



Shaping the Future of
Drug Development

Visualizing and Cleaning Safety data to aid Causality Assessment

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- Introduction
- Causality Assessment in Pharmacovigilance(PV)
- Methods & Results using R
- Conclusions

- Unsolicited (spontaneous) Individual Case Safety Reports (ICSRs) is one of the main sources of safety data to perform analytics/ causality assessment for Signal detection and Aggregate reports.
- Such spontaneously reported cases usually do not have enough information for a robust causal assessment.
- This kind of data is large and “dirty”, this being the rule rather than an exception
- Wrangling of such data by Safety Physicians and Scientists often consumes 60-70% of their time.

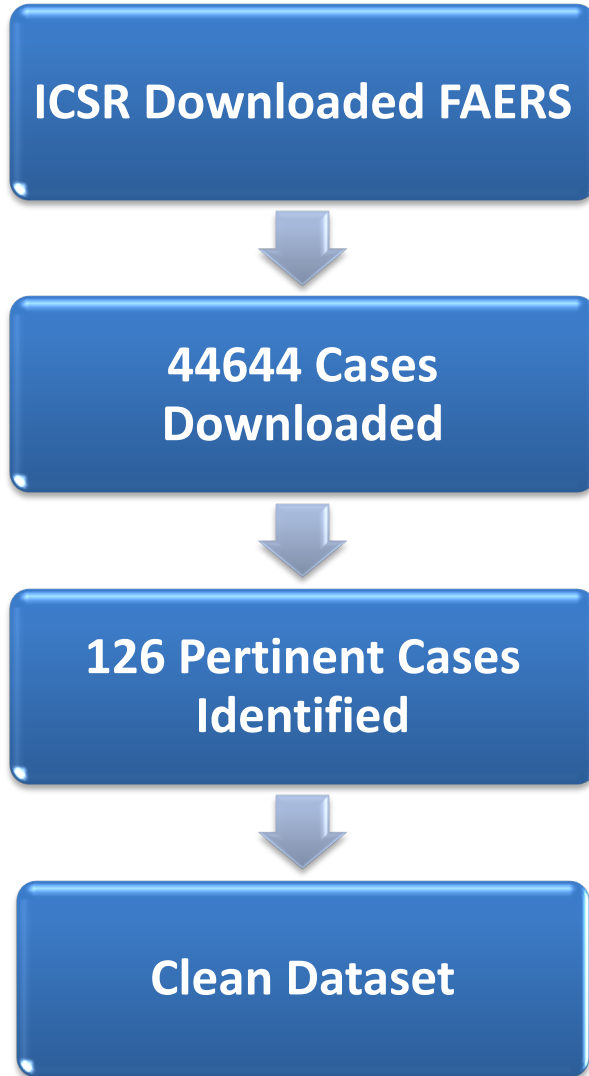
Causality Assessment in PV

- Causality assessment (CA) is the assessment of a relationship between a drug treatment and the occurrence of an adverse event.
- The popular method of causality assessment in pharmacovigilance is loosely based on the Hill criteria.
- The following parameters-strength of association, temporality, consistency, theoretical plausibility, coherence, specificity in the causes, dose response relationship, experimental evidence, analogy.

Common Criteria considered for Causality Assessment in PV

- Time to Onset (TTO): This determines the time taken for the event to occur after the drug is consumed.
- Concomitant Medication (ConMed): Medication consumed by patients along with suspect product are called concomitant medication.
- Medical History/Co-morbidities (CoM/Med History): Medical history and co-morbidities are used to assess an alternate explanation for the adverse events reported.
- Dechallenge/Rechallenge (De/Rechll): The act of stopping the suspect medication of the adverse event is called dechallenge. If the medication is again introduces as therapy and the adverse event appears again is called a positive rechallenge.

Methods & Results using R



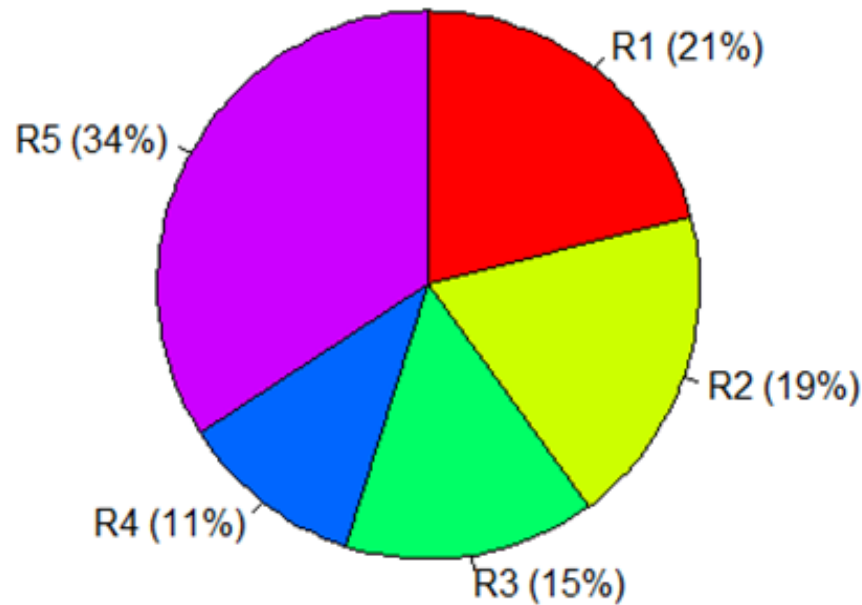
Zoledronic Acid 2013-2017 Q2

Using R Filtered Cases using SMQ “Hepatic Failure”

Proceeded to clean data using R

Methods & Results using R- Ranking

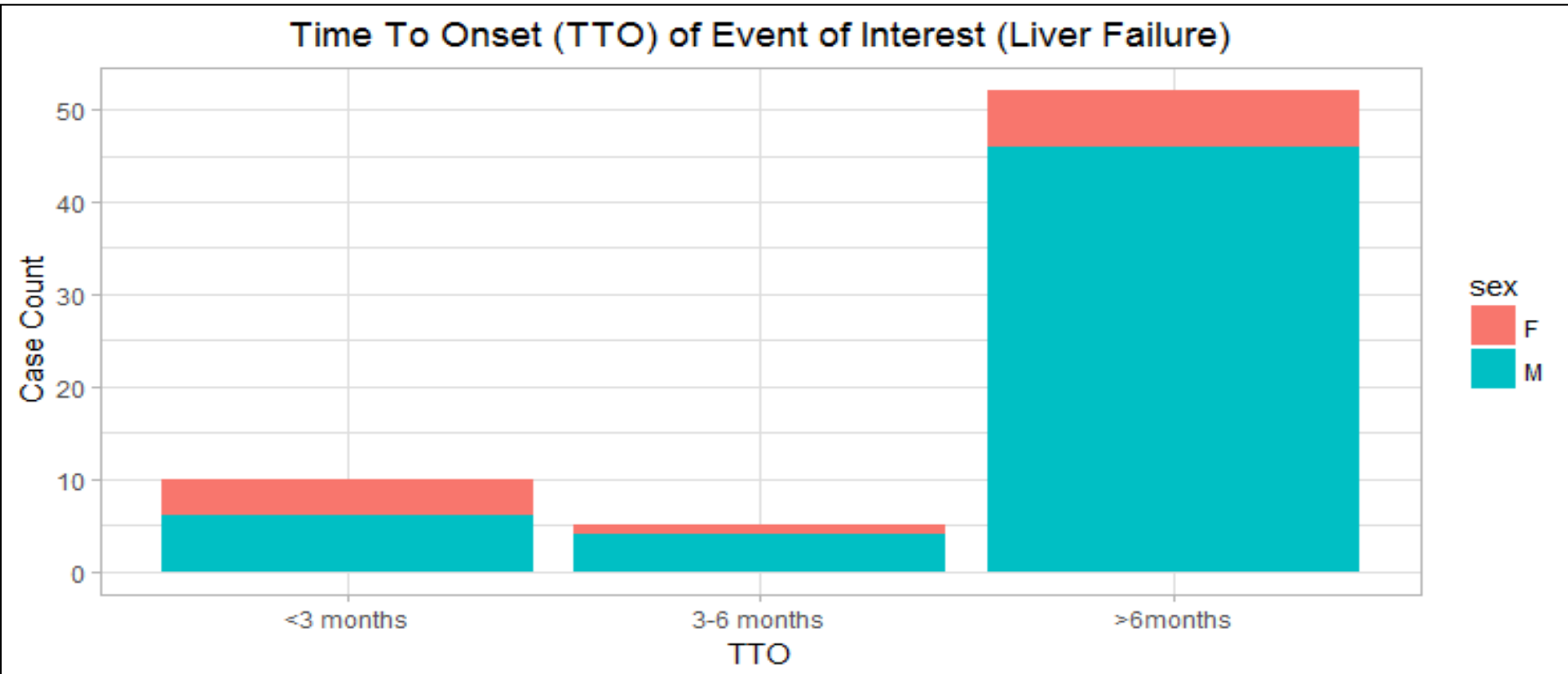
Ranking of cases based on information available within cases



Rank 1 for Highest information content to
Rank 5 for Lowest information content

Ranks	Information Content based on causation criteria
R1	TTO + ConMeds + CoM/Med History + De/Rechl + Narr
R2	TTO + ConMeds + CoM/Med History + De/Rechl
R3	TTO + ConMeds + De/Rechl + Narr
R4	TTO + ConMeds + CoM/Med History + Narr
R5	Absence of all 5 criteria

Methods & Results using R- TTO



This visual indicates the time frame by which the event occurred after initiating therapy. It also takes into consideration the gender of the patients.

Methods & Results using R- ConMed

Concomitant Medication Reported in 71 of 126 Cases

Negative (64%)

Question – In which of the cases should we focus on causality assessment?

Answer – Concomitant Negative

Positive (36%)

 Negative = Not known to cause liver failure
 Positive = known to cause liver failure

A list of all medication causing liver dysfunction was prepared and compared with the reported concomitant medication using R.

Methods & Results using R- CoM/Med History

Co-morbidity/Medical history Reported in 72 of 126 Cases

Negative (70%)

Question – In which of the cases should we focus on causality assessment?

Answer – CoM/Med History Negative

■ Negative = Co-morbidity/Medical history not related to liver failure
■ Positive = Co-morbidity/Medical history related to liver failure

A list of all medical conditions causing liver dysfunction was prepared and compared with medical condition reported for each patient using R

Methods & Results using R- Challenge **Cytel**

Dechallenge and Rechallenge Reported in 47 of 126 Cases



Question – In which of the cases should we focus on causality assessment?

Answer – De-challenge positive

Using R, all cases with de-challenge and re-challenge were isolated and identified. There were no cases with re-challenge information. Among the de-challenge reported cases, a positive de-challenge is a potent indicator for a causal association.

- Cases with Positive Dechallenge + Negative CoMeds & CoM indicates a causal association between the drug and event.
- A manual task which would have taken at least more than full working day was achieved in less than 10 minutes.
- Granularity of the dataset can be represented for easier analysis.
- Such programs promote visualizations in safety regulatory documents

Thank You
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