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Do we need to involve patients in clinical study report lay summaries?

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ABSTRACT

Translating complex clinical regulatory documents into versions that are understandable to patients and the general public was never going to be an easy task, but it is a very necessary, important, and now legally mandated one. This article argues that the advent of the clinical trial results lay summary requirement has highlighted the need for patient involvement in clinical trials at the very earliest stages, not just during the trial itself, and that the involvement of the patient community can not only make the final lay summary much easier to produce, but can also enrich the clinical development process and make the results much more fit for purpose for patients themselves.

The clinical study report lay summary

After many years of writing regulatory documents for clinical research, one becomes very familiar with crafting, structuring, and writing documents for a regulatory audience. This entails writing documents constructed for the way they are read by regulatory reviewers, which assumes a scientifically sophisticated reader and is more concerned with directing the reader to the information rather than explaining the information itself. However, the introduction in 2014 of the requirement for a lay summary of the clinical study report meant that suddenly medical writers had to acquire the skills and ability to write for patients and the general public.[1–4]

This was largely embraced by the pharmaceutical industry as a way to reach out to non-specialists and provide them with clear, unbiased information to help them understand the clinical development process and to hopefully increase confidence and trust in the pharmaceutical industry itself. In addition to more (and better) health information being demanded by patients and the general public, the pharmaceutical industry is also aware that providing clear, unbiased information to patients not only fulfils a legal requirement, but also has benefits in terms of patient engagement and compliance. A recent review of health literacy and informed consent for clinical trials showed that study participants' comprehension improved when the information they were given was simplified, and this, in turn, led to greater patient satisfaction and confidence in their decisions.[5]

Of course, writing in a non-technical style was not completely new for many writers, as documents like the patient information sheet/leaflet (PIL) always needed to be written using a vocabulary that was comprehensible to non-specialists. This, however, only covered the actual language used – there were still problems in making these documents readable for patients and the general public, and studies have also highlighted serious issues with PIL design characteristics, such as type size and paper quality that negatively impact their use.[6] Thus, presenting the results of clinical studies for patients and the general public presents new challenges, especially in terms of what results to present and how.

Lies, damned lies, and statistics…

There are many aspects to presenting study results to patients and the general public that are challenging, and these have been well described previously.[4,7,8] Most difficulties begin with the fact that clinical trial results are often presented in tables and graphs. The understanding and interpretation of standard clinical research graphical techniques, such as error bars, forest plots, Kaplan-Meier graphs, or box-and-whisker diagrams are not skills that most members of the general public have, and yet describing and interpreting the results of medical interventions can be almost impossible without them.

Statistics are particularly difficult for even medical specialists to understand. Most people could probably understand that the primary efficacy analysis is meaningful based on whether the results are considered statistically significant or not, but trying to explain why the results of secondary analyses, which are also described using statistical significance but are not supported by statistical power, can seem like an almost insurmountable obstacle. It is even questionable whether this is worthwhile for patients and the general public, since the secondary analyses do not give definitive answers in the same way that the primary analysis does.

However, not presenting some of the results can lead to accusations of cherry-picking from many patient advocates, as it can be interpreted as an attempt to hide some of the results of the study.

More importantly, in many studies the efficacy measure that really matters to patients is not the primary one but rather one of the secondary measures. This commonly occurs when the primary analysis uses a surrogate marker for a disease that is more easily measured and quantified (such as the amount of a substance in the blood) rather than a direct measure of relevance to patient welfare, such as length of hospital stay or other measures of quality of life. This conflict between results that can be quantified (and described with statistical testing), and measures that have real meaning for patients' lives (but are often subjective and hard to describe) is central to much of clinical research and the cause of many of the main challenges when describing clinical studies to patients and the general public.

Medical writers do not usually need to consider this when writing for regulatory agencies, and rarely deal with "patient-centred outcomes" unless describing a study involving patient-reported outcomes or writing specifically for patients (often in the medical communications arena). Although regulatory agencies routinely request that the relevance to patients of any measure be demonstrated, this is rarely considered a key

aspect of the planning and design of clinical trials and drug development. When producing summaries of trial results for patients and the general public, this conflict can become painfully apparent and difficult to resolve.

Thus, there is growing awareness and momentum for the early involvement of patients in clinical trial design. For example, the latest advice given by Diabetes UK for "Writing a good lay summary" asks the researcher to consider "Were the questions and outcome measures informed by patients' priorities, experience, and preferences?"[9] Incorporating their feedback as early as possible (ideally during informed consent production) also allows the wording used in the informed consent form to be used in the lay summary, which not only increases patient comprehension and familiarity, but eases the medical writing process because text can be used that has already been developed, tested, and approved by the pharmaceutical sponsor company.[10]

Surely, if patient advocate groups could identify variables that would be of the most importance and relevance to patients prior to the design and running of the study, then these variables could be given a special status in the analysis and described in ways that could be more easily understood to the general public than the use of statistics alone.

Do we know what patients want and need?

We know that the pharmaceutical industry's perception (and also that of some clinicians) of what patients really want and need from patient information can be different from reality.[11] Nevertheless, it is vital that we understand these requirements, and we can only ensure this by reaching out to patients and patient advocate groups and involving them in the clinical development process.

The lay summary is a description of what happened in the clinical trial, and since it is aimed at patients and the general public, it must be relevant for them. This is not a "one-size-fits-all" exercise, since what can be deemed to be relevant depends on many variables, including the patient group, the condition under investigation, and the stage of development of the drug or treatment.

It is also important to offer patients and the general public some context surrounding the results, so that they can understand how and where the new drug or treatment fits into the current armamentarium, and who it is likely to be most useful for. Finally, it is crucial that not only is the information presented in a clear and unbiased way, but that there is some reminder or explanation that a study's results should not be taken in isolation, and that clinical development requires many studies (sometimes with contradictory results) and ongoing testing before a medicine or treatment is considered fit for prescription to the public.

The involvement of patients in the development of the lay summary can help the medical writer (and therefore the pharmaceutical company) to address these issues by highlighting the particular areas of concern and relevance to the patient group that the document is aimed at.

However, health literacy[12] remains an issue. A World Health Organization study found that almost 50% of adults have problems with, or inadequate, health literacy.[13] To make sure that health literacy considerations are accounted for, it is important to include members of the target audience in the assessment (and preferably the preparation) of lay summaries, and this is advised by the EU in the Clinical Trial Results guidance.[14,15] It has also been shown that this can increase the readability and comprehension of lay summaries by the target audience.[16]

Of course, the reality of clinical development means that it can be difficult to involve patients at the very start, but even having them "user test" the final lay summary can bring huge value and make the document much more useful for patients,[17] and so this should be considered as a minimum. This agrees with our own findings that consulting patients or patient advocates has offered valuable insights into the development of lay summaries.

There is finally yet another potential benefit from greater and earlier involvement of patients and the general public in clinical development. The pharmaceutical industry currently suffers from a decidedly mixed reputation in popular media. The press seems to delight in occasional scandals and examples of "bad actors" to pillory the industry as a whole as immoral and greedy. Much of this is based on misinformation which finds fertile ground in the profound ignorance of most of the general public about drug development and clinical trials. However, by involving patients and their needs to a greater and earlier degree in the development process, the industry further stands to gain an improvement in public understanding, acceptance, and thus approval of the pharmaceutical industry and the ways in which new disease treatments are developed.

Conclusion

It is clear that involving patients in the crafting and development of the lay summary of clinical trial results not only helps medical writers (and the pharmaceutical industry) to produce more helpful, useful, and fit-for-purpose documents, but it is also an excellent opportunity for the industry to engage directly with their target audience. The goal should be to produce documents that can and are actively used by patients and the general public to understand critical information about the medicines they are prescribed and take.

However, patient engagement can and should be taken a step further. The way that clinical studies, and in fact most clinical research, is conducted may make perfect scientific or statistical sense but can miss the mark as far as patients are concerned. Although the values of a particular electrolyte in the blood may be a convenient way of measuring disease progression in a clinic, there might be far more relevant measures for the patients. Involving patients at the start of the clinical development process during the planning of clinical development and study design can save time, money, and bring positive outcomes for everyone. ■

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