Paper CM09

Building Your Central Monitoring Team: Players, Skills, Structure, & Communication

Christina Dinger, PRA Health Sciences Kansas City, United States
Lynn Demings, PRA Health Sciences, British Columbia, Canada

Disclaimer

The content of this position paper reflects the opinions of the authors. Any views and recommendations stated within this paper are those of the authors, and they do not represent the positions of their employer.

Abstract

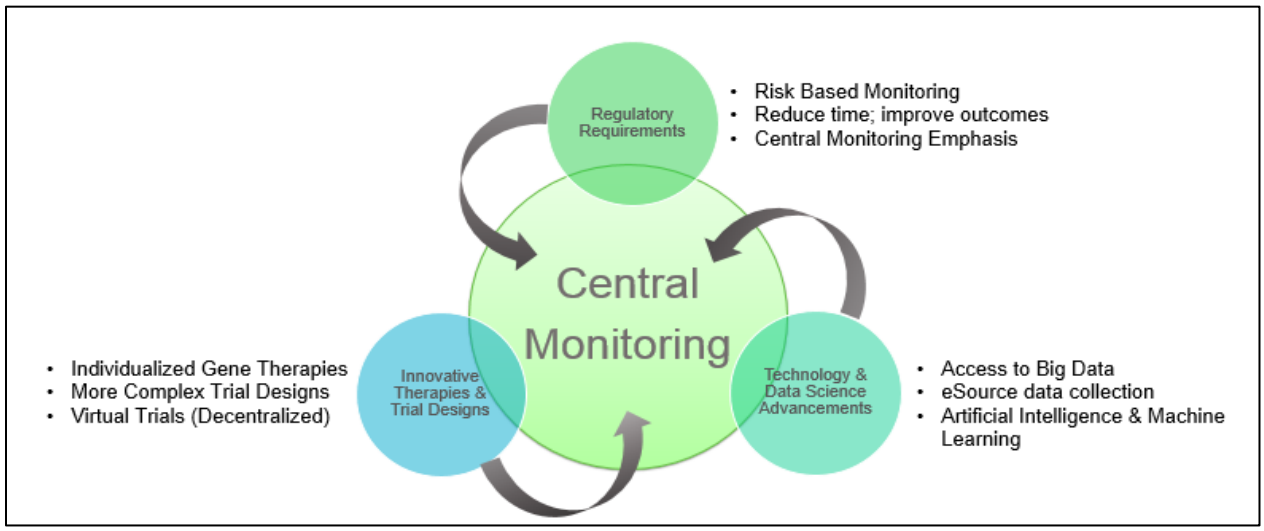
To embrace the paradigm shift towards Central Monitoring, organizations must develop a structure that meets the needs of clinical trials operating today, but also supports the evolution and expansion of Central Monitoring as the primary means for monitoring data.

This paper will outline key components necessary for organizations to create a foundation that facilitates the incremental growth and expansion of Central Monitoring. It will discuss the cross-pollination and integration of roles needed to assemble a nimble project team ready to meet the demands of a complex digital trial. Lastly, it will provide a scalable and cost-effective Central Monitoring model that harnesses technology and data science.

Central Monitoring Drivers:

Since 2011 organizations have reacted to risk-based regulatory guidance and implemented changes in how they operationalize clinical trials. As part of taking a Risk-Based Monitoring (RBM) approach endorsed by the FDA, EMA, and MHRA, organizations have applied data analytics to monitor and trend clinical data centrally, giving rise to Central Monitoring. More than just an industry buzz phrase, Central Monitoring is the quintessential paradigm shift in how clinical trials are monitored. This shift is not just a reaction to regulatory guidance but also driven by technology advancements and complex study designs that require fundamental changes in the industry.

Figure 1.0: Drivers Supporting Central Monitoring



The EMA guidance document (2013), recommends implementing central monitoring and describes it as:

Document review, data review, and analysis performed remotely from the investigator site by the sponsor to examine the data collected in order to check compliance, identify unusual data patterns, deviations from protocol or missing or invalid data. Examples of central monitoring techniques include checks of submitted documents (e.g. checklists for TMF content completed by investigators, training evidence etc.), clinical data checks (e.g. range checks, calendar checks etc., rate of reporting adverse events), compliance data/metrics checks (e.g. number of reported deviations from the protocol, rate of reporting adverse events… etc.).(P. 3)[1]

Per the EMA's definition, the realm and scope of Central Monitoring covers far more than data analytics. It also encompasses validation reviews (typically sequestered as data management activities), medical and safety reviews, and traditional clinical monitoring tasks performed on-site by a Clinical Research Associate (CRA). Monitoring and review activities that were previously dispersed across many roles and departments, per the EMA's definition, are now consolidated into the same categorical review type, Central Monitoring. Grouping all off-site review types into a unified unit can create synergy, agility and efficiency within an organization, if the organization is structured appropriately.

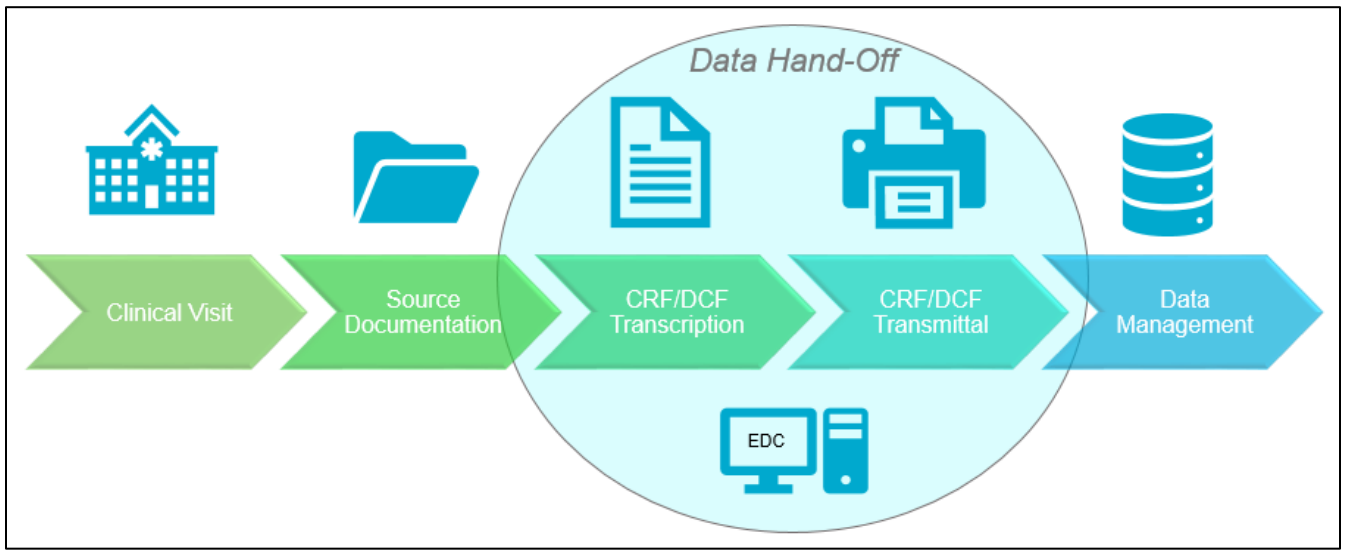
LEVERAGING CENTRAL MONITORING CAPABILITIES WITHOUT SYSTEMATIC REORGANIZATION IS LIKE PUTTING A ROUND PEG IN A SQUARE HOLE.

Central Monitoring – Where does it fit?

While regulatory agencies support Central Monitoring as a viable mechanism to propel clinical research, many organizations are struggling to embed and integrate Central Monitoring into their organizational framework. When pulling back the curtain to determine why organizations are struggling, the reasons become clear. The scope of organizational changes required go far beyond creating a Central Monitoring team. To successfully employ Central Monitoring and leverage technology advances, organizations must realign their staff, processes, and for CRO's, their service offerings and revenue structure to support it.

Specifically, the Clinical Operations and Data Management service offering model applied in many CRO and Sponsor organizations does not support a comprehensive Central Monitoring approach and the flow of data in our digital society. This bifurcation was established when paper CRFs reigned supreme and a clear hand-off point from Clinical Operations to Data Management existed. The flow of clinical data from a site was linear and required the transmission of clinical data from one entity to another with processing steps along the way (see figure 2.0 below). With the advent of Electronic Data Capture (EDC) efficiencies were gained by the electronic transmittal of data and queries; however, the hand-off between Clinical Operations and Data Management tasks still prevailed and the boundary lines remained intact. According to a recent Society of Clinical Data Management (SCDM) Reflection Paper (2019), the introduction of new technologies often results in increased complexity and cost rather than efficiencies. The paper goes on to say that, "*The full potential of EDC has not been realized as most implementations ended-up converting existing inefficient paper process inside an electronic tool,*" (p. 4).[2]

Figure 2.0: Linear Flow of Data from a Site



Today, the linear flow of data is diverging at a record pace and the transmittal points between Clinical and Data Management tasks are blurred, and in many instances, completely gone.

- Each year more clinical data is captured directly from study participants through eSource devices. Several companies surveyed during a 2018 SCDM forum stated that over 70% of clinical data volume is **not** coming from EDC (p. 13).[3]
- Integration of Electronic Health Records (EHR) directly to EDC systems or cloud-based solutions eliminates transcription from source documents and Source Document Verification (SDV) (Rocca, et al, 2019).[4]
- Decentralized (i.e. virtual) study designs are being deployed to support patient centricity and to make study participation more assessible by collecting data virtually -- outside the traditional clinical setting (Medidata, 2019).[5]

Despite these advances and the benefits digitization brings forth, organizations are not able to capitalize on them because the organizational structure, processes and supporting personnel are not adapted and positioned

appropriately. Business units and roles established to conduct clinical trials 25 years ago are still in place and relatively unchanged in responsibilities and skill set.

Preparing for the Future – Reshaping the Organization & Its People

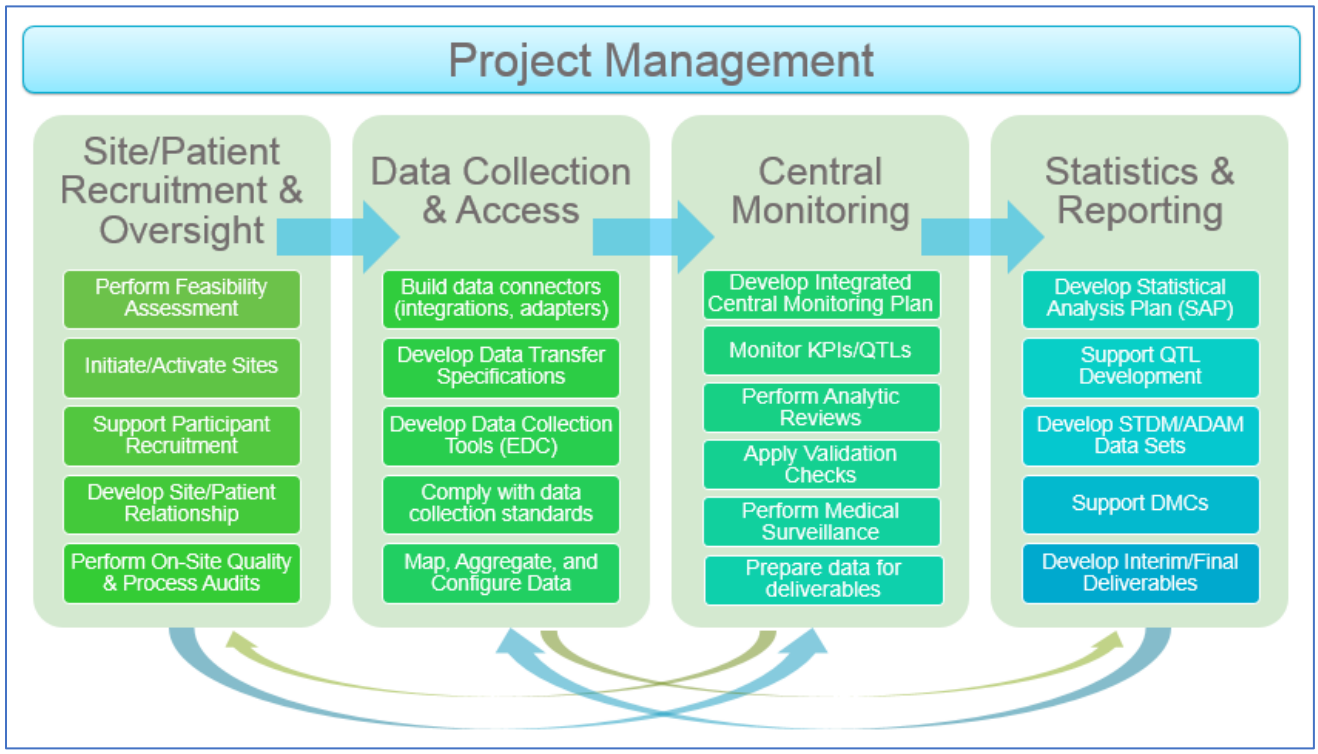
To establish a comprehensive and scalable Central Monitoring approach, an organization must address key components including:

- Creating an organizational framework to harness *Big Data* and support Central Monitoring
- Removing department silos to develop a unified Central Monitoring business unit
- Integrating and cross-pollinating roles to promote collaboration & efficiency
- Embedding Data Science into Central Monitoring to empower Central Monitors

Setting a New Organizational Framework

There are four operational pillars required to support a clinical trial under the oversight of Project Management. These pillars can serve as the framework for an organization and represent core business units or service offerings. Like architectural structures, each pillar relies on the strength of the other pillars to carry their load. It is an interdependent relationship that requires equal parts, give and take, to successfully conduct a clinical trial.

Figure 3.0: Operational Pillars - Key Tasks & Interdependent Relationship



The key changes illustrated in Figure 3.0 from what is seen in many clinical research organizations today, are the two middle pillars which are linked to the up-shift in *Big Data* and the need to review it centrally. Data collection & access tasks typically scoped under Data Management to perform back-end processes (i.e. activities after the data is monitored on site) must now support front-end processes (i.e Central Monitoring). The de-coupling of data collection & access tasks from other Data Management activities, represents a major shift from the how many organizations align and scope their services today**.**

Establishing a Data Collection & Access Pillar; Linking & Standardizing Data

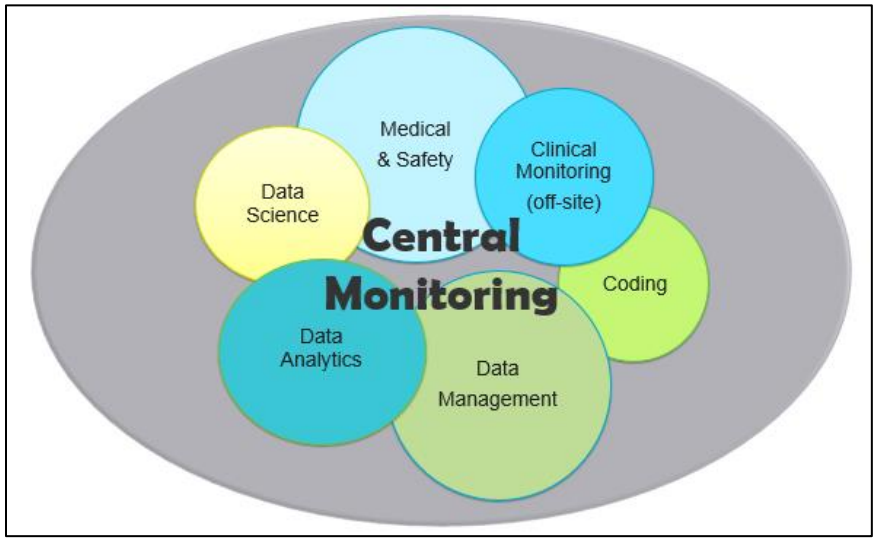
As digitized data becomes more prevelant, the ability to collect and standardize data from a plethora of sources is essential to support Central Monitoring capabilities. Data wrangling, or the ability to gather and aggregate *Big Data*, has given rise to Data Engineers. Data Engineers prepare data to be analyzed. They build connectors, and data collection tools that allow for the integration and translation of data from various sources to create an optimal data ecosystem for Central Monitors to operate (Aghabozorgi, Lin, 2016).[6]

In the absence of a highly skilled team of Data Engineers, Central Monitors struggle to access data and structure it in a way that connects with other data or systems. Managing multiple data sources and disparate data is a common issue in the industry and if not addressed, can lead to many inefficiencies and additional risks to the study (i.e. significant delays in data access and inability to aggregate data to identify risks and issues). It is reported that Data Scientists spend roughly 80% of their time preparing or wrangling data and only 20% of their time applying predictive modeling and developing algorithms (Qureshi, 2018)[7]. Additionally, without a dedicated business unit to jointly build data systems (e.g. EDC) and wrangle eSource data, it is difficult to employ data mapping standards, automation opportunities, and integration best practices that create efficiency returns for Central Monitoring and also Statistics and Reporting. Thus, to capitalize Central Monitoring capabilities and create efficiencies, it is critical to develop a business unit devoted to building robust data consortiums for Central Monitors to operate.

Unifying Central Monitoring; More than just a Paper Exercise

With the shift towards Central Monitoring, many of the departments and roles that were once separated as individual business units (e.g. Data Management, Data Analytics, Medical Surveillance, Medical Coding, etc.) are joined under the categorical umbrella of Central Monitoring. The paper exercise of grouping service offerings together within the Central Monitoring realm, without the heavy lifting involved of reshaping the organization, processes, and reporting structures, will not produce the desired outcome. As depicted in figure 4.0 below, the departmental silos still exist, and Central Monitoring does not operate as a cohesive team. Although the various business units that comprise Central Monitoring have points of interconnection, each business unit functions as a separate entity within the organization. Monitoring roles (e.g. Data Coordinators, Data Analysts, Medical Reviewers, etc.) are segregated by business function and there is no real accountability or alignment overseeing all central monitoring activities. This fragments the data review process, creates gaps in some areas and redundancies in others, and disperses overall accountability which ultimately lowers quality and increases costs.

Figure 4.0: Central Monitoring – A Conglomerate of Silos



An integrated organizational structure is needed to align all the roles performing Central Monitoring activities. The departmental barriers and multiple organizational reporting lines must be softened or completely removed. While Central Monitors may be delineated by specialty or area of review (e.g. Medical Reviewers), they must all report through the same Central Monitoring business unit, and a unified, trial-specific central review plan must be employed.

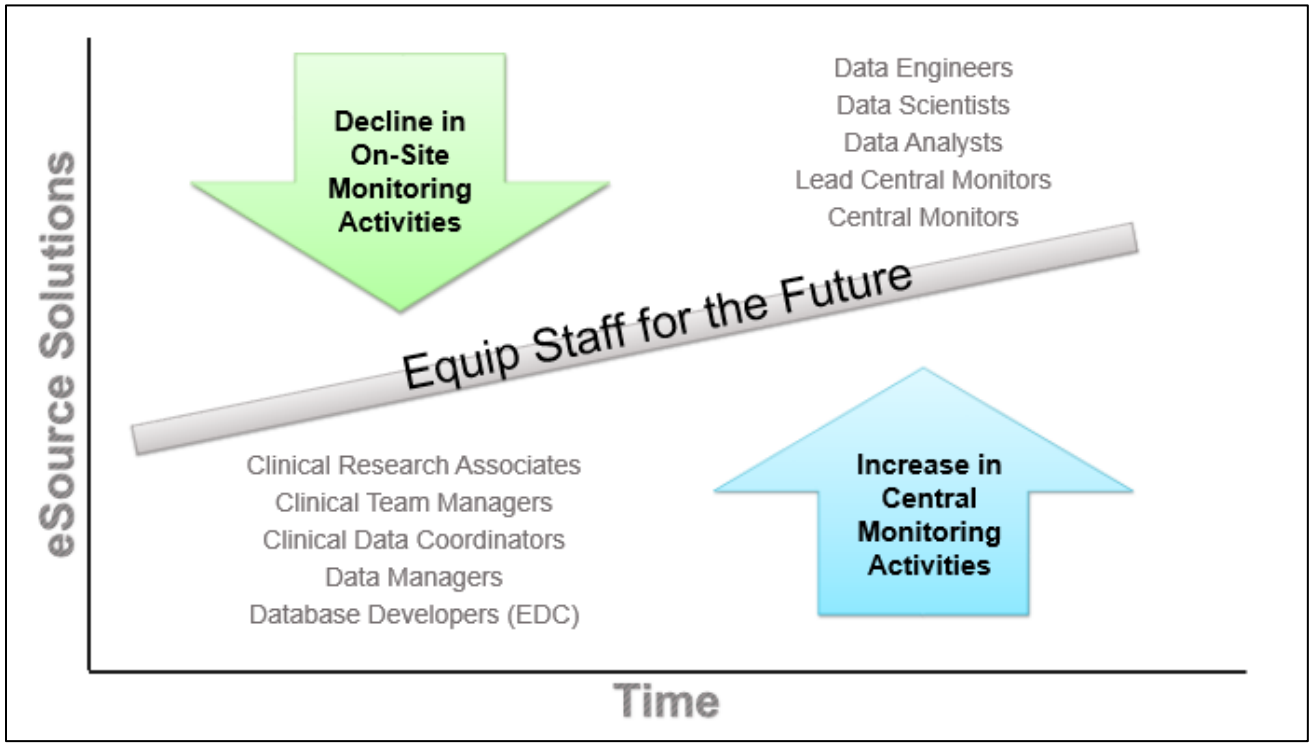
There are many technology systems on the market that support the end-to-end, unified Central Monitoring model. Such cloud-based platforms provide out-of-the-box data analytics and visualizations that can be cascaded and provisioned to central monitor workflows for action. These technology solutions when paired with a unified Central Monitoring team create a strong engine for success and allow for traceability, accountability, and agility within the project team.

Role Integration and Cross-Pollination

By developing a dedicated business unit to collect and wrangle data and similarly creating a unified Central Monitoring business unit, the overlap and connection points between previously segregated functions will surface and the integration of tasks into consolidated roles will follow.

The cross pollination of knowledge to facilitate the consolidation of roles will take time, but organizations can take steps now to develop an incremental plan that moves the resource needle (i.e. people in place and skillset) to match the evolution of the industry.

Figure 5.0: Shift in Roles Over Time



There is a global shortage of Data Scientists, Data Engineers and Data Analysts. Colleges and universities have added new curriculums to address the shortage, but the gap remains high and is not expected to close anytime soon. Pair the global shortage with the prerequisite of having clinical research experience and the shortage is even more pronounced. The August 2018 Linked In Workforce Report found that there were more than 151,000 data scientist jobs going unfilled across the U.S.[8] Similarly, Data Engineering remains an in-demand job

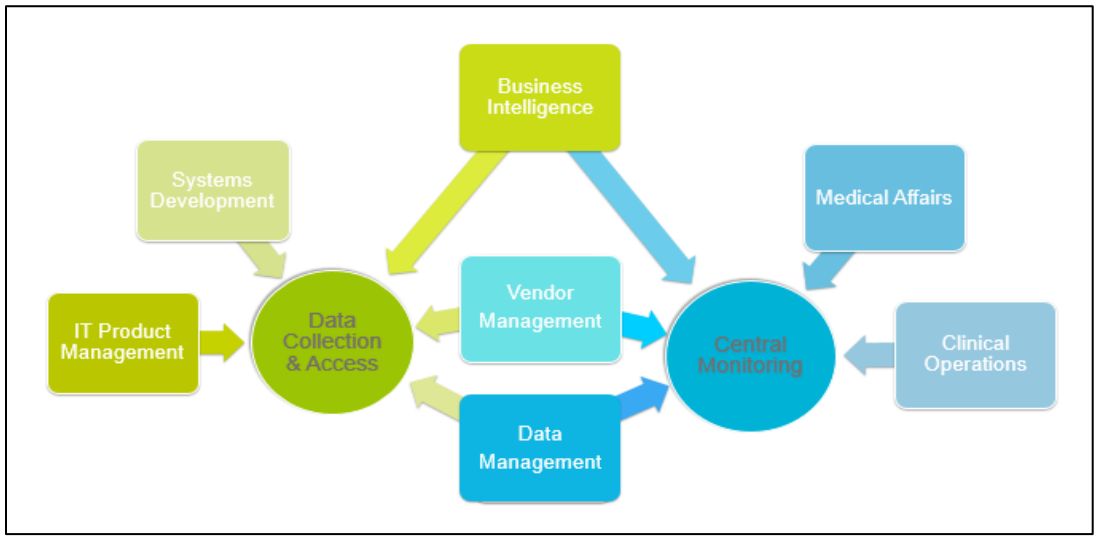
according to a 2019 report, (Kolakowski, 2019).[9] In order to be prepared for the future and overcome the workforce shortages, an organization must develop the skills internally by investing in its most important asset, its people.

While the role names used within Clinical Research will change to align with the evolution of Data Science and leveraging *Big Data*, most of the 'new' roles do not require an entirely different skillset, but rather adaptation and growth. For example, CRAs must adapt to performing previously on-site clinical reviews in new ways, centrally. Thus, they will require data analytic training, so they are familiar with how to review and draw actionable insights from data visualizations.

Bringing together employees from different disciplines to join forces allows for natural cross-pollination of knowledge and skills to influence and support each other. [10] This creates a well-rounded team with different perspectives and Subject Matter Experts (SME). (See figure 6.0)

Organizations should take the initial step of reviewing current roles and compare those to the fundamental skillsets needed to develop future roles within Central Monitoring and Data Access and Collection. Then, they can identify individuals already capable to serve in the new capacity and those that can quickly develop the skills needed for the new role(s). From there, change management plans and career development ladders can be created accordingly. While each employee has different aptitudes and is unique in education and skillset, preparing for the roles of the future should be exciting and give employees the opportunity to assess different positions and career avenues within the organization. This in turn creates employee buy-in and engagement in the change, rather than uncertainty and resistance.

Figure 6.0: Transferable Skillsets & Cross-Pollination



TECHNOLOGY SOLUTIONS ARE INTEGRAL TO MEET THE NEEDS OF DIGITAL TRIALS; HOWEVER, THEY ALONE WILL NOT DICTATE SUCCESS. AN ORGANIZATION'S ABILITY TO RETAIN, DEVELOP, AND RECRUIT THE TALENT NEEDED TO LEVERAGE TECHNOLOGY IS WHAT WILL DICTATE SUCCESS.

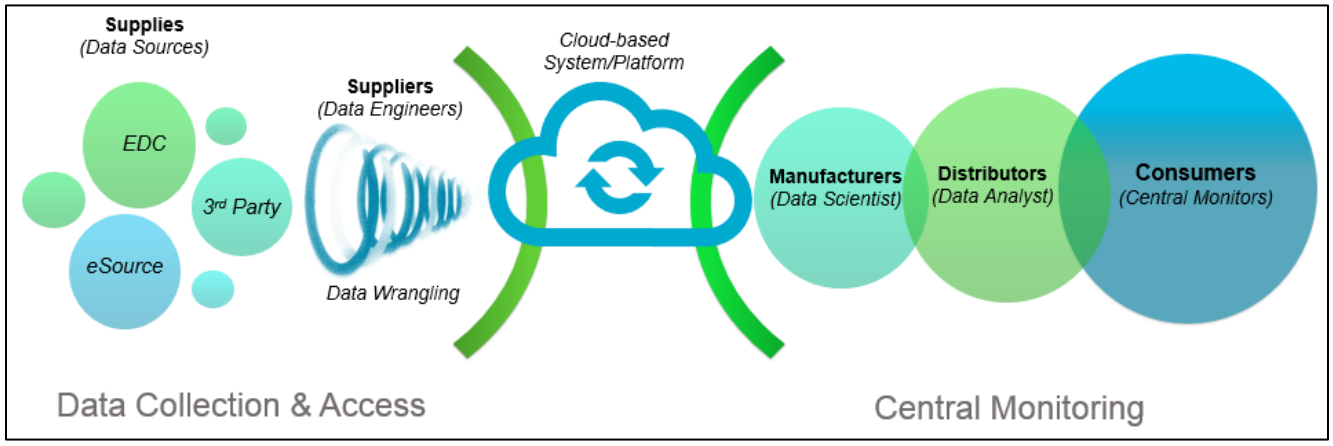
Structuring a Scalable & Well-Provisioned Central Monitoring Business Unit

When building out a scalable and cost-effective Central Monitoring Unit, it is recommended to maintain a relatively flat structure that ensures the right people are in place to make decisions and take action. While the Central Monitoring business unit will likely be the largest in headcount as data digitization expands, only a few operational role layers should exist, and a single Central Monitor Lead should be assigned per trial.

Additionally, organizations must leverage Artificial Intelligence (AI), and Machine Learning (ML) where possible to maximize the efficiency and effectiveness of Central Monitors. This requires a core group of Data Scientists embedded in the Central Monitoring business unit. By embedding Data Scientists in the business unit, synergy and expertise with Central Monitoring system(s), tasks, and key players are achieved. *"This ensures that data scientist will have the context needed to work effectively with their business partners and the opportunity to develop meaningful personal relationships to get buy-in for ideas and initiatives,"* (Do, 2017). [11]

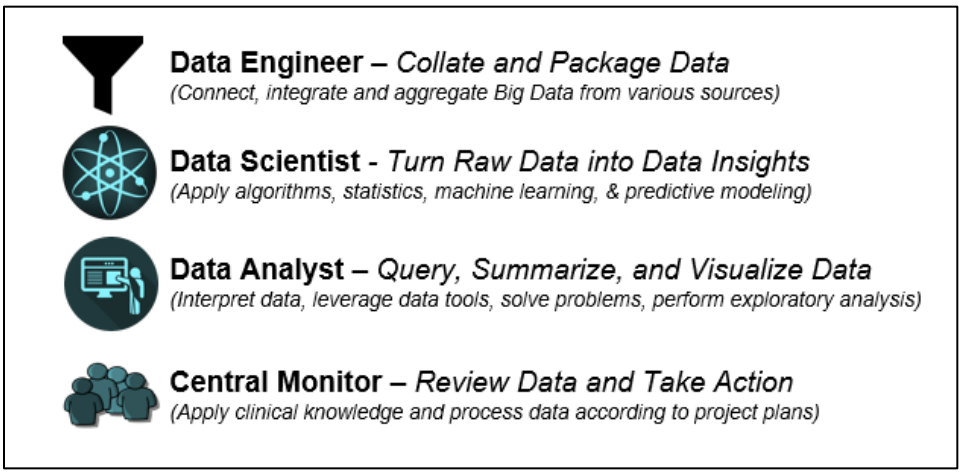
Additionally, it allows for a "Bottom-Up AI" design to be utilized that leverages skillsets which allows scalability and cost containment. In a Bottom-Up approach, "*Data Analysts shape the data, understand the problem, and help design the solution. They then work with Data Scientists to find the best approach and validate results*," (Qureshi, 2018). [12] This allows a small Data Scientist team to serve the needs of a large Central Monitoring business unit. It leverages the clinical and analytical knowledge Data Analysts bring forth so that Data Scientists can quickly understand the problem, quantify the business need, and develop a solution. It also promotes career advancement and can organically serve as a mechanism for Data Analysts to develop into the next generation of Data Scientists.

Figure 7.0: Consumer Product Supply Chain Analogy



An analogy to represent the "Bottom Up AI" model and the overall flow of data from eSources to Central Monitoring is the consumer product supply chain (see figure 7.0). In this analogy the Data Engineer acts as the supplier. The Data Engineer understands the raw supply needs of his/her customers and collects, builds and packages the supplies accordingly. The Data Scientist is the manufacturer; the Data Scientist's job is to turn the raw supplies into usable/consumable products to meet the needs of the consumer. The Data Analyst is the product distributor and his/her role is to understand the needs of the consumer and to provision, educate and share the products available with them. The Data Analyst role is bi-directional as he/she also serves as the liaison between the consumer and manufacturer and drives the pipeline of new products. Lastly, the Central Monitor represent the consumer. The Central Monitor applies the products distributed to perform central monitoring tasks and take necessary actions.

Figure 8.0: Leveraging Big Data to Perform Central Monitoring– Key Roles



While the Central Monitoring structure is straight-forward with the 3-Layer operational design, there are many ways an organization can position and assign resources within the structure. To achieve cohesiveness and scalability, most organizations would benefit from having Data Scientists serve as global roles within Central Monitoring to support the needs of the entire business unit. With-that-said, it is up to the organization how best to position Data Analysts on a study. There are many workable possibilities and each of them come with pros and cons that must be considered. For example, should a Data Analyst be assigned to each trial or should Data Analysts provide support at a program or therapeutic indication level? If Data Analysts are assigned to individual trials do they serve as the Lead Central Monitor too (i.e. oversee and are accountable for all Central Monitoring tasks for the trial)? These are the types of questions that must be asked and debated to determine the best fit for the organization.

Conclusion: Key Take-Aways & Considerations

Clinical Research Organizations should optimize their business structure to leverage *Big Data* and maximize the potential of its greatest asset– not data, not technology, but its employees to meet the needs of the future.

Organizations must re-think how they cost, plan and operationalize a clinical trial and develop an incremental approach to meet the demands of the future. This likely includes merging many business units and departments and the cross-pollination and consolidation of roles.

The change management scope outlined in this paper is vast, but is doable if a clear vision is established, buy-in at all levels is obtained, and an incremental plan with clear goals is executed.

For Contract Research Organizations (CRO) a crucial part of the change management will include educating and gaining the buy-in of their clients. Industry wide discomfort with RBM exists and confusion abounds with each company's implementation of RBM varying from another. The CRO must have a 'stand-up' model that is easy to understand, cost-effective and versatile to gain their client's trust and business.

> *"NOT FINANCE. NOT STRATEGY. NOT TECHNOLOGY. IT IS TEAMWORK THAT REMAINS THE ULTIMATE COMPETITIVE ADVANTAGE, BOTH BECAUSE IT IS SO POWERFUL AND SO RARE."* [13]
>
> PATRICK LENCIONI (P. VII)

Sources

[1] European Medicines Agency (2013). Reflection paper on risk-based quality management in clinical trials. https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-risk-based-quality-management-clinical-trials_en.pdf

[2, 3] Nadolny, Zambas, Torche, Bhardwaj (2019). The Evolution of Clinical Data Management to Clinical to Data Science. Society for Clinical Data Management https://scdm.org/6588/

[4] Rocca, Asare, Esserman, Dubman, Gordon (2019). Source Data Capture from EHRs: Using Standardized Clinical Research Data. Federal Drug Administration https://www.fda.gov/media/132130/download

[5] Medidata (2019). Virtualizing Clinical Trials. https://www.medidata.com/wp-content/uploads/2019/05/Virtualizing-Clinical-Trials_Medidata_White-Paper-May-19.pdf

[6] Aghabozorgi, Lin (2016). Data Scientist vs Data Engineer, What's the difference? https://cognitiveclass.ai/blog/data-scientist-vs-data-engineer

[7] Qureshi (2018). How to Turn Data Analysts into Data Scientists. https://www.healthcatalyst.com/insights/healthcare-data-scientists-steps-leveraging-data-analysts

[8] LinkedIn (2018). August LinkedIn Workforce Report: Data Science Skills are in High Demand Across Industries https://news.linkedin.com/2018/8/linkedin-workforce-report-august-2018

[9] Kolakowski)2019). Data Engineer Remains Top In-Demand Job https://insights.dice.com/2019/06/04/data-engineer-remains-top-demand-job/

[10] Arbuckle (2017). What does Cross-Pollination in Business Mean? https://bizfluent.com/info-8547100-crosspollination-business-mean.html

[11] Do (2017). What is the most effective way to structure a data science team? https://towardsdatascience.com/what-is-the-most-effective-way-to-structure-a-data-science-team-498041b88dae

[12] Qureshi (2018). How to Turn Data Analysts into Data Scientists. https://www.healthcatalyst.com/insights/healthcare-data-scientists-steps-leveraging-data-analysts

[13] Lencioni (2002). The Five Dysfunctions of a Team. Jossey-Bass