Widening Gaps between the Hare and the Tortoise: How Clinicians Catch Up the Advances in Basic Research

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Introduction

Recent advances in various aspects of medicine are so overwhelming – to name a few, Omics, big data, artificial intelligence (AI), and endless pipelines of new therapeutics… – that individual clinician feels inevitable helplessness and anxiety of lagging behind. In contrast to the hare in Aesop's allegory, hares in reality do not sleep, and make the gaps between the hare and tortoise even wider and wider. Thus, clinicians in practice can't dream of keeping abreast with advances presented in front of their eyes. This leads to a regression to safe already knowns or a blind acceptance of unknowns, either of which is not thought to be desirable.

As for me, I'm always overwhelmed at sheer amounts of supplementary data accompanying Omics studies – for example, tables beyond typesetting limitations and figures beyond my intellectual limitations. I'm always surprised at the unexpected findings presented in the big data studies, and at the same time suspicious of whether this association is authentic or whether this finding is causal. About AI, I not only admire the technological feat which is unimaginable decades ago, but also feel uneasy anxiety for advancing AI-doctors replacing humans. In the flood of brochures advertising new drugs, I'm lost in confusion what is the real position of this drug in the therapeutic ladder of my own. In short, I was the helpless tortoise just looking at the hare running away out of my sight.

Rebooting

I found unexpected consolations from the article by John Ioannidis.1,2 These articles confirmed my long-

standing suspicions for the authenticity and usefulness of innumerable reports on the ever expanding lists of medical journals. While reading the articles and thinking about their meanings, I am developing a good habit of critically assessing the quality of the reports. In addition, I obtained some – not full – immunity to overwhelming data of Omics study, since I've learned that most of the associations revealed in the Omics study would be false positive, requiring tests of reproducibility before accepted as true positive.

Another firm ground on which I can stand by myself was one of my mentor's remark on the status of clinician. He repeatedly mentioned that, "Theorists, they produce articles easily, even proving that their previous theory was wrong makes another new article. In contrast, practicing clinicians, they hardly publish, because their subjects, i.e. patients, never change, and they could not find something new so easily." When I read big data articles, I always reflect why I or my great preceding mentors missed these associations found on big data. In most cases, I think that the associations are just statistically significant, not clinically significant. I firmly believe that our professions – past, present and future – are too meticulous to miss important clinical symptoms or signs or associations, and our patients are rarely changed in terms of clinical presentations. Thus I think it is really hard to find "something" new under the sun.

But there is no rule without exceptions. Thus there can be something new under the sun, and this truly holds to new therapeutic modalities, for example, new biologics adopted for old disease. Although, in most cases, new therapeutics start with great fanfare and expectation, but later disappear without trace, however, in some cases, new therapeutic agents could be a game-changer. In such circumstances, clinicians should be cautious not to be misguided by the advertisement of pharmaceutical companies. There are several commonly encountered tricks by the company – comparison with the placebo (not with active drug), outcome measure with surrogate markers (not with genuine health parameters), and exaggeration of outcome with relative ratio (instead of absolute incidence). Clinicians have to learn reading between the lines. The best way to avoid these traps is to raise your hand and ask for clear explanations not to the salesperson of the company, but to the colleague expert doctors who participated in the clinical trials to find the efficacy and safety of new therapeutics. An informal conversation with an expert at a meal is worthwhile to read thousands articles.

Back to the basic

The mentor who taught me the invariable nature of patients also gave me another important lesson about the clinician's duty as a care giver. "Both dermatologist and pathologist look at the same pathology slide for biopsy specimen of skin disease. Pathologists try to give correct diagnosis, but dermatologists should not satisfy finding correct diagnosis. When viewing slide and thinking about the diagnosis, dermatologists have to answer what can

be done for patient, at the same time." Given the diagnosis, clinicians should always think of what they can DO for patients.

Considering this duty of clinicians to do something for patients, clinicians should assess the advances of medicine in terms of practical usefulness. Many articles are thought to have little practical value – they are published only for the sake of publishing itself. This is consistent with what Ioannidis asserts in his 2016 PLoS article2. Ioannidis's 2005 article1 indicate the other requirement that decent article for clinicians should has – that is authenticity.

From the above mentioned two critical aspect of decent article – authenticity and usefulness, I suggest a work flow to assess new advancements of basic research as a clinician (Fig 1). First, divide the articles into two categories – what I am familiar with or not.

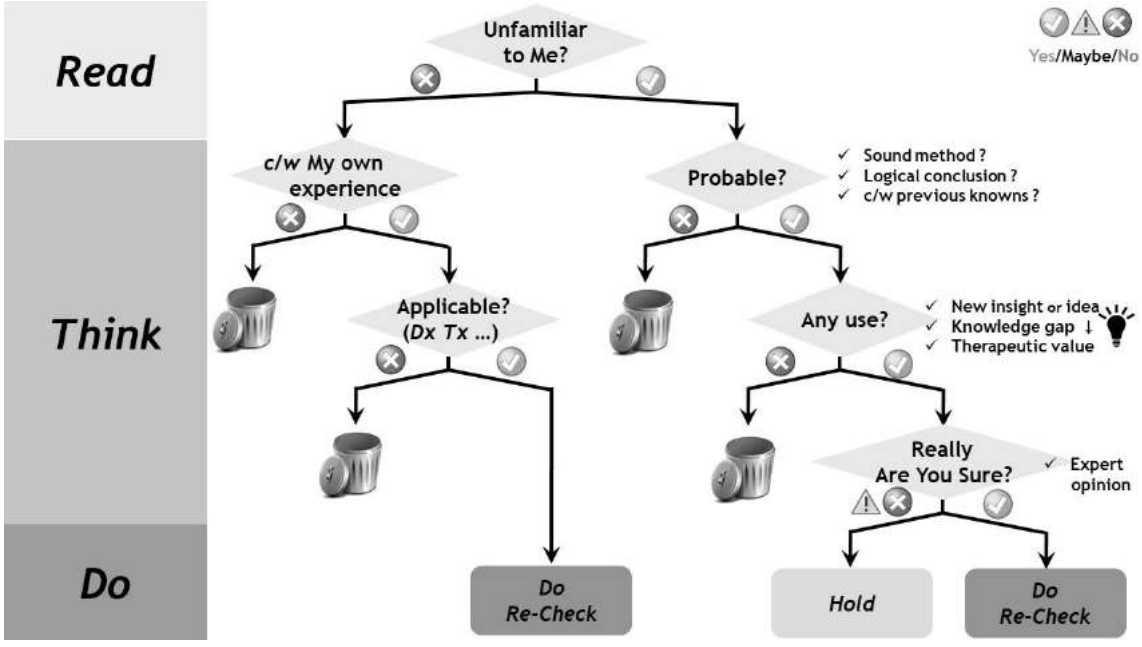

Figure 1. Work flow for incorporating or discarding new advancements in basic research.

In case of familiar subjects, I check whether this article is consistent with what I've already known – my own test for authenticity. If not, just throw it into trash bin. Although, consistent with my experience, if there is no practical applicability for my practice, I regard it as an article for the sake of publishing itself. If there is something applicable for my patients with not so much costs (real money, risk…), I think clinicians should not hesitate to apply new advancements to the care of their patients. However, clinicians should re-assess both cost and benefit again and again with their own experiences. Those advancements which survive the test and re-test would be applied to patients with more confidence and be used to expand what's already known.

In case of unfamiliar subjects, check whether the contents of the articles are probable or not. Based on sound method and logical inference from the results, the findings could be true. However, if findings are not consistent

with known findings of other articles, better to throw into trash bin. For those articles which survive the test of authenticity, then check the usefulness. Because we are not lazy professions at least in our clinical fields, and there could rarely be something new under the sun in clinical medicine, the usefulness for us would be suggestion of new insight in our fields or new tools crossing knowledge-gap. Another source of usefulness stems from the new therapeutics which open new therapeutic horizons in clinical medicine. Considering that most of great advances introduced with great hope turned out to be disappointing later in the history of medicine, for the unfamiliar truths, I think it is necessary to pass another safety test before applying them to patients. As mentioned before, expert opinion may be reliable short cut in this final stage of verification. As is true for familiar truths, re-assessment is mandatory for the final survivor of these verification process.

Concluding remarks

In spite of all the handicaps and limitations that individual clinician has, he/she can't afford the luxury to be idling in the patient care – between the two extremes of regressing into comfortable but outdated practice habit and succumbing to trendy but risky new waves. Clinician have to do the right things for their patients.

Another mentor of mine underscored the attitude of scientists, and summarized it as "read-think-do". I think it can be applied to the vigilant clinicians: clinicians should READ not to fall behind ever-advancing medicine, but they critically THINK on what they READ not to fall into a trap, then DO what they could for the patient care not to fall into status of "all talk no action".

References

1. Ioannidis J. Why Most Published Research Findings Are False. PLoS Med 2005;2(8):e124.
2. Ioannidis J. Why Most Clinical Research Is Not Useful. PLoS Med 2016;13(6):e1002049.