



Lot more than a patient's data

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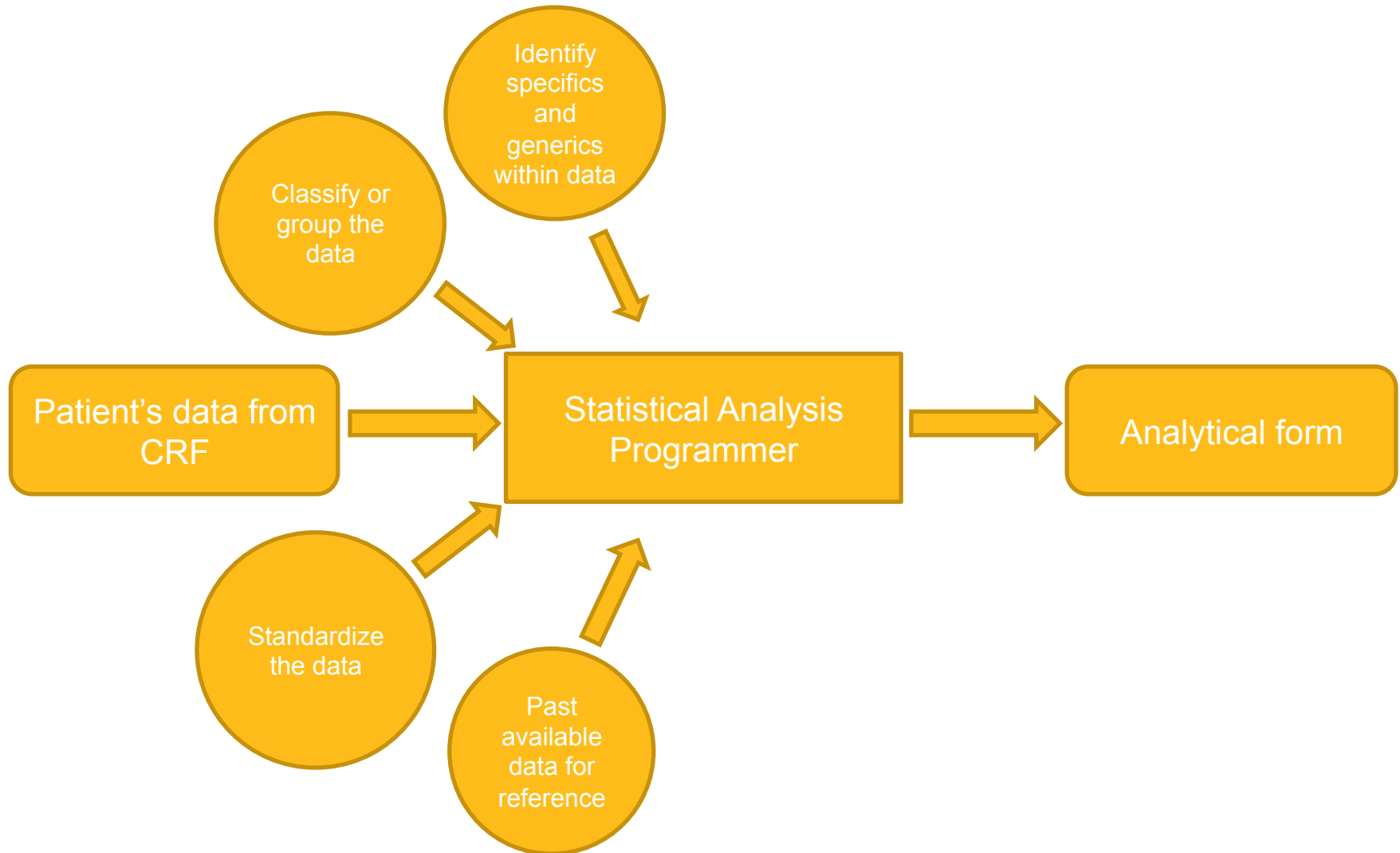
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Introduction and purpose

- data references or external information
- Understand the above and their contribution in clinical data analysis.
- A few key examples and their basic purpose.
- No programming aspects mentioned

Opening thoughts



Dictionaries: Classification or grouping of data

Adverse events

1. BACKACHE

2. Back Injury

3. Back pain related to muscle strain

MedDRA
(Medical Dictionary for
Regulatory Activities)

Concomitant medications

1. ASPRIN

2. COLDRIN

3. DISPRIN

4. CETIRIZINE

WHODrug
(World Health
Organization Drug
Dictionary)

Dictionaries: MedDRA

Body System Organ Class (SOC)	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT
High Level Group Term (HLGT)	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT	INJURIES NEC	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT
High Level Term (HLT)	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT	SITE SPECIFIC INJURIES NEC	MUSCULOSKELETALAND CONNECTIVE TISSUE PAIN AND DISCOMFORT
Preferred Term (PT)	BACK PAIN	BACK INJURY	MUSCLE STRAIN
Lowest Level Term (LLT)	BACKACHE	BACK INJURY	MUSCLE STRAIN
			
Reported AE term in CRF	BACKACHE	Back Injury	Back pain related to muscle strain

Standardized MedDRA Query (SMQs)

In addition to the classification of events using MedDRA dictionary, we also have Standardized MedDRA Query (SMQs) that groups preferred terms (PTs) according to the medical condition the event falls under.

Example:

SMQ Level 1 Name	Hypertension	Hypertension	Hypertension
	↑	↑	↑
Body System Organ Class (SOC)	Cardiac disorders	Metabolism and nutrition disorders	Investigations
	↑	↑	↑
Preferred Term (PT)	Hypertensive heart disease	Metabolic syndrome	Blood pressure increased
	↑	↑	↑
Reported AE term in CRF	Hypertensive heart disease without heart failure, benign	Metabolic syndrome	blood pressure elevation

Unit conversion [Reference datasets]

Data (eg. Laboratory, vital signs, ECG tests) could be collected / measured in different units at different sites and laboratories because of the different conventions followed at different sites.

Site	Patient	Vital sign test	Result value	Result Unit	Standard result (in SI)	Standard Unit (SI)
101	1011	HEIGHT	67	IN	170.2	cm
101	1011	WEIGHT	193	LB	87.5	kg
102	1021	HEIGHT	62	IN	157.5	cm
102	1021	WEIGHT	55	Kg	55	kg

The **conversion factors** and the **decimal places** up to which the converted values to be shown are the two requisites for performing conversions of any measured values.

Two reference datasets—CONVERSION and PRECISION

CONVERSION:

Parameter	Original units type	Pre-conversion Unit	Conversion unit type	Post-Conversion Unit	Conversion factor processor	Conversion factor
WEIGHT	SI	kg	SI	Kg	MULT	1
WEIGHT	SI	kg	US	LB	MULT	2.204622
WEIGHT	US	LB	US	LB	MULT	1
WEIGHT	US	LB	SI	Kg	MULT	0.453592

PRECISION:

Parameter	Unit	Precision Type	Precision Number
WEIGHT	LB	DECIMAL PLACES	1
WEIGHT	kg	DECIMAL PLACES	1
HEIGHT	IN	DECIMAL PLACES	0
HEIGHT	cm	DECIMAL PLACES	1

Clinically notable abnormalities

Reference ranges help to flag the abnormal values. In order to further identify if these abnormal values are clinically significant (i.e. notable abnormal) or not, we flag based on a set of criteria.

- defined for each applicable lab test to identify the notable values
- not standard for all the trials, but are specific to each study
- defined in the protocol by clinical and safety experts

Clinically notable abnormalities (cont..)

Protocol 1:

Lab test	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hemoglobin in g/dL (Female)	11.0 - 12.0	9.5 - 10.9	8.0 - 9.4	<8.0
Hemoglobin in g/dL (Male)	12.5 - 13.5	10.5 - 12.4	8.5 - 10.4	<8.5

Protocol 2:

Lab test	Notable Abnormality value
Hemoglobin in g/dL (< 16 years of age)	≥ 2 g/dL decrease from baseline (or) <8.5 g/dL
Hemoglobin in g/dL (≥ 16 years of age)	≥ 2 g/dL decrease from baseline (or) <10 g/dL

Clinically notable abnormalities

(cont..)

A simple example on vital signs to understand why the grade ranges for a parameter could be different from one trial to another trial.

Normal and clinically notable abnormal values for vital sign tests

Vital sign test	Normal (mm/Hg)	Notable abnormal (Lower) (mm/Hg)	Notable abnormal (Upper) (mm/Hg)
Systolic Blood Pressure (SBP)	<120	90	140
Diastolic Blood Pressure (DBP)	<80	60	90

Normal and clinically notable abnormal values for vital sign tests (If the trial conducted on Hypertensive patients)

Vital sign test	Normal (mm/Hg)	Notable abnormal (Lower) (mm/Hg)	Notable abnormal (Upper) (mm/Hg)
Systolic Blood Pressure (SBP)	≥ 120	either ≤ 90 + decrease ≥ 30 or < 75	either ≥ 180 + increase ≥ 30 or > 200
Diastolic Blood Pressure (DBP)	≥ 80	either ≤ 50 + decrease ≥ 20 or < 40	either ≥ 105 + increase ≥ 20 or > 115

Safety concerns specific to drug

- SAS programmers could also receive information about the safety profile of a drug (i.e. AEs of special interest and risks) from Drug Safety and Epidemiology team that will need to be reported.
- These could include adverse events reported in:
 - past conducted trials,
 - published literature reports,
 - epidemiology data,
 - preclinical data,
 - competitors data
 - and some of the observed AEs or SAEs in an ongoing clinical trial that could potentially raise a safety concerns
- Please see the paper for examples of risks

External/ Open source data

- Reference to the information available as open source:
 - Publication data from trials conducted in the past or
 - from general surveys, literature.

“Whether the death rate in our trial is more, or less than what is observed in the literature?”

A few details about the trial:

- We have conducted a clinical trial using treatments active drug “Ta” and Placebo “Tp” on patients with disease “Da”.
- It is tested on patients with age above say 55 as the disease “Da” is mostly observed in elders.
- The planned analysis for death rate is by age groups say 55-<65, 65-<75, 75-<85 and >=85 and by gender.

External/ Open source data (cont..)

1. Death rates observed in our trial.

Category	Death rate observed in Active treatment [Ta] (Males) (Per 1000)	Death rate observed in Active treatment [Ta] (Females) (Per 1000)	Death rate observed in Placebo treatment [Tp] (Males) (Per 1000)	Death rate observed in Placebo treatment [Tp] (Females) (Per 1000)
55-<65	8.6	5.8	9.8	6.1
65-<75	21.2	14.9	23.4	15.5
75-<85	58.8	42.1	59.4	43.1
>=85	155.4	125.5	158.4	126.1

Note: The numbers shown in the table are hypothetical for illustration.

2. Death rates observed in general population.

Category	Death rate observed in general population (Males) (Per 1000)	Death rate observed in general population (Females) (Per 1000)
55-<65	10.9	6.5
65-<75	23.5	15.8
75-<85	58.7	42.3
>=85	155.7	123.1

Note: The numbers shown in the table are hypothetical for illustration.

Note: The most relevant and recent data available in the literature or publications should be used for the analysis. These references/ sources will be provided by qualified Safety and Epidemiology personnel.

Trial Design Model (TDM)

- Trial Design Model can:
 - serve as a reference throughout the trial.
 - provide a standardized way to describe the study trial and allows reviewers to:
 - Clearly and quickly grasp the design of a clinical trial
 - Compare the designs of different trials
 - Search a data warehouse for clinical trials with certain features
 - Compare planned and actual treatments and visits for subjects in a clinical trial.
- Trial design datasets includes:
 - Trial Visits (TV),
 - Trial Arms (TA),
 - Trial Elements (TE),
 - Trial Inclusion/Exclusion (TI) and
 - Trial Summary (TS).

Conclusion

- classify or standardize the data,
- identify patterns within data
- compare against the past available or the reference data etc. using a wide variety of supplemental information.

In this presentation, we discussed typically used standard dictionaries, reference datasets and the information from safety, clinical, statistical and other teams.

However, there could be several other supplementary data specific to the disease or therapeutic area.

Thank you...!!

