Progress in Cancer Care: The Hope, the Hype, and the Gap Between Reality and Perception

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Many of the recent advances that have been made in cancer care have been, although arguably important, relatively modest. Sometimes, however, these modest, incremental advances have been presented, discussed, or at least perceived by medical and lay audiences alike, as major advances or so-called breakthroughs. Discussions of the actual data and frank delineation of the limits of the true contribution of a new agent are often met with responses such as “Is that all it does?” or “Why did I think it did so much more?” Why are perceptions and reality so frequently disparate? One important, and correctable, reason is a widely accepted use of terminology that inadvertently facilitates, and at times even encourages, an overly optimistic interpretation of stated results. Although adopted with the best of intentions to instill optimism into a difficult situation, to provide for gentle and compassionate communication of devastating news, or to provide statistical and technical accuracy, still the effect in too many cases has been, in the long run, exactly the opposite of what was originally intended. Under the guise of scientific or statistical rigor, the use of certain terms in fact serves to regularly permit us to hear, whether said or not, an overstatement of accomplishments. The terms are technically correct, and an expert in the field will have no problem accurately understanding what is being stated. However, when these terms are used to communicate the same information to a less specialized medical audience, even more so, to the public, misunderstandings frequently occur. We are not discussing here the objective results of the trials, nor the relative merits of various metrics used to report those trials but, rather, the subjective interpretations and common misinterpretations of those data, based not on what the numbers said, but on what was said about the numbers.

This article does not represent a systematic review of publications to address the frequency of specific concerns, but rather offers some general qualitative observations for consideration. Outlined herein are several examples of such terminologies with potential for ambiguity and recommendations for modifications of these terms that would diminish these opportunities for misunderstanding. Such changes would encourage a more direct accounting of our successes and failures and would facilitate more rational expectations on the part of patients, more accurate understanding on the part of clinicians, and more accurate representation of the relative benefits of a therapy versus its costs and its risks.

A recent press release about a clinical trial result quoted a knowledgeable individual as saying how gratified he was that patients could now be offered a treatment with a “significant” survival advantage. Few doctors, fewer laymen, and even fewer patients reading that statement would have assumed that in fact this advantage was an extension of median survival by a total of 6 weeks. The more precise term to use would have been a “statistically significant” survival advantage. By allowing the omission of the clarifying adverb, we at best permit, and at worst tacitly encourage, the assumption that “significant” is synonymous with “substantial.” So my first recommendation for improved clarity in communication is that we not accept the unmodified word “significant” when describing an advance in cancer care, but rather should require an appropriate modifier, such as “statistically significant,” if that is what is meant, or “clinically significant,” if that is what is being claimed. For claims of clinical significance, a necessarily subjective determination, the actual benefit should be concurrently stated, such that if a person wishes to offer the opinion that a 6-week, or 6-month, or 6-year survival benefit is “clinically significant,” a clear statement of the actual extent of that benefit would be immediately present, so that the reader could evaluate whether he or she agrees with the author’s interpretation.

Also worthy of consideration is the often misunderstood use of the term “highly significant.” Even if we use the more accurate “highly statistically significant,” the misperceived implication of this term too often can be that the greater degree of significance, as indicated by the substantial number of zeros in the P value, implies a greater benefit. This is, of course, not the case. What it implies is a greater confidence that the difference reported is a real phenomenon and is not due to chance. A study that shows a 2-week median survival advantage with a P value of .04 differs from a study that shows a 2-week median survival advantage with a P value of .0004 only in that we are a hundred times more confident that the difference in the second study is a real phenomenon and not the result of chance; the second study does not show a superior survival advantage to the first. Thus a second recommendation for improved clarity is that when reporting a statistically significant difference between two groups, it would be most informative to report the actual difference between the two outcomes and then report
the treatment is highly statistically significantly better than a comparator is unnecessarily vague. If the survival benefit is a median of 2 weeks, or 2 months, or 2 years, let’s state that first and then tell the reader how certain we are that the reported difference is real and not due to chance.

**FREEDOM FROM PROGRESSION-FREE SURVIVAL**

The term “progression-free survival” is both desirable and problematic because it has the all-important word “survival” in it. Indeed, many patients and clinicians have been confused into believing that a treatment showed a survival benefit, when in fact, progression-free survival data were all that had been reported. This is not a matter of debating whether progression-free survival is a reasonable surrogate for overall survival, but, rather, this represents an emphasis of the fact that they are two very different end points, and that the term “progression-free survival” advantage can too easily be misread or misheard as a statement of an overall survival advantage. Thus a third recommendation for improved clarity in communication of cancer results is to replace the too-easily misunderstood term “progression-free survival” with the more precise, if less rosy, term “progression-free interval.” This term more accurately reflects the true meaning of the concept, which, in general, is the time from when a treatment is started until the time that it is no longer controlling the cancer. Because it is fully understood by all that if the patient has died, the treatment is no longer working, it is therefore not necessary for either accuracy or clarity to have the word “survival” included in the term. Announcing that a study demonstrated a “statistically significant improvement in the progression-free interval” would be a far clearer and more accurate representation of the actual achievement than the currently accepted “significant improvement in progression-free survival.”

**IF THE DEATH RATE IS REDUCED, HOW COME THEY ALL DIED?**

A randomized study in patients with incurable cancer that compares two survival curves may accurately and correctly report that the “risk of death was reduced by 20%.” Although this is a fully correct use of technical statistical terminology, many clinicians and much of the lay audience for this sort of information lack the rigorous statistical training to correctly understand this use of this terminology. The easily assumed but not correct implication of the colloquial use of the statistical statement is that 20% fewer patients died, and therefore these 20% were essentially cured. This, of course, was not the case; in a trial that describe a chemotherapy regimen report that it was “well tolerated” or had “tolerable toxicity,” or the subtle variant, had “manageable toxicity.” Here again, the layman reading the report can logically mis-assume that the regimen in question was not like all those other chemotherapies that we hear about, but rather was more like taking an over-the-counter analgesic or a vitamin tablet. Therefore, a fifth recommendation for improved clarity in communication is to disallow the subjective and essentially meaningless terms “well tolerated,” “tolerable toxicity,” and “manageable toxicity” from reports and descriptions of cancer therapy. Toxicities would best be communicated by simply reporting them, without editorializing. The reader can decide whether the toxicity reported is or is not at an acceptable level, given the severity of the disease and the benefit of the therapy.

In conclusion, we have made many important advances in cancer treatment over the past decades, and we can be proud of these accomplishments, but many of the steps forward have been small ones, and there is still much more work to be done. It is counterproductive to foster the perception of greater success than has actually been achieved, as this would risk jeopardizing our credibility, setting our patients up for disappointment, and fostering a complacent acceptance of modest, incremental advances in cancer drug development. If we, the physicians who are reporting, reviewing, and publishing these trials, eschew terminology that can facilitate misunderstanding, we will have taken a major step toward improving the accuracy with which our communications are understood.

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