

Role of Data Analytics Functions in studies utilizing Real World Data (RWD) for Submissions

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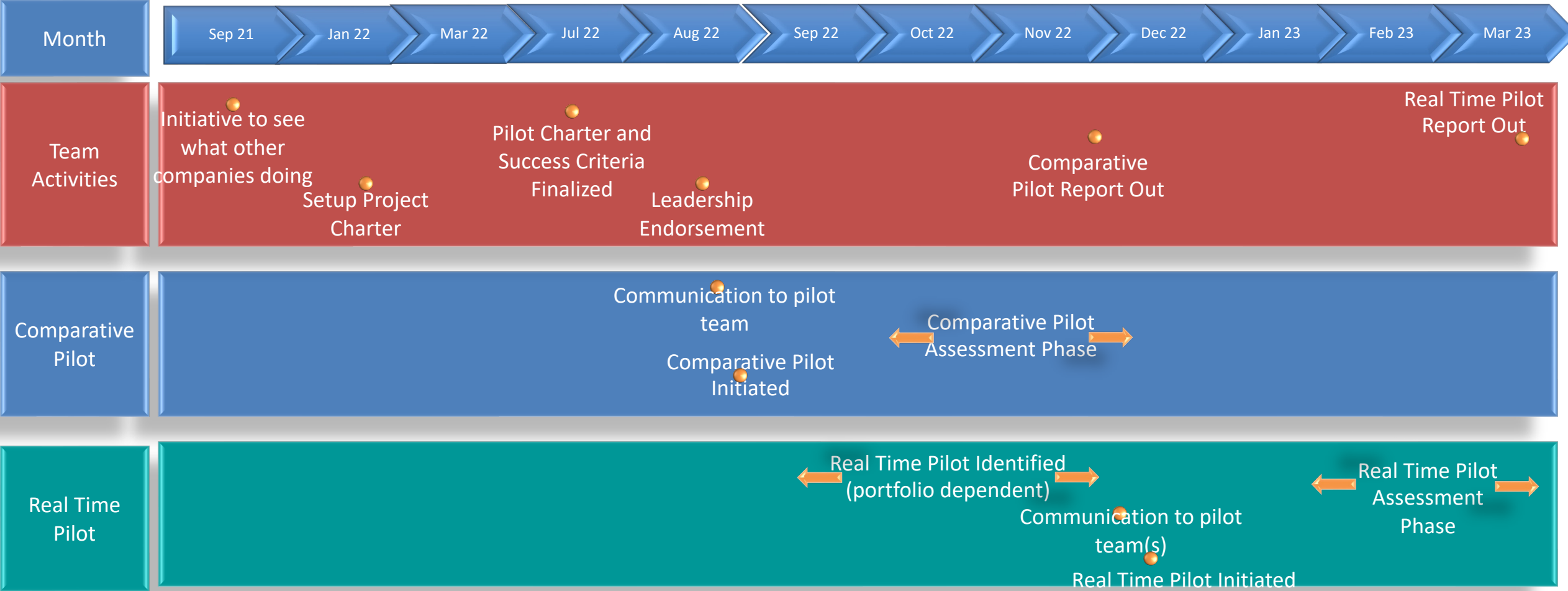
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Real World Data playbook and Risk Management

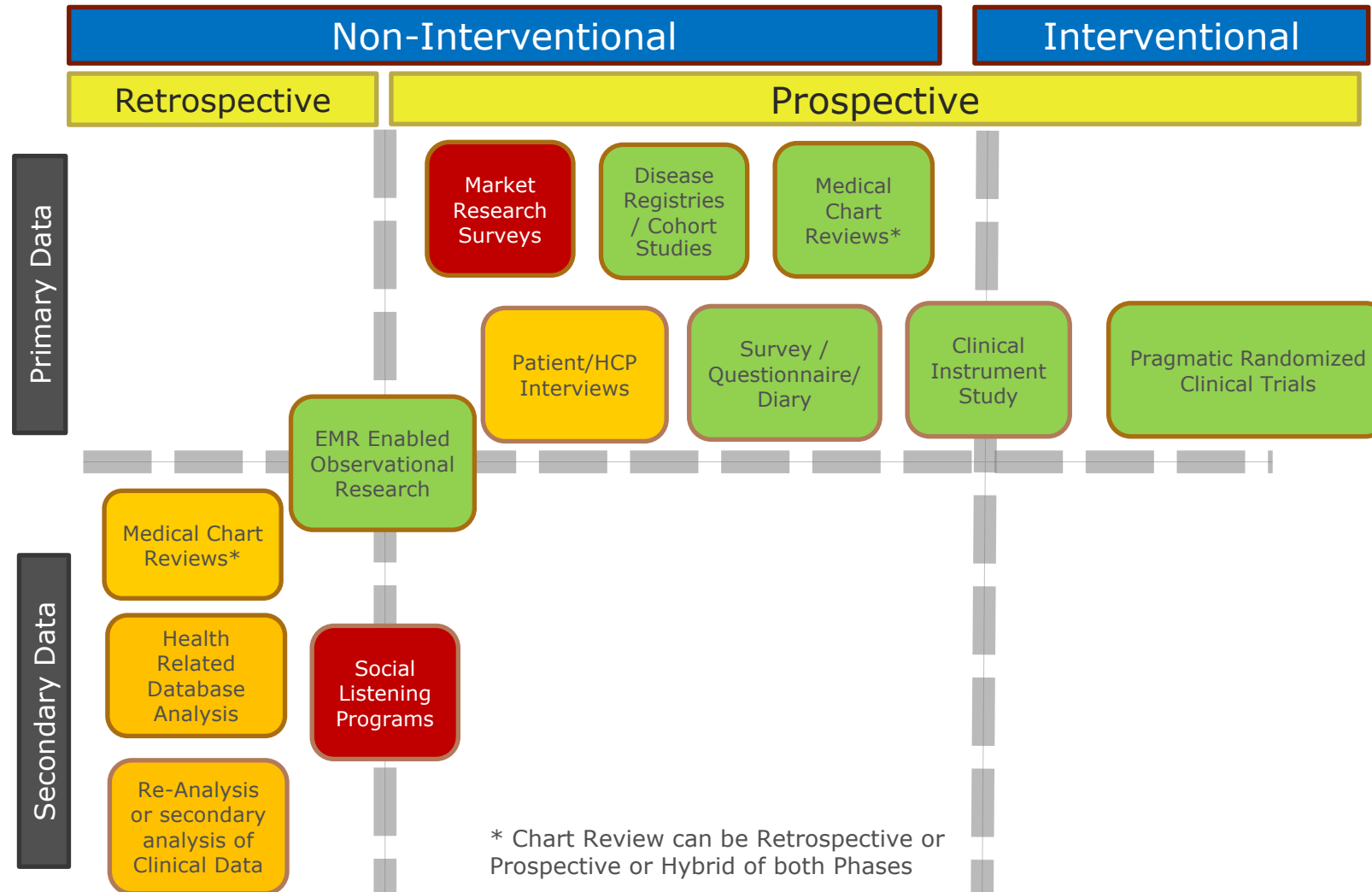
1. Industry and Regulatory focus on using RWD to support regulatory decision making.
 - The main regulators have all released guidelines on the use of RWD in regulatory decision-making
2. Development of the Janssen Real-World Data Playbook
3. Increase in number of Janssen RWE studies in the regulatory setting
 - This led to more requests from the business for support from Risk Management Department



Risk Management NIS/RWD Support Pilot Timelines



What type of NIS could Risk Management Support?



Note: For Retrospective studies limited RM-CM support could be provided in de-risking of protocol

Dealing with Real World Data



Will the data assist with answering the question?

When to discuss this topic within cross-functional teams?

Is the data from the vendor what you need. Is the quality sufficient?

When will we receive this and in what format?

Relating and transforming this data to standards

How compliant for submissions will it be – will it be acceptable?

Is the analysis viable? Can valid conclusions be drawn?

Case Study:

Drug A - Background & Overview

- Current standard of care therapy for Metastatic Urothelial Cancer (mUC) is shown to have a low response for subjects with the specific tumor biomarker alterations we are targeting with Erda
- Study was a Phase 2, open-label study to evaluate efficacy and safety of Drug A in patients with locally advanced or mUC with select FGFR mutations and gene fusions

Risk/Risk-mitigation

Unlike Clinical trials, data from RWD sources are not robust as there are no established standards for data collection, transformation, cleaning process, etc... Some common risks are listed below



Early engagement of Stats and Programming is vital to overcome these risks.

Risk	Risk-mitigation
Data not fit for Purpose e.g. Imbalance comparison groups	Request and review frequency of all key data fields before 'third party' agreement
Insufficient data integrity and/or traceability	Ensure integrity of source data and data transfer agreement (DTA) in place
Non-Standard source data and formats not consistent/usable	If possible, acquire data in a standard format
Data Anonymization methods insufficient	Review vendor source data imputation rules, anonymization methods and privacy policies
File transfer issues (Non-cumulative files, changes in data structure)	Incremental files (as per DTA)

FDA Questions

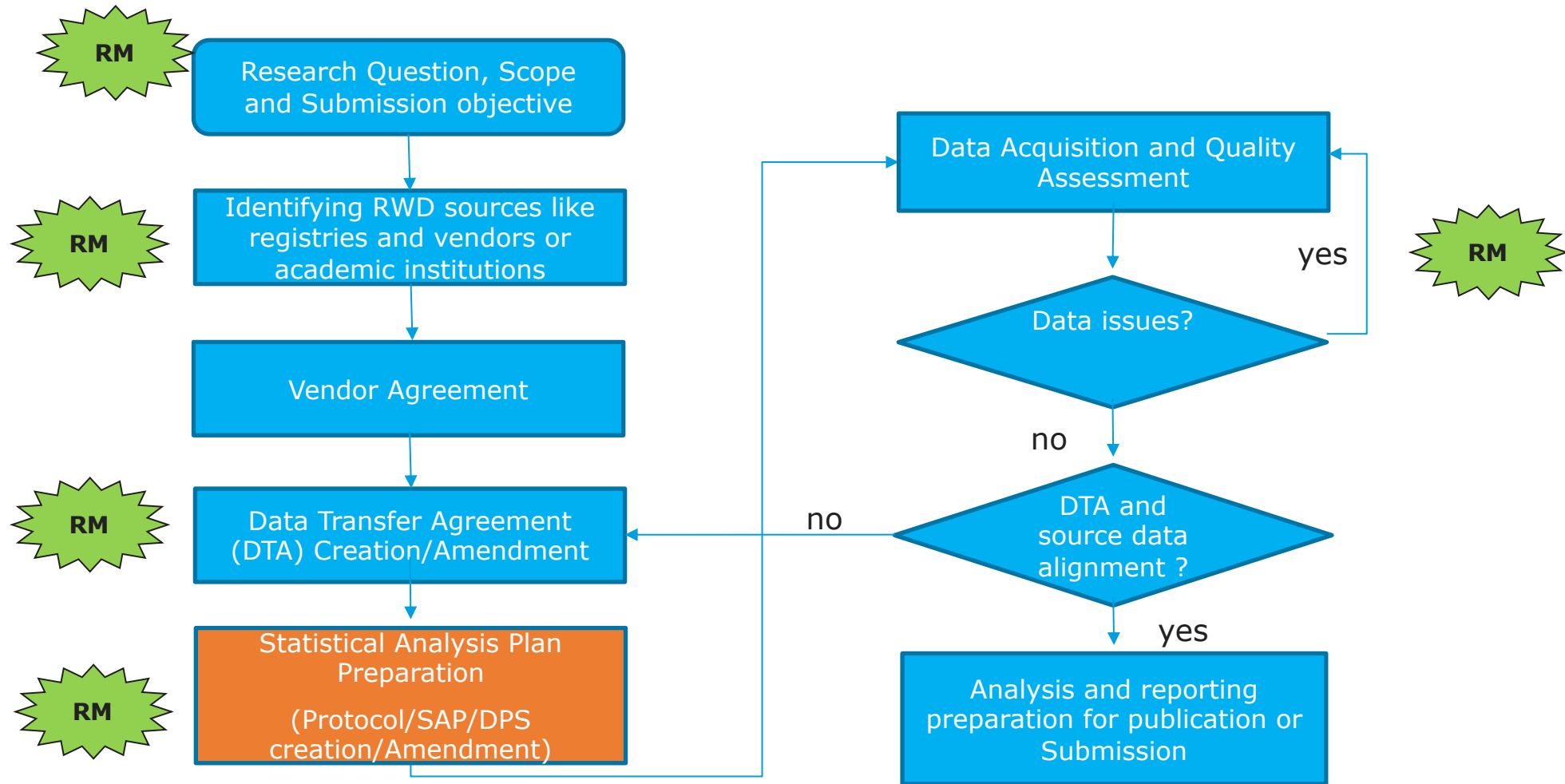


FDA Questions	Janssen Response
In RWE, X number of patients have been treated, why Y in the analysis?	Patient flow details are described in the submission package
How reliable is the diagnosis information and line of therapy in the EHR from the RWE vendor	EHR recorded diagnosis dates and all therapies received, which were captured from both structured records in database and unstructured records from free text clinical notes. Reviewer and abstractor reviewed these data and consolidated them into the database.
RWE patients represent the general 'disease under study' patients?	The demographics seem to suggest they reflect the general disease under study patients. Note these are primarily patients from community practice and not reflective of clinical trial population
Are there any of the disease under study patients in the RWE database excluded due to lack of determination of genomic data ?	Since the genetic status is a key analysis variable, we did not obtain any data from patients who did not have genomic results.

General Comments about External Control Arm

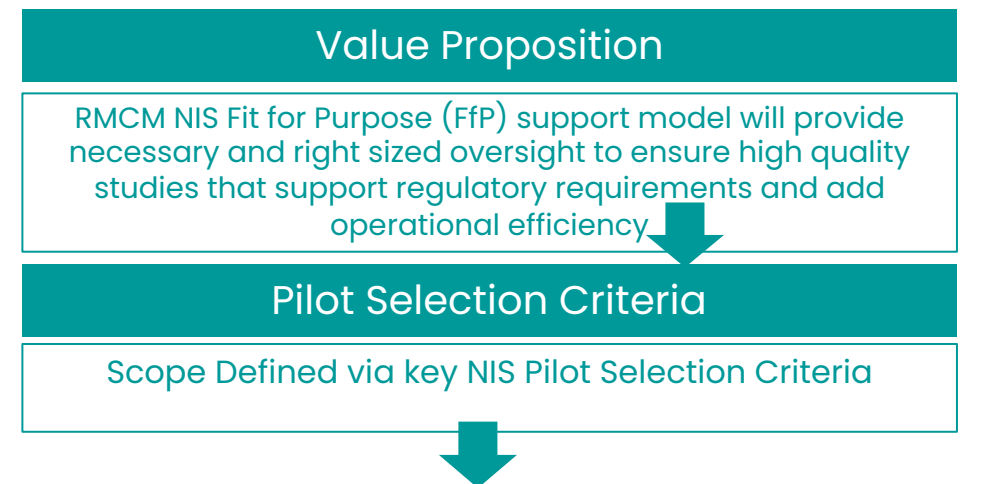
- ✓ Finding a matching population is key
- ✓ Align vendor provided data is adequate to fulfil the objectives of the ECA study, after applying IE criteria
- ✓ Quality of response data from external source is sufficient – RECIST data for response assessment
- ✓ Multiple sources of external data – may broaden the coverage, but introduce duplication
- ✓ May include non-standard data derivations and analyses as compared to a typical trial

RWD Process Flow

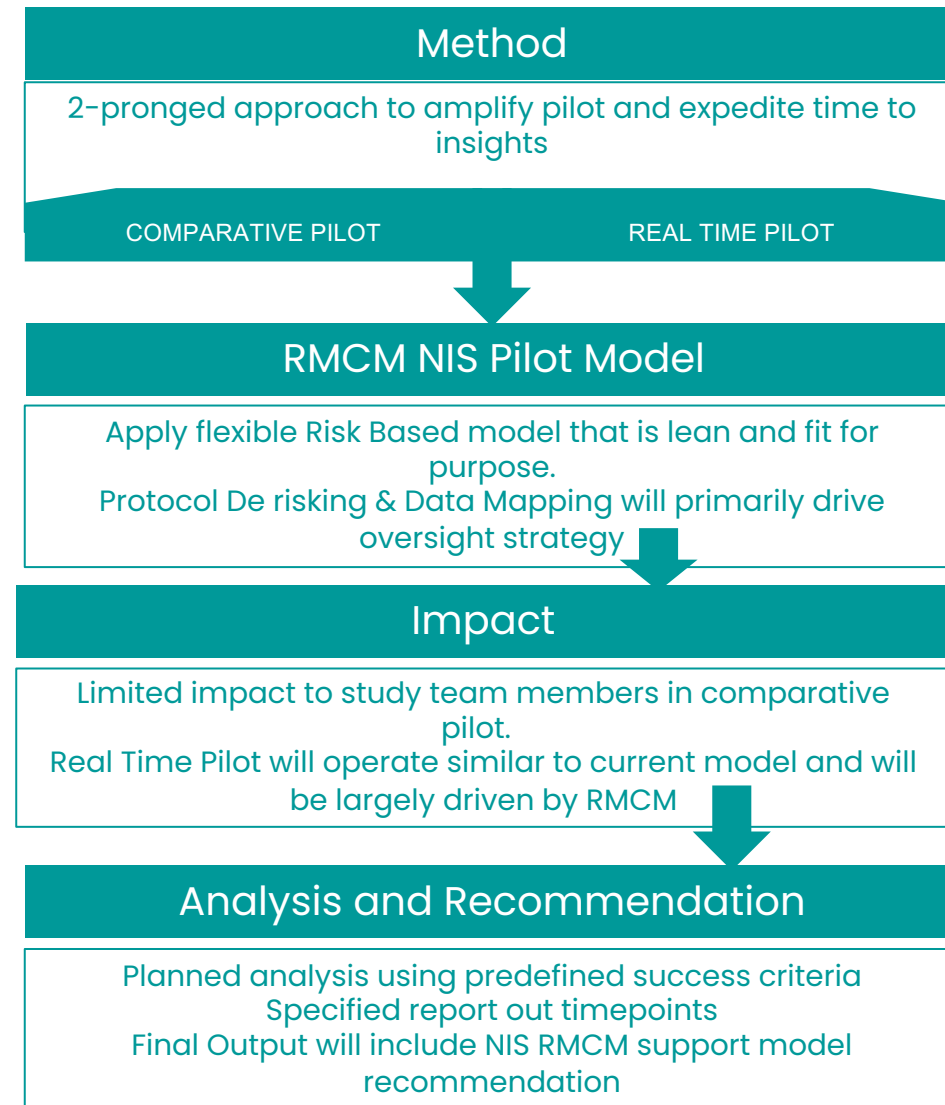


RM – Risk Management

NIS/RWD Portfolio Pilot Overview



RMCM NIS Trial Support Criteria



So – what is in the Playbook?



- Background information on RWD sources and types of studies
- Insights into considerations for Protocol review
- Tips for engagement with vendors supplying RWD and engagement with Health Authorities
- Data Fitness concepts and how Programmers can support in these activities
- Guidance for cross functional collaboration
- RACI for activities surrounding data ingestion, assessment of data relevancy and reliability
- Standardization and Analysis and Reporting approaches for RWD
- Links to relevant HA guidances and trainings

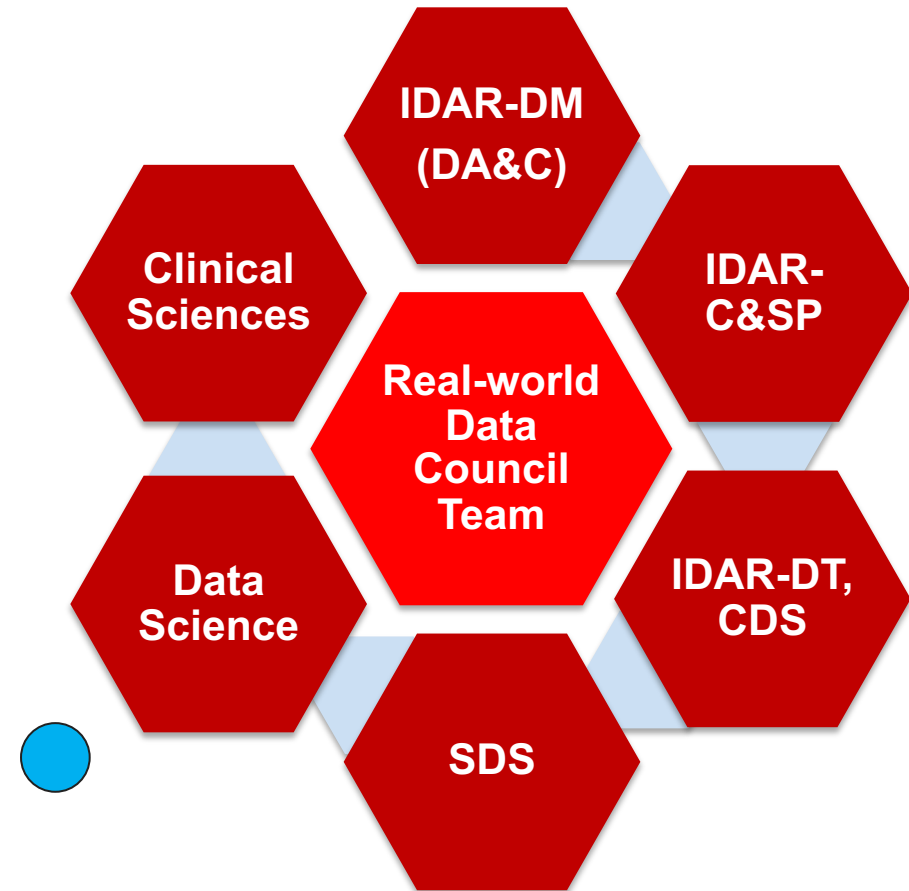
Playbook Demonstration

Real World Data Council

- Risk Management joined the initiative late but now fully involved in updating the RWD Playbook to include Risk Management
- Consultative partners – Clinical Operations, Business Partners
- Learnings from our own NIS/RWE Pilot studies are to be incorporated in to the RWD Playbook and in how Risk Management can best support these type of studies

Advice:- Include Risk Management at start of process. Part of RWD or Consultancy

Risk Management Input



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Made Together.

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Just the beginning...Ongoing initiatives

Considerations
for Protocol
Review and Risk
Management

Data Privacy
Process

Reviewers Guide

Operational
Manual and Data
Dictionary

Data Sciences
collaborations on
data translations

Data
implementation

Feasibility
analysis/Quality
assessments



thank you!