Objective and numerical method of finding value and selecting importance of medical knowledge, studies and publications

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SIGNIFICANCE

Putting worth on research and selection of studies by importance are crucial in medical innovation. Practical applications include choosing personal study topics, publication review, study grant selection, and decisions of spending or misspending billions in public health. Multiple studies raised alarm that current methods perform poorly in reproducibility, prediction of best research and objectivity. I propose using the metrics how much disease burden is reduced and calculating objective, numerical research value. The concept is that worth of medical research is not subjective but can be reproducible and numerically quantified. The method increases transparency by giving decision makers an externally accountable proof, and frees peer reviewers to check scientific integrity. Its numerical form can capture small differences important in competition between studies.

ABSTRACT
Finding value and selecting knowledge by importance are crucial in medical innovation. Applications include individuals designing research, funding organizations selecting grants, journals – publications, institutions – priorities in public health and health policy, and decision makers spending or misspending billions of research funds. Currently finding value of knowledge is done by peer review together with checking scientific integrity. Multiple studies raised alarm that it performs poorly in prediction of highest citations, bias, transparency and quality. The resulting problems include perception of slow medical progress and wasting funds and time. I introduce a standard, objective and numerical method for finding value of medical research. It measures disease burden prevented by new knowledge contained in a study or a publication. In its simple form, it is calculated using disease prevalence, disease burden, and efficacy of the therapy. It can be modified for risk of failure, early stage research and for ethical considerations. The process is described step-by-step in terms common in medical practice. A quick estimate is often sufficient. The advantage is objectivity, since it is calculated from real world data. This gives transparency and externally accountability to decision making. The second advantage is a numerical form. This can measure small differences in research value which, in sharp competition, determine which studies are selected. A researcher can calculate the value of own future effort. Institutions might ask to provide it at submission.

ARTICLE

Introduction

Important task in medical innovation is finding value of medical knowledge or selecting more versus less important research (1-8). It is performed whenever an individual researcher chooses a study topic. Further practical applications are selecting manuscripts in academic publishing (9,10), selecting grants during science funding review (2-6,11-14), and in choosing research priorities and
trying to reduce waste in public health and health policy (1). The results are decisions to spend or misspend tens of billions of research funding annually.

Currently finding value of medical knowledge is partially subjective. Institutions and journals use peer review, which also checks for scientific integrity. However, multiple studies in the last two decades raised alarm that peer review is remarkably inefficient in estimating value of research (5,6,8,10,11-15). Quality of prediction which research turns most valuable, by number of publications, citations (2,3,6,14) or several other metrics (13,14) is low (2,3,6,10,13,14). Journals frequently reject papers which become groundbreaking after publication elsewhere (10). Reproducibility of opinions between reviewers and journals is also low (5,8,10,11-13). Common accusations are also bias against novel topics and directions of research (5,9,13), and lack of transparency (1,3,8,13,15). Resulting problems include journals struggling to improve content, perception of wasting medical spending and science funding (1,3,13,15), and time at every level, from an individual researcher to nation-wide policies, perception of too slow progress in medicine (1,9,13), and poor image of medical research both within the research community and in the public (9).

Finding value of medical research additionally lacks precision (6). Sharp competition results in that only 10-15% of eligible research grants (6,16,17), and 4-10% manuscripts in top journals (18-21) are accepted. Later, one publication can spawn a multi-million grant, and a single grant or publication can make or break a career of a researcher (14,22,23). Because small differences in quality determine which studies go to the small minority which becomes successful (6,14), and average better than random (6) to moderate (4,7) quality of the evaluation is not sufficient (1,7,9).

Although the weakness of peer review became well documented during two decades, it persists because no better solution was found. Suggested modifications included changing selection or
motivation or reviewers (1,7), reviewing by a larger group or a community (24), or modifying
human reviews by scoring methods or algorithms (25). None of these became universally accepted.
They all share the inherent bias: they are based on personal opinions (8,13,15), not objective and
prone to be challenged (13). This also means that a branch of business which manages multi-billion
funds, which medical research is, has relatively poor central metrics (1,13). Other branches of
business developed stricter standards (e. g. 26).

Results

The concept

I propose to evaluate biomedical knowledge using objective and numerical research value. To avoid
semantic misunderstanding: the research value should not be confused with monetary value.
Knowledge includes research studies, grant applications, publications, and manuscripts. All these
are pieces of knowledge or future knowledge, which are evaluated by science reviewers using
broadly similar criteria. I propose using an objective metrics derived from the prime objective of
medicine: protecting human life and health. The medical knowledge should be valued by how much
disease burden it prevents. Numerical research value is, in its simple form, calculated by
multiplying disease prevalence, disease burden and efficacy (established or expected) of the
therapy.

The concept is perhaps most intuitively understood by an example. Imagine that a medical doctor
reads two reports about two therapies. The therapy A allows saving lives of 100 people annually.
The therapy B allows saving lives of 200 people annually. This is a simplified example and all other
factors are equal. The doctor could reasonably say that the piece of knowledge B is exactly twice as
valuable as A. This shows, that the value of knowledge for medicine can be based on the facts in the
real world and that it could be measured in exact numbers.
The advantage of this approach is objectivity, because it comes from real world numbers such as disease prevalence, disease burden and efficacy of the therapy. They are externally verifiable and have relatively limited scope for interpretation. This makes decisions explainable and externally accountable. The latter is valuable to any official who needs to justify the decision making.

The second advantage is that the value is quantitative, so potentially very precise. The value can contain a margin of error, which it can be also expressed in numbers. Currently decisions are made using qualitative adjectives like 'important', 'very important', 'breakthrough', or essentially appeals to majority: 'of big general interest', 'considered important' etc. Compared to these, numerical research value allows making decisions with much more clarity.

**Extension to risk of failure, basic and early stage research and portfolios of studies**

Numerical research value can also be extended to risk of failure of a study. For example, clinical trials in large majority do not result in a reliable therapy (27-29). Therefore the research value of a clinical trial should be divided by the probability of failure of clinical trials at a given stage. This way, the risk can be narrowed down.

Preclinical research, pure science research and one-off reports carry risk of failure even larger than a clinical trial. Probability of a drug candidate to pass to a phase I of trial is on average 0.29–0.35 (30-32), varying from 0.23–0.7 between disciplines (32). I did not find a number how many pure science and one-off reports result in a practical therapy. As an interim solution I suggest calculating value of a preclinical research as 0.3 of a phase I clinical trial in the same discipline. This, however, is likely an overestimate.
Effort currently put into research can be included in research value, too. A new researcher entering a popular field faces a risk that competitors will solve the problem. Unless the researchers expect a synergy, the law of diminishing returns applies. In this case, the research value might be divided between the working groups in the field, or by estimated probability of success. This avoids the possible mistake that 100% researchers and funds would go to the single most common disease.

Calculations can be also applied to the choice of several not exclusive options. An institution which can pick several or a portfolio (3) of projects, could use methods similar to constructing an optimal portfolio of options (33).

In some cases, exact numbers are impossible to get. In this case they may be replaced by estimates. Nevertheless, narrowing down the uncertainty in the well explainable way is still helpful for decision.

In many practical situations, a quick estimate of research value is enough for a decision. For example, often one needs to choose between two options. Then, quick estimate of key factors, and knowing that one relative research value is much bigger of another, is sufficient for a decision.

Methods

A practical step-by-step guide to objective research value of a manuscript or a study

Note, as said above, that a quick estimate is often enough in practice.

1. Choose the metrics.

An easy mistake would be to trying to compare the incomparable, for example lifetime cases worldwide with cases per year in the USA. The metric should be common to all compared cases,
appropriate to the topic and objective. The metric can include impact of the disease (mortality, quality-adjusted life years, disability-adjusted life years, financial cost, other), time frame (lifetime occurrence, occurrence per year, or other) and geographical scope (worldwide, in a country etc).

A researcher can define the metrics for oneself. A journal or a grant committee could select the metric for the field of study and ask the submissions to use it, unless a good reason is given.

Generally, the criteria of a metric mentioned earlier in the above lists are preferable to latter ones, for example mortality over life quality. The appropriate recalculation could be used. However, the latter criteria are better in some disciplines, for example for non-lethal diseases. Additionally, a simple recalculation may be inappropriate for the impact of the disease, because the opinion in society is that life has no absolute priority over quality of life. Here the metrics partially depends on subjective ethical considerations.

2. Obtain the burden of the disease in concern according to the metrics. If an effect is measured over the existing therapy, a correction is needed.

3. Calculate the numerical research value itself – the disease burden lowered. Multiply the burden of the disease by efficacy of the therapy (actual or expected). For example, if mortality was reduced twofold, divide the disease burden by two.

4. For the early stage research, estimate probability of passing to the therapy. In case of clinical trials, divide by a rate of failure of trials appropriate for the discipline and type of study (27-29). For a pre-clinical research or single case study, the worth is even lower (30-32). If no data are available, I suggest an estimate of 0.3 of a phase I of a trial but it can be an overestimate.
5. Theoretically, the research value could be modified by applications outside the field of study. For example, drugs for one type of cancer are often active against other types. If there is a well-founded belief that it is possible, value of other areas can be added. However, I did not found the numbers in literature how often such extensions occur. An ideal modifier here would be a number of therapies found extensible between the disease areas, divided by all attempts (including the number of therapies tried and failed).

The above guide could be modified appropriately to a medical area. Note, that small differences in numbers may come from imprecise original data and be spurious.

Ethical considerations could warrant modification. Note, however, that the ethical principle of lowering disease burden is already the principle of the method. Particular ethical considerations can often be helped by calculations of research value. As an example, it is possible to calculate which patients are neglected by the current medical research. To calculate what help already is available for a particular disease, concentrate on the point 2. above. Calculate the burden of the disease if no therapy was used. Calculate separately what proportion of this burden is lowered by the existing therapies. This shows objectively which diseases are neglected and how much. Particular effort should be directed at these. Such efforts might fit into the general medicine portfolio (see above) as a low-hanging fruit, where small, targeted effort can produce big results.

Discussion

A researcher can use the concept as a purely personal guide to which research is worth undertaking and which publications to read. Further application is publication review and science funding review of research grants. Here, journals and funding institutions could calculate the research value by themselves, or ask submissions to include the calculated research value and its original
components. These bodies could also decide to produce guidelines to the authors containing, for example, preferred metric to use. This will reduce the burden on peer reviewers who are notoriously overworked (7,10,13). In this setup, peer reviewers check faster whether the research value was calculated properly, and can focus on scientific integrity: whether the research is scientifically valid, methods will produce the results, results support conclusions etc.

The method itself is a scientific novelty. It introduces the idea that research value of medical research is not a subjective whim, but can be objective and can be numerically expressed. The general understanding in the medical community that some matters are objectively important and others not so becomes formalized using a generally agreed metrics of disease burden. The method is reproducible, in the sense than every researcher using the same data on disease burden, chance of success of clinical trials etc. should arrive at the same number. This greatly increases objectivity and reduces human bias, even if there is still some scope for interpretation. The result is providing decision makers with transparency and external accountability of their actions, important for example in medical spending.

There are cases when exact calculation of objective research value is impossible or impractical. This concerns, for example, the very early stage research, which is currently missing estimates of probability of developing into a practical therapy. Even then, the method can be useful by providing brackets of uncertainty, or a relative choice, for example choosing one early stage research before another.

The value can be also used as an objective metrics in general research: in cost analysis and more broad science pricing and research pricing in health economics, public health and health policy, trawling medical research for the purpose of data science in metaresearch, bibliometrics, scientometrics and science of science. It might also be adopted, together with citations ranks,
impact factor etc., for research quality assessment, evaluating scientific output, academic productivity and scientific achievement. Interestingly, it allows comparing research from very different branches, for example cardiology with oncology, as long as the metric is the same.

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