accidents are not AEs (63) it is actually improper to exclude accidents from AEs. The layperson can readily appreciate the fact that drugs can cause drowsiness, or result in impaired vision (64) where the result is an accident that produces injury.

c. Classification of adverse events by considerations used by statisticians

Adverse events can also be classified according to how a biostatistician would approach the data. These approaches include the following reporting (65):

- AEs by intention to treat (ITT) analysis
- AEs by per protocol (PP) analysis
- Use of a severity threshold, that is, reporting of AEs only above a certain severity grade
- Use of a prevalence threshold, that is, reporting of AEs occurring only above a certain percentage of patients
- Outcomes of AEs, such as treatment discontinuations, dose reductions, and withdrawals from the study.

Although these types of adverse events generally fall under the umbrella of the biostatistician serving a clinical study, a typical medical writer will be familiar with all of these concepts.

d. ITT analysis versus per protocol analysis

Clinical trials in regulated settings require collection of data on safety and efficacy. The FDA grants marketing approval for drug products based on a review of safety and efficacy data (66). The European Medicines Agency also requires that clinical trials provide data on safety and efficacy (67).

Safety data may be analyzed in ways that are different than for efficacy data. ITT analysis, modified ITT analysis, and per protocol analysis have been applied differently for safety and efficacy data. Where safety analysis is presented from a clinical trial, it is typically presented by way of ITT analysis, as the FDA requires all subjects exposed to the drug be reported in the safety analysis (68).

Efficacy can be assessed by ITT analysis, but also by methods that apply to more restricted and smaller groups of study subjects. It is often the case that safety is assessed

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