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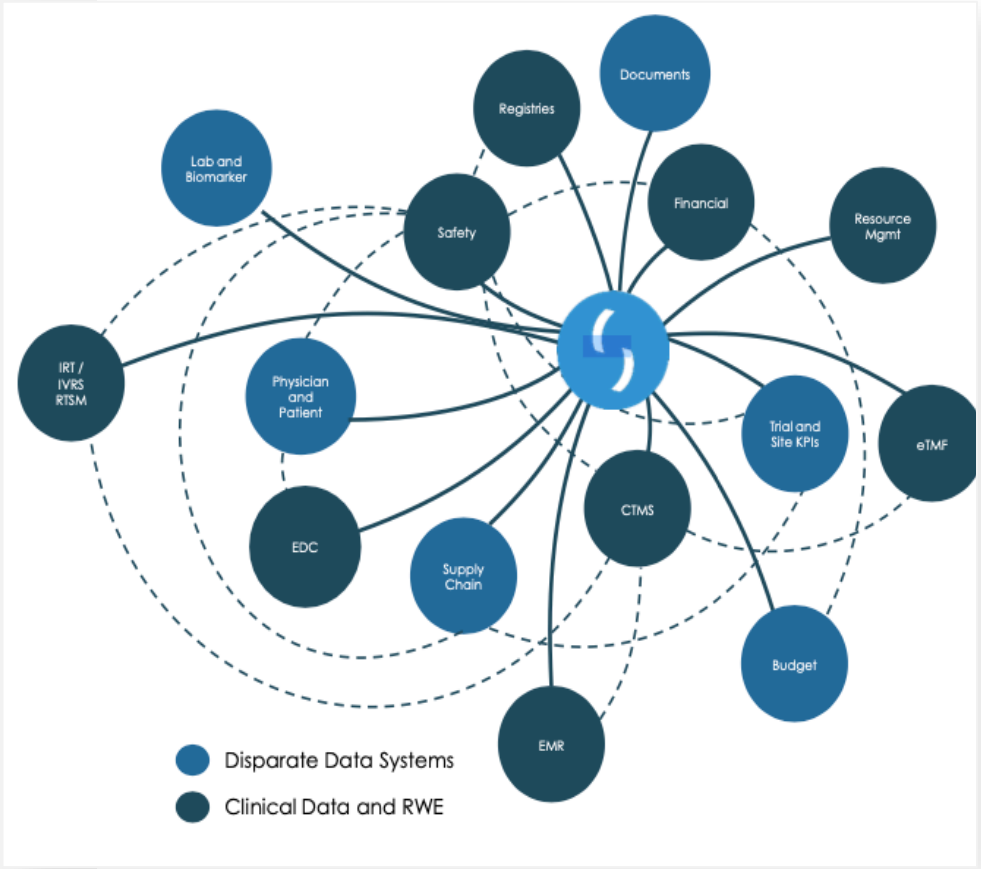
The Asia Pacific CRO

Digital Innovation in Clinical Development

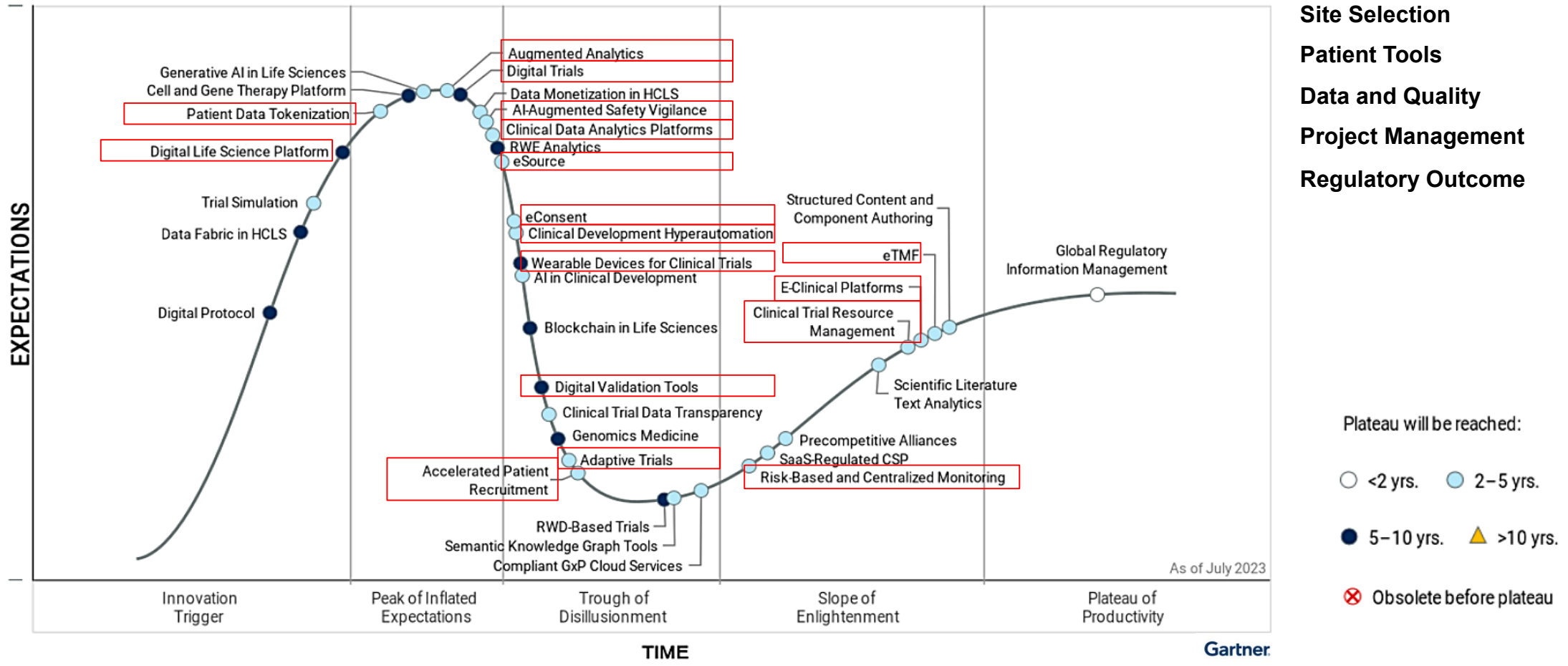
Michael Stibilj, COO, Novotech

Digital Innovation in Clinical Development

- Clinical Development is a complex and diverse endeavor
- Exciting innovation is happening across the industry, with new technology, new processes and approaches and levels of data integration that were previously dreamed about
- Application of artificial intelligence with machine learning and generative AI have the potential to revolutionise how we design and manage clinical trials
- We need to learn how to use these tools and experiment with different approaches and be prepared to change the ways we have worked
- Many of these innovative tools are only at the beginning of their application lifecycle, insights are already being gained, but new application of current tools and new tools will continue to develop



Hype Cycle for Life Science Clinical Development, 2023



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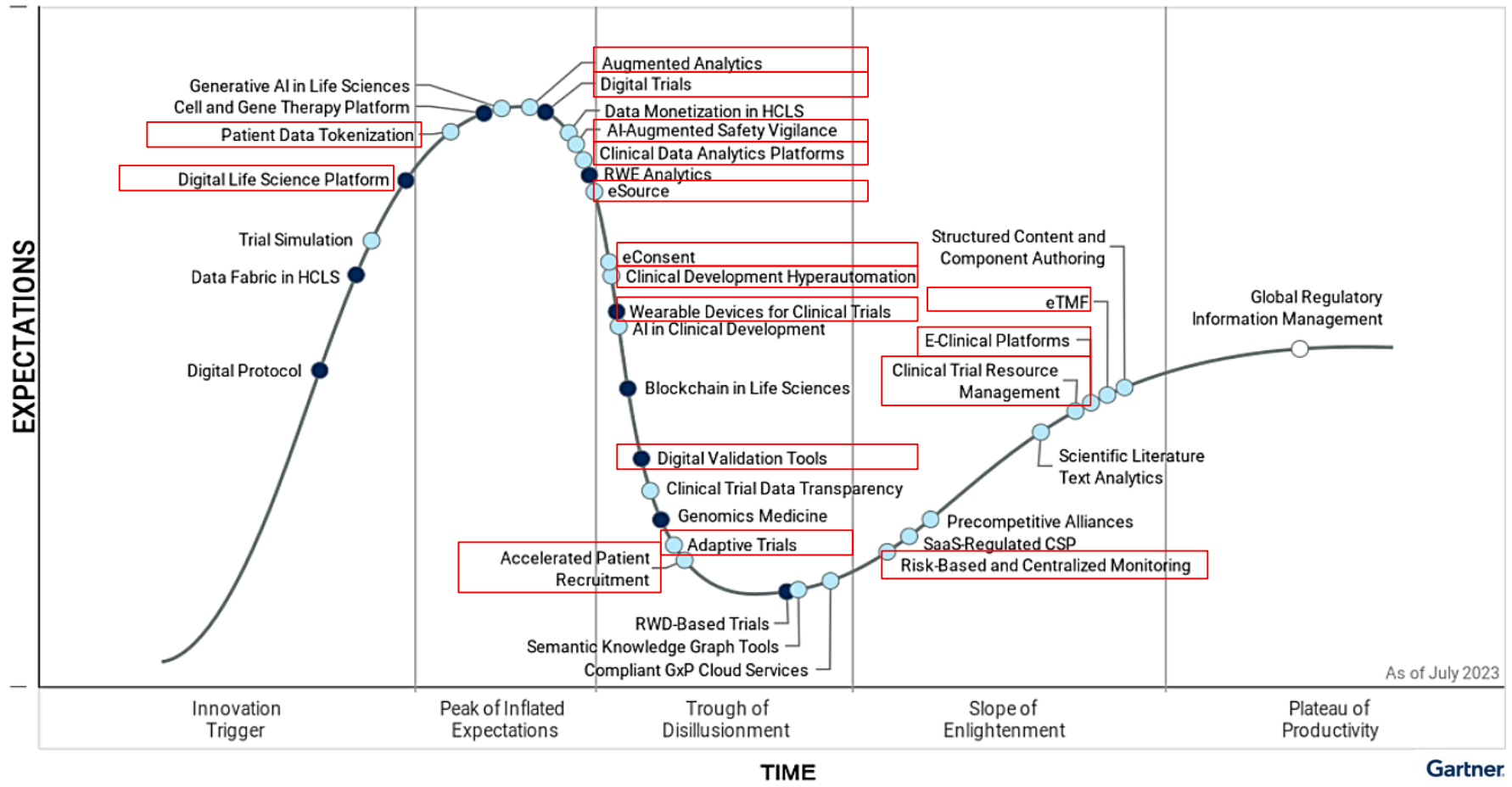


Site Selection

Patient Tools

Data and Quality

Project Management

Regulatory Outcome

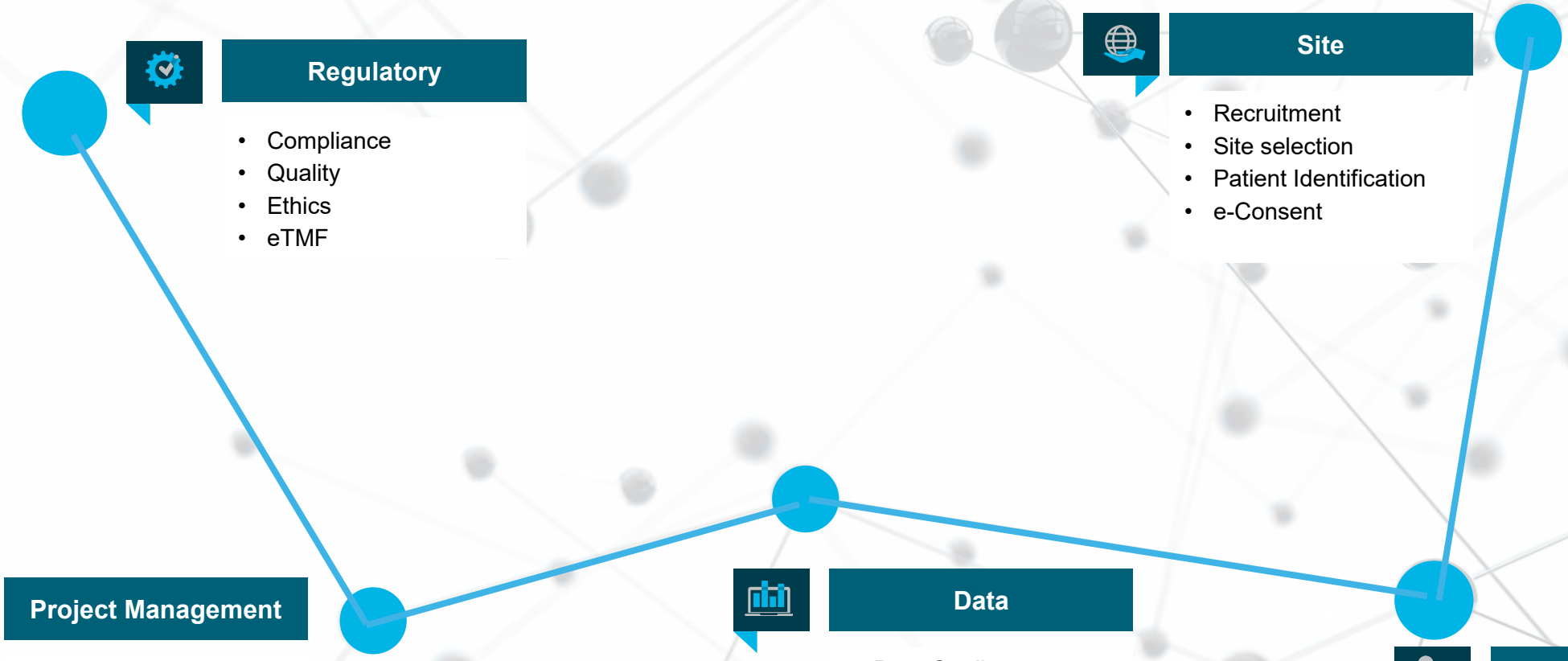
Plateau will be reached:

○ <2 yrs. ◔ 2–5 yrs.

● 5–10 yrs. ▲ >10 yrs.

⊗ Obsolete before plateau

Clinical Development is a Complex Network of Data



Regulatory

- Compliance
- Quality
- Ethics
- eTMF

Site

- Recruitment
- Site selection
- Patient Identification
- e-Consent

Project Management

- Project Planning
- Study Oversight
- Risk Management
- Trend Analysis
- Analytics
- RBM/ RBQM

Data

- Data Quality
- CRF Design
- Cleaning
- CDISC Analysis
- Novel Endpoints

Patient

- Patient Safety
- Data Collection
- e-DC
- e-PRO
- Trend Analysis

Site Selection

Possibly one of the most critical decisions after the protocol design

- Site Selection and ultimately patient recruitment the critical factor in terms of project timelines
- It has been reported that globally two-thirds of sites fail to meet their initial recruitment target and 80% of studies are late completing recruitment
- By using cutting-edge analytics to stitch together multiple data sets, we can enable evidence-driven site selection (Medidata AI & Deep6, Oncoshot)
- Multiple companies working on analysing data from EHRs, insurance records, disease registries, etc - to identify new and previously inaccessible patient pools (Prospection, Medical Director)

Study Feasibility Planning

SITUATION:

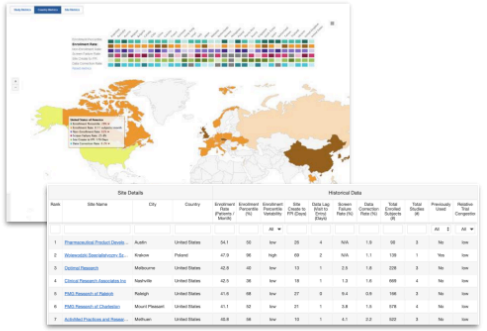
A mid-sized Biotech company was planning a CAR-T program of studies targeting DLBCL, a highly competitive indication. They needed to identify high performing sites with DLBCL + CAR-T experience while avoiding highly-congested sites, which would also determine final country selection

APPROACH: 6 Mo. Engagement

- **Segmented sites** by CAR-T capabilities and site trial congestion as well as related indications across multiple regions globally to identify the greatest global cross section of potential sites & countries for their eventual program expansion
- **Identified** list of problem sites that didn't enroll a single patient
- **Created multiple Forecasts** of the Phase 1 trial under different countries and site scenarios for better directional understanding

IMPACT:

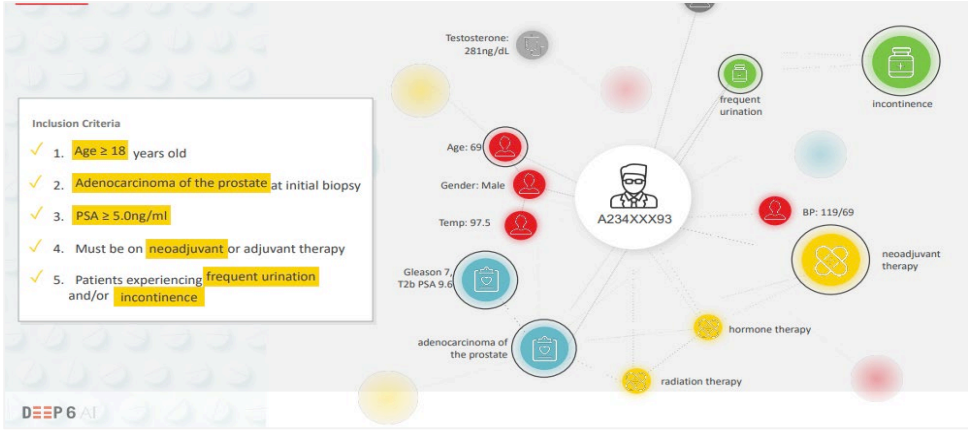
- **On track to meet planning goals under a more robust, confident plan,** for a very complex patient population



MEDIDATA

DASSAULT SYSTEMES

Precision Matching Populations to Inclusion/Exclusion Criteria



Patient Identification

Genomic Profiling is Changing Treatment Practices and Patient Outcomes

- Precision Medicine requires patients with very specific genotypes, often representing <10% of the patients presenting with the indication under study

- Precision oncology offers patients targeted therapies that **improve patient outcomes**
  - 1 in 3 patients who undergo genomic screening have more treatment options
  - 5% response rates in Non-matched agents Vs 27% response rates in Matched-Targeted Agent treatment [1]

- Novotech working with Omico in Australia and their national clinical trial network of 43 centres to pre-select sites and also implement decentralised clinical trials across the network

- Artificial intelligence used to analyse unstructured clinical data, including doctors' notes, pathology reports, and operating notes, to find patients that best match clinical trial criteria

- Big data analytics to identify high-potential locations where trial participants can be found (Deep6 AI, Omico, Oncoshot)

- In addition, using portals to increase the efficiency of training and communication for investigators and staff, prior to and during the study

PrOSPeCT - the **P**recision **O**ncology **S**creening **P**latform **E**nabling **C**linical **T**rials

- Open and track clinical trials at strategically selected sites across Australia
- Undertake Comprehensive Genomic Profiling of 20,000 patients
- Mulitplex IHC testing for proteins of interest also available
- Generate report for referring physician
- Link patients with appropriate biomarker-driven clinical trial
- Patient retains autonomy with regard to decision making
- Target conversion rate of over 50% screened patients moving into clinical trials

To Date:

- 7000 Patients Screened
- 3991 Treatment Recommendations
- 800 Referring Clinicians
- 608 Clinical Trial Referrals

Bringing Precision Oncology to Australian Cancer Patients

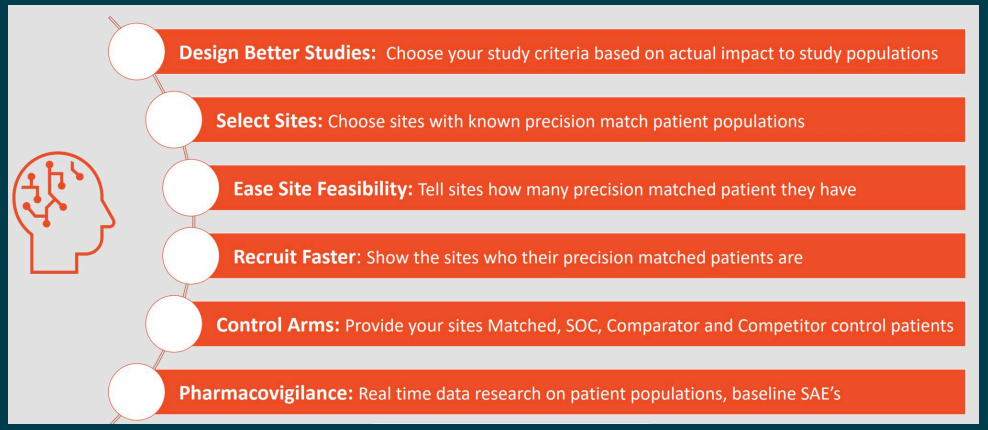
Ref 1: Paluri RK, *et al. Sci Rep* 2020;10:7935.

Patient Recruitment

Recruitment Related Tools

- As a reminder, 80% of studies are reported as being late completing recruitment
- Numerous avenues for digital innovation applied in clinical trials to interact with patients
  - Digital patient identification and recruitment strategies
  - Increasing use of digital advertising, but also adoption of social media, SOE targeting methodologies to be able to reach out to potential participants
  - Digital recruitment, beyond advertising pre-screening potential patients and moving towards e-consent both face-face and remotely
- These digital strategies enable the quick identification, screening, and enrolment of participants for clinical trials (Prospection, Medical Director, PenCS).
- Recruitment accounts for roughly 40% of the collective clinical trial budget of US pharma companies

- Many solutions rely on algorithms, AI, and/or natural language processing (NLP) to match patients to trials based on their medical records (Deep6)
- More recently, regulatory authorities are asking about the diversity and inclusiveness of clinical trial participants, requiring additional strategies to target different ethnic and socio-economic groups



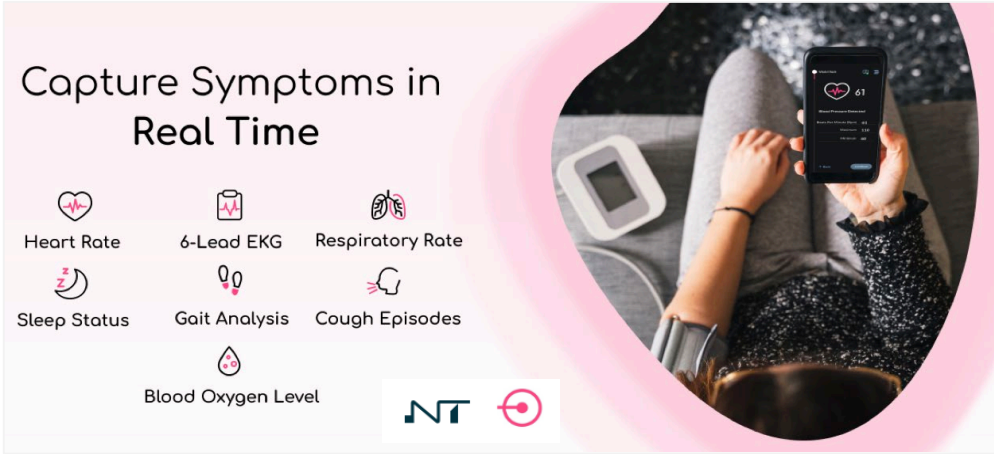
Patient Monitoring

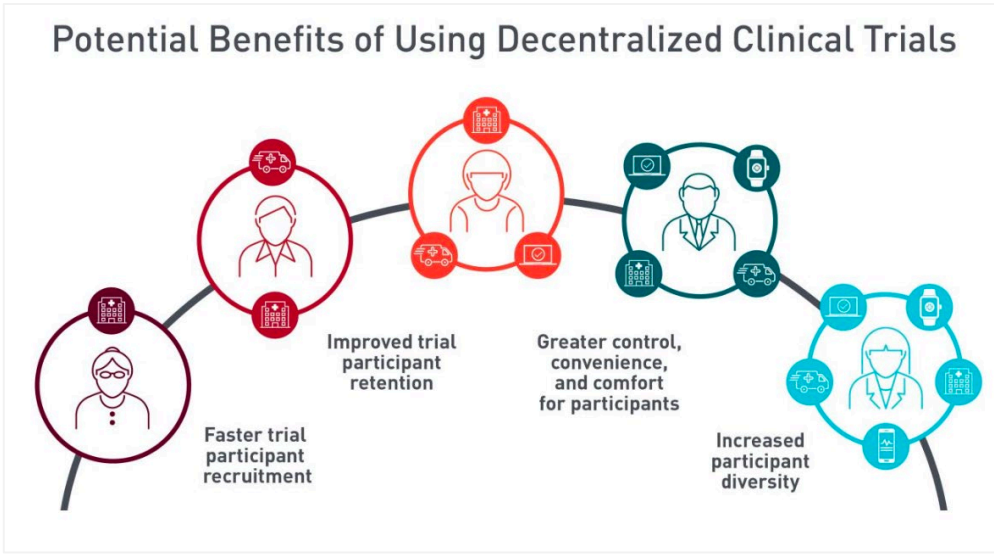
Patient Monitoring and Safety Related Tools

- Digital innovation in trial monitoring has gained momentum with more investment in real-world evidence. Patient reported outcomes (PROs) are now more frequently being collected in trials

- Passive data collection is starting to become more prominent, leveraging sensors in mobile phones and various biosensors and ‘wearables’.
  - Utilizing smartphone cameras to capture data such as ingestion of medication
  - Tracking movement in home (ObvioHealth)
  - Monitoring phone usage to track conditions. Assessing typing and touch screen kinematics to assess neurodegeneration (nQMedical)

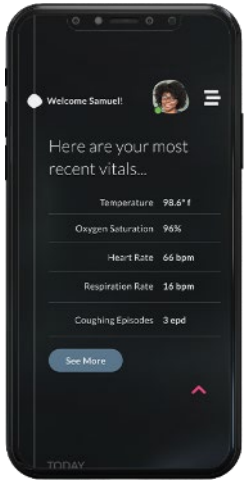
- These tools can also reduce the burden on trial participants and boost retention

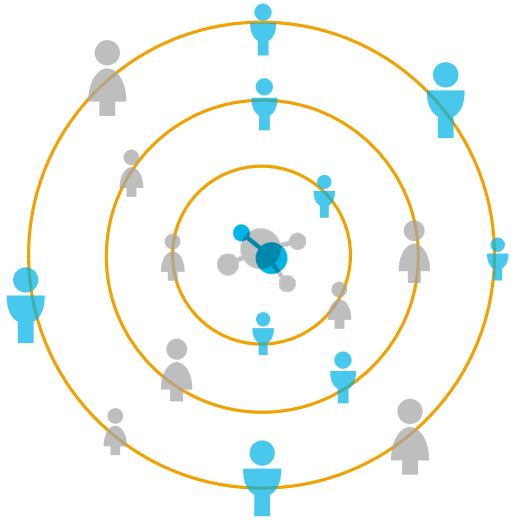




Patient Experience

Digital or Decentralised Clinical Trials





Patient Engagement Model

- Virtual Site Capabilities
- One of the first to offer a patient-centric BYOD app

Seamless Ecosystem

- End to end virtual and hybrid trial platform
- e-Consent
- e-PRO enabled
- Cloud Native

Tech & Team

CRO Services + Virtual Site Team

- Clinical researchers and scientists
- Health technologists
- Patient support team

ObvioHealth Launched in 2017 and Partnered with Novotech in 2021

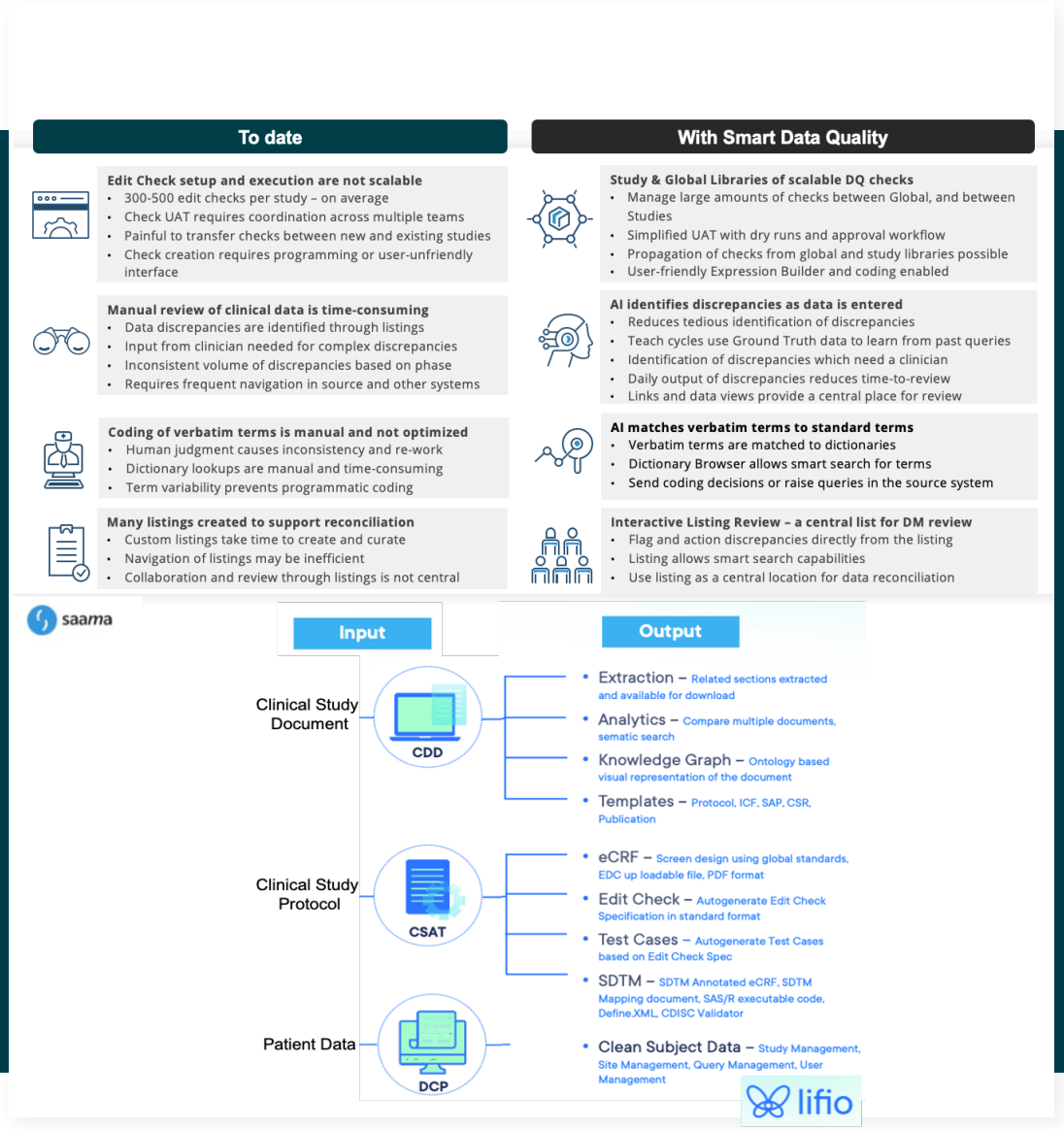
Data Quality

AI supported Data Cleaning

- e-DC has been a standard for the past 20 years, we are now seeing e-DC being better integrated with other data collection tools and also project management tools to provide a more complete data view of the patients and the trials (Veeva, ObvioHealth, Medidata)

- Machine Learning tools are being applied to data cleaning of more complex datasets that previously required manual review of multiple data listings by data managers and medical monitors (SaaMa)

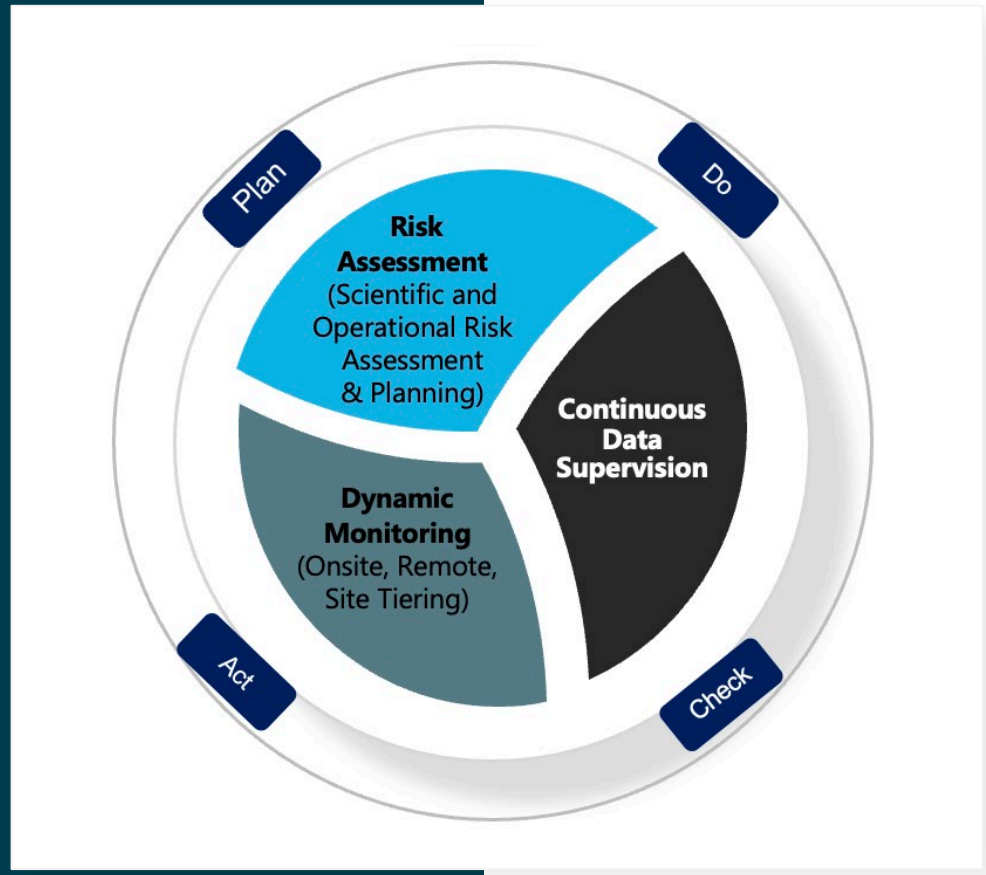
- Mapping e-DC to SDTM has been a challenging process that traditionally consumes large amounts of time and resources. Effective use of technologies such as machine learning can help standardize data sets, integrate legacy data, and improve data analysis and visualization (SaaMa, Lifio)



Clinical Project Management

Information and Insights

- Clinical Project Management revolves around communication and coordination
- Successful clinical trial project execution involves a significant amount of planning and risk management
- For that we need data and more importantly we need insight
- Digital tools are enablers for successful clinical project execution. Taking the focus away from creating and collecting the data, creates the space to identify insights
- New insights enable better decisions or allow decisions to be taken earlier
- Many of these tools are at the beginning of their application lifecycle yet insights are already be gained
- New applications of current tools and new tools are in development these have the potential to transform how we design and manage studies



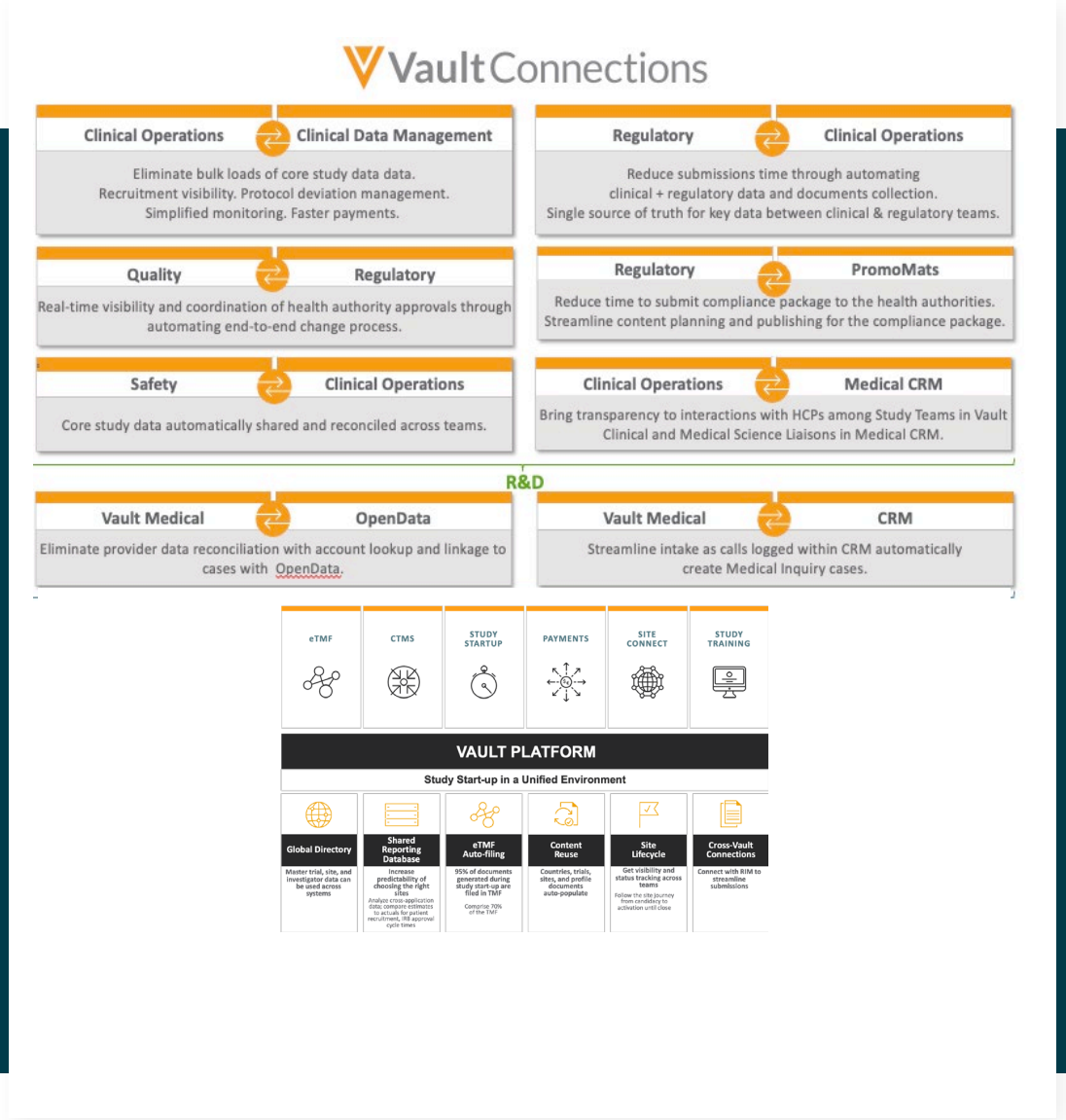
Digital Integration

- Integrating digital tools helps realise the value of the tools individually and collectively,

  CTMS historically tracked what had happened. With integration and interoperability through workflows and shared data CTMS truly becomes a “Clinical Trial Management System” and we can manage ‘what is happening’ and ‘what is going to happen’

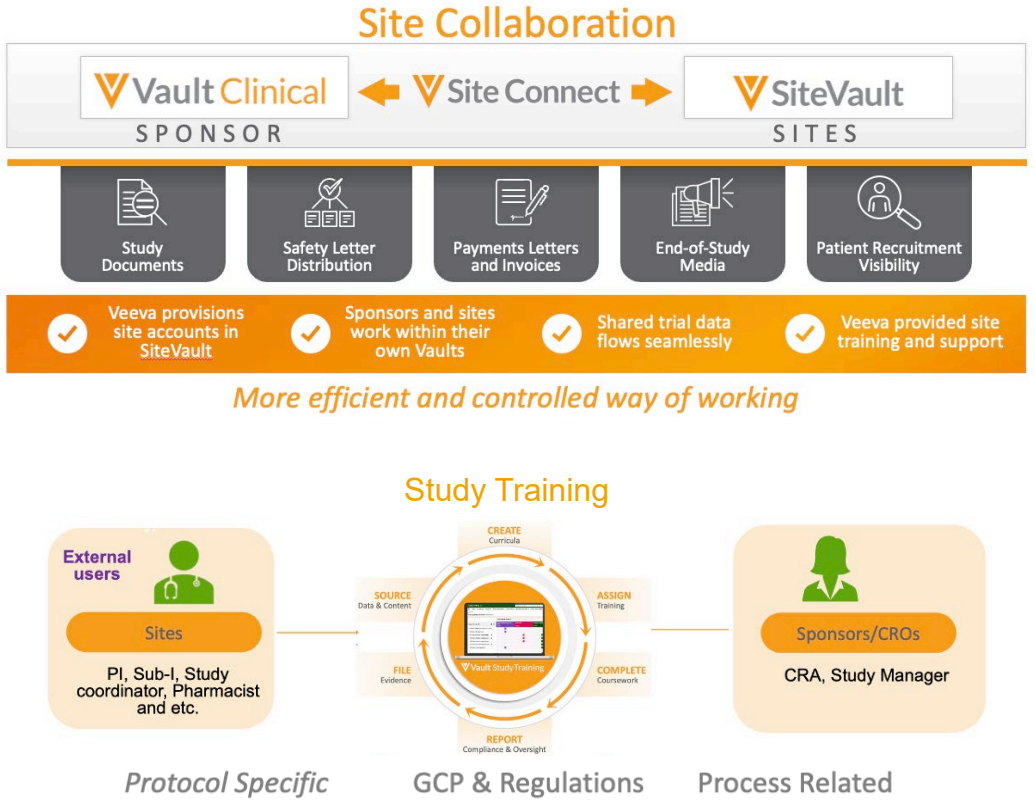
- APIs between platforms extend the reach from one platform to form an organisational eco-system (Veeva, Medidata, Salesforce, Oracle) from providing historical data to real-time data

- We still use dashboards and reports, but the real ‘management’ comes through the use of workflows, thresholds and directed actions



Inter-Operability

- Inter-operability between digital tools enables different teams and partners to work collaboratively
- Data and outputs shared to support transparency and communication
- Workflows to help direct the required actions and provide real-time view to status of process
- Tracking and reporting on status to support regulatory compliance, for example Study Training (Veeva)



Risk Based Quality Management

Data Management

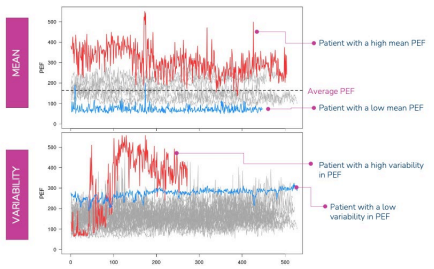
Discrepancies
AE/Med Coding
Reconcile SAEs
Lab Data Review

Centralized Monitoring

Medical/Safety Reviews

Mean & Variability Tests to Detect Anomalies in PEF

Peak expiratory flow (PEF), a person's maximum speed of expiration, as measured with a peak flow meter.



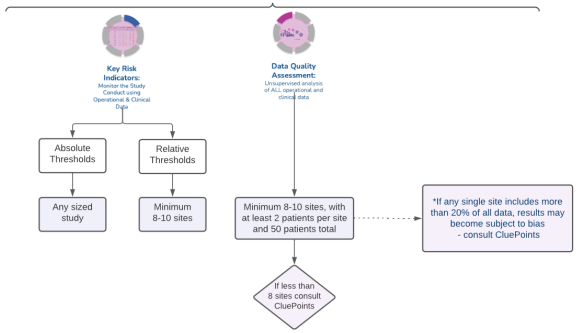
Site Monitor

Move away from 100% SDV

Confidence in data quality & integrity

Efficient and effective when on site

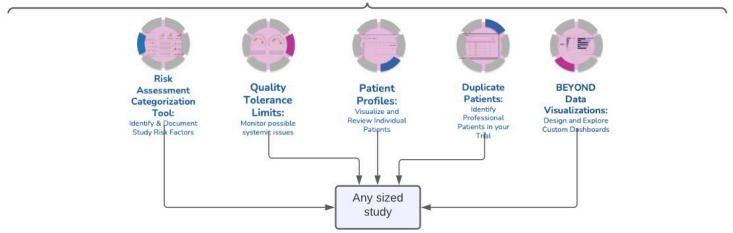
Site (and Country) Level Analyses



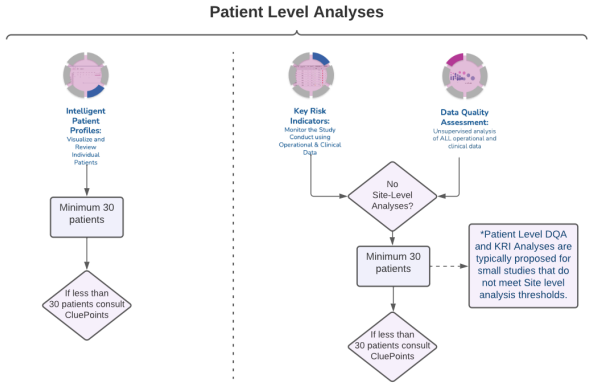
CluePoints

CENTRAL MONITORING PLATFORM

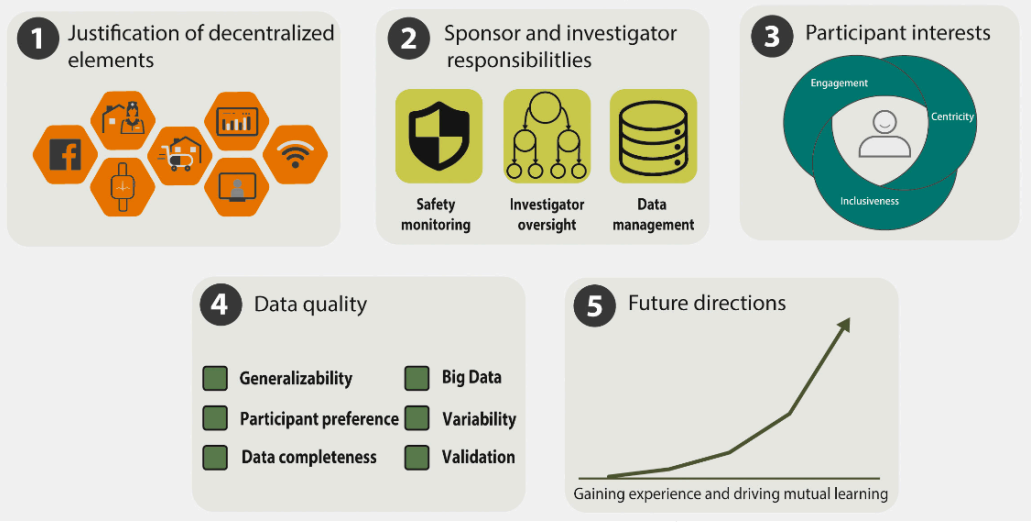
Risk Assessment / Study Level Limits / Duplicate Patients & Data Visualisation



Patient Level Analyses



Regulatory View on Adoption of Digital Tools



De Jong et.al, Clin Pharm & Therapeutics Aug 2022

Benefits

- Improve accessibility, diversity of trial participants
- Improve retention in clinical trials by moving trial activities to participants' homes and local surroundings
- Ability to identify and attract potential participants

Opportunities

- Reduced participation burden
- Facilitate participation of underserved communities in clinical trials to ensure the trials are more representative of race, socio-economic
- Adoption of new surrogate markers, endpoints to assess disease burden in the real-world and quality of life

Concerns & Risks

- Concerns regarding investigator oversight and participants' safety with limited face-to-face contact.
- Need to validate new technology and surrogate markers in parallel to the utilisation
- Ensure that the digital tools are incorporated during the protocol design stage of the trial

If Not Now, When? If Not You, Who?

Challenges and Barriers to the Adoption of Digital Innovation

We are a conservative industry,

- We are dealing with patient safety, without full evidence of the safety of the product
- We are taking a lot of investment risk on behalf of the sponsor

The regulatory foundations are the same – foundations from GCP

- But, we need to work with multiple regulatory authorities
- Each authority has different opinions that need to be anticipated and considered

However, in my opinion

- We need to be working with these tools to ensure they mature, in the clinics
- The potential benefits are real, in terms of speed to market for patients and the industry

We need to be taking informed and considered approaches to experiment and validate

- They are all not an all-or-nothing approach, it's important that we adopt and adapt to different situations
- Engage with all stakeholders during the protocol design process
- Some technologies and approach will require fit-for-purpose protocol design and conduct considerations
- We always need to be considering safety monitoring

The Opportunity is around us and ahead of us

NOVOTECH™
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“Digital Transformation is like a Bamboo Plantation-Bend but don't break. Be flexible yet firmly rooted. Show resilience while highly sustainable!”

— **Narayanan Palani,**