CluePoints

The Risk-Based Data Management (RBDM) Revolution

ACDM Conference 2024

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Agenda

Examine the concept of Risk-based Data Management and the concurrent industry focus areas that are moving us in that direction

- The Challenge
- Efficiency
- Technology
- Data Science
- Risk-based Data Management
- Summary

The Challenge

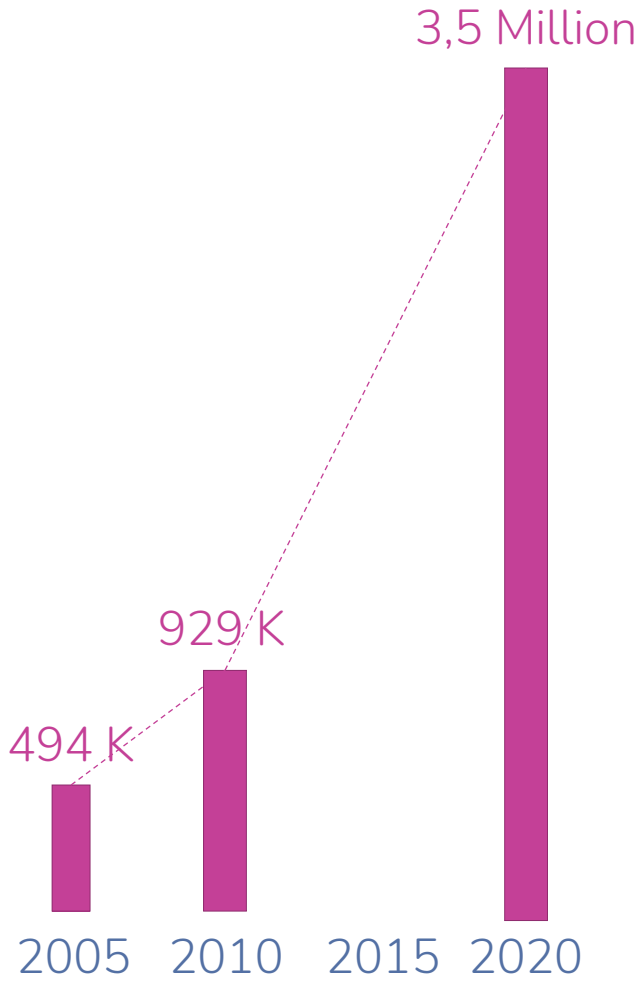
The evolving landscape of clinical development

Evolving Landscape – More Data

The typical Phase III protocol collects

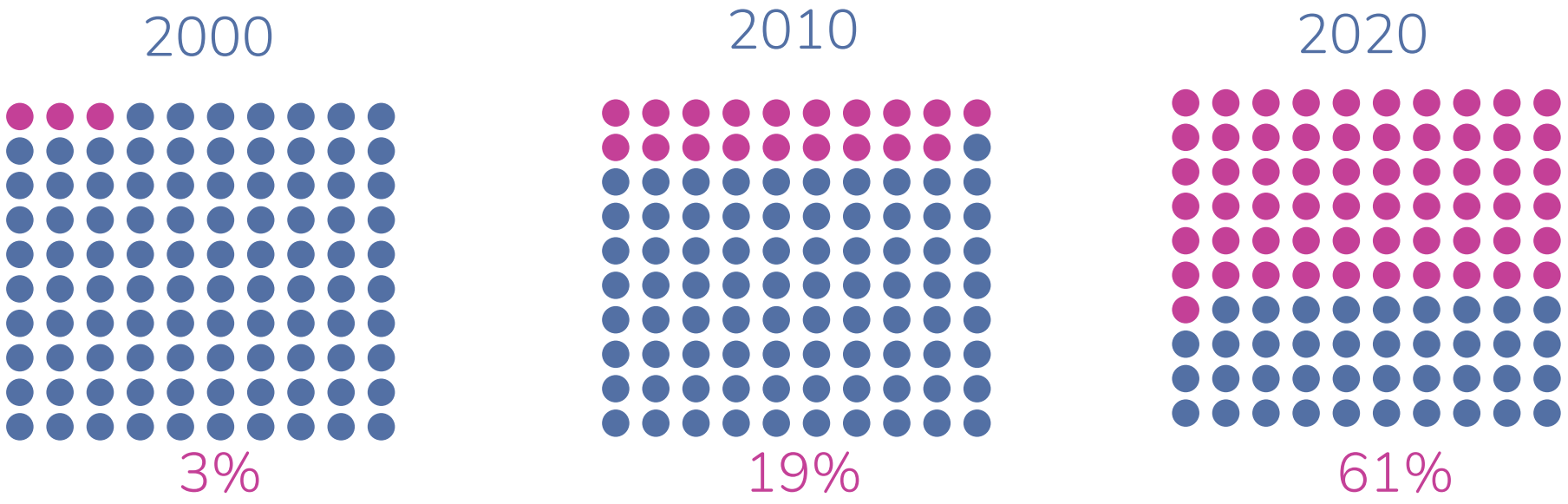
in average 3,5 Million data points,

7 times more than 15 years ago.[1]



[1] Getz K, Smith Z, Kravet M. Protocol Design and Performance Benchmarks by Phase and by Oncology and Rare Disease Subgroups. Ther Innov Regul Sci. 2023 Jan

Evolving Clinical Trial Landscape: Precision Medicine

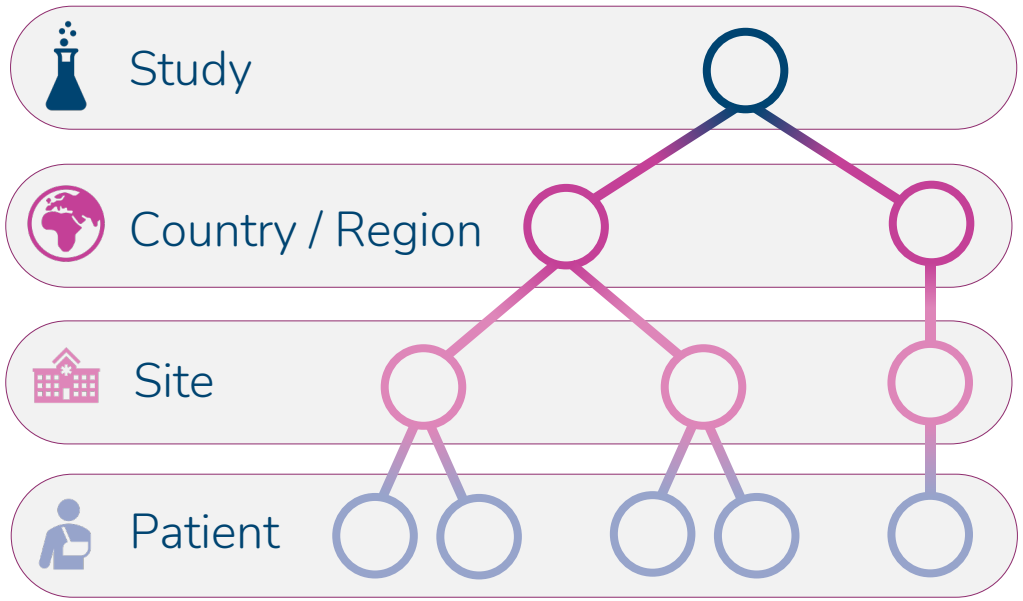


The percent of drugs in R&D that are personalized medicines has raised from 3% in 2000 to 61% in 2020 [1]

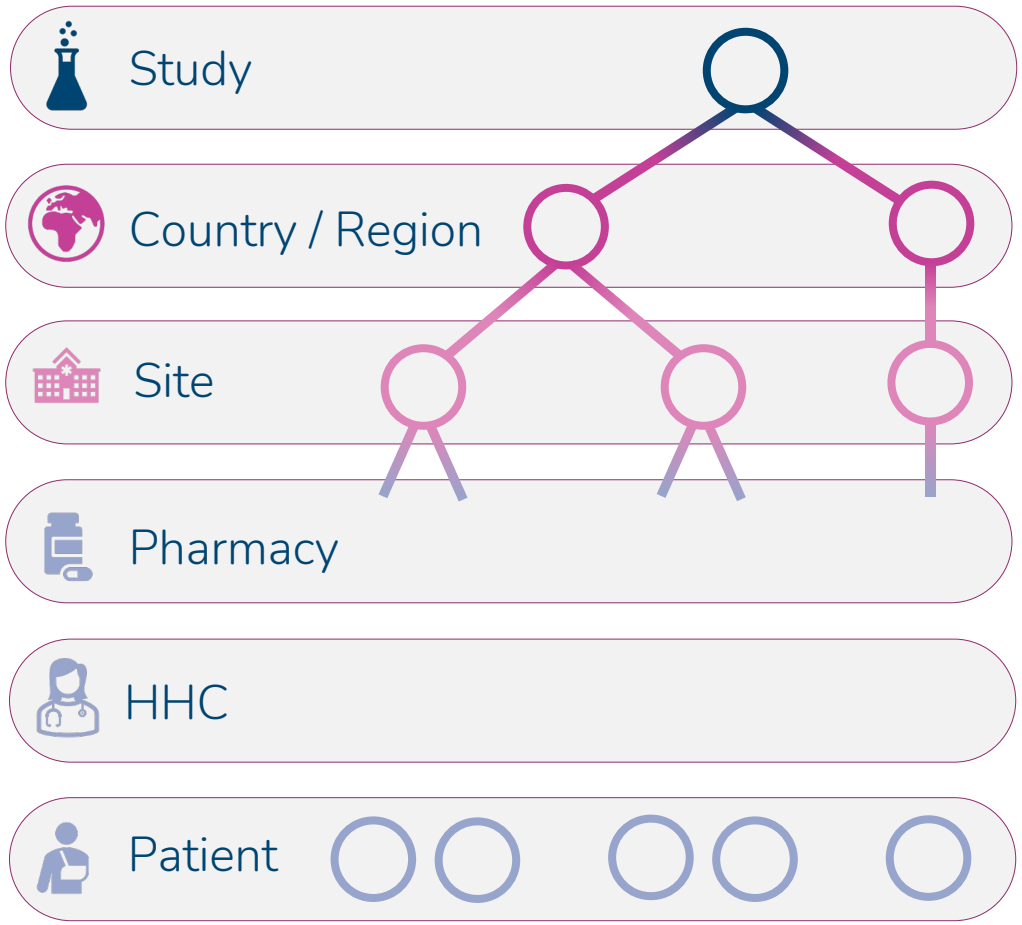
[1] Getz K, Smith Z, Kravet M. Protocol Design and Performance Benchmarks by Phase and by Oncology and Rare Disease Subgroups. Ther Innov Regul Sci. 2023 Jan

Evolving Landscape - Decentralized Trials & New Dimensions of Risk

Traditional Study



Hybrid & Fully Decentralized Study



New independent sources of study activity and data collection that could impact data reliability and patient safety.

Introspective Industry Focus On Data Management

Efficiency

Overarching identification of processes and tasks that:
'just take longer than they should !'

Can we simplify or find a more efficient approach ? Marginal gains ?

Shifting Technology Landscape

Availability of AI/ML solutions that provide time, efficiency and quality benefits

Can we enable our resources to deal with more complexity ?

Data Science

Increased capacity to identify quality issues that matter.

Supplement traditional compliance and conformity controls

Risk-based Data Management

Provision of Data Management oversight that is focused, proportionate and flexible based on Risk Assessment and identification of Critical to Quality factors and Critical Data.

Overlap and common benefits across all

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Risk-based Data Management

Risk-based Data Management

What do we mean by “Risk-based Data Management” ?

- The targeted and efficient application of clinical data management practices to clinical trials
- Designed to maximise the value of DM activities on any given trial
- Moving away from “1 size fits all” strategies
- Driven from a QbD Approach & Risk Assessment in the same way that monitoring is

Efficiency

Efficiency …… (and redundancy)

Data Management

Site Monitors (CRAs)

Medical Monitors

"Each variable is reviewed

17 times"

(on average)

Efficiency. Can anybody help us find a better way ?

What tasks soak up time and resource ?

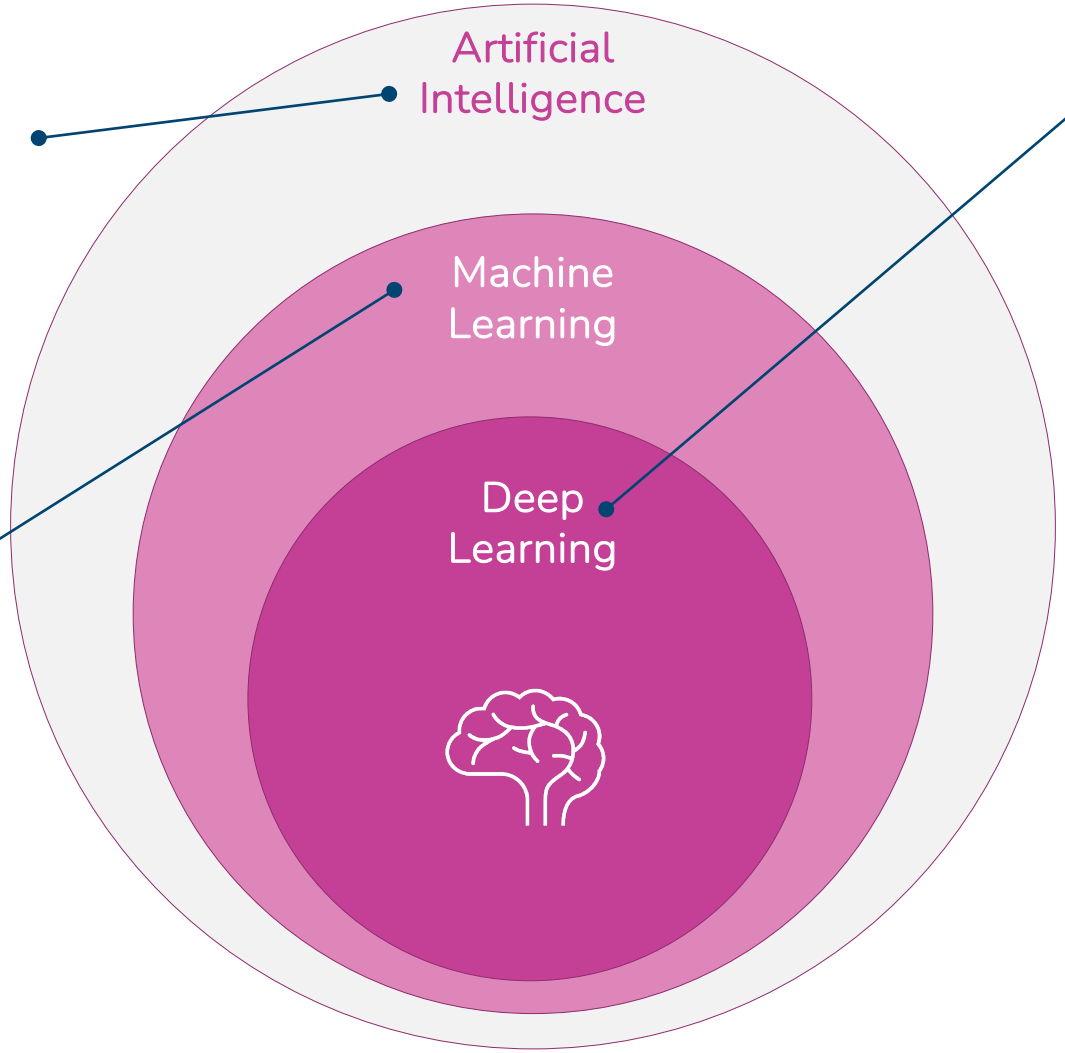
- Data review and raising manual queries is resource intensive
  - Development & Validation of Listings and DM Review outputs
  - DM Review work and raising queries
  - How many outputs become queries ?
  - Do the queries result in value ?
- Coding of data
  - Only so much data codes automatically, leaving manual burden
  - Synonym management to boost auto-coding is painful
  - Frequent thesaurus changes compound the problems
- Data Standards and Data Conversion
  - Life is good for ‘core’ data. Established capabilities for swift conversion
  - Difficulty comes with the ‘edge case’ data
- System Configuration and Validation .....

Shifting Technology Landscape

AI vs Machine Learning vs Deep Learning

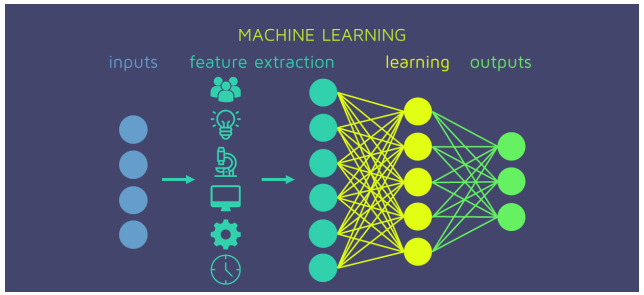
AI: Mimicking the intelligence of behaviour of humans.

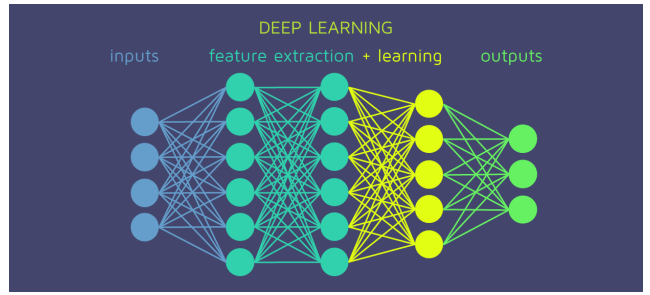
ML: Learning from data "training" without programming a complex set of rules.



DL: Technique inspired by our brain's own network of neurons "neural networks" and involves multiple layers (typically >3).

- Directly learns from data without need for business knowledge and heavy feature extraction steps.
- Learn new scenarios easily
- Flexibility in learning any correlation
- Not constrained by assumptions





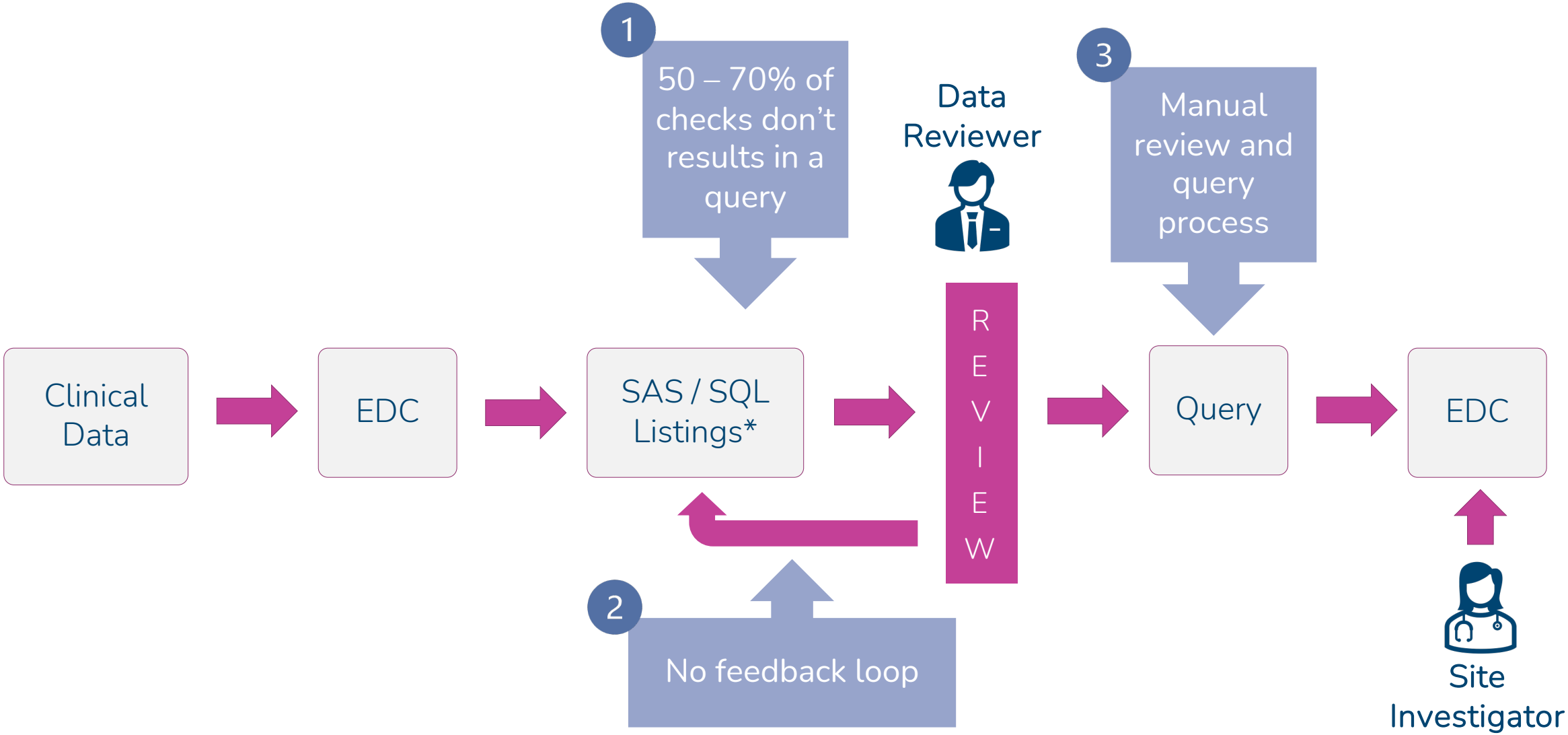
Supervised Learning?

Present the algorithm with many examples of labelled data, …

…the algorithm learns the rules to make a prediction on new data

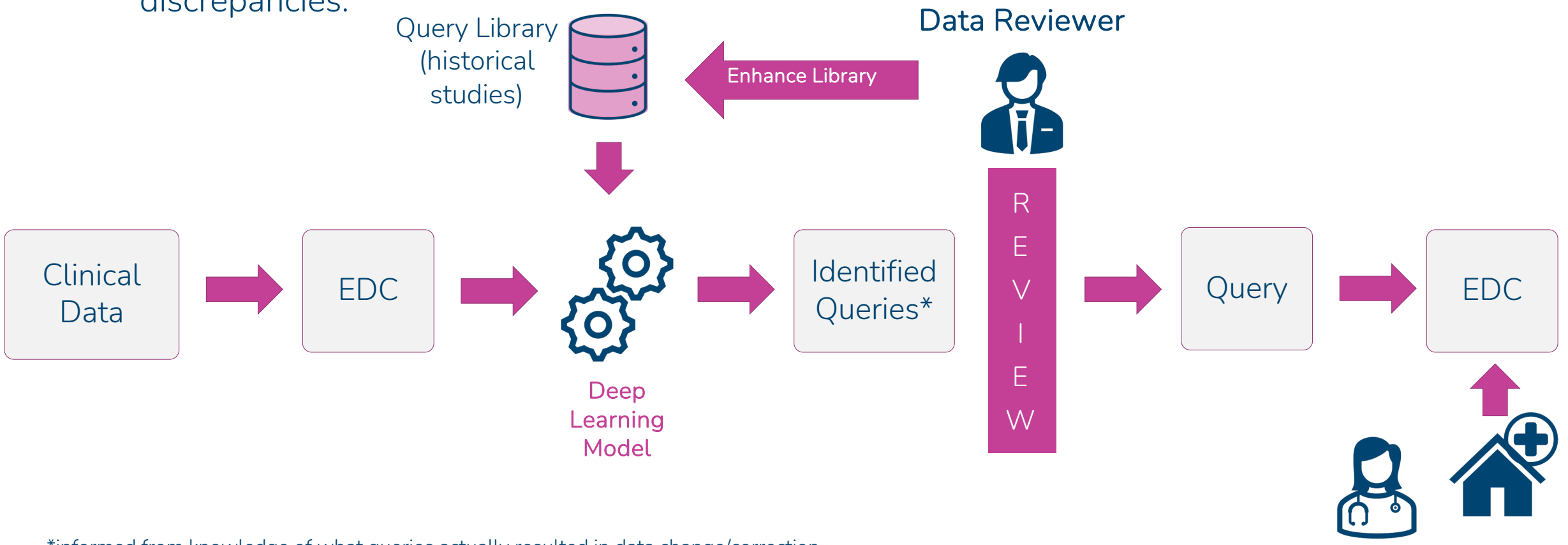
Prediction: sheepdog

Data Queries: Current Process



AI Driven Detection of Data Queries: How?

Approach: Use a database of queries manually created in previous studies to train a supervised DL model to automatically detect data discrepancies in the data, and to identify relevant data fields that provide supportive evidence and explain the nature of the data discrepancies.



*informed from knowledge of what queries actually resulted in data change/correction.

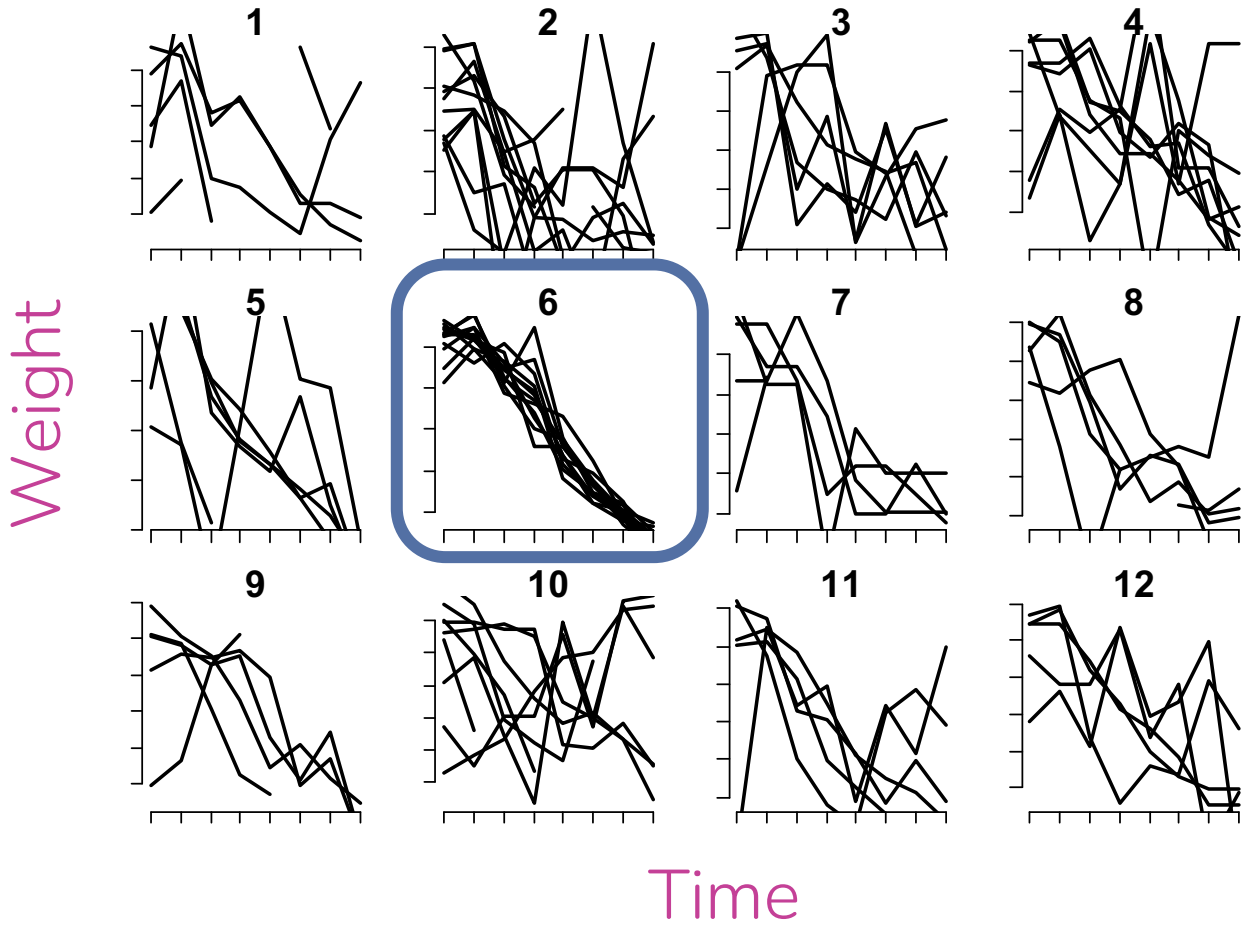
Use Case: Data Anomaly Detection: Value Creation Opportunity

Data Anomaly Detection & Query Generation

1	2	3
Reduce False Positives	Feedback Loop	Improve Reviewer Efficiency
Improving the % of anomaly predictions that result in a query being raised		Reduce the time required evaluate queries through automation Reduce repeat work
Reduction for 50-70% FP to 17%		Reduction from 6-7mins to 1.5 mins

Data Science

Data Science and Detecting Systemic Abnormalities

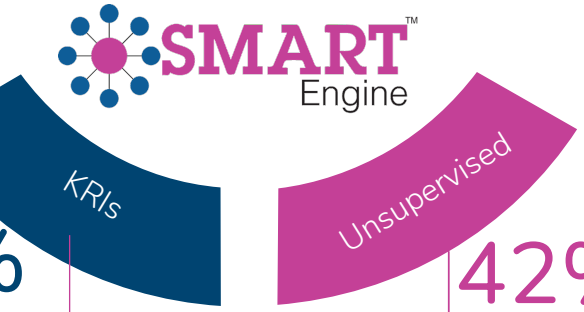


Central Statistical Monitoring

Programmatically Interrogating:

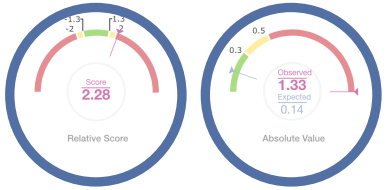
- Every Data Source
- Every Data Point
- Audit Trail Data

Confirmed, Identified Risks via Data Science



- Protocol & GCP Compliance
- Study Equipment / Technology
- Data Cleaning / Data Entry

By Center



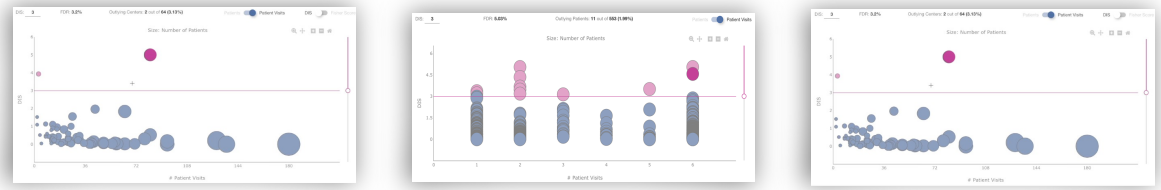
Absolute and Relative thresholds

The Score is computed by the SMART engine and reflects how atypical a center is compared to the other centers (observed vs. expected).

By Center

By Patient

By Region



Unsupervised analysis of all clinical and key operational data

Detection of anomalies at site, patient and region level that remain undetected using traditional techniques.

Reference: S. Young, D. Beaudry, V. Pomerantseva, J. Rowe, The Eradication of False Signals in Monitoring, *Applied Clinical Trials-09-01,2022, Volume 31, Issue 9*

Risk-based Data Management

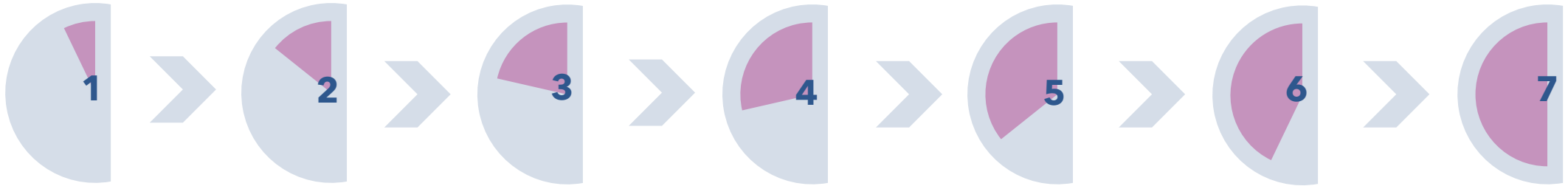
Remember Section 5 of ICH E6 (R2) ?

- Huge emphasis on cross-functional risk assessment
- Including Data Management

High
Medium
Low

- Centralised Monitoring
- Site Monitoring – SDV & SDR
- Data Management ?

Applying the same concept to Data Management



5..0.1 Identification of **Critical Data and Processes**

5.0.2 **Identification** of Risks

5.0.3 **Evaluation** of Risks

5.0.4 Risk **Control**

5.0.5 Risk **Communication**

5.0.6 Risk **Review**

5.0.7 Risk **Reporting**

- Data Management Risk Assessment – Why ?
  - Confirmation of Critical Data from a DM perspective
  - Opportunity to assess each moving part in the data collection strategy
  - Opportunity to assess complexities of data flow
  - Opportunity to consider Audit Trail Review scenarios
  - Opportunity to flex downstream DM practices
  - Promote Risk-based thinking across the team

High

Medium

Low

- Data Management
  - Aligned to Critical Data
  - Reduced Edit Check Configuration
  - Reduced Listings Review
  - Data Sampling Strategy

Exciting times for Data Management

1

Focused and Efficient through a Risk-based Approach to Data Management

2

Leverage new ways to support traditional pain points and increase identification of issues that ‘matter’

1. Risk-based Data Management provides:
    - Opportunity to deliver focused oversight and save against ‘1 size fits all’ approaches
    - Release bandwidth to deal with new data and more complex operational scenarios
2. Shifting Technical Landscape and Data Science provides:
    - Detect risks earlier and with greater accuracy and from new sources
    - Detect risks that ’matter’ in addition to traditional compliance and consistency

Thank You.

Questions?