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Use proper indicators of change in neuropsychological studies

Abstract

Some indicators have been proposed in biomedical research to index the reliable change of measurements after the intervention or treatment. A good indicator should have simple statistical property and can be easily used by people without formal statistical training. Our analysis shows that many mistakes occurred in medical publications in the application and interpretation of the indicators, especially in the statistical distributions of the indicators. In this paper we summarize some typical mistakes and give correct formulas.

Keywords: practice effect, normal distribution, linear regression

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Abbreviations: SDI, standard deviation index; RCI, reliable change index; SRB, standard regression-based; PE, practice effect

Introduction

Repeated measurements have been widely used to study a change of outcomes in clinical neuropsychology, see Chelune et al.,[1] Du et al.,[2] Frerichs & Tuokko,[3] Hinton-Bayre,[4] Jacobson & Truax,[5] Levine et al.,[6] Ouimet et al.,[7] Sherman et al.[8] and Zahodne et al..[9] To measure the change at the individual level, we first need to define a meaningful indicator of the change. A well-defined indicator should be interpretable both biologically and statistically. The statistical distribution of the indicator should be easily accessible to biomedical investigators.

Recently, Duff[10] reviewed some indicators that have been used in medical journals. After reading Duff 's review paper, we have found several serious mistakes. Some of the mistakes are associated with errors that have appeared in the reference papers cited by Duff.[10] Our survey shows that the statistical distributions of the indicators discussed in Duff[10] are wrong. These mistakes may lead to invalid inferences and cause serious problems for biomedical investigators without appropriate statistical background. The purpose of our paper is to point out some of these mistakes, to explain the reason of these mistakes, and further to correct these errors.

Fundamentals of change indicators

In order to have an appropriate definition of the indicator for the change, we first discuss some fundamental facts. For a randomly selected individual in the experimental group, let T_1 and T_2 denote the measurements at time 1 and time 2, respectively. T_2-T_1 is the change from time 1 to time 2. Let M_1 and M_2 be the population mean values of the measurements of the control group at times 1 and 2, respectively. The change of the individual effect in the experimental group after adjusting the practice effect (PE) is $(T_2\text{-}M_2)\text{-}(T_1\text{-}M_1)=(T_2\text{-}T_1)\text{-}(M_2\text{-}M_1)$, see Duff.[10] Suppose the standard deviations of T_1 and T_2 are S_1 and S_2 with the correlation coefficient r_{12}. Then the standard deviations of T_2-T_1 and $(T_2\text{-}T_1)\text{-}(M_2\text{-}M_1)$ are the same and they are equal to $\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}$. The standardized change and the standardized change after adjusting PE are respectively. These two formulas are the fundamentals of construction of indicators of change

$$\frac{T_2 - T_1}{\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}}$$

$$\frac{(T_2 - T_1) - (M_2 - M_1)}{\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}}$$

Mistakes in the use of indicators in medical publications

In this paper, we focus on two types of mistakes that have appeared in Duff.[10]

a. Order of operations

b. Statistical distribution of the indicators. Similar mistakes also appeared in some publications cited in Duff.[10]

Order of operations

In Equation 1 of Duff,[10] the formula of the standard deviation index (SDI) is defined as

$$SDI = T_2 - T_1 / S_1 \qquad (1)$$

Order of operations is a fundamental part of elementary school math, see for example Ewen & Nelson.[11] One of the rules of the order of operations is that multiplication and division have higher priority than addition and subtraction. According to this rule, the right hand side of (1) is the same as

$$T_2 - (T_1 / \mathrm{S_1}) \quad (2)$$

For example 80-94.5/11.46=80-(94.5/11.46)=80-8.25=71.75.

Anybody with knowledge of elementary school math should obtain this result. However, on p.255 of Duff,[10] the calculation is 80-94.5/11.46=-1.26, which is totally wrong.

A closer look at the Duff[10]'s result found that to calculate 80-94.5/11.46, he first calculated 80-94-5, which is -14.5, and then divided it by 11.46, which is -1.27. The rules of the order of operations are not fulfilled here and it appears that the incorrect assumption made that T_2-T_1/S_1 is the same as (T_2-T_1)/S_1.

It is clear that the author does not understand the rules of the order of operations. He simply assumes that T_2-T_1/S_1 is the same as (T_2-T_1)/S_1. In fact, for the measurement data, the right hand side of (1) appears to be in error. For example, suppose the unit of T_1 and T_2 is kilometer (km). Then the unit of S_1 is also km. Physically, then the expression T_2-(T_1/S_1) is meaningless.

In the following discussion we examine Duff[10] 's formulas with the appropriate orders of operations.

For example, the SDI should be of the form

$$SDI = (T_2 - T_1) / \mathrm{S_1} \quad (3)$$

Equation 1 of Duff[10] also reported several other indicators, which we assume are of the following forms:

a. The reliable change index (RCI)

$$RCI = (T_2 - T_1) / SED \quad (4)$$

b. The RCI controlling for practice effect (PE)

$$RCIPE = [(T_2 - T_1) - (\mathrm{M_2} - M_1)] / \mathrm{SED} \quad (5)$$

c. The Iverson[11] RCI controlling for practice effect (PE):

$$RCI'_{PE} = [(T_2 - T_1) - (M_2 M_1)] / SED_{Iverson};^{11} \quad (6)$$

d. The standard regression-based (SRB) change formula

$$SRB = (T_2 - T_1) / \mathrm{SEE} \quad (7)$$

The expression of SED, SED Iverson,[11] and SEE will be discussed in relevant sections.

Statistical distributions of indicators

The paragraph designated 'Methods for Assessing Reliable Change' on p.253 in Duff,[10] T_1 and T_2 are said to be the scores at times 1 and 2, respectively; and S_1 and S_2 the standard deviations of control group at time 1 and time 2, respectively. Under Equation 1 on the same page, S_1 and S_2 are said to be the standard deviations at time 1 and time 2. According to the paper, there is one control group and one experimental group. It seems that T_1 and T_2 should be measurements at times 1 and 2 of the experimental group, as the outcome of interest is the change of the experimental group. If this is true, S_1 and S_2 should be the standard deviations of the experimental group instead of the control group at times 1 and 2, respectively. It is not reasonable to standardize the measurement of the experimental group using the standard deviation of the control group unless we assume these two groups have the same standard deviations.

As discussed in sections above, the standard deviation of T_2-T_1 is $\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}$. If ($T_1$,$T_2$) has a bivariate normal distribution, then T_2-T_1 also follows a normal distribution. If we further assume that there is no change between times 1 and 2 (which means T_1 and T_2 have the same mean values), then has the standard normal distribution.

$$\frac{T_2 - T_1}{\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}}$$

We discuss the distributions of some indicators listed in Equation 1 in Duff.10

The distribution of SDI in formula (3): From above we know that SDI in (3) does not follow standard normal distribution. We cannot compare the SDI with the quantile of the standard normal distribution to see whether there is a significant change from time 1 to time 2. Unfortunately, on p.254, Duff[10] assumes SDI has the standard normal distribution, which appears to be in error.

The distribution of RCI in formula (4): In Equation 1 of Duff,[10] Hence, RCI does not follow the standard normal distribution. It also does not make sense to compare it with the quantile of the standard normal distribution to check if there is signi cant change from time 1 to time 2.

The distribution of the Iverson RCI in formula (6): According to Equation 1 in Duff,[10] Hence, RCI'PE does not follow the standard normal distribution either. We cannot compare RCI'PE statistic with the quantile of the standard normal distribution to evaluate if there is a significant change from time 1 to time 2.

The distribution of SRB in formula (6): It is trivial to prove that b_{est}=$r_{12}S_2$/S_1, not S_2/S_1 as has been reported in Equation 1 in Duff,[10] and $SEE_{est} = S_2\sqrt{1 + r_{12}^2}$. The formula of SEE_{est} in Equation 1 of Duff[10] appears to be incorrect.

Our discussions indicate that none of the indicators reviewed in Equation 1 of Duff[10] follow standard normal distribution. Unfortunately, Duff[10] and some medical publications compared those indicators with the quantile of the standard normal distribution to evaluate the change from time 1 to time 2. This practice is inappropriate and should be avoided in future medical research.

Correct formulas of indicators

In this section we present correct formulations for these indicators listed in Duff.[10] With these formulas, the investigators can compare statistics to the appropriate quantiles of the standard normal distribution to check whether a reliable change has occurred between time 1 and time 2. Note that all indicators discussed above are in the form of the critical part is to find the correct standard deviation of the change.

$$\frac{change\ from\ time\ 1\ to\ time\ 2}{standard\ deviation\ of\ the\ change}$$

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Here are correct forms of those indicators

The standard deviation index (SDI)

$$SDI = \frac{T_2 - T_1}{\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}}$$

The RCI controlling for practice e ect (PE)

$$RCI_{PE} = \frac{(T_2 - T_1) - (\mathrm{M}_2 - M_1)}{\sqrt{S_1^2 + S_2^2 - 2r_{12}S_1S_2}}$$

a. The standard regression-based (SRB) change

$$SRB = \frac{(T_2 - M_2) - (\mathrm{r}_{12}\, S_2 / \mathrm{S}_1)(\mathrm{T}_1 - M_1)}{S_2\sqrt{1 - r_{12}^2}}$$

Since the numerators of the RCI and the Iverson[11] RCI are exactly the same as those of SDI and RCIPE, respectively, we no longer need to introduce them.

Conclusion

In this paper, we point out some common mistakes related to indicators of change used in the medical literature. Some authors utilize (active language) the wrong distribution to compare the indicators and to determine whether a reliable change has occurred. Some indicators were redundant and not well defined.

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Conflict of interest

The author declares no conflict of interest.

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