Paper AR05

iCDM - interactive dashboards that innovate central data monitoring at Danone Nutricia Research

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ABSTRACT

With an integrated approach and the use of automation and digital technologies, central data monitoring can bring substantial benefits for quality, patient safety, operational efficiency and costs. Danone Nutricia Research (DNR) initiated a project named 'interactive Central Data Monitoring' (iCDM). This project encompasses the development and roll-out of dashboards, development of methodology and the implementation of new process and data flow. iCDM fits into DNRs strategy on data and digitalization. In this paper we will discuss the technical approach, present the iCDM dashboard design and functionalities, share the project challenges and learnings, and reflect on the organizational journey.

INTRODUCTION

In 2018 Danone Nutricia Research (DNR) implemented a new analytics environment linked to a major upgrade of its Statistical Computing Environment (SCE), see Vervuren & Ferran (2019). This was part of a bigger strategic initiative around data and digitalization that aimed to advance DNR's clinical systems as well as the use and governance of clinical data. The new systems implemented had two major components. The data processes of the common functions in Biometrics (Data Management, Statistical Programming and Statistics) were serviced and innovated by the new SCE, the SAS Life Science Analytics Framework (LSAF). The other component, tightly linked to the LSAF platform, consisted of a set of software solutions, that was referred to as 'Virtualization and Visualization' platform ('V&V'). As the name indicates, this platform offers visualization capabilities. Because of this hybrid set-up, functions and teams outside Biometrics, like clinical study teams, could be serviced while respecting data access restriction linked to data privacy, confidentiality or blinding. Jointly, LSAF and V&V enabled improvements of existing processes and practices within Biometrics, as well as the development and application of digital innovations with a broader scope. Interactive Central Data Monitoring or iCDM is one those.

CENTRAL DATA MONITORING

ICH GCP defines Centralized (data) monitoring (CDM) as "a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons." CDM processes provide monitoring capabilities that can complement and reduce the extent of on-site monitoring and help identify unreliable data, safeguard subject safety and protocol compliance by focusing oversight on the most important aspects of study conduct. Building a successful CDM capability requires the availability of enabling technologies, focused on the translation of data into information that can result in appropriate actions (Gough *et al*., 2016).

RISE OF THE iCDM PROJECT

The iCDM project started as a bottom-up initiative that found its roots in early work by the V&V implementation team. While the LSAF platform was supporting concrete, existing processes and work practices, V&V offered generic (BI) capabilities. These had a clear role and purpose in the data strategy, but there were no specific use cases or projects to support. To overcome that, the V&V team performed an information needs analysis early in the project (2018). One of the use cases that stood out as having a potentially high impact against a modest development effort was 'Trial Management / Study Performance'. The underlying needs identified through interviews with study managers, clinical researchers and data managers were:

- display drop outs; gain insight in reasons and characteristics of the subjects
- monitor informed consent and randomization
- track data issues and monitor quality (comparable to data review by data managers, yet on a different level)
- visualize outliers
- easily view planning and timing of visits and milestones
- distribution of primary outcome parameter
- monitor site performance

Based on this, the V&V team prototyped several 'study performance' dashboards, which got positive feedback when demonstrated to the various stakeholders. A crucial event, which led to the launch of the iCDM project, was a meeting with a lead study manager who was trying out an improved central data monitoring process. Using conventional processes and tools (i.e. static displays), this CDM process sought to identify quality, safety and operational risks based on the continuous monitoring of data and risk indicators to enable study teams to respond earlier and more proactive to potential issues. Another goal of this improved process was to better track site

performance, and to focus more on site contacts and on-site visits based on identified issues. The opportunities and synergy by combining efforts, and use the V&V dashboards in the context of this improved central data monitoring process, were quickly recognized; thus the iCDM project was born.

In the first year following its launch the iCDM dashboards were successfully piloted in two nutrition clinical studies, based on which the project sponsors requested iCDM to be applied in all new clinical studies that were eligible for the approach. To accommodate this ambition, the project was expanded to include new activity tracks. Also, next to study managers and BI specialists, the team's expertise was broadened by including a statistician and a clinical researcher. Currently the project knows the following activity areas:

- Methodology (with particular attention to Quality Tolerance Limits)
- Working procedures (decision tree, dashboard menu card, requirements gathering, work instructions)
- Central monitoring execution + Study team collaboration & support
- Dashboard development
- Business case

DATA STANDARDIZATION AND END-TO-END DATAFLOW

The implementation of the V&V platform with its visualization software and the possibility to deploy dashboard with access proper control, was the primary enabler of iCDM's interactive dashboards. Yet, the full iCDM process could not have been established without two other developments:

- Automated data flow from the electronic data capture system (EDC) system to the V&V platform via the statistical computing environment (LSAF)
- Implementation of standardized data structures (i.e., SDTM datasets)

At the beginning of the project, data could only be transferred via manual extractions from the EDC system and a manual upload into LSAF by a data manager. This was followed by another manual action: running SDTM conversion programs by a programmer. Thus, transfers were time-consuming and required coordination between the data manager and the programmer of the study at hand. As a result, data in the iCDM dashboards were refreshed on a weekly basis only. While data transfers between LSAF and the V&V environment were automated from the beginning, end-to-end automation of the dataflow was only possible after (1) an automated data extraction from the EDC system was made possible, (2) implementation of an SDTM data conversion workflow in LSAF. With the end-to-end automated flow in place (see fig. 1), daily data extractions were scheduled for all active studies in the EDC system, followed by an SDTM conversion in LSAF and upload to the V&V platform and into the dashboard for all applicable studies. The move from once-weekly to daily data refreshing made a big difference to the dashboard users, and effectively made continuous monitoring come alive.

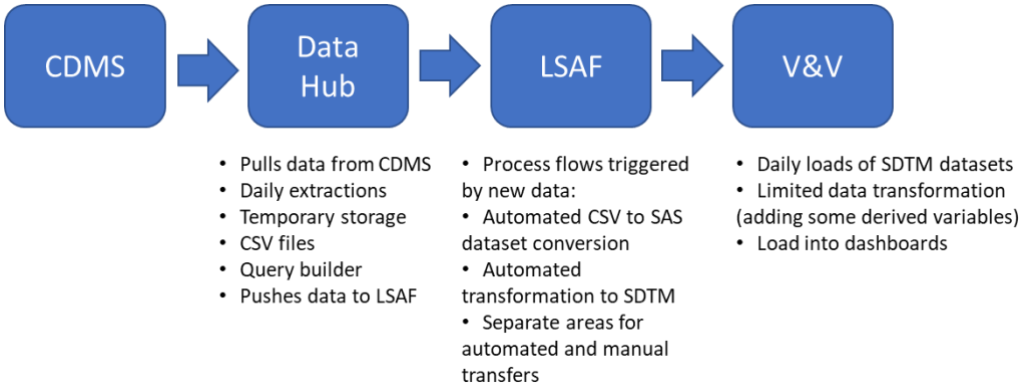

Figure 1: End-to-end data from from CDMS to iCDM dashboards in the V&V platform.

The knowledge of SDTM and the capability to produce SDTM datasets was already in place. However, the work that had generated this (see Vervuren & Gijsbers, 2018) was based on completed studies. The production, mostly via outsourcing, of SDTM datasets very early during study conduct, demanded some adaptations to the conversion process. These involved:

- Availability of high-quality sample data (representative data values, records in all datasets, coherence between related datasets) to serve as inputs for conversion programming,
- Complete and up-to-date documentation of extensions, modifications and exceptions to the SDTM standard within DNR (the "DNR SDTM Implementation Guide")
- Availability of annotated CRFs (consistent with DNR SDTM-IG)
- Maturation of the available conversion toolbox (e.g., macros, programs, metadata structures)
- Strengthening of the oversight and collaboration process

These improvements are currently in progress. Together they are expected to accelerate and streamline our SDTM conversion process, ensuring early availability of well-defined SDTM datasets to feed into the iCMD dashboards.

INVESTMENTS AND BENEFITS

After the successful pilots further investment in the project as well as the decision to deploy iCDM as part of standard processes required insight in investments and benefits/returns. To this end, the project team conducted a financial analysis based on estimated cost and savings. The following efficiency areas were identified:

- Data Review Meeting: reducing the number of bespoke TLFs + more efficient preparation for DRMs across functions
- On-site monitoring: reduction of monitoring costs by reducing time spent by CSMs/CRAs. (Sertkaya *et al*., 2016; Agrafiotis *et al*., 2018)
- Periodic Medical Review: rendering obsolete the creation of bespoke TLFs.
- Data Management: effiency in query resolution (Agrafiotis *et al*., 2018) and eliminating the need to create overviews in Excel
- CAPA handling/resolution: reduction of issues and incidences. (Agrafiotis *et al*., 2018)(Atwaru *et al*. 2016)
- SDV: drive and enable reduction of source data verification through focused/risk-based monitoring

For each of these efficiency areas cost savings were calculated as a reduction of total effort (time), which was then translated to a monetary saving. As to investments, a distinction was made between one-off (or start-up) costs and recurring costs.

One-off investments: (a) Project team FTe and external fees, (b) Advancing data standardization process
Recurring costs: (a) Platform hosting, (b) Dashboard development, (c) Data preparations, (d) Continuous improvements.

Next, using the total investments and cost saving per study, a six-year projection (fig. 2) was made with the following assumptions/parameters:

- Efficiencies gained in the first two years were 50% and 75% respectively of the estimated amounts (the first year in this analysis was the third year in the project)
- One-off investments were loaded only on the first two years
- Three to four studies were projected per year (based on expected eligible studies)
- Recurring costs were fixed per study and year
- A representative mix of study lengths was taken. SDTM conversion and dashboard development costs were taken at the start of the study, whereas savings were split over the years.

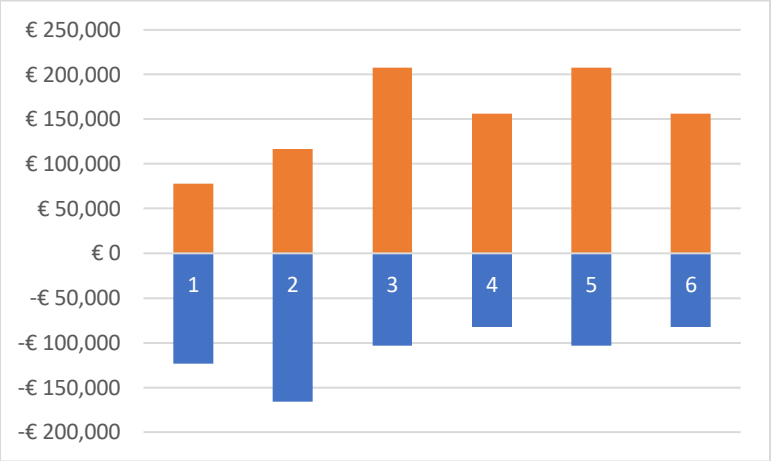

Figure 2: Six year projection of estimated investments (negative amounts; blue bars) and savings (positive amounts; orange bars) based on running three to four studies per year. See text for estimates and assumptions.

This analysis showed net savings from the third year onwards and a break-even point also around the third year (following two years of prototyping and piloting).

CDM DASHBOARDS

Data visualizations were developed for all SDTMs domains and they were grouped into a ‘Quality and Progress’ and a ‘Safety and Subject profile’ dashboards. Next to SDTM datasets some operational data had been extracted from the CDMS (and transferred via LSAF), feeding into the Query status and SDV reports. Several examples are shown below (fig 3-5). The functionalities and uses/actions of these and other examples were demonstrated during the conference presentation based on realistic sample data.

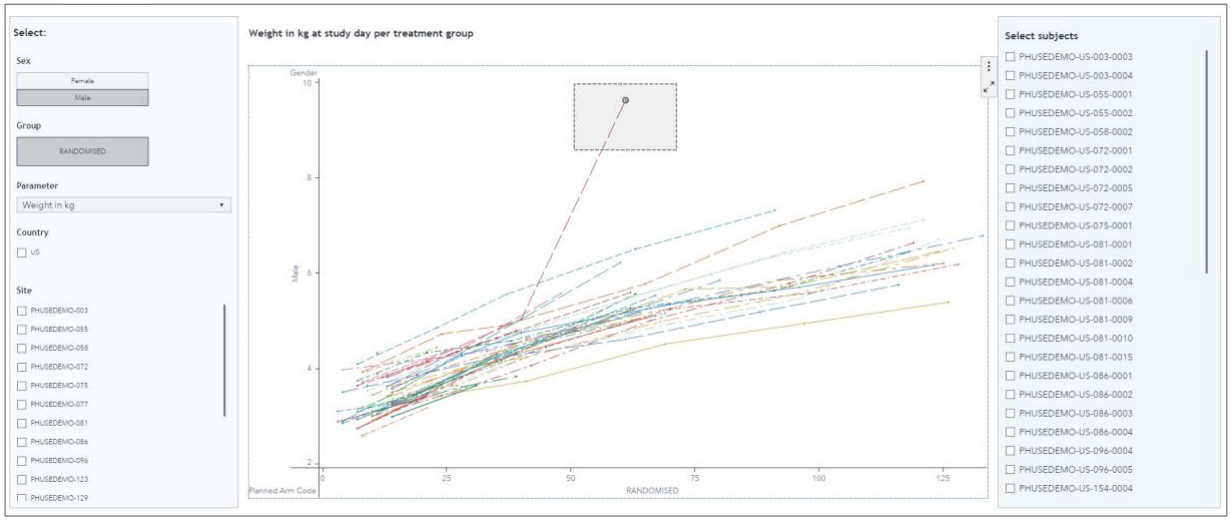

Figure 3: Growth curves allowing quick identification of outliers

Figure 4: Visit window overview helps in visit planning and identify issues with sites

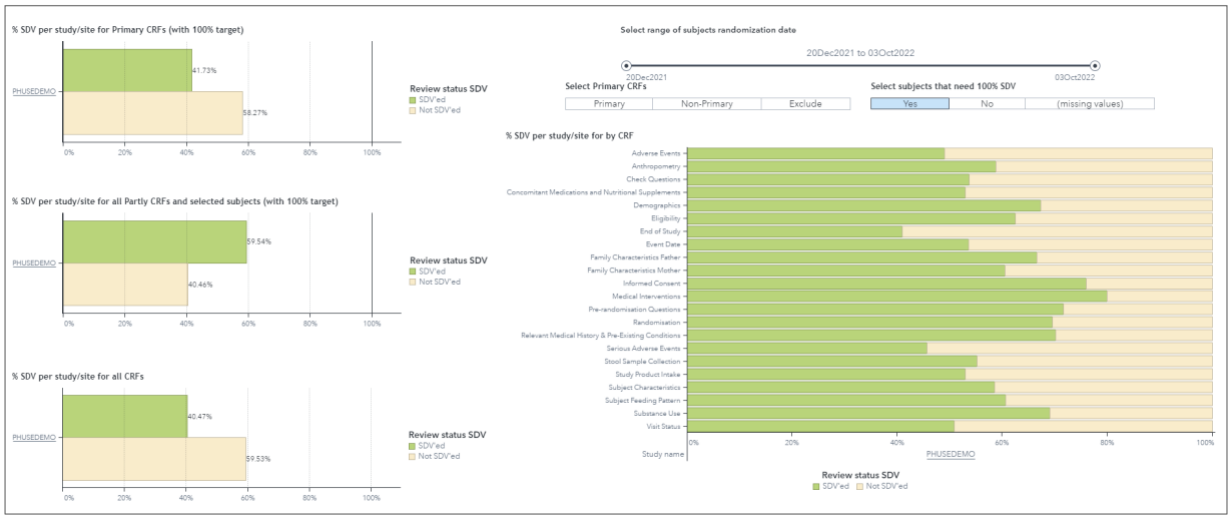

Figure 5: SDV information aids in spotting unnecessary SDVs versus backlogs

CONCLUSION

Well-designed, interactive dashboards make data come alive, and they are a great tool to discover and understand the data and trends therein. Yet, such a technical advancements alone are not enough. Central monitoring activities rely on the skills of people, well-defined processes, and technologies that enable the translation of data into information, and resulting actions and decisions (Gough *et al*., 2016). Within DNR several advancements and initiatives in technology, process improvement and standardization came together in recent years, and boosted the development of central data monitoring. Having powerful dashboard in place, and with good progress on methodology and process development, and clear cost efficiencies, there is strong basis to continue the transformation and digitalization of central data monitoring at DNR.

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ACKNOWLEDGMENTS

The authors would like to thank the current and former members of the iCDM project team, Sonia Amodio, Willem de Bruijn, Margriet Veldhorst, Irene Jongenelen and Linda Beijk, as well as the project sponsors, Gerda van Wijhe, Egbert Biesheuvel and Heidi Sonnemans. Further, we are indebted to V&V project team, especially Annemarie Lutz and Frank Dietvorst, and to Herman Ament for his key contributions in setting up the end-to-end data flow.

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