In the Beginning—There Is the Introduction—and Your Study Hypothesis

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Writing a manuscript for a medical journal is very akin to writing a newspaper article—albeit a scholarly one. Like any journalist, you have a story to tell. You need to tell your story in a way that is easy to follow and makes a compelling case to the reader. Although recommended since the beginning of the 20th century, the conventional Introduction-Methods-Results-And-Discussion (IMRAD) scientific reporting structure has only been the standard since the 1980s. The Introduction should be focused and succinct in communicating the significance, background, rationale, study aims or objectives, and the primary (and secondary, if appropriate) study hypotheses. Hypothesis testing involves posing both a null and an alternative hypothesis. The null hypothesis proposes that no difference or association exists on the outcome variable of interest between the interventions or groups being compared. The alternative hypothesis is the opposite of the null hypothesis and thus typically proposes that a difference in the population does exist between the groups being compared on the parameter of interest. Most investigators seek to reject the null hypothesis because of their expectation that the studied intervention does result in a difference between the study groups or that the association of interest does exist. Therefore, in most clinical and basic science studies and manuscripts, the alternative hypothesis is stated, not the null hypothesis. Also, in the Introduction, the alternative hypothesis is typically stated in the direction of interest, or the expected direction. However, when assessing the association of interest, researchers typically look in both directions (ie, favoring 1 group or the other) by conducting a 2-tailed statistical test because the true direction of the effect is typically not known, and either direction would be important to report. (Anesth Analg 2017;124:1709–11)

“Therefore, since brevity is the soul of wit, And tediousness the limbs and outward flourishes, I will be brief, your noble son is mad.”

William Shakespeare (1603), The Tragedy of Hamlet, Prince of Denmark; Act 2, Scene 2

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A cross-sectional study of the British Medical Journal, Journal of the American Medical Association (JAMA), The Lancet, and the New England Journal of Medicine revealed that before 1945, their scientific articles were organized in a manner more like a book chapter with individualized headings associated with the subject.1 Although recommended since the beginning of the 20th century, the conventional Introduction-Methods-Results-And-Discussion (IMRAD) scientific reporting structure was not adopted by these leading medical research journals until the 1950s, became predominant in the 1960s, and has only been the standard since the 1980s.1

In this, first in a series of planned basic statistical tutorials, we address (1) creating the vital yet ostensibly under appreciated and often (at least initially) poorly written Introduction section of a manuscript; and (2) the basics of inferential hypothesis testing. We have chosen to highlight the studies and articles by Patel et al,2 Chau et al,3 and Faroni et al,4 which were published in Anesthesia & Analgesia, as examples of a well-constructed Introduction with a well-defined study hypothesis.

CRAFTING THE INTRODUCTION OF THE MANUSCRIPT

The Introduction should be focused and succinct—composed of not more than 300 to 400 words. With few exceptions, it ideally contains only 5 short paragraphs. Each paragraph serves a specific purpose, as described below. The well-crafted Introduction collectively serves as the “hook” that captures the reader’s attention. Patel et al,2 Chau et al,3 and Faroni et al4 present such a well-crafted Introduction.

The first paragraph describes the significance of the topic. The significance includes the pathophysiology, epidemiology, and impact of the clinical condition. For basic science studies, the major roles and implications of the subcellular, cellular, and/or organismal mechanism(s) are highlighted.
The second paragraph provides the background on the topic. The background includes only the most pertinent previous studies and their key findings. It is not intended to provide an exhaustive review of the literature. No present study results are included in the Introduction. Any comparison of the present study’s findings with that of previously published work belongs in the discussion.

The third paragraph defines the rationale for study. The rationale identifies the 1 or 2 key gaps in the current fund of knowledge or understanding that motivate the present study—the question(s) it seeks to address. A good research question should clearly follow the “FINER” criteria and thus be Feasible, Interesting, Novel, Ethical, and Relevant.

The fourth paragraph lists the a priori study aims or objectives, which are directly tied to the stated study’s rationale. They are limited to preferably 1 or 2 and at most 3 in number. These expressed study aims or objectives form the backbone and roadmap of the rest of the manuscript. Additional study aims or objectives cannot be introduced later in the article—seemingly as an afterthought or the product of haphazard post hoc data mining.

The fifth and final paragraph clearly states the primary study hypothesis and, if appropriate, the secondary study hypothesis. Any stated study hypothesis is a direct and logical extension of a listed study aim or objective. A study hypothesis should be specific, naming, and distinguishing primary and secondary outcome variables. For example, instead of stating: “We hypothesize that intervention X reduces complications, length of stay, and 30-day mortality”—expand to state: “For our primary aim, we tested the hypothesis that intervention X reduces complications, length of stay, and 30-day mortality”—expand to state: “For our primary aim, we tested the hypothesis that intervention X reduces the incidence of any major postoperative cardiac complication compared to control in patients undergoing coronary artery bypass grafting surgery. Secondarily, we tested the hypothesis that intervention X reduces length of stay and 30-day mortality in this patient population.”

THE BASICS OF INFERENTIAL HYPOTHESIS TESTING

Inferential statistics essentially allow one to make a valid inference about an association of interest for a specific population based on data collected in a sample. Unknown population parameters representing the association of interest are estimated from the study sample. Population parameters are expressed using Greek letters (eg, μ, P, ρ, β), whereas sample variables and their estimates of these parameters are expressed using Roman letters (eg, p, r, b).

In all research, it is vital to appreciate that inference is not based on data or subjects in the research study, but rather on the population of interest that the study targets. Hypothesis testing involves posing both a null and an alternative hypothesis. The null hypothesis proposes that no difference or association exists on the outcome variable of interest between the interventions or groups being compared. In single-group studies, authors might test the null hypothesis that a parameter such as a correlation or slope equals some predetermined constant (typically, zero).

The goal of each study is to assess the veracity of this claim of “no effect,” “no difference,” or “no association.” We do so by comparing the groups on the observed data using statistical tests, which incorporate both the observed difference (the “signal”) and the observed variability (the “noise”), and constructing a test statistic that can be thought of as a “signal-to-noise ratio.” We then reject the null hypothesis regarding the population parameter if there is sufficient evidence against it—in other words, if the signal-to-noise ratio is large compared to what we would expect if the null hypothesis were true. Details on how this statistical testing is done will be presented in later tutorials.

The null hypothesis (H0) is conventionally notated for various study designs (Figure 1) with subscripts 1 and 2 referring to the groups being compared. For example, in Patel et al,2 the null hypothesis would be stated as “H0: μ1 = μ2,” where μ1 and μ2 represent the population mean values for groups 1 (lidocaine) and group 2 (no lidocaine).

The alternative hypothesis is the opposite of the null hypothesis and thus typically proposes that a difference in the population does exist between the groups being compared on the parameter of interest. The alternative hypothesis implies that there is a relationship or association between 1 variable and another or that there is an effect of 1 variable on another in the population. Note that the formulation of the alternative hypothesis simply changes the null hypothesis sign from an equal (“=” sign) to a non-equal (“≠” sign). The alternative hypothesis (Ha) is thus noted differently (Figure 2).

- H0: μ1 = μ2, or equivalently, μ1 − μ2 = 0, for comparing groups on a population mean
- H0: P1 = P2, or equivalently, P1 / P2 = 1, for comparing groups on a population proportion
- H0: ρ = 0 for the population correlation coefficient (e.g., correlation between age and mean arterial blood pressure)
- H0: β = 0 for a population regression coefficient (e.g., slope of mean arterial blood pressure regressed on age, or log-odds ratio for relationship between exposure and a binary outcome like mortality)

Figure 1. Conventional notation for the null hypothesis (H0).

Figure 2. Conventional notation for the null hypothesis (Ha).
Most investigators conventionally seek to reject the null hypothesis (H0) because of their expectation (or hope) that the studied intervention does result in a difference between the study groups or that the coexisting factor has an effect or association. Therefore, in most clinical and basic science studies and manuscripts—including in Anesthesia & Analgesia—the alternative hypothesis (Ha) is typically stated, and the null hypothesis (H0) is not. Also, the alternative hypothesis is typically stated in the direction of interest or the expected direction.

For example, in the highlighted study and article by Patel et al,2 the authors do state the alternative hypothesis (Ha) as “We hypothesized that the intraperitoneal instillation of lidocaine would reduce postoperative pain scores after elective cesarean delivery.”

In the article by Chau et al,3 the authors also state the alternative hypothesis (Ha) as “We hypothesized that the onset of labor analgesia would be most rapid with the CSE, followed by the DPE, and slowest with the EPL techniques.” However, in the last paragraph of their Introduction, Chau et al could more clearly differentiate their primary and secondary aims—for example: “Our primary hypothesis was that the onset of labor analgesia,” and then “Secondarily, we sought to determine if overall analgesia characteristics and side effects would favor the DPE technique.” Furthermore, their Introduction should directly align or coincide with their statistical methods, in which they instead focus on the primary outcome in only 2 of the 3 intervention groups: “The primary outcome of the study was time to NPRS ≤ between the DPE and EPL groups.”

Finally, in the article by Faraoni et al,4 the alternative hypothesis (Ha) is stated succinctly as well: “We hypothesized that children with preoperative anemia undergoing noncardiac surgery would have an increased risk of in-hospital mortality.”

However, it is customary and usually expected that the nonequality on the parameter of interest implied by the alternative hypothesis be assessed using a 2-tailed test statistic, because superiority or inferiority cannot be definitively known ahead of time. It is for that reason that in the alternative hypothesis formulations stated previously, we used a not equal to sign (“≠”) instead of a 1-directional greater than (“>”) or less than (“<”) sign. An intervention that is expected to have a positive effect may in fact have a negative effect or vice versa. A 2-sided or 2-tailed test statistic is therefore needed to make sure that a true effect in either direction be appropriately tested and thus captured by the study.

**REFERENCES**


