



Real World observational studies and the challenges in data collection

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Disclaimer: The views and opinions expressed in this presentation belong solely to the presenter and do not necessarily reflect those of the presenter's employer, organization, committee, or any other group or individual. The purpose of this presentation is to highlight the data collection challenges encountered while working with primary databases in Non-interventional studies. No data or confidential information belonging to Novo Nordisk has been utilized in this presentation.

What are Non-interventional studies

Primary and Secondary data collection

Characteristics of RCT and RWE studies

Challenges in data collection and handling

What are Non-interventional studies?



Source: Google; For representation purposes only

A NIS* is a study where:

- The study product is prescribed in a manner consistent with routine clinical care.
- The prescription of the medicine is clearly separated from the decision to include the patient in the study.
- No additional or diagnostic or monitoring procedures shall be applied, and epidemiology methods shall be used.

NIS - Non interventional study

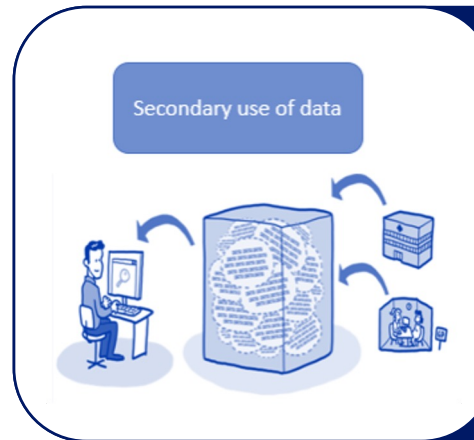
* The full definition of a Non-interventional Study comes from the European Commission in: Clinical Trials - Directive 2001/20/EC

Primary and Secondary data collection

Observational studies that uses data collected from patients and health professionals for



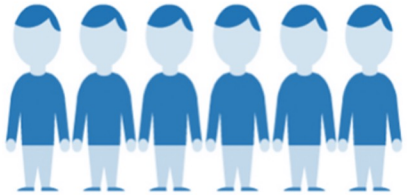
Study Purpose are **Primary data**, where the data collected is directly obtained from the study participants.



Other than study purpose are **Secondary data collection**, where the data collected is from existing data that has been previously collected.

Characteristics of RCT and RWE studies

RCT



- ☐ Strict inclusion and exclusion criteria and hence Homogeneous population
- ☐ Standardized treatment
- ☐ Low risk of bias
- ☐ Better adherence and persistency to the allocated treatment
- ☐ Treatment efficacy

What happens under ideal conditions?

RWE



- ☐ Few inclusion and exclusion criteria and hence Heterogeneous population
- ☐ Routine clinical care
- ☐ High risk of bias (but depends)
- ☐ Adherence and persistency are less to the allocated treatment
- ☐ Treatment effectiveness

What happens when no one is watching?

RCT : Randomized clinical trials RWE : Real world Evidence

Source: Google ; For representation purposes only

Reference: [Real-world Evidence versus Randomized Controlled Trial: Clinical Research Based on Electronic Medical Records - PMC \(nih.gov\)](#)

Challenges in data collection and handling

Inform consent visit

Late identified Screen failures

Long in-study duration

Intermediate visit



Informed consent visit



Scenario 1:

- V1 visit is the “Informed consent and treatment initiation visit V1*”
- Informed Consent can be signed any day prior to the visit or on the day of the “Informed Consent and Treatment Initiation visit (V1)” provided that the patient has received verbal and written information and has had sufficient time to consider his/her participation.

	Informed Consent and treatment initiation visit	Intermediate visits according to local clinical practice	End of study visit
Visit number	V1	V2.X	V3
Time of visit (weeks)	0	1-33	34-44

What happens ?

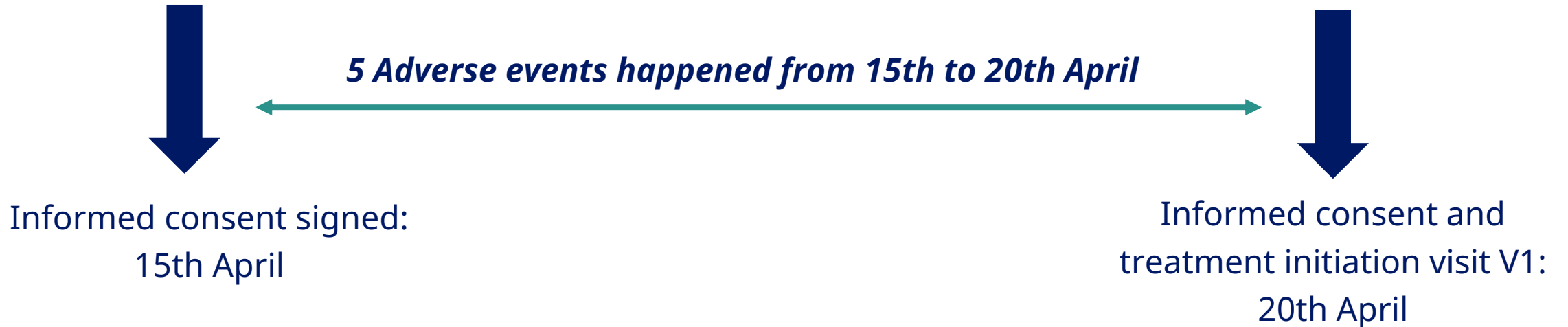
The reference start date for the in-study observation period is the date of the “Informed Consent and Treatment Initiation Visit V1” and participant signs IC prior to study visit V1.

**Consequently, both IC and Treatment initiation should happen on same day at V1*

IC- Informed consent

Informed consent visit

Case: Informed consent signed prior to “Inform consent and treatment initiation visit V1”



Informed consent visit



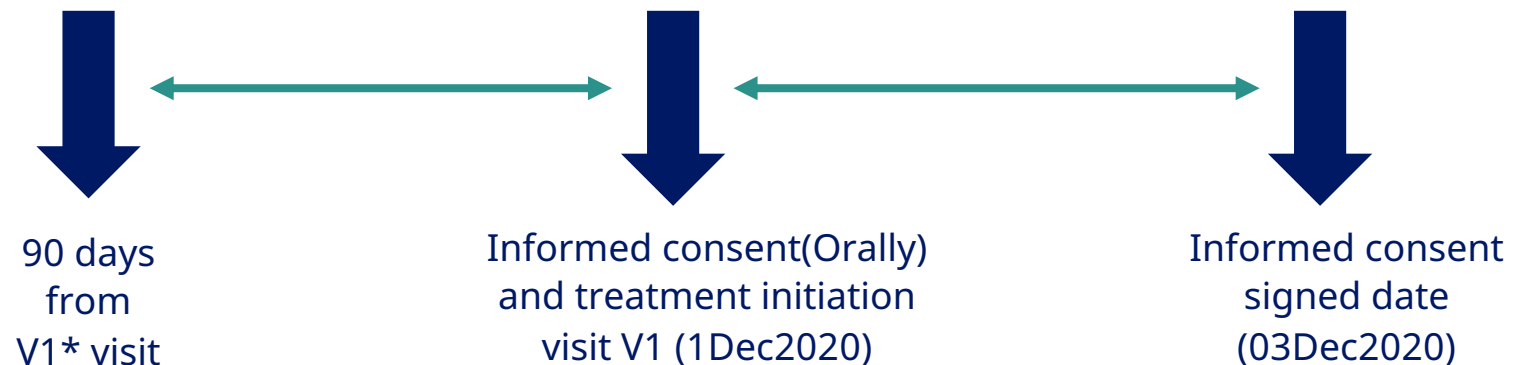
Scenario 2:

Informed consent obtained Orally at V1 visit which is “Informed consent and treatment initiation visit V1” and signed later with different date from V1 visit.

What happens ?

Baseline measurements collected withing 90 days from “V1* visit” for some parameters in the study and IC signed later to V1 visit.

Considering actual IC date as reference start date will tend to lose some assessments at baseline



* Informed consent and treatment initiation visit V1

IC- Informed consent

Informed consent visit

Considering different scenarios in NIS , what is the appropriate reference date ?

Reference date = Minimum(V1*date ,Informed consent date)

Late identified Screen failures



Source: Google; For representation purposes only

- In NIS studies screening is not strictly adhered
- Patients enter the study without meeting some IE* criteria
- Later identified as Screen failures
- Excluded from analysis

Scenario: Study requires patients to be naïve to some medication as per study IE* criteria

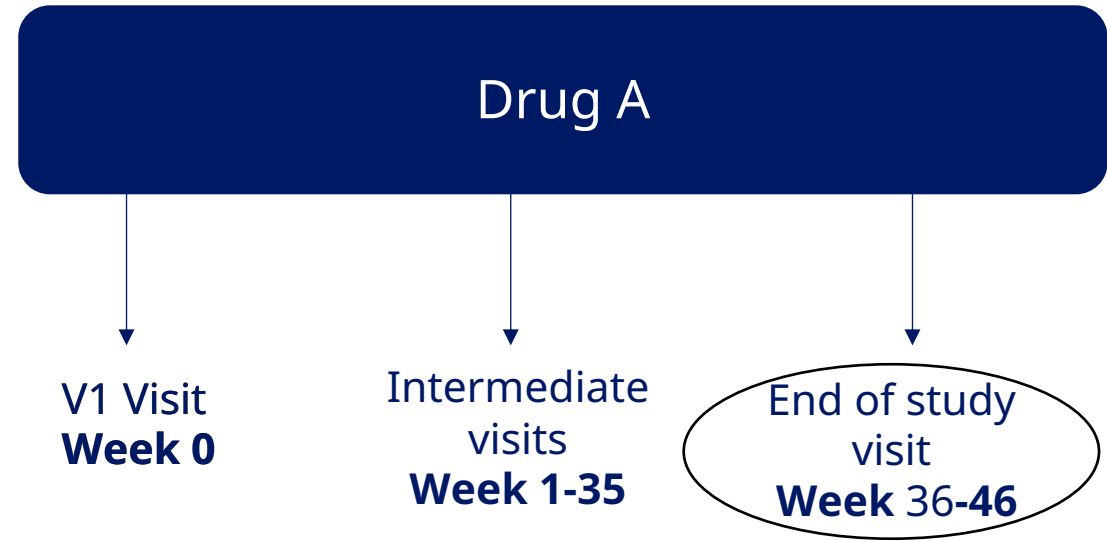
Early surveillance by Medical specialist

Long in-study duration

Scenario: EOS visit for couple of early enrolled patients collected until the **LPLV** of the last enrolled subjects leading to long in-study duration

To ensure patients adhere to the protocol study duration and to efficiently use data collected

- Protocol defines window for the EOS visit instead of keeping it fixed visit.
- Protocol clearly states that duration should be “X weeks considering **individual patients**” instead of “Duration should be X for the study”.



EOS: End of study

LPLV: Last patient last visit

Intermediate visits

- Patients can come for Intermediate visits any number of times i.e., no fixed visits.
- Data may not be collected at the same time-point for all patients

Due to this ...

- Fixed visits in summary table
- Completeness of data is impacted

To account for missing data, statisticians used **MMRM** model in their statistical analysis.

	Inform Consent and treatment initiation visit	Intermediate visits according to local clinical practice	End of study visit
Visit number	V1	V2.X	V3
Time of visit (weeks)	0	1-33	34-44

Laboratory parameters - summary - full analysis set			
Total			
Total Cholesterol			
V1			
N			x
Mean (SD)			xx.x (XX.XX)
Median (IQR)			xx.x (XX.XX)
Min ; Max			XX ; XX
V3			
N			x
Mean (SD)			xx.x (XX.XX)
Median (IQR)			xx.x (XX.XX)
Min ; Max			XX ; XX
Tryglycerides			
V1			
N			x
Mean (SD)			xx.x (XX.XX)
Median (IQR)			xx.x (XX.XX)
Min ; Max			XX ; XX
V3			
N			x
Mean (SD)			xx.x (XX.XX)
Median (IQR)			xx.x (XX.XX)
Min ; Max			XX ; XX

Thank you !



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