Intention to treat analysis

**Intention to treat.** Part of the mnemonic for judging the quality of therapy RCTs: \textit{ABCDFIX}.

**Intention-to-treat principle**

Once subjects are randomized, they should be analyzed in the group they were first randomized to, even if they never received treatment, discontinued the trial, or crossed over to the other group.

Intention-to-treat analysis is generally the primary analysis of a randomized controlled trial. It is of particular importance when patients have dropped out or crossed over from one treatment arm to another in done a therapy RCT. (Glasziou 2003)

Drops outs and crossovers present a serious problem because the remaining groups may no longer be comparable. Analyzing the results based on intention to treat can help correct for this problem.

Applying the intention-to-treat principle

Some studies deal with drop outs by excluding the participants from the analysis. This form of analysis is sometimes called “as per protocol,” “efficacy,” or “analysis by treatment administered.” The reported outcomes include only those who completed the research protocol. “Although investigators can use information from such an analysis to estimate the intervention’s efficacy in those who actually received it in the intended intensity or dose for the intended interval, this estimate is likely to be seriously flawed.” (Montori 2001)

There are a number of reasons the intention to treat principle is applied (some are very technical). Here are two of the most cited (Dawes (2005).

- Intention to treat reflects the way treatments may perform in the general population because patients do drop out from care. Participants in clinical trials may not adhere to the protocol due to any number of reasons. They may have moved away, may have found the treatment protocol too difficult to follow, may not have felt that it was helping fast enough, or may have been suffering from side effects. In this case the results might mask the fact that a particular intervention
had more side effects than reported or the program was too difficult to follow—facts that would be important to a physician considering the intervention under study.

- Intention to treat preserves the baseline groups achieved by randomization. As Dawes writes if drops outs are not included, “one is not sure whether the differences you may see [how the groups responded to care] are a result of your manipulation of the data after a trial.”

For the reasons above, intention to treat analysis is a way of decreasing the chances that we may be over estimating the effect of a therapy.

Although failing to report an intention-to-treat analysis may not always be a fatal flaw, it is thought to considerably decrease the quality of the study and leave the validity of the results open to question.

On the other hand, the intention-to-treat analysis is not a perfect solution to the problem. When drop outs and cross overs are counted as a treatment failure, it may discount how effective a treatment may be in a highly motivated, compliant patient. In other words, "when treatment is effective but nonadherence is substantial, the analysis following the intention-to-treat principle underestimates the magnitude of the treatment effect that will occur in adherent patients." (Montori 2001)

Determining if intention-to-treat analysis was used

Clinicians evaluating a randomized trial need to know if the researchers applied the intention-to-treat principle. A quick approach is to scan the Methods section of the published report looking for the phrase "intention-to-treat."

“Two surveys of randomized controlled trials published in major medical journals during 1993–1995 (Ruiz Canela 2000) and 1997 (Hollis 1999) found that half of the reports used the term ‘intention-to-treat analysis.’ Unfortunately, the term was not always used appropriately.” (Montori 2001)

Example

Here is a paragraph from the Results section of a study (Rompe 2007) that UWS students submitted a CAT on.

“In accordance with the CONSORT statement for reporting randomized trials, all statistical analyses were done on an ‘intention-to-treat’ basis to avoid overestimation of clinical effectiveness. All patients were included for statistical calculations, regardless of the treatment actually received and regardless of subsequent withdrawal or deviation from the protocol, i.e., loss to follow-up. Missing responses (2 of 25 in group 1, 1 of 25 in group 2, 2 of
25 in group 3) were imputed as the last observation carried forward. The last observation was defined as the last observed value before the initial management, i.e., in cases lost to follow-up. It was supposed that there was no improvement from the basic evaluation.”

This is an excellent example of a description of the intention to treat analysis.

**Verdict: Intention to treat analysis was done.**

**Bottom Line**

- Look for the phrase “intention to treat” in the methodology or result section of the paper.
- If you cannot find this statement, but there were no drop outs or cross overs, there is no problem.
- If there were drops outs or cross overs and an intention-to-treat analysis was not done, this is usually considered a significant weakness and there is a danger that the results are not as robust as they appear.
- If the researchers claim to have done an intention-to-treat analysis, this is a strength, especially if they actually describe how it was applied. Be aware, however, that it is not always done correctly. There are ways to more closely exam the results to see if the analysis was applied properly, but they are outside the scope of this lesson.

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**References**

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Montori, VM,Gordon H. Guyatt GH, Intention-to-treat principle CMAJ November 13, 2001; 165 (10)
