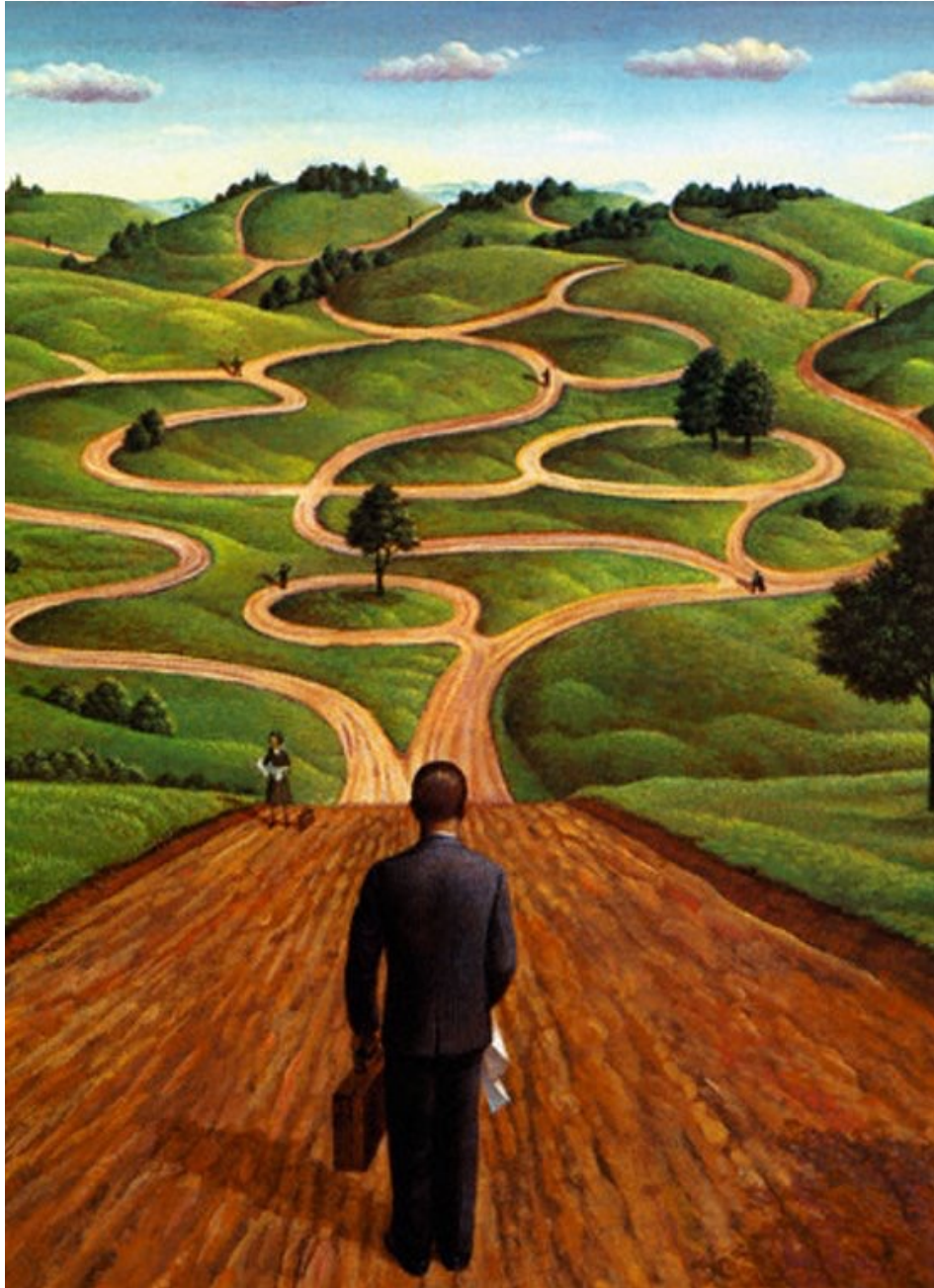




Does no errors equal high quality?

Julie Solbjerg Appel

Sanna Herrgård

Statistical Monitoring Specialist

DM Process & Innovation Specialist

Agenda

RBQM in Novo Nordisk

- Framework
- Strategy
- Skill types
- Types of monitoring

RBDM & ATR

- Background & purpose
- Approach

Conclusions

- Collaboration across skill types

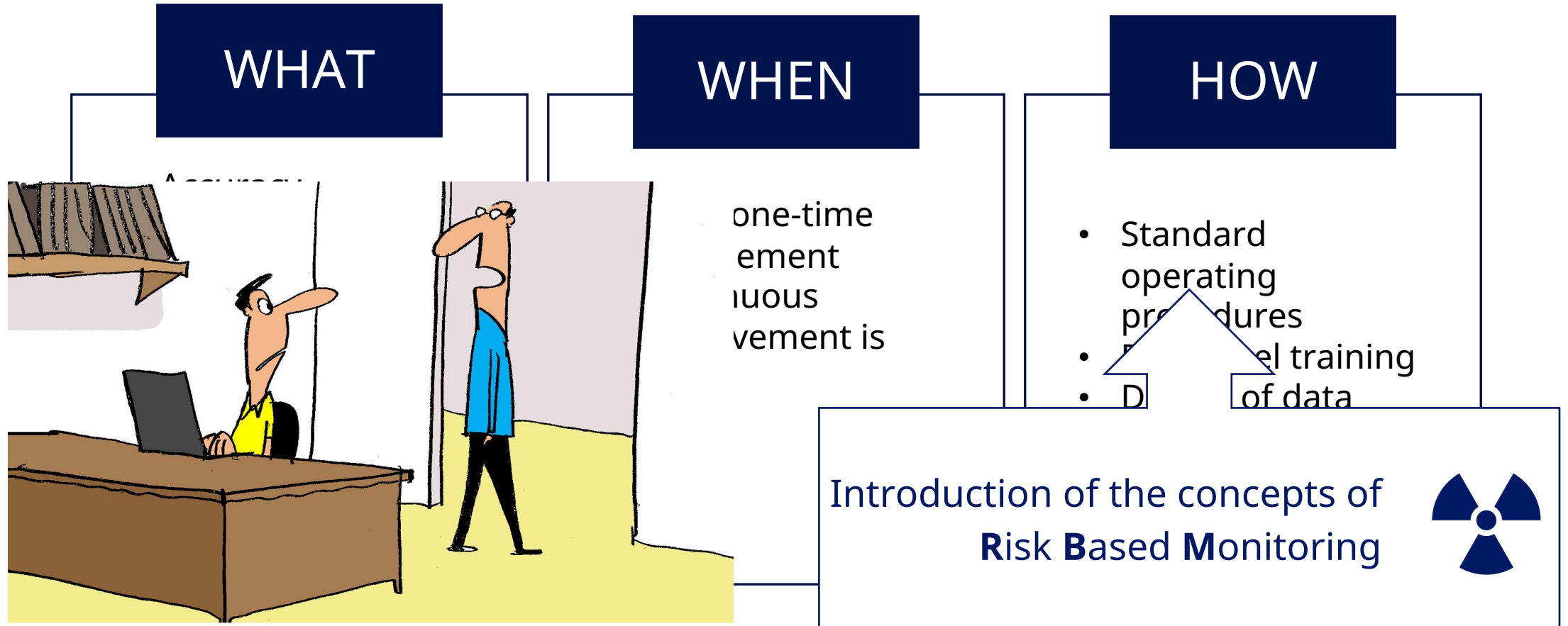
Statistical monitoring

- Background & purpose
- Approach

Case

- Screening bias
- ATR dashboard

Data Quality



"WE'RE ALL ABOUT INTEGRITY HERE. BY THE WAY, IF MY WIFE CALLS, TELL HER I'M NOT IN."

Risk Based **Quality** Management in Novo Nordisk

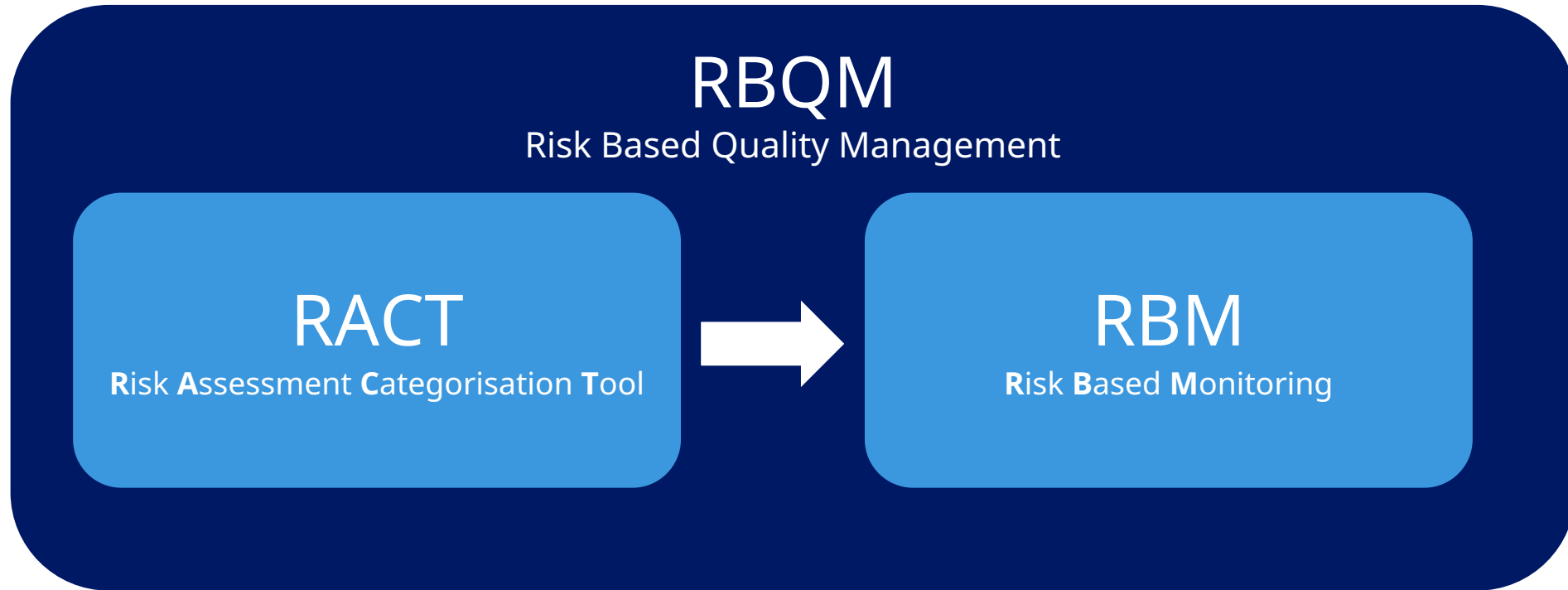
RBQM in a nutshell



It is about
knowing and managing
your trial risks and only do focused
monitoring where needed!

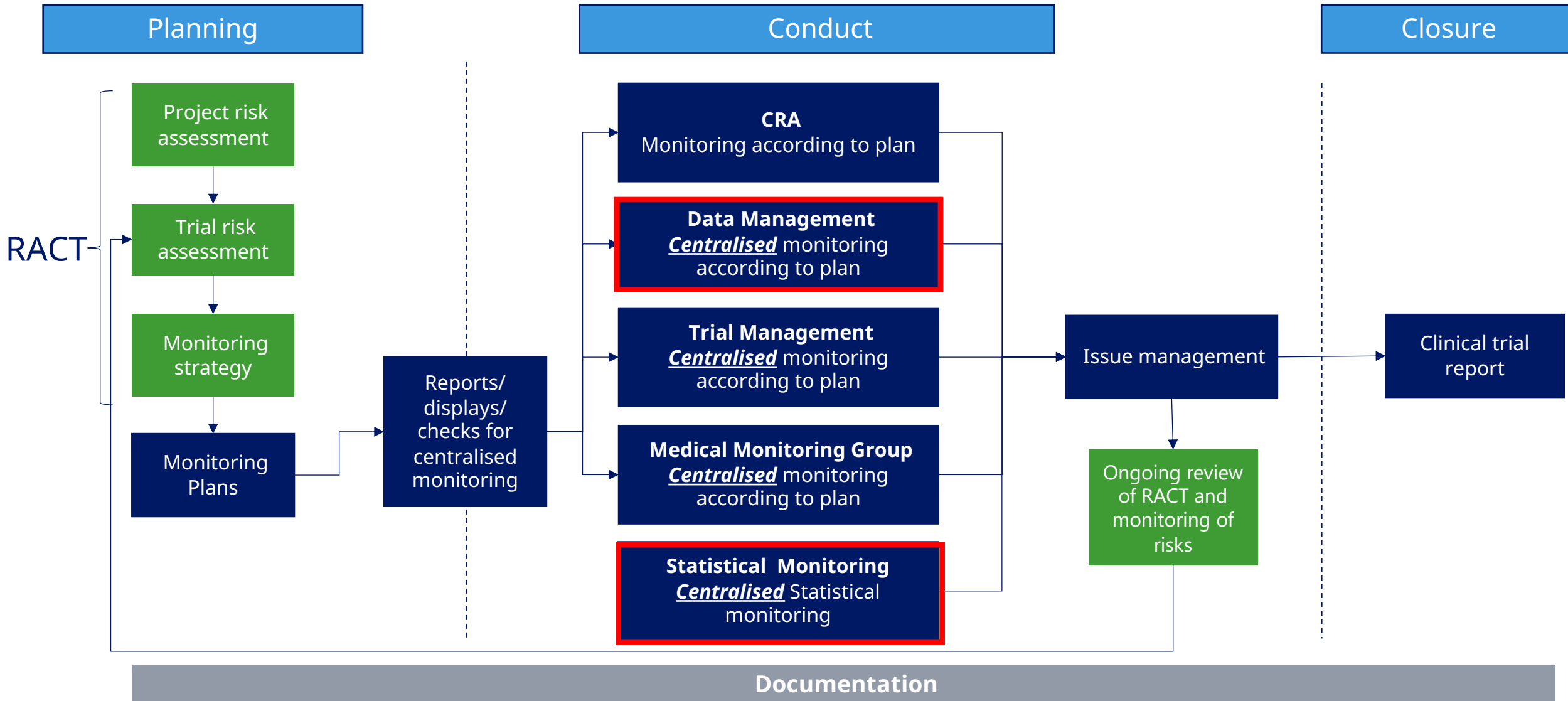
It is not about
taking risks!

Changing from RBM to RBQM



RBQM is the agreed monitoring strategy decided on in the risk assessment process (RACT)
RBQM covers both the RACT and RBM processes

Overall RBQM process



Statistical monitoring

Statistical Monitoring



An approach to monitoring of data using statistical methodology and visualisations



Exploratory by nature



Iterative with a frequency depending on complexity of trial



Risk based approach but with different focus



Key Risk Indicators

- Small number of variables
- Focus on important risk factors
- Exceeding pre-specified thresholds
- Requires specific reports on trial level

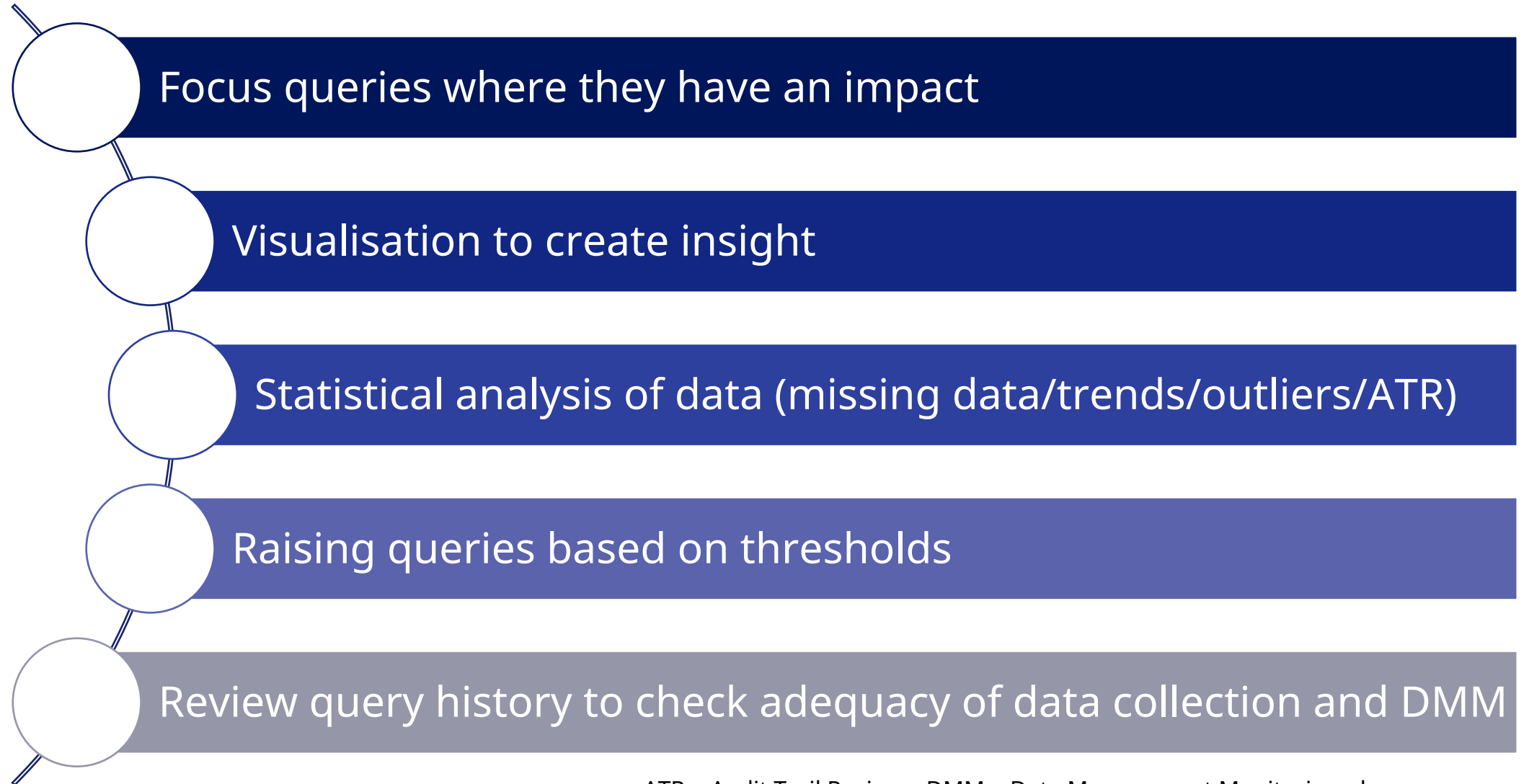


Statistical monitoring

- All available variables
- Focus on statistical differences in comparing sites
- Utilising all data and formats using a large number of analyses
- Statistical and exploratory analyses may be applied across many trials

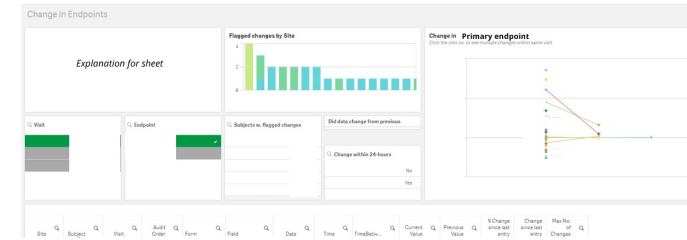
RBDM - ATR

What is RBDM

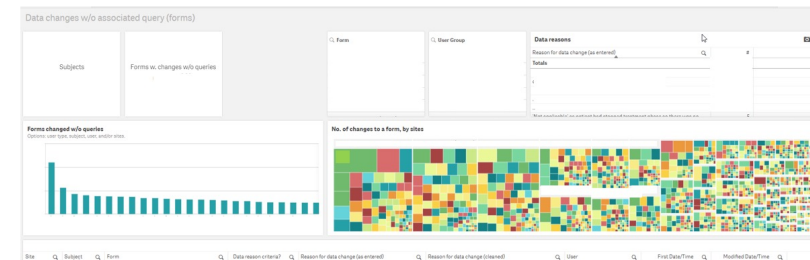


Audit Trail Review (ATR)

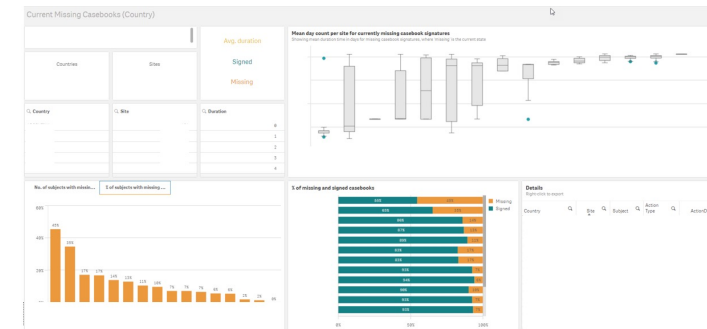
- ATR of GxP systems is a requirement
- New activity for most sponsors
- Novo Nordisk has built a visual data analytics application to support ATR of EDC data
- Use cases stem from Industry position paper [Downloads \(eclinicalforum.org\)](https://www.eclinicalforum.org/downloads)



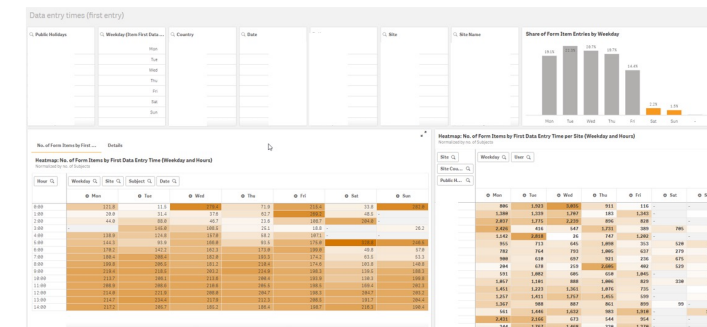
Primary endpoint



Data changes without associated query



Missing casebook signatures



Data entry day and time

Why is ATR part of RBDM?

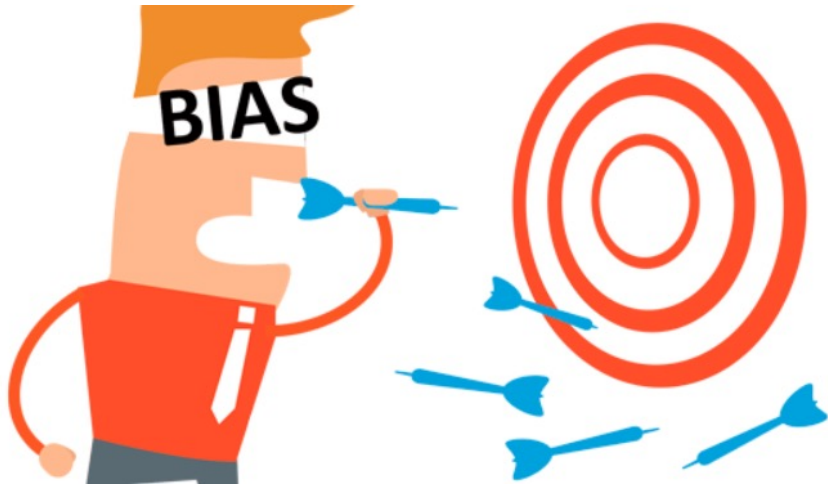
- Audit trails contain millions of rows of data → need to understand trial risks and identify relevant visualizations
- ATR or risk-based audit trail monitoring?



Case

TEAM NOVO NORDISK
Professional cycling team

Screening bias



case

- At the **screening visit** a patient is scored resulting in eligibility criteria being met
- At the randomisation visit, the patient is scored more **objectively**

consequence

- **non-eligible** patients randomised
- sub-optimal patients will potentially **dilute trial results**
- potential **safety issues**

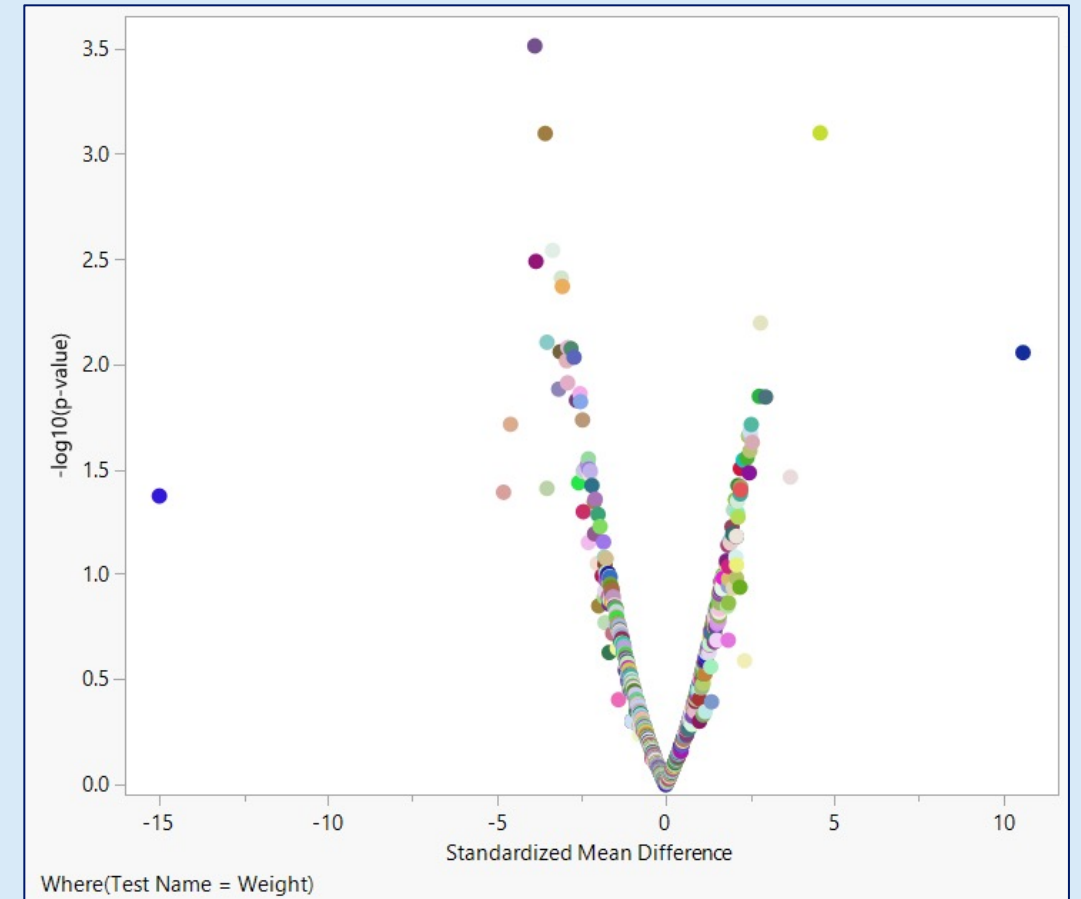
analysis

- Identify **within-site changes** in values between screening and randomisation visit
- Compare site differences to identify sites that **may falsify screening data**

Case study: NN test study

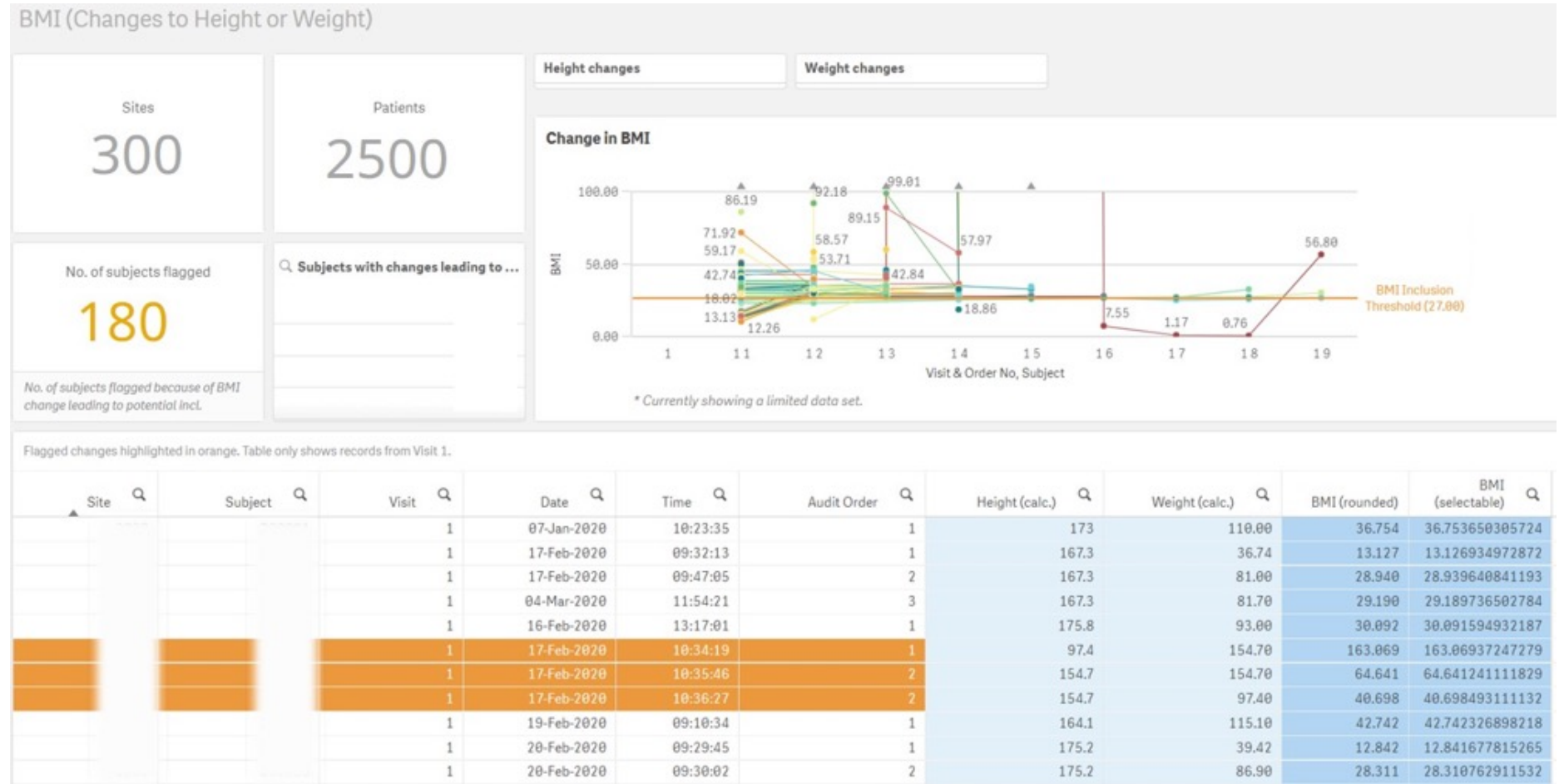
- Inclusion criteria: BMI > 27 kg/m²
 - Height (visit 1 only), weight (visit 1 & 2)
- Changes in weight data for all sites are analysed
 - Volcano plot identifies records where data change significantly between V1 and V2
 - No significant P-values but two sites seem to be different

Variable	Site	Mean difference	No of patients
Weight	A	0,95 kg	3
Weight	B	-1,25 kg	2

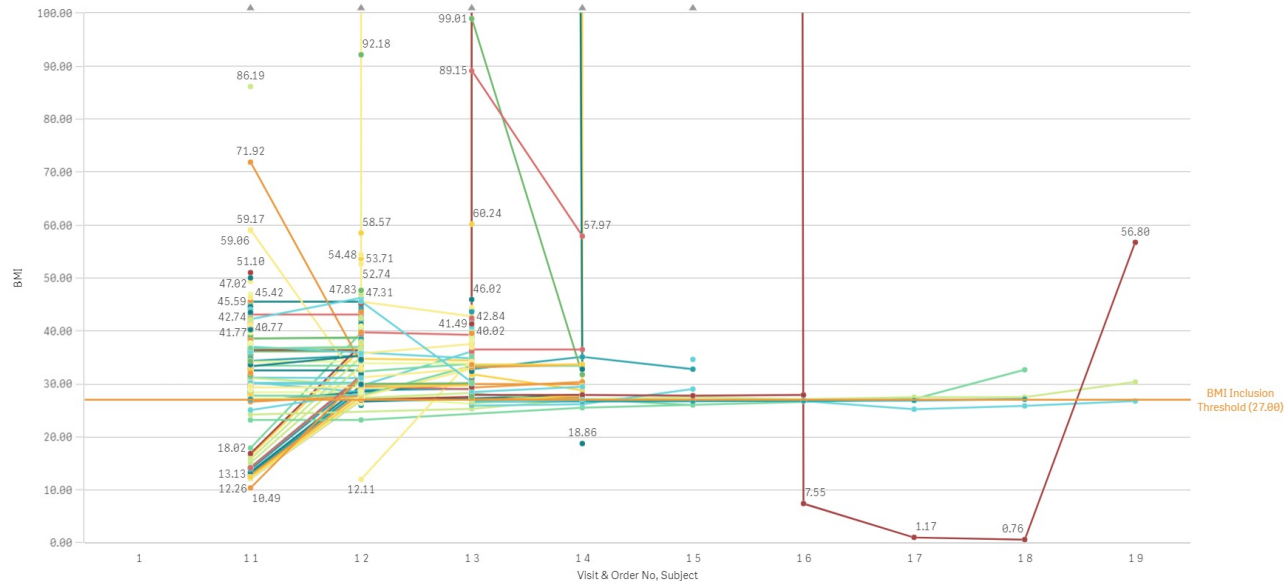


ATR dashboard

*Flagged patients:
Patients with
changes
within 24
hours
leading to
inclusion in
the study*



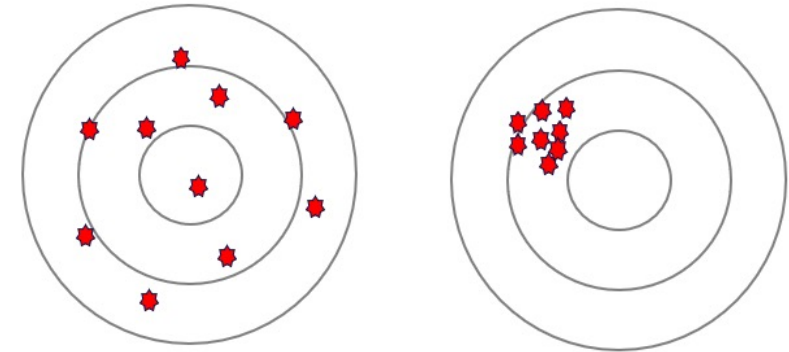
ATR dashboard – systematic & random errors



Subject	Initial entry	Current value
1	1232,8 kg	132,8 kg
2	18,7 m	1,87 m

Patients to be investigated:

- Changes made within a short time span
- Minor changes
- Repeated changes



Targeting data that matters



Remove
obvious
random
errors

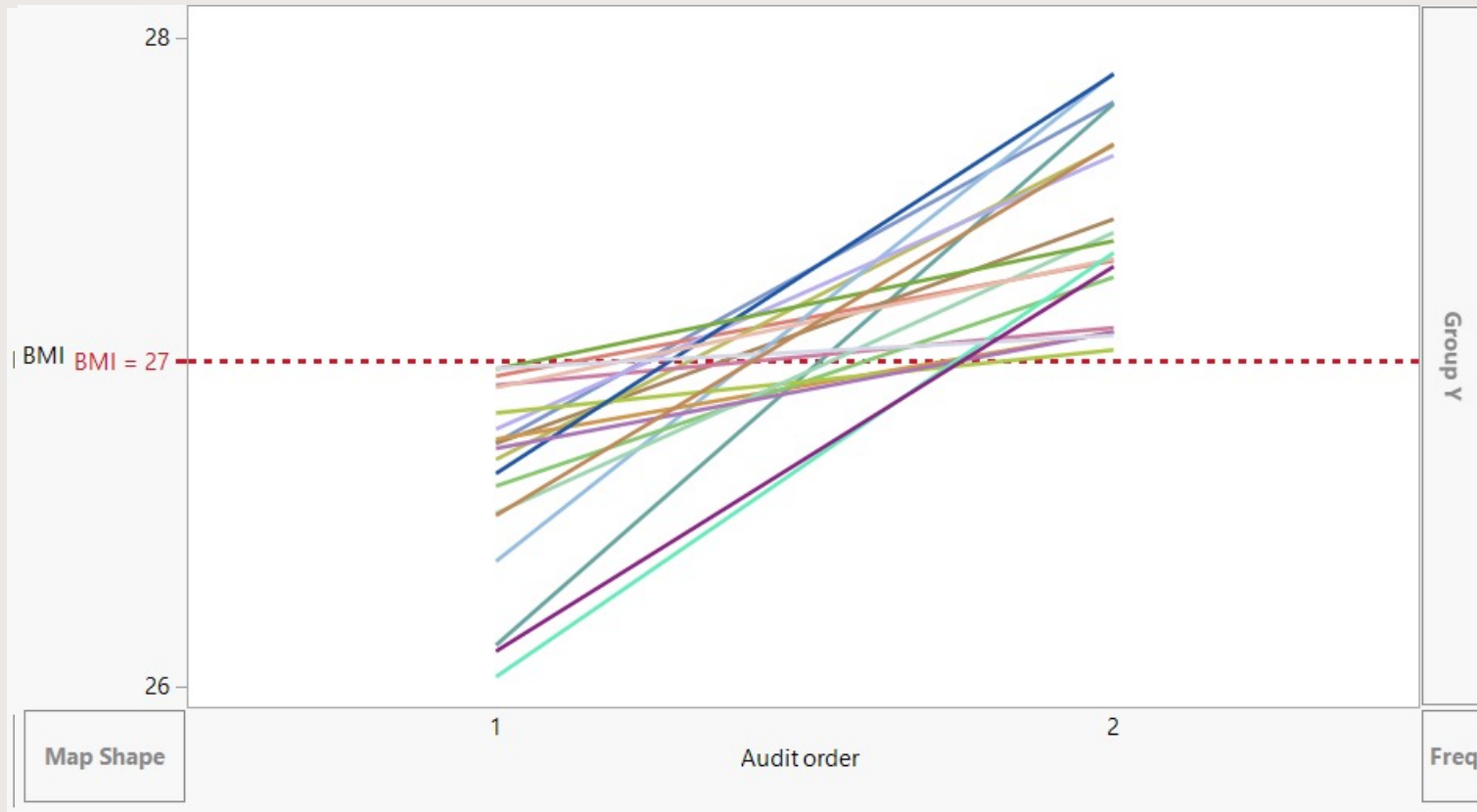
Large height or weight changes

Large BMI changes

Outliers

Initial BMI value > 27

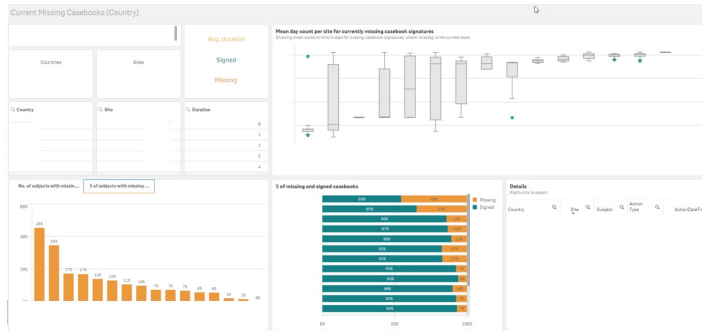
Data analysis



We are left with the data that matters and further scrutiny can begin



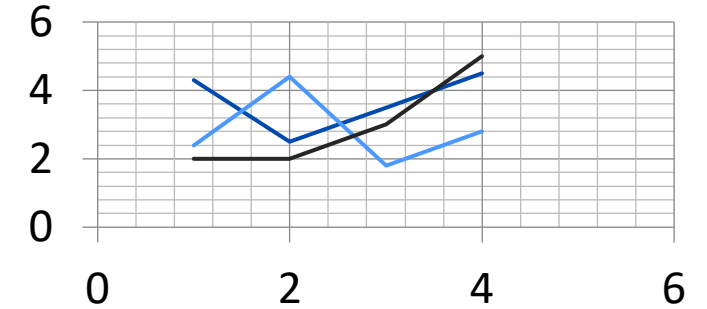
Impact of ATR and statistical monitoring



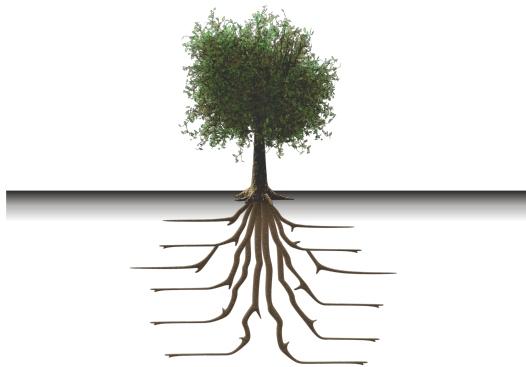
ATR & Statistical monitoring



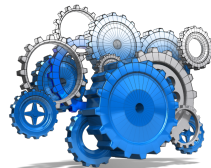
Findings from ATR



Trending across sites or trials



Root-cause analysis



Processes, systems, standards and training



Patient

Conclusions

- Our perception of what constitutes good data quality is changing
- Collaboration between ATR and statistical monitoring activities will enable us to identify trends previously uncovered
- This collaboration will ultimately help us improve processes, training, systems and standards
- Everyone benefits - Novo Nordisk, sites and patients



Thank you

- Questions?

