Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

doi: 10.5455/2319-2003.ijbcp002612

Educational Forum

Small size sampling?

Rakesh R. Pathak*

Department of Pharmacology,
C.U. Shah Medical College,
Surendranagar 363001, India

Received: 21 September 2012
Accepted: 25 September 2012

***Correspondence to:**
Dr. Rakesh R. Pathak,
E-mail: rr_pathak@yahoo.com

ABSTRACT

Though small size samples can be planned and justified based on scarcity of time, money and manpower, there are situations making more accuracy a must and needing larger samples sizes. That's why rare adverse drug reactions are identified only after a drug comes into the market and a large population is exposed to it. There are many more reasons for increasing the sample size and requirement of the study decides which criteria of accuracy should be tightened the most (e.g. avoiding type I error is more important or type II error).

Keywords: Type I error, Type II error, Cohort, Statistical predictors

Yes, the same heading as in the previous issue of the journal[1] but with a "question mark" this time! Would the small size sample work all the while? Are all the large sample studies just wastage of time, money and effort?

A quote from the bible of pharmacology would be exemplary - "a cohort study must follow at least 10,000 patients who are receiving the drug to detect with 95% confidence one event that occurs at a rate of 1 in 3300 and that event can be attributed to the drug only if doesn't occur spontaneously in the control population"![2]

Let's solve this sum ourselves. If we permit 1% margin of error and consider the situation worldwide (population >300,000,000) we can find the number by standard chart of the research advisors (2006) or online calculator.[3,5]

But here the case is not that simple. Here the λ (mean event rate) is 1 in 3,300 or 0.0003030303….for this λ, and the power (the probability that the mean event rate is greater than that specified) of 0.95, and critical tolerance = 1 (i.e. the prevalence is greater than the mean event rate we have already set) - the sample size of 10,000 (for an incidence rate of 0.0003, it is 9986 - to be exact) can be found from the table[4] - that too if the incidence of the adverse event (supposed to be due to the drug) is "not spontaneously occurring in the population" as already stated.[2]

Up to phase III, total number of people exposed to a new drug is not as high as this and that's why many rare adverse drug reactions are identified only after a drug comes into the market and a large population is exposed to it and this exposed population is reassessed in phase IV study of pharmacovigilance called post marketing surveillance.

Many more reasons are there for larger size sampling as we can verify from the sample size calculating program.[5] In a population of 20,000, error level of 5% and 95% confidence level leads to a maximal samples size of 377.[4] It's to be noted that at 50% response distribution i.e. when there is equal chance of the outcome to occur or not, the sample size is maximum.

But error level of 1% with the same 95% confidence level, leads to a maximal samples size of 6489 and if error level of 1% with the confidence interval of 99% is considered, the required sample size becomes 9068.[4] In the last case, relieving only the error level to 5% (and confidence level remaining up to 99%) decreases the sample size down to 643.[4]

Thus the required level of accuracy of conclusion also influences the sample size. Now "how do these different statistical predictors of accuracy of conclusion (viz. confidence level, permitted level of error etc.) manifest in the real life problems" is hinted ahead.

Just to start with, by reducing the risk of type I error (or α error - i.e. false positive, erroneously rejecting the null hypothesis in favor of alternate hypothesis) we tend to increase type II errors (or β error i.e. false negative, erroneously accepting null hypothesis).[6]

Seeing the result of a clinical trial, type I error means that the test treatment is taken to be effective when actually it is not. And FDA or any other supervising body would try

to minimize this error and prohibit unwarranted permissions.[7]

But type II error implies that test treatment is taken as ineffective when actually it is. And the drug companies investing a lot of money in discovering a drug are more interested to minimize this type II error. Accordingly, the two approaches vary in fixing the criteria of accuracy.[7]

Suppose a camera system installed in a car tries to determine whether certain blobs it sees on the road are pedestrians or not. And if it misses anyone to acknowledge as pedestrian, there are increased chances of hitting someone - obviously type II error is more important here.[8]

Alike is the case where medical imaging software tries to find and mark suspicious regions, which could be a serious tumor. Likewise, if a medication with some fatal side effect is being tested, type II error would be obviously more important.[8]

But suppose a prosecutor is trying to prove that the defendant is guilty using a blood test. Here type I error is more important as innocent person should not be punished.[8] The same is true when a factory wishes to make sure whether a costly innovation is worth it or not.[9]

For screening test of HIV in blood donors, false positive is not that dangerous and small type I error is allowed and cheaper tests are used but when it comes to the diagnosis in patients, much costly test are used to avoid this false positive labeling.[10]

REFERENCES

1. Pathak RR. Small size sampling. Int J Basic Clin Pharmacol 2012 Aug;1(1):43-4.
2. Oates JA. The science of drug therapy. In: Brunton LB, Lazo JS, Parker KL, editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 11th ed. New York, NY: McGraw-Hill; 2005:135.
3. The Research Advisors. Sample Size Table. Available at http://research-advisors.com/tools/SampleSize.htm. Accessed 9 September 2012.
4. Explanations and Tables for sample size for rare events. Available at http://www.stattools.net/SSizRareInc_ExpTab.php. Accessed 10 September 2012.
5. Raosoft. Sample size calculator. Available at http://www.raosoft.com/samplesize.html. Accessed 10 September 2012.
6. Bland M. An introduction to medical statistics, Third Edition. Oxford University Press, Great Britain, 2000.
7. Chow SC. Controversial Statistical Issues in Clinical Trials. Chapman and Hall/CRC Press, Taylor and Francis, New York; 2011:22.
8. Introduction to probability and statistics for computer engineers. Available at http://www.cmpe.boun.edu.tr/courses/cmpe343/fall2010/PS8%20Key.pdf. Accessed 9 September 2012.
9. Levine DM, Krehbiel TC, Berenson ML. (2010). Business Statistics: A First Course, 5th ed., Upper Saddle River, NJ: Prentice Hall; 2010: 295.
10. Type-1-error. Available at http://www.nationmaster.com/encyclopedia/Type-1-error. Accessed 5 September 2012.