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Society for Clinical Data Management
DATA DRIVEN

Improving data quality on Oncology trials through RBM

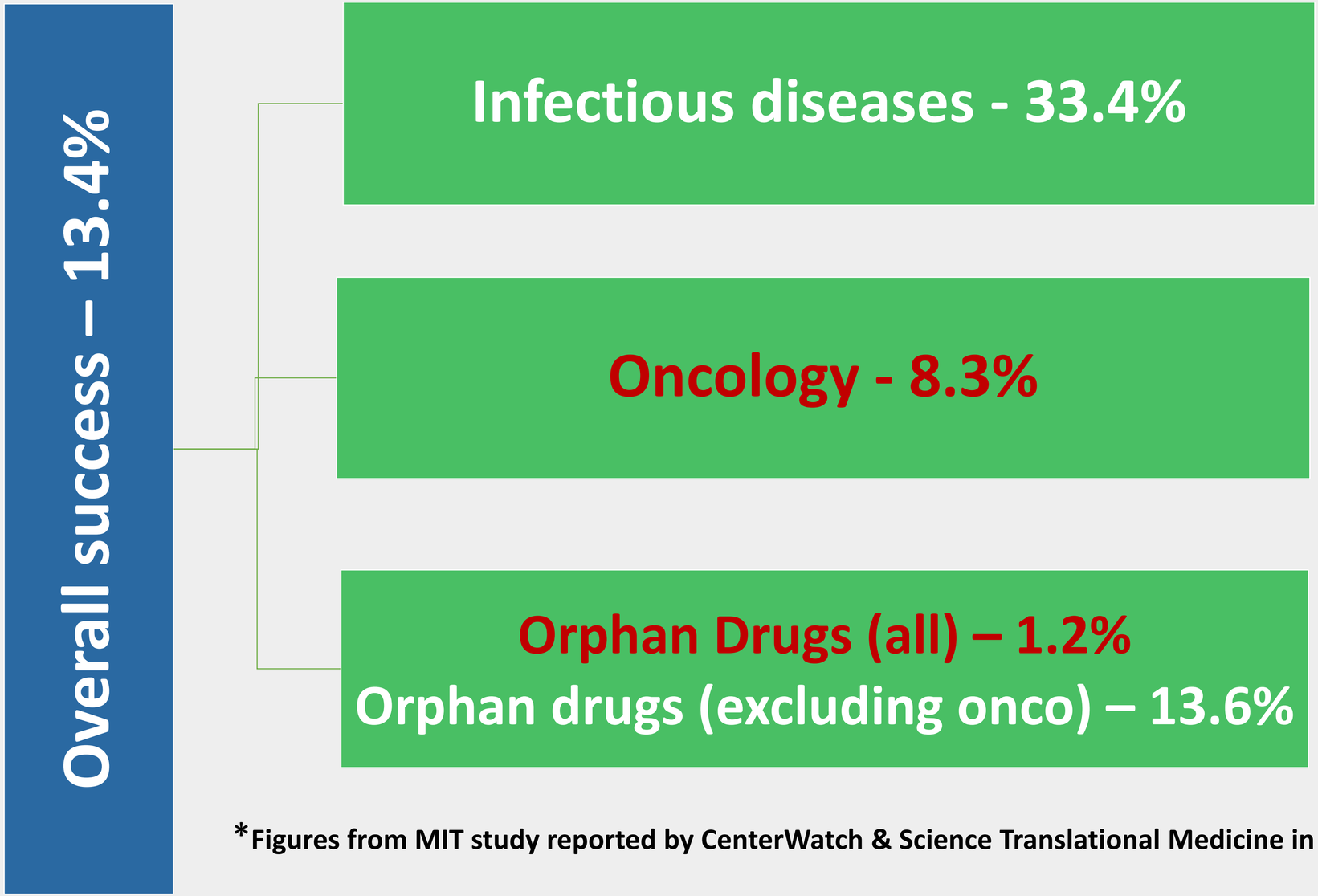
Case Studies

Society for Clinical Data Management
DATA DRIVEN

PPCE rely on us

TABLE OF CONTENTS

Clinical Trial Success rates from First-in-Human to Regulatory Approval



*Figures from MIT study reported by CenterWatch & Science Translational Medicine in Feb 2018

Increasing Durations on Oncology trials

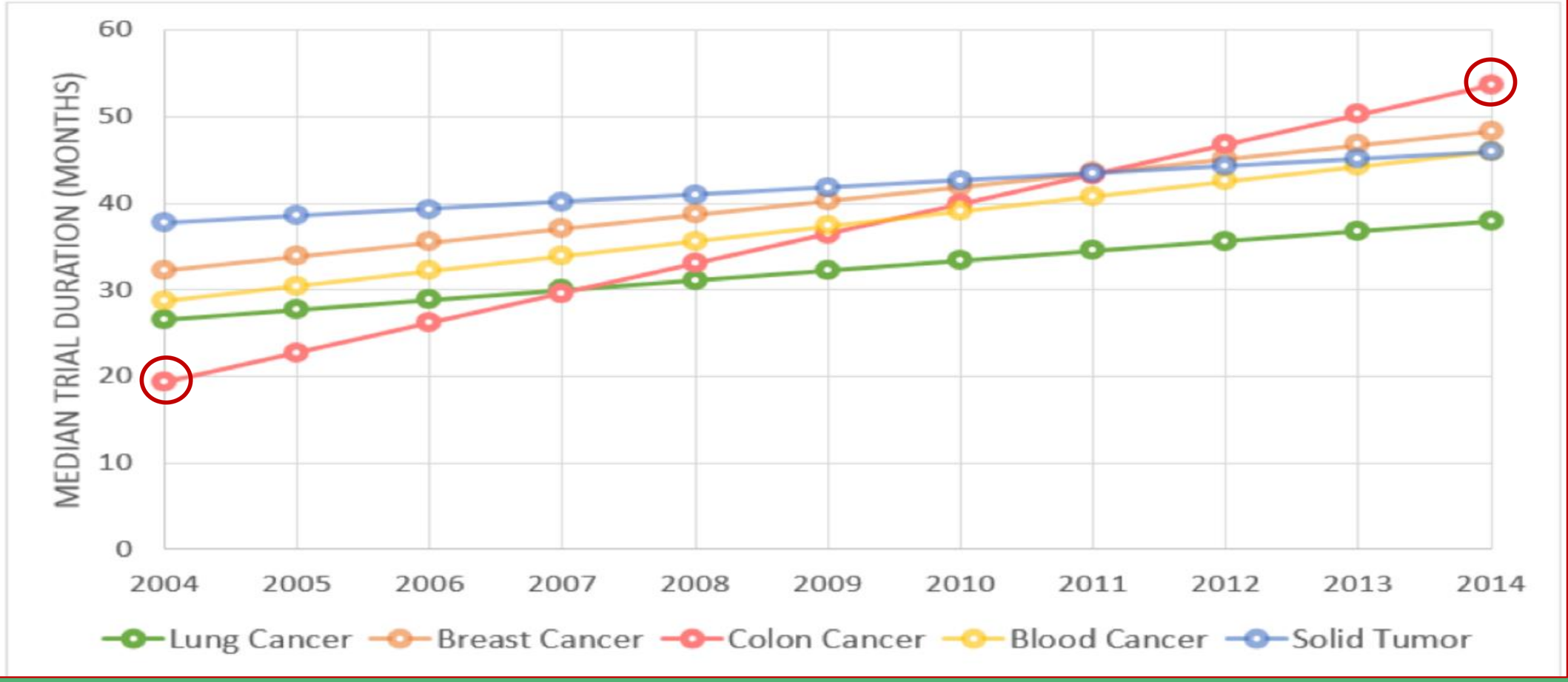
(From 23 to 39 months)

Figure 1: Median Trial Duration: Oncology Trials (Source: Karmadata)

*Published in Applied Clinical Trials

Increasing Durations on Oncology trials

Figure 2: Trendline Analysis of Oncology Trial Duration by Disease (Source: Karmadata)



*Published in Applied Clinical Trials

Increasing Durations on Oncology trials

Cancer type	Percentage increase in duration from 2002-2005
Colon	178%
Leukemia	60%
Breast	50%
Lung	42%
Solid Tumors	22%

*As per Applied Clinical Trials

Reasons for Increasing Durations

*White Paper by Moe Alsumidaie and Peter Shchiemann, Ph.D

- Delayed subject enrollment
- Increased procedural frequency
- Phase III & IV: Average Inclusion Criteria *3
- Phase III & 4: Adverse Events ↑122%
- Investigative sites ↑58%, randomized patients ↓18%
- Superior SOC treatments Vs. death as a primary endpoint

Reasons for Increasing Durations

*White Paper by KMR Group

- Increased complexity of trial designs
- More factors for testing: biomarkers, multiple diseases
- Increase in numbers of exploratory endpoints
- Operation and running of Clinical Trials

Reasons for Increasing Durations

*White Paper by KMR Group

1. Site selection and initiation

2. Site performance

3. Database design

4. Data cleaning and data review

Applying RBM:

Examples, Anecdotes, Case studies

The case for Good Preparation to mitigate risks through the course of a study

1. Risk-based Selection criteria

and

Initiation procedures

- Previous performance metrics available?
- Previous similar protocols?
- Familiar with use of RECIST criteria?
- Initiation involved all staff responsible for data capture at site? Stand-ins?
- Database design 100% ready at the time of initiation?

Site Performance Metrics

*Medidata Edge

Site Overview

Site Grade	Study Grade
B	A+
8	421
Total Patients	Total Patients
2.62	2.38
Percent Discrepancies	Percent Discrepancies
3.48	3.27
Average Discrepancy	Average Discrepancy

High Risk Patients

Patient	% Discrepancies
4561002	5.16
4561008	4.35
4561007	4.18
4561010	3

The case for Quantification & Vizualization to support Risk Monitoring

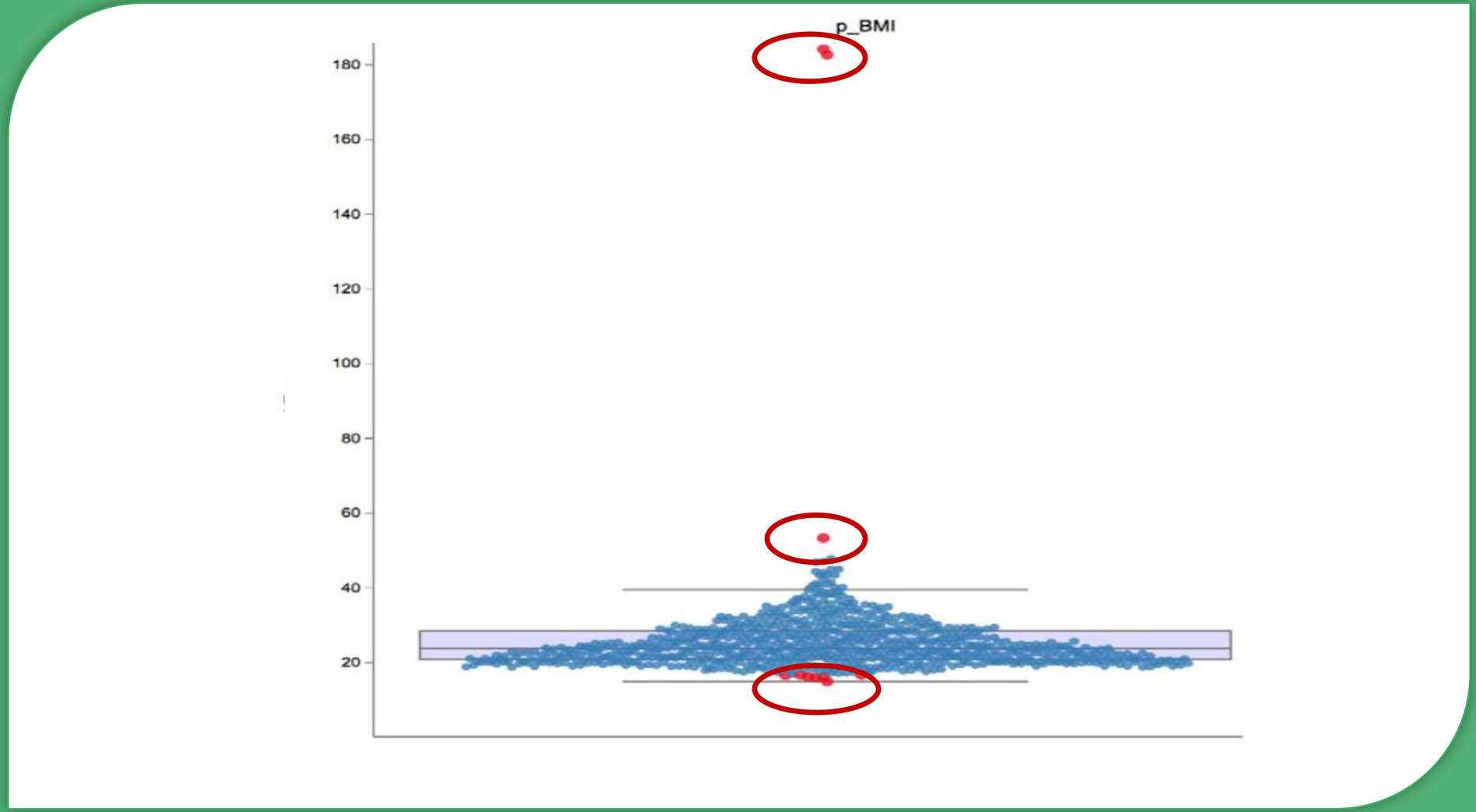
2. Mitigating Site Performance Risks

- Metrics & Monitoring
- Quantification & Benchmarking
- Feedback loop for course correction
- Regular Refresher training

Site Performance Metrics

BMI outliers

*Medidata Edge



Site Performance Metrics

Date comparison discrepancies

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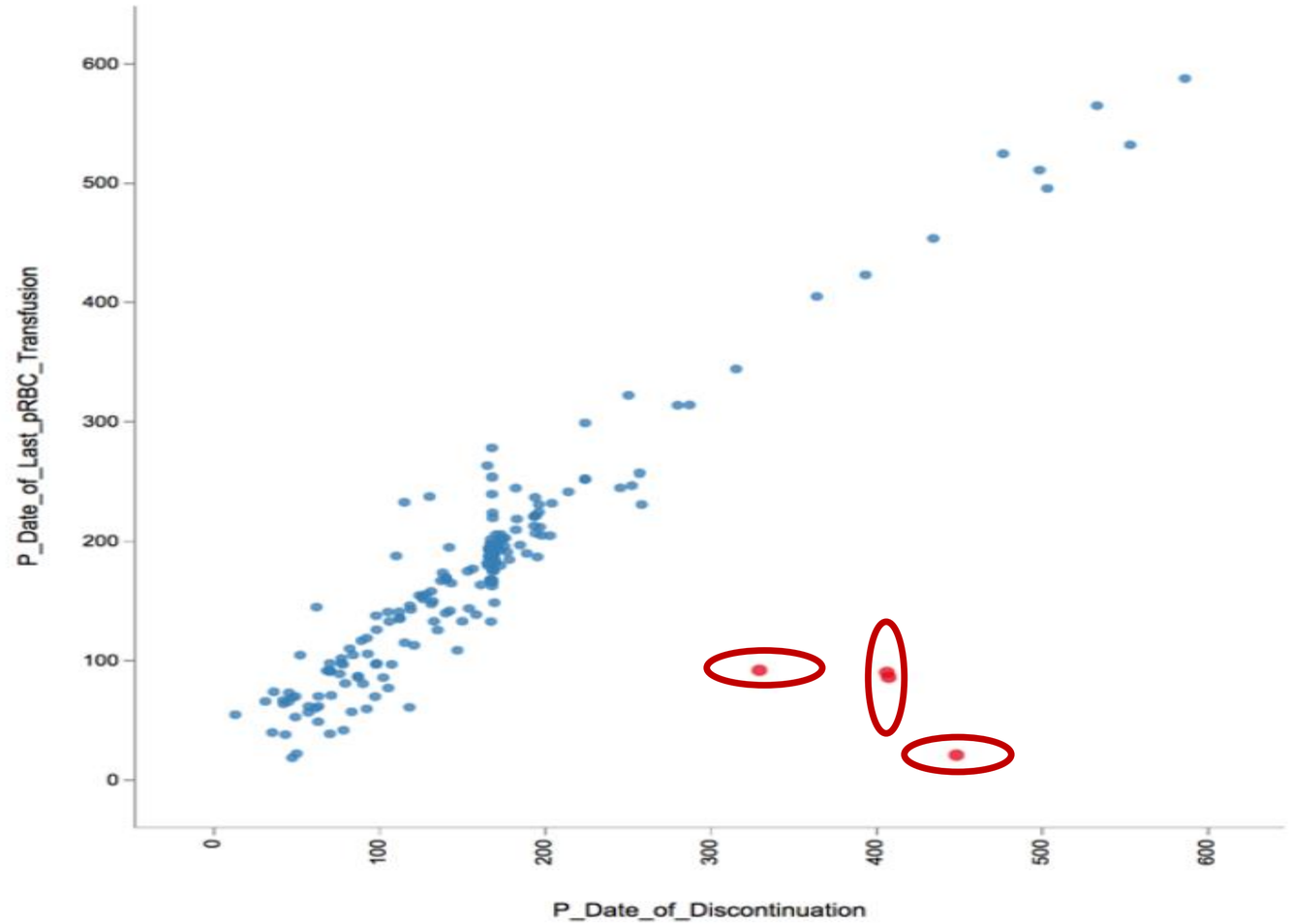


The case for subject matter experts at Risk Assessment stages

3. Optimizing Database Design to mitigate Data Quality risks

- User friendly design
- Clear Data Capture instructions
- All options available to support clean data
- Validation of adherence to RECIST criteria, such as:
  - Computation of OS and PFS
  - Consistency of lesions sequence

Case Study 1: Optimizing Database Design - NTL

RADIOLOGICAL ASSESSMENT SCREENING (1)

- Radiological Assessmen
- Tumour Assessment - Target Lesions
- Tumour Assessment - Non-Target Lesions (Screening)

CRF History

0202003 - Tumour Assessment - Non-Target Lesions (Screening)

Treatment Week	00
Were non-target lesions present at Screening?	Yes
Date of Tumour Assessment	04 JUL 2016

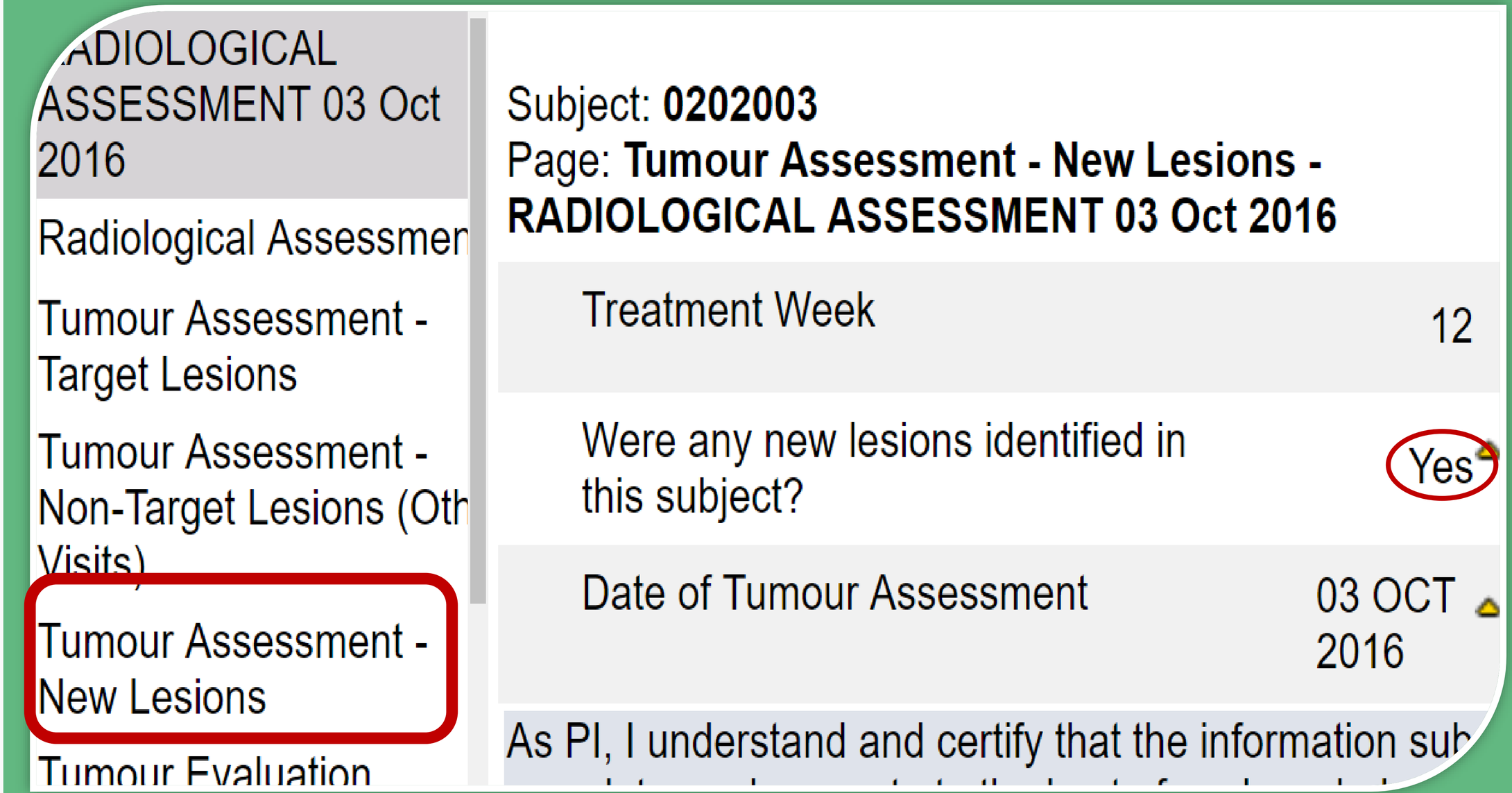
#	Lesion Number	Site	Method of assessment
1	01	MEDIASTINAL LYMPH NODES	CT scan
2	02	POSTERIOR MEDIASTINAL LYMPH NODE	CT scan
~~3~~	~~03~~	~~LUNG METASTASES, BOTH LUNGS~~	~~CT scan~~

Case Study 1:Optimizing Database Design - NTL

- RADIOLOGICAL ASSESSMENT 03 Oct 2016
- Radiological Assessmen
- Tumour Assessment - Target Lesions
- Tumour Assessment - Non-Target Lesions (Oth Visits)
- Tumour Assessment - New Lesions
- Tumour Evaluation
- CRF History

2	02	POSTERIOR MEDIASTINAL LYMPH NODE	Present	CT scan
~~3~~	~~03~~	~~LUNG METASTASES, BOTH LUNGS~~	~~Unequivocal progression~~	~~CT scan~~
~~4~~	~~04~~	~~MULTIPLES LIVER METASTASES~~	~~Unequivocal progression~~	~~CT scan~~
~~5~~				
6	03	LT PORTAL VEIN THROMBOSIS (NEW LESION)	Present	CT scan

Case Study 1: Optimizing Database Design - NTL



Case Study 2: Optimizing DB Design – Lymph Node as TL

ıge: Tumour Assessment - Target Lesions - RADIOLOGICAL ASSESSMENT SCREENING (1)

Treatment Week	00
Date of Tumour Assessment	06 DEC 2016

#	Lesion Number	Site	Method of assessment	Longest diameter
1	1	S8 HEPATIC MASS	CT scan	44 mm
2	2	S7 HEPATIC NODULE	CT scan	17 mm
3	3	CELIAC TRUNK LYMPH NODES:	CT scan	40.0 mm
4	4	RT PERICARDIAL LYMPH NODE	CT scan	49.0 mm

Sum of longest diameter	150.0 mm

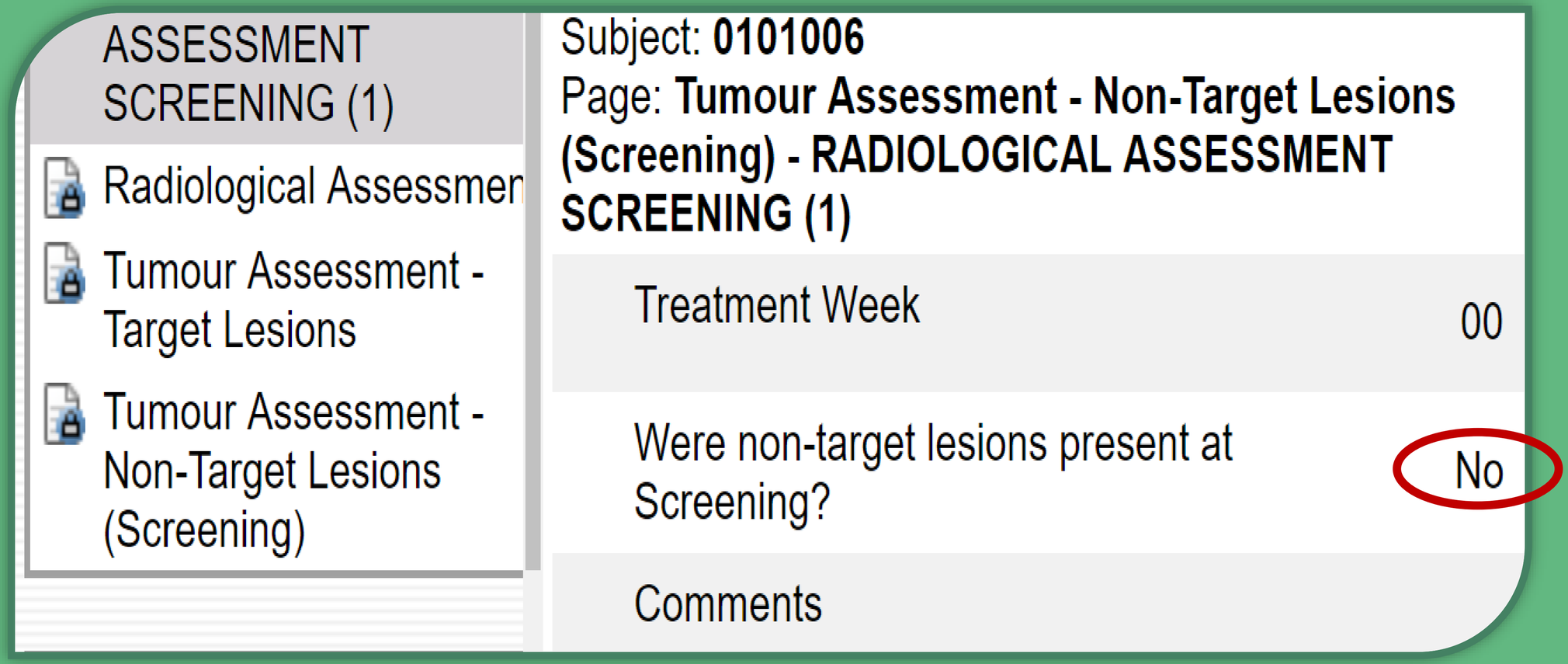
The case for Risk Assessment inputs in the QC plan

4. DM: Identifying QC parameters for real time course correction

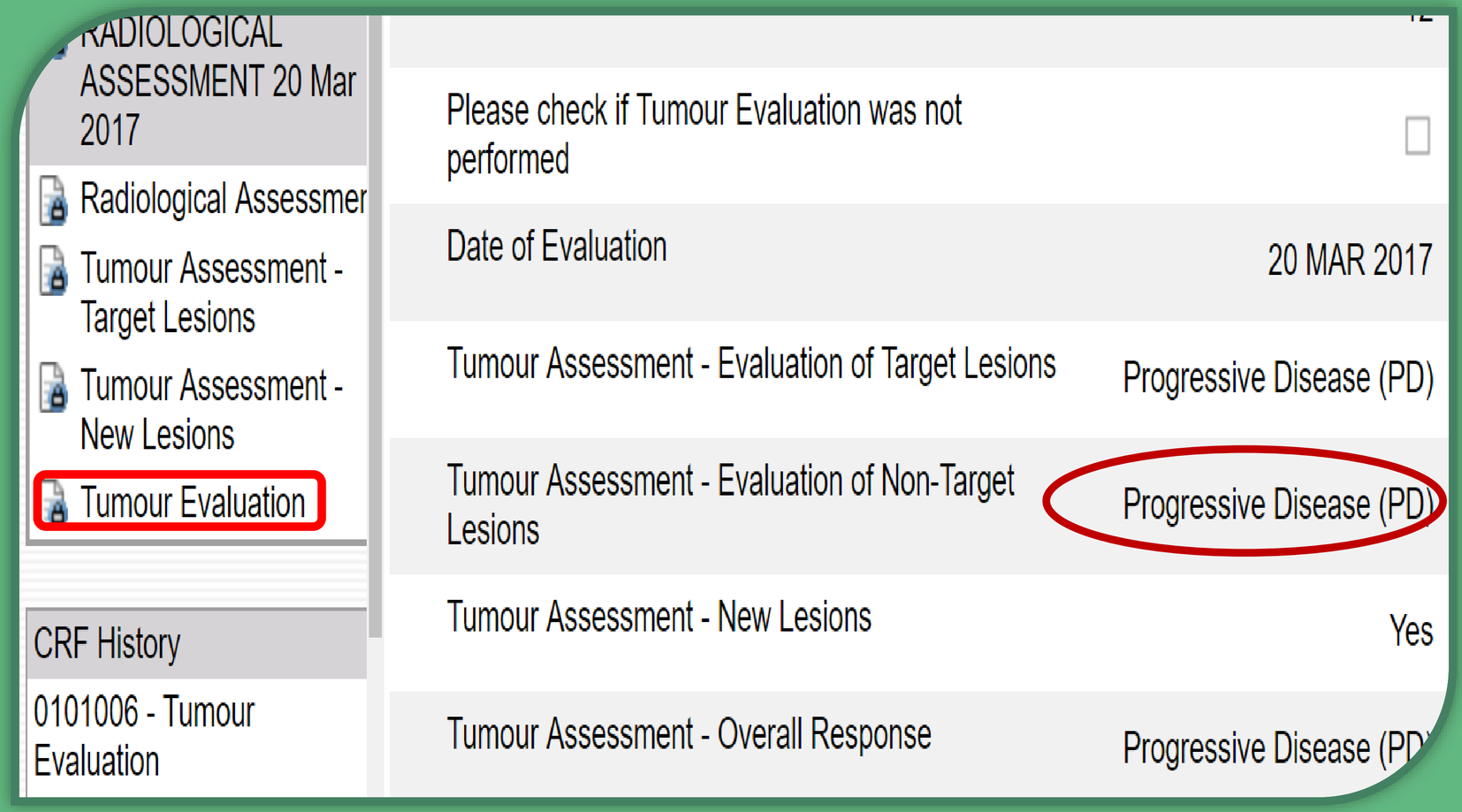
- Use historical data and experience to clearly identify Data Quality Risks
- List risk mitigation measures as check parameters in the QC plan
- **Develop Skill Matrices:**

  Training and evaluation of QC personnel prior to deployment on a study
- Ensure effectiveness/currency of the QC plan and RA through regular QA audits

Case Study 3: Optimizing Data Quality at DM



Case Study 3: Optimizing Data Quality at DM



Case Study 4: Optimizing Data Quality at DM

Adverse Events

CRF History

0102001 - Adverse Events

0102001 - Adverse Events Status

0102001 - Palliative Radiotherapy

4	BLOOD BILIRUBIN INCREASED	4 NOV 2015	Yes		GRADE 1	Not Related	Not Resolved
5	BLOOD BILIRUBIN INCREASED	19 NOV 2015	No	3 DEC 2015	GRADE 3	Possibly Related	Resolved
~~6~~	~~ASCITES~~	~~4 NOV 2015~~	~~No~~	~~16 NOV 2015~~	~~GRADE 2~~	~~Not Related~~	~~Resolved~~

Case Study 4: Optimizing Data Quality at DM

PRIOR AND CONCOMITANT MEDICATION AND THERAPIES (1)

Prior and Concomitant Medication and Therapie Status

Prior and Concomitant Medication and Therapie

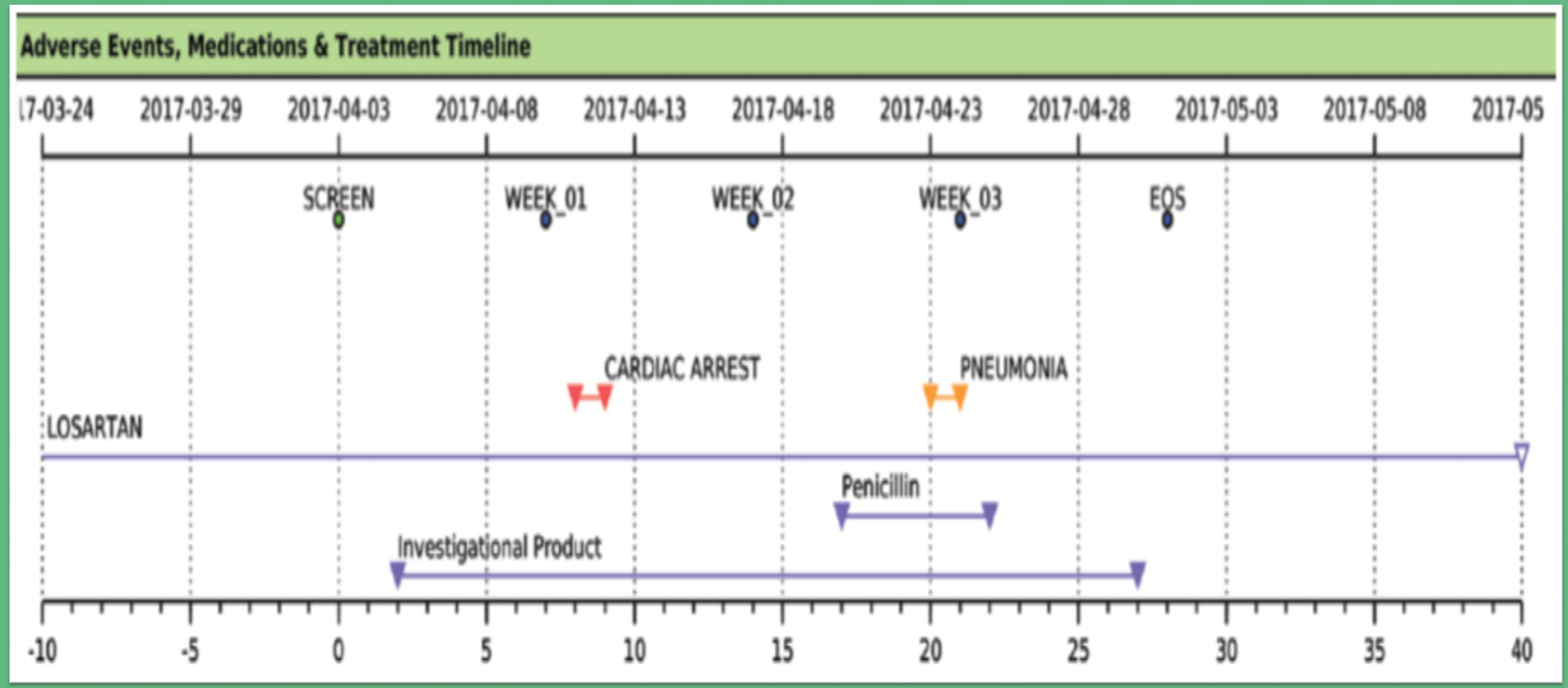
CRF History

0102001 - Prior and Concomitant Medication and Therapies

26	KONAKION (VITAMIN K)	MH8	10	mg (Milligram)	QD (every day)	IV (intravenous)	17 DEC 2015	No	17 DEC 2015
27	LACTULOSE SYRUP	MH5	10	mL (Milliliter; cm3)	TID (three times a day)	PO (oral)	6 NOV 2015	No	6 NOV 2015
28	LACTULOSE SYRUP	MH5	10	mL (Milliliter; cm3)	QD (every day)	PO (oral)	15 NOV 2015	No	15 NOV 2015
29	FUROSEMIDE	AE6	40	mg (Milligram)	QD (every day)	IV (intravenous)	6 NOV 2015	No	6 NOV 2015
30	LORATIDINE	AE18	10	mg (Milligram)	PRN (as needed)	PO (oral)	18 DEC 2015	No	20 DEC 2015
	LORAZEPAM	PROPHYLAXIS			QD (every		20		20

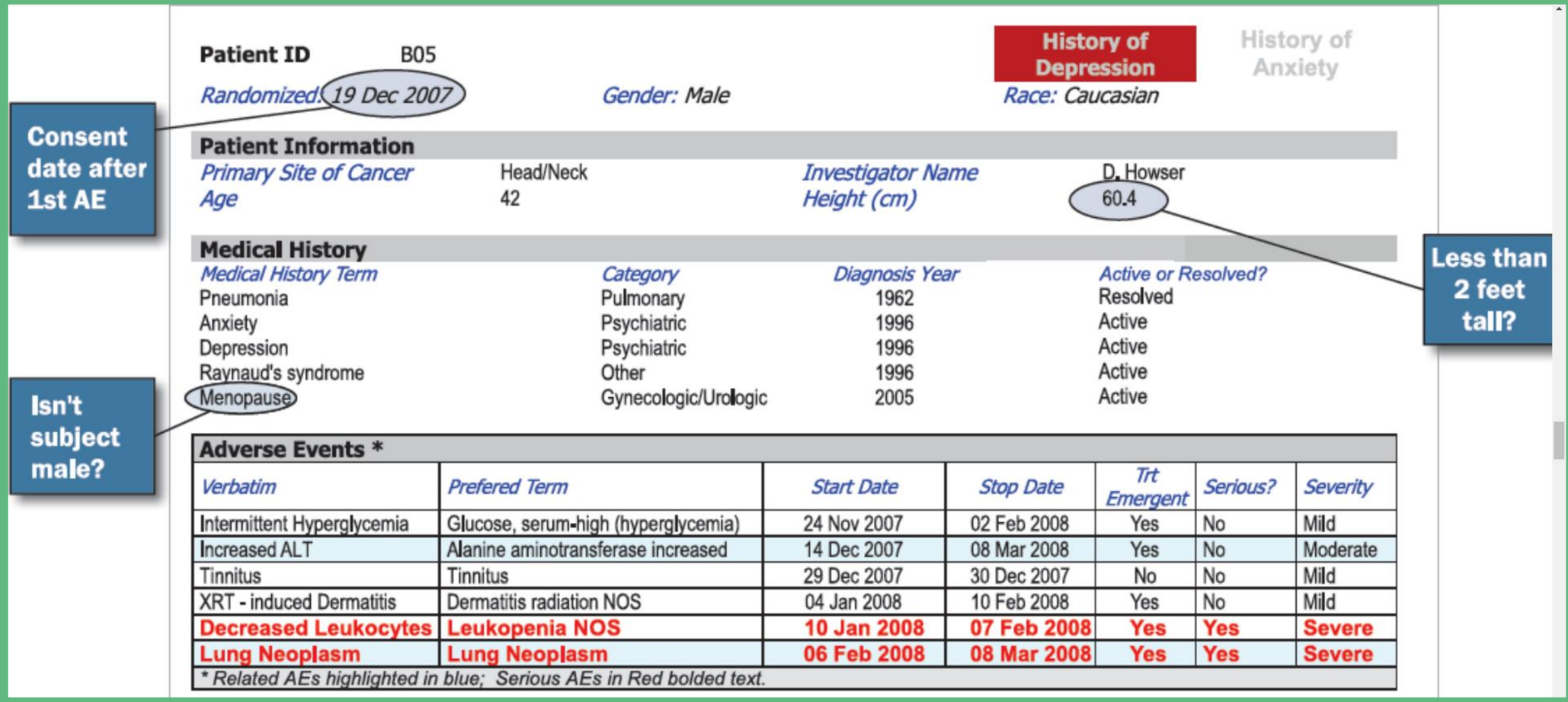
The case for Analytics to support your RBM approach

*Medidata Edge



The case for Analytics to support your RBM approach

*Medidata Edge



Patient ID B05

Randomized: 19 Dec 2007 *Gender:* Male *Race:* Caucasian

History of Depression

History of Anxiety

Consent date after 1st AE

Patient Information

Primary Site of Cancer	Head/Neck	*Investigator Name*	D. Howser
Age	42	*Height (cm)*	60.4

Less than 2 feet tall?

Medical History

Medical History Term	*Category*	*Diagnosis Year*	*Active or Resolved?*
Pneumonia	Pulmonary	1962	Resolved
Anxiety	Psychiatric	1996	Active
Depression	Psychiatric	1996	Active
Raynaud's syndrome	Other	1996	Active
Menopause	Gynecologic/Urologic	2005	Active

Isn't subject male?

Adverse Events *

Verbatim	*Prefered Term*	*Start Date*	*Stop Date*	*Trt Emergent*	*Serious?*	*Severity*
Intermittent Hyperglycemia	Glucose, serum-high (hyperglycemia)	24 Nov 2007	02 Feb 2008	Yes	No	Mild
Increased ALT	Alanine aminotransferase increased	14 Dec 2007	08 Mar 2008	Yes	No	Moderate
Tinnitus	Tinnitus	29 Dec 2007	30 Dec 2007	No	No	Mild
XRT - induced Dermatitis	Dermatitis radiation NOS	04 Jan 2008	10 Feb 2008	Yes	No	Mild
Decreased Leukocytes	**Leukopenia NOS**	**10 Jan 2008**	**07 Feb 2008**	**Yes**	**Yes**	**Severe**
Lung Neoplasm	**Lung Neoplasm**	**06 Feb 2008**	**08 Mar 2008**	**Yes**	**Yes**	**Severe**

** Related AEs highlighted in blue; Serious AEs in Red bolded text.*

The case for Analytics to support your RBM approach

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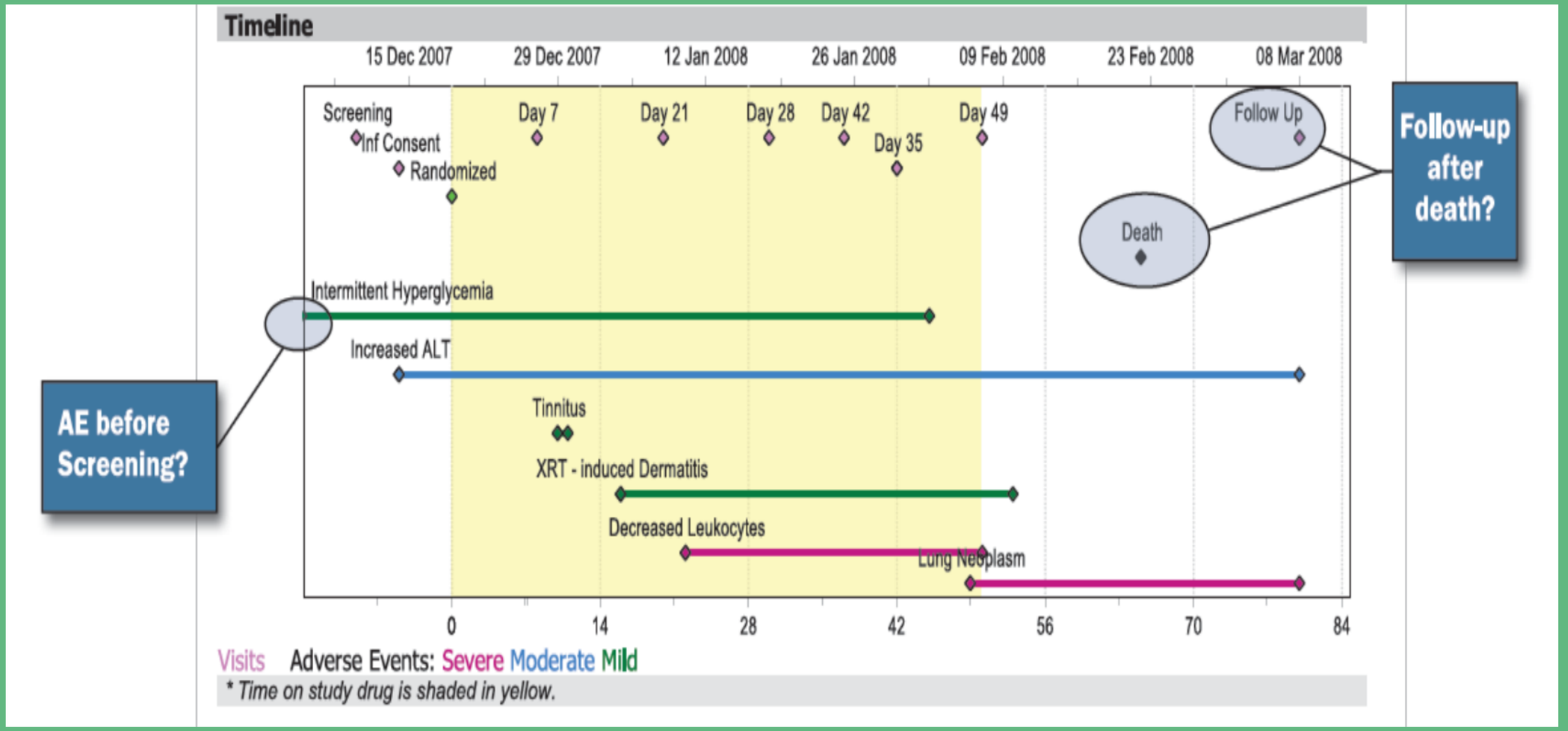

The case for Analytics to support your RBM approach

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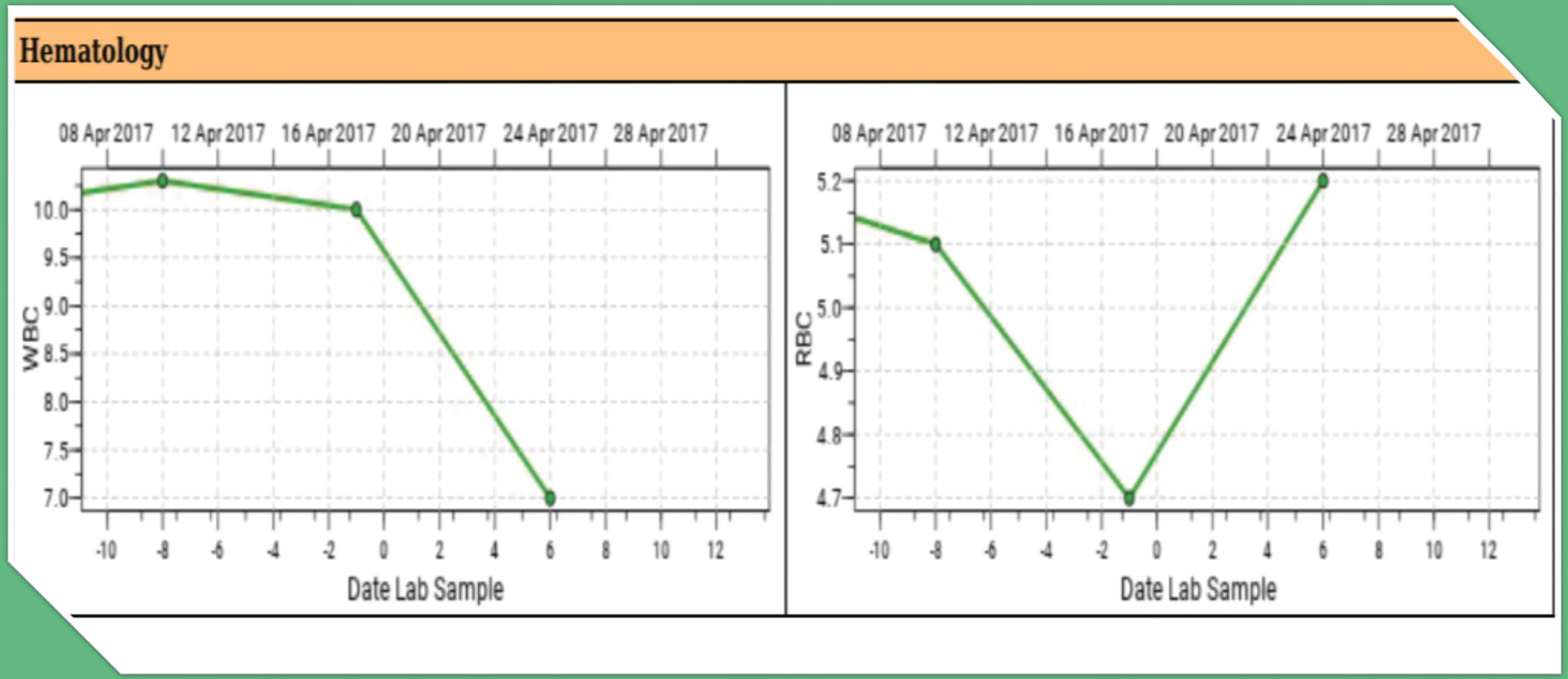

Begin at the beginning	• Start with the Risk Assessment!
Make it practical	• Integrate into trial monitoring parameters
Educate on risk parameters	• Use QC to ensure currency of your RA
Visualize to Quantify	• Use analytics to measure whether risks are under control
Use data real-time	• Use data trends for fact-based decision making

QUESTIONS?

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