Loss to Follow-up in Clinical Trials – Implications and Prevention

Sir,

Loss to follow-up (LTFU) refers to participants who have not returned for continued care or evaluation in the trial, this results in incomplete ascertainment of the primary outcome for participants randomized in the trial.[1] LTFU can severely compromise the trial's internal and external validity and results in a kind of selection bias, especially when the drop rates are different between the groups or the participants who drop out are different in terms of exposure, outcome, or prognosis than from those who continue the trial. It is one of the quality indicators of the trial and a large number of LTFU implies poor design and quality of the trial. In addition, it increases the cost and duration of the study as more resources are spent on trying to trace these participants and in the recruitment of new study participants.[2] A systematic review by Akl *et al*. concluded that plausible assumptions of outcomes for the participants who were lost to follow-up could change the interpretation of findings.[3] In general, <5% loss leads to little bias, while >20% poses serious threats to the validity of the study.[4]

There can be many reasons for LTFU. The patient may move to other geographical locations and therefore unable to travel, may have suffered some other illness, may disappear, suffer unreported death, or may not wish to attend the clinic where the study is being undertaken. In some cases, the patient may lose interest in the study, may choose to discontinue treatment either due to side effects or very good results, or may choose to cross over to another intervention. Other logistical reasons may also cause LTFU such as participants may change their names, addresses, and phone numbers. In general, studies with longer follow-up have more LTFU as in the case of large prospective cohort studies. Identifying the cause for LTFU due to discontinuation is important as it gives an indication as to whether the intervention is beneficial or may actually be causing more harm either physically or mentally to the participant.

A few strategies to reduce LTFU are careful study design and training of staff so that follow-up of participants is done in a culturally and sociodemographically sensitive manner. Recruitment should target motivated subjects and those who are easy to trace and contact. A pilot study may be conducted in which issues related to follow-up such as multiple visits, lengthy questionnaires, and multiple injections can be identified. In addition, previous studies using similar interventions or methodology can be studied, and factors leading to LTFU identified. Reducing the gap between follow-ups and providing incentives, especially for compensating the loss of wage and travel costs, may also help. In addition, scheduling visits for follow-up which do not affect their work for example during weekends may help. It is very important that the participants are made to feel important and understand the nature and implications of the study. The research staff should be sympathetic to the participant's grievances and try to address them as soon as possible. Developing a plan to implement routine data quality checks and mechanisms to retain and contact participants goes a long way in reducing LTFU.[5]

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Conflicts of interest

There are no conflicts of interest.

Satvinder Singh Bakshi, Vinoth Kumar Kalidoss[1]

Departments of ENT and Head and Neck Surgery and [1]Community and Family Medicine, AIIMS, Guntur, Andhra Pradesh, India

Address for correspondence: *Dr. Satvinder Singh Bakshi, Department of ENT and Head and Neck Surgery, AIIMS, Mangalagiri, Guntur - 522 503, Andhra Pradesh, India.*
E-mail: saty.bakshi@gmail.com

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