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Brief Article

Endpoints in Clinical Trial

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Introduction

Endpoints are variables monitored during a study to document the impact of treatment on how a patient feels (for example, pain, dyspnea), functions (for example, ability to walk or exercise) and survives(for example mortality, stroke)[1]. Typical examples are myocardial infarction, stroke, and mortality. Most clini-cal studies categorize endpoints as primary, secondary, exploratory, and surrogate. The primary end-points are essential to establish the effectiveness of intervention[2]; secondary endpoints support the pri-mary endpoint and additional effect[3], and exploratory endpoints explore new hypotheses.

Primary endpoints

Primary endpoints are essential for defining the efficacy (of the therapy/drug/intervention) and its mea-surement. Primary endpoints are clinically meaningful and contemplate the accepted norms and stan-dards in the related field of research. However, as described by the inclusion and exclusion criteria, there should be sufficient evidence that such a variable can provide a valid and reliable measure of clinically relevant and essential treatment benefits in the patient population. The primary endpoints are important for two main reasons: (a) the primary endpoints are essential to establish the effectiveness of the inter-vention, and (b) these are used for the sample size calculation. Investigators are bound to prespecify the primary endpoints before the commencement of the trial. This bound the authors to analyze only prede-fined variables rather than testing every possible variable until one is statistically significant.If the investi-gator redefines the primary endpoints, the results are likely biased (i.e., inaccurate or not meaningful).

Although the single primary endpoint is the ideal strategy to find the unbiassed impact of the in-tervention, dramatic improvement in morbid and mortal events has limited the number of events that will eventually happen in a defined time frame. Considering a single variable as the primary outcome thus may lead to exposure of ineffective treatment to a large population. So investigators collate mortal and morbid events with two or more endpoints to increase the expected numbers of events, thus balancing statistical power and precision[4-5] Variables incorporated in composite endpoints are consistently defined and have a common pathophysiological mechanism.

Table 1 : Primary endpoints Key Points

Used for defining efficacy and its measurement
Used for calculating the sample size
Investigators are bound to prespecify the primary endpoints.
Redefining the Primary endpoint after the commencement of the study is not permissible.
The collation of multiple variables to form a composite endpoint is acceptable with a predefined rule.

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Table 3 : Examples of endpoints in different specialities

Cardiovasular Disease

Individual end point	Composite endpoint	Surrogate endpopint
Total and cause specific mortality	CVD Mortality/MI/Stroke	Serum level of C-Reactive protein
Disease recurrence(e.g., MI, angina, stroke)	Fatal or nonfatal MI/Stroke/heartfailure	Serum cholesterol levels
Bleeding	Hospitalization for MI/Stroke	Blood pressure finding
Vascular complications		Frequency and type of cardiac arrhythmias
Quality of life		Anginal symptoms
Functional status		6 minute walk

Respiratory Disease

Individual end point	Composite endpoint	Surrogate endpopint
Total and cause specific mortality	Progression free disease survival(death or decline in forced vital capacity)	Serum IgE Levels
Respiratory symptoms(e.g., cough, wheezing)	Exercise capacity	Multiallergen screen
Disease exacerbation		Nitric oxide
Quality of life(e.g., asthma quality of life questionnare)		Complete blood count

Gastrointestinal Disease

Individual end point	Composite endpoint	Surrogate endpopint
Total and cause specific mortality	Sustained disease remission without treatment(e.g., corticosteroids) and mucosal healing	
Clinical remission	Bowel damage scores	
Hospitalization		
Mucosal healing		

Source:Individual and Composite Study Endpoints: Separating the Wheat from the Chaff. Am J Med. 2014 May;127(2):379-384). Used with permission.

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