COMPETING RISKS AND ANALYSIS OF FAILURE TIMES

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Abstract
A competing risks is an event that either hinders the observations of the event of the event of interest or modified the chance that this events occurs.
Competing risk occurs when subject can experience one or more events or outcomes which compete with outcomes of interest.
In a typical analysis of time to event data competing events may be censored or incorporated into composite end points. The presence of competing events violates the assumptions of independent censoring which is the basis of standard survival analysis techniques.
The paper deals with principles of the competing risk analysis and approaches for analysing data with competing events.
Keywords: competing risks, failure rates, ,Kaplan- meier estimate

Introduction:-
We refers to the events as "Competing events" in a sense that they compete with each other to deliver the events of interest and the occurrence of one type of events will prevents the occurrence of the others. As a result we call the probability of these events as "competing risks" in a sense that the probability of each competing events somehow regulated by the other competing events.
Competing events are competing risks events that compete with the primary event of interest such that they preclude the occurrence of the primary events.
The topics of competing risk events and the estimation of the cumulative incidence of an event of interest have been discussed by several authors.
Ignoring competing events in the analysis might lead to biased effect estimation of the exposure on the outcome. The Cause Specific Hazard function generates the classical Concept of Hazard Function to the Competing risk setting and it describes the Rate failure from one event type in the presence of the other.
The Fine-Gray Method models the Subdistribution Hazard Function with the assumptions that
Subject who experience competing events remain at risk along with those who survive all events and are not censored.
A Proportional Hazard Model for the Cumulative Incidence functions with covariances by treating the Cumulative Incidence Function curves as Subdistribution Function was proposed by Fine and Gray[1999]. The Subdistribution Function is analogous to Cox Proportional Hazard Model except that it models a hazard function as known as Subdistribution Hazard derived from a Cumulative Function.
The Method is popular for handling competing events.
The cause-specific CIF using weighted versions of standard estimators in an alternative way to be estimated was proposed by Geskus et al[2011].
The theoretical concepts underlying the estimation of Cumulative Incidence of an event using a variety of models is reviewed by Gail et al[1975].
The Subdistribution Model might be consistent in restricted time ranges but this assumption needs to be formally justified Latouche at el [2013].
The Fine and Gray subdistribution hazard function for event type c can be expressed as

$$Hc, cif(t) = \lim_{\substack{\Delta t \\ for\ c'\ not\ equal\ to\ c}} \frac{\Pr(t < Tc < t + \Delta t \ / Tc > t\ U\ Tc' \leq t)}{\Delta t}]$$

The above function estimates the hazard rate for event type c at time t based on the risk set that remains at time t after accounting for all previously occuring events types which includes competing events . The random variable Tc denotes the time to failure from event type c .
Cause Specific Hazard methods:-
The cumulative incidence function quantifies the risk of failure from a particular event type when there are competing risks.
Censored observation approach is taken in the application of the logrank test and Cox[1972,1975] Semiparametric a model as well as in Nonparametric estimation in the Cumulative hazard for a particular Cause Nelson et al[1972].

Methods for the analysis of cause specific failure data in epidemiological setting have been developed by Crowley and Hu [1977] Holt [1978]Prentice et al[1978] and kalbfleisch and Prentice [1980] as a natural extension of the methodology used in the construction of multiple decrement life tables.
The cause specific approaches has a long history of application [Prentice et al [1978]. In contrast the model of Fine and Gray[1999] targets the subdistribution function directly and has become a very popular choice in practice.
The cause specific hazard function $hc(t)$ at time t is the instantaneous rate of failure due to cause C conditional on survival until time t
or later it is defined as

$$hc(t) = lim \frac{P(t < T < t + \Delta t\,, \delta = c\ /T > t\ )}{\Delta t}$$
$$c = 1,2,3 \dots \dots \dots \dots \dots . . C$$

The cause specific hazard function gives the instantaneous failure rates at time t from event type c.
The cause specific approaches treats competing events as censored also considers the conditional risks of the event of interest had the competing event not occurred.
A key concept in competing risk analysis is the distinction between competing risk events and censoring.
Consider T as the duration between the time origin and the occurrence of an event. Censoring is the process which prevents us from fully observing this T .In particular right censoring occurs when we know that an event has not occurred prior to some time C but we can no longer follow the individual to measure T exactly and hence only observe

$$Z = \min(T\,, C)$$

A method to estimate the cumulative incidence of a specific event based on an extension of the Cox proportional hazard regression model was developed by Tsai et al[2001]..

Competing risk data:-
Competing risk data arises when subject can potentially fail from multiple causes but experiencing failure from one cause.
On the other hands proportional hazard models for cause specific hazard are easy to fit and offer a more natural interpretation in terms of rate ratio.
Since the probability of failure of a certain type depends on the rates of other competing events.

Regression Model for the competing risks:-
Regression models are employed to access the effect of various risk factors on the occurrence of a certain type of events. In competing risks setting this type of analysis commonly carried out using one of the two methods Cox model or the Fine-Gray model.
The Cox proportional hazard model is called a semi parametric model because there are no assumptions about the shape of the baseline hazard function.
Cox model can be applied to analyse competing risk data in the presence of multiple causes of failure.
It is important to note that when competing events are very rare or not affected by exposure both Fine-Gray and Cause -Specific hazards Methods will generate similar results.

Fine-Gray Regression model:-
It is based on an alternative failure rate summary of measure the subdistribution hazard function. Fine -Gray model makes similar assumption about Subdistribution Hazard Function as those made in Cox model for Cause Specific hazards. The model assumes that the subdistribution hazard in two groups are proportional to each other at every time point and the magnitude of the ratio of those two hazards is estimated from the data.
The analysis result of the Fine and Gray Model are summarised by subdistribution hazard ratio which reflects the effect of each covariates has on the risk of the event of interest. The interpretation for cause specific hazards and subdistribution hazards are different.
A non- parametric estimate of $Exp\ \{\ cause - specific\ cumulative\ hazard\}$ is provided by the kaplan-meier Kaplan and Meier [1958] where extraneous causes of failure are treated as censored observations.
Censoring means the total survival time for that subject cannot be accurately determined. This can be happen when something negative for the study occurs such as the subject drop out or lost to follow up or required data is not available.
Kaplan-meier estimate is one of the best options to be used to measure the fractions of subjects living for a certain amount of time after treatment.
Suppose that the survival times including censored observation after entry into the study of a group of n
Subjects are $t_1\,, t_2\,, t_3\,, \dots \dots \dots . t_n$ the proportion of subject $S(t)$ surviving beyond any follow up time $t_\times$ is estimated by

$$S(t) = {}_i^{\Pi} \frac{r_i - d_i}{r_i}$$

where t_x is the target survival time less than or equal to t.
And r_i is the number of subjects alive just before time t_i and d_i denotes the number who died at time t_0 where i can be any value between from 1 and x.
For Censored Observation

$$S(t_i) = \frac{r_i - d_i}{r_i} \times\ S(t_{i-1})$$

The Kaplan Meier estimate is the simplest way of computing the survival over time in spite of all difficulties as associated with subjects or situations.
In preparing Kaplan- Meier Survival analysis subject is characterized by three variables

(I) The serial time
(II) Their status at the end of their serial time
(III) The study groups they are in

The kaplan Meier Curves estimates the Survival curve i.e descriptive statistics.
Kaplan Meier Curves are an often used statistical tool that helps determine the likelihood of experiencing an adverse outcome over a period of time.
Censoring has an effect on the survival rates.
Censored observations that coincides with event are usually considered to fall immediately after the event.
censoring removes the subject from denominator I.e individual are still at risk.
The kaplan -meier curves and estimate of survival data becomes a familiar way of dealing with differing survival times when not all the subjects continue in the study.
The Hazard ratio is the measure of association.
The Cox regression allows the analysis of the influences of the predictive factors ie Covariates.
The log-rank test compares the survival over the entire curve between two groups. In doing so it compares the observed values so what would be expected given that the null hypothesis is true.In medical research the null hypothesis is most often that there is no treatment effect.

Conclusion:-
The Cox cause specific hazard approaches and the Fine Gray approaches used in competing risk analysis are illustrated with considering Censoring . The paper also focuses on Kaplan - Meier estimation approach and Fine and gray regression model with theoritical point of view of illustration.

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