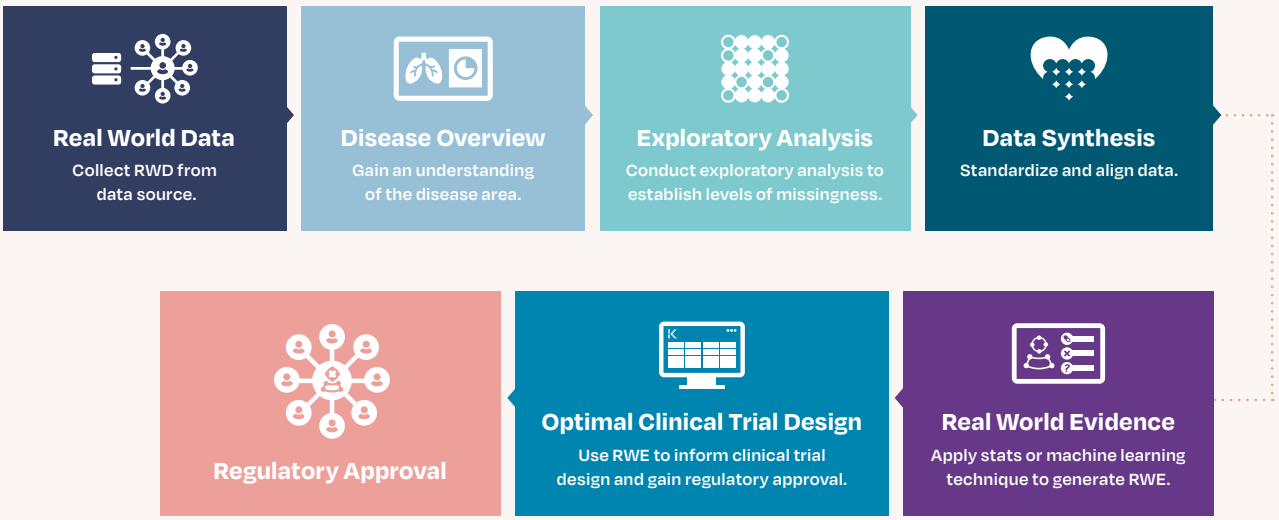

Figure 2. Using RWD to generate real-world evidence (RWE) in clinical trials.

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FDA guidance on the use of RWE to support regulatory decision-making for medical devices (1) emphasises the importance of having a pre-defined common set of data elements, a common definitional framework (i.e., data dictionary), and pre-specified time intervals for data element collection and outcome analyses.

The Data Science team:

- derived and documented elements including key aspects related to data missingness, data integrity and alignment, and derivation of clinical time-to-event outcomes such as progression free survival.
- employed a rigorous, pre-specified procedure of patient selection from the RWD without knowledge of the single arm trial results to reduce any potential form of bias.

The Results

Collation of a real-world data cohort

As each of the prespecified search criteria required for the study was applied to the RWD registry population the pool of eligible candidates narrowed from thousands to low hundreds and then to tens. These were used to construct a RWD cohort.

Feasibility of using a synthetic control arm

Finding external control data that matches the specifications of the single arm trial can be challenging, especially in small populations and rare diseases when specific eligibility criteria are required, for example, prior treatment regimen or disease severity.

Sufficient patient-level data was identified and filtered from the RWD registry for use in a synthetic control arm. The synthetic control arm was successfully validated for a clinical trial investigating a particular oncology subpopulation who had a specific disease and treatment history.

The Impact

The company investigating a candidate therapeutic for a disease for which there are usually small populations were able to:

- **Use RWD in a synthetic control arm** for their study to replace enrolling patients
- **Generate sufficient data for their study** despite the small target population
- **Save recruitment time, costs and patient burden.**

References

1. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Guidance for Industry and Food and Drug Administration Staff' issued August 31, 2017.

Why Exploristics?

Expertise In Early Development

The development of investigational drugs is a complex and expensive process with many risks. For over ten years our teams have been supporting and de-risking clinical development with their in-depth statistics and modelling expertise. Our study planning, statistical analysis and programming services add value to early stage development programmes by ensuring they deliver the robust evidence needed for incisive, informed decision-making.

With many of our development solutions built around our unique **KerusCloud** platform, we can provide exceptional, bespoke, end-to-end biostatistics support from strategic decision-making and protocol development to analysis, reporting and stakeholder engagement.

Robust Evidence Packages

The unique offering of our comprehensive biostatistics services in combination with **KerusCloud** ensures that Exploristics can help to generate strong evidence packages to support regulatory engagement or investment, accelerating development timelines and increasing the value of pipelines.

Let's talk!

If you'd like to discuss this case study further or learn more on how our **technology enabled services** can support your development project, please contact our VP of Sales & Marketing, Abbas Shivji, at **abbas.shivji@exploristics.com** or **book a call**.

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