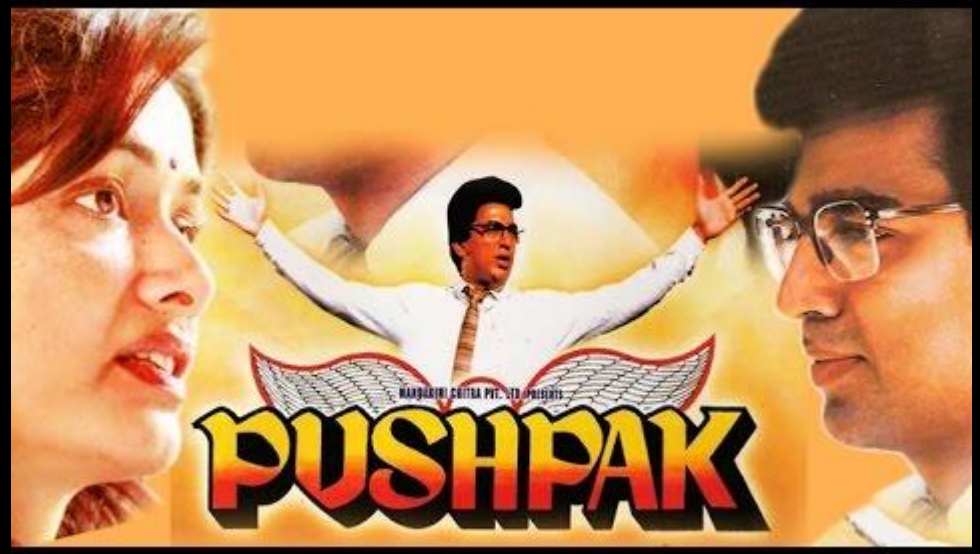
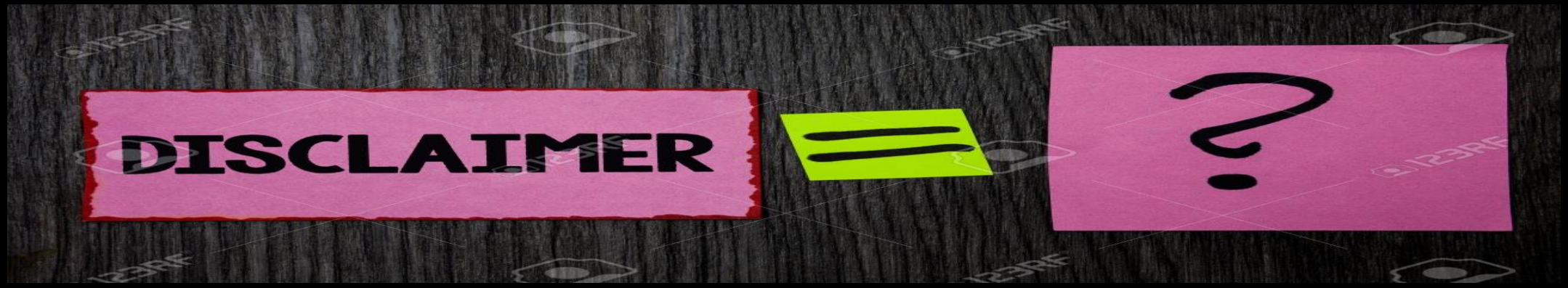
Observational study: Journey of film without dialogues into Super-hit movie



Seema Shah

30-Mar-2019



All facts/techniques appearing in the slides are from my industrial experiences . Any resemblance to your facts/techniques, is not coincidental/may be we have worked together/discussed.

“Data Science (Past, Present, Future)"

Status on Facebook

In Reality

Investigator initiated studies

Ethical independent clinical research conducted by qualified third-party investigators

- to ensure we better understand the benefit/risk profile of therapies, as well as to explore new opportunities to address unmet medical needs.

What is an Observational study?

An observational study is a type of study in which individuals are observed or certain outcomes are measured in an only observational manner.

No attempt is made to affect the outcome (for example, no treatment is given). It is also reference to as a non-interventional study.

- Utilize data that are already routinely collected as part of patient's medical care
- Patient does not have to attend for study visit or fill in any questionnaires (Depends upon design of study)
- Laboratory testing performed according to clinical need – will be more frequent if patient is ill or requires investigation

Difference between

Observational study

Clinical trials

Observational Studies

Checks

- Study visits
- Data entry
- Representative?
- Loss to follow-up
- Data quality

Observational database

- As and when patient attends for care
- Often electronic transfer of data
- Often includes all patients – therefore representative
- May be difficult to assess as some patients attend infrequently
- Difficult to regulate

Challenges for Data management

- Milestones estimation
- Cleaning of data
- Partial dates or missing data: Retrospective data
- Structural changes (OC Database vs eCRF)
- Delay in Site responses

Challenges for Statistician

- Statistical Analysis Plan
- No visit schedule
  - Visit window
  - Extended/long intervals
- Unstructured data
- Can we simulate/generate data using statistical model: Yes, we can but in agreement with clinics; however we should know data and behavior of data (distribution)

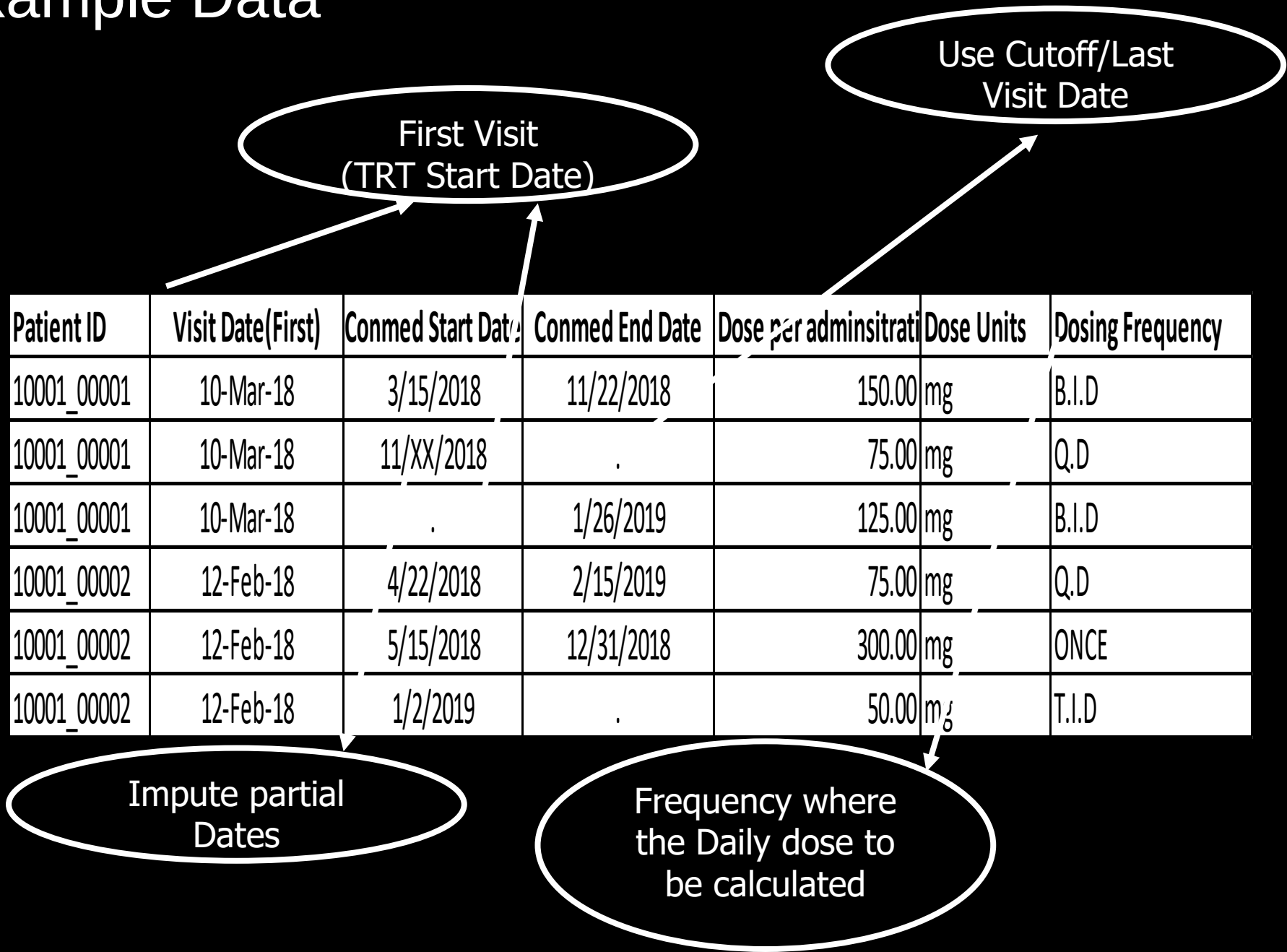
Challenges for Statistical SAS programmer

- Program specifications
- No Drug Administration Record panel (DAR)
- Partial dates and derivation of duration

Non interventional studies

- No DAR panel
  - Exposure for NIS from Concomitant for a specific drug
- AE reporting
  - TEAE?
  - SAE?
  - AESI?

Example Data



Patient ID	Visit Date(First)	Conmed Start Dat	Conmed End Date	Dose per adminsitrati	Dose Units	Dosing Frequency
10001_00001	10-Mar-18	3/15/2018	11/22/2018	150.00	mg	B.I.D
10001_00001	10-Mar-18	11/XX/2018	.	75.00	mg	Q.D
10001_00001	10-Mar-18	.	1/26/2019	125.00	mg	B.I.D
10001_00002	12-Feb-18	4/22/2018	2/15/2019	75.00	mg	Q.D
10001_00002	12-Feb-18	5/15/2018	12/31/2018	300.00	mg	ONCE
10001_00002	12-Feb-18	1/2/2019	.	50.00	mg	T.I.D

Complications

- Concomitant data is always a tough to read one.
- First & Foremost we need to identify whether it is a prior/Conmed or Prior & Conmed.
- We only fetch the records -Concomitant (during the study period)
- Out of which based on the dosing frequency we have to re-derive the full cycle of the dosing happened (between Start & End dates)
- Frequencies (QD, ONCE) – Once daily
- Frequencies (B.I.D) – Twice daily
- Frequencies (T.I.D) – Thrice daily

- For the below example patient received medication from 15-Mar-2018 till 22-April-2018 (39days of duration)
- Dosing frequency is MWFS (Mon, Wed, Fri, Sun – 50 mg) & TTS (Tue, Thu & Sat - 100mg). We need to program to get the weekday information starting from 15-Mar till 22-Apr, apply the dose accordingly & calculate cumulative dose & Average daily dose so on.
- All other dosing information as selected as per the frequencies specified.

Patient ID	Conmed Start Date	Conmed End Date	Dose	Dose Units	Dosing Frequency	Other, Specify	CMD_ST	Day	Dose_Given	Cumulatvie	AVG daily dose
10001_00001	3/15/2018	4/22/2018	150.00	mg	OTHERS	MWFS-50mg TTS-100mg	3/15/2018	Thursday	100	100	
10001_00001	3/15/2018	11/22/2018	150.00	mg	OTHERS	MWFS-50mg TTS-100mg	3/16/2018	Friday	50	150	
10001_00001	3/15/2018	11/22/2018	150.00	mg	OTHERS	MWFS-50mg TTS-100mg	3/17/2018	Saturday	100	250	
10001_00001	3/15/2018	11/22/2018	150.00	mg	OTHERS	MWFS-50mg TTS-100mg	3/18/2018	Sunday	50	300	
							.			.	
							.			.	
10001_00001	3/15/2018	11/22/2018	150.00	mg	OTHERS	MWF-50mg TTS-100mg	4/22/2018	Sunday	50	2800	**71.7949**

References

- Google surfing for all images
- https://www.roche.com/research_and_development/who_we_are_how_we_work/investigator-initiated-studies-portal.htm
- https://www.novartis.com/sites/www.novartis.com/files/novartis-investigator-initiated-trials.pdf
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530977/
- https://www.ncbi.nlm.nih.gov/books/NBK11597/