e) Impact of new technologies on Clinical Data Management

Opportunities offered by emerging technologies have the potential to revolutionize Clinical Development and dramatically change CDM at its core. Those will enable Clinical Data Scientists to proactively contribute to study designs via creative and innovative data capture methods. These opportunities will fuel the evolution of Clinical Data Management to Clinical Data Science by automating repetitive tasks like query management and surfacing impactful data issues truly compromising the scientific integrity of the clinical trials. Clinical Data Scientists will have to lead root-cause analysis and come-up with potentially complex remediations. Eventually, Clinical Data Scientist SMEs will continually "train" and monitor expert systems to improve their accuracy in detecting issues. Eventually, some systems might autonomously act to prevent further risks. Clinical Data Scientists powered by intelligent systems and assisted by Virtual Clinical Data Managers will handle the rising complexities stemming from the new study designs and omni channel data collections systems (i.e. from diverse sources and systems).

6. Evolution of the Clinical Data Management Role

The people aspect of the changing landscape cannot be underestimated. As the new data sources and supporting technological advances are taking a foothold in the Clinical Research domain, the role of the Clinical Data Manager will become much more complex. This change is at the same time a blessing and a challenge. It offers new opportunities to data experts who have been viewed as the central steward of clinical data quality - the Clinical Data Manager. However, it is a dramatic shift leading to the need to upskill and prepare CDM professionals. Overall, this is a unique opportunity to re-shape our identity for years to come.

a) CDM at the Cross-section of Risk-Based Study Execution

With the adoption of risk-based principles articulated in ICH E6 (R2), CDM is at the cross-section of fit for purpose (i.e. Risk-Based) study execution. As examples, Clinical Data Scientists will need to:

- **Proactively Manage Risk**: The Risk Assessment must go beyond the typical risks impacting study timelines, deviation from data standards or identifying critical data and processes. Risk Management must start with risk prevention (i.e. Quality by Design) by identifying threats prior to the first patient being enrolled into the study. So, Clinical Data Scientists must assess risks associated with protocol design, study-set, country involved, profile of sites selected, deviations from Standard Of Care and any other study execution activities which have the potential of leading to errors that could negatively impact the credibility and reliability of the trial results.
- **Identify systematic or process driven data issues** including those stemming from trial-design and study conduct factors such as rate of enrollment, technologies used, etc. The key will be to efficiently and reliably monitor such risks through the holistic review of **all** clinical and operational data (i.e. finding data patterns and anomalies across studies, countries, sites, and patients).
- **Manage risk associated with rather complex data flows** resulting from disparate data sources.
- Understand **risk-based approaches** when conducting clinical studies in a **patient centric and decentralized environment**.

b) Foundational Clinical Data Management Competencies

While the role is evolving, several of the foundational competencies for a Clinical Data Manager remain the same. For example, the following are essential building blocks:

- Attention to detail
- Therapeutic area knowledge
- Communication skills in articulating complex data findings to the trial teams
- Systematic data review and trending
- Project Management
- Design of data collection tools

c) New and Refined skillset

CDM Leadership and Subject Matter Experts must proactively guide the transition of their staff from Clinical Data Manager to Clinical Data Scientist. Organizations must consider how to best combine or split responsibilities across role(s) to leverage internal expertise and talents. Additionally, while this already exists in some companies, CDM organizations must consider the best approaches to centralized data monitoring. This will require the use of data review and analytical skills to aid site monitoring teams to efficiently run onsite and remote site monitoring activities.

Ultimately, to remain the most effective and relevant, CDM professionals will need to build on the core CDM skillsets and focus on emerging opportunities offered by technology, regulations and Clinical Development strategies.

Some of the emerging skillsets include:

- Robust **critical thinking and process knowledge**. The nature of issues identified though advanced analytical capabilities will lead to root cause analysis and corrective actions. These will mostly entail adjusting processes moving forward to prevent re-occurrence as oppose to just correcting data.
- Broader **cross functional collaboration**. For example, Clinical Data Scientists will have to consider the recruitment strategy and outcome of study, country and site feasibility. Clinical Data Scientists will have to tailor data collection systems, data review strategies, and training requirements (at study, countries, sites and patients level) that consider the risks associated with the expected patients and sites diversities (e.g. geographical, cultural, experience, etc.).
- Ability to align the flows of data with the need of the **next generation clinical protocol** so that:
  1. Data can be collected to "ensure human subject protection and the reliability of trial results"[4],
  2. Existing data can be made fit for use to meet protocol endpoint such as generating trustworthy evidences from Real-World Data (RWD).
- **Deep knowledge of data** including the characteristics of different types of data, such as EHR data from inpatient vs. outpatient from a biorepository. Understanding the implications of data context, quality, source, amount, and workflow[14].
- **Advanced analytical and technical skills** to interrogate and mine high volumes of data from a variety of data sources. Clinical Data Scientist must drive the development of tools extracting meaningful insights to detect potentially unreliable data threatening the validity of the trial results.
- High level **understanding of Artificial Intelligence methods** and scope of applicability.

- Ability to help build and test machine-learning algorithms to detect patterns of missing data, outliers, trends and/or lack of variability which can be applied as a standard within their therapeutic area or set of studies with or without human supervision.

7. Conclusion

The drivers for change explored in this reflection paper clearly illustrate the necessity for CDM to keep pace with the Clinical Research industry evolution and anticipate the downstream impact on the overall CDM and health development processes down to the study level. The rise of big and complex data stream, the availability of innovative technologies, the maturity of Artificial Intelligence, the adoption of new study designs and the evolutions of regulations are already starting to reshape what CDM means today. The divide between clinical trial data and Real-World Evidence is collapsing quickly. These changes are no longer buzzwords used to attract people at conferences, but a reality we all must tackle.

It is no longer possible to blindly apply a "one size fits all" approach and continue with our current approaches. No one could expect SOPs to pre-define all data processing variations resulting from the factors highlighted in figure 5. We are entering an exciting era where quality by design, critical thinking, risk-based and fit for purpose approaches will prevail. Our mission is to set a roadmap toward **Clinical Data Science** which requires the evolution of our skillsets, processes, technologies and best practices.

In this data and patient centric framework, CDM will play a strategic role in ensuring the reliability of the trial results and support the transformation that Clinical Research needs.

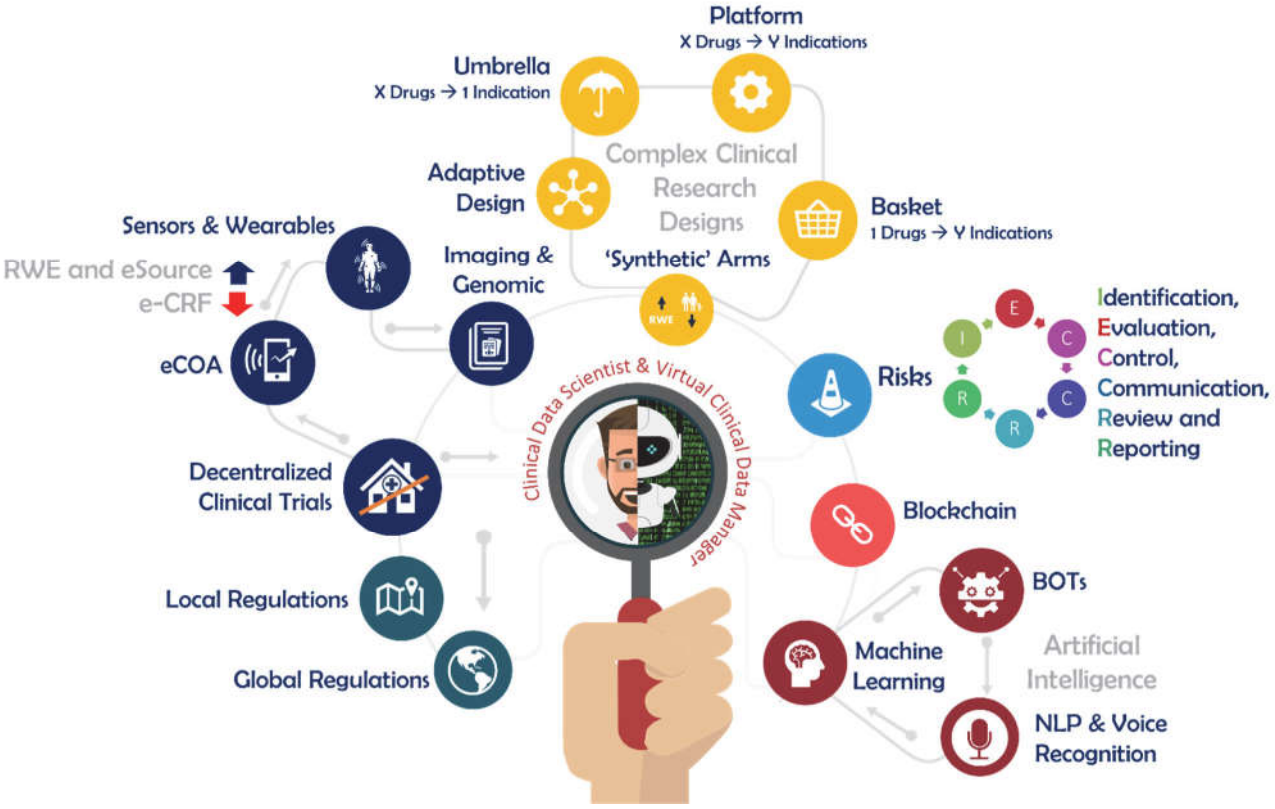

Fig 5. The rising complexity of the CDM Role