Lay titles for clinical trials: Is industry achieving the balance?

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Abstract
Titles of clinical trials may directly influence whether patients, caretakers, or healthcare professionals will want to obtain more information about the trial. Major clinical trial registries require lay titles (referred to as “brief” or “public” titles) that are understandable to the public. However, devising adequate lay titles is challenging. In this study, we assessed the quality of lay titles from Phase II/III and III clinical trials registered in ClinicalTrials.gov in 2021. Assessments included the presence of recommended elements, use of technical terms, an expert assessment of adequacy and informativeness, title length, and the use of acronyms. A large proportion (72%) of lay titles did not include all recommended elements, contained technical terms (73%), and were not adequate according to experts (51%). Often, brevity was given precedence over content and understandability. Generally, lay titles with acronyms had better ratings in all assessed categories. These results suggest that industry sponsors can do more to create lay titles that better inform patients and healthcare providers.

Introduction
Titles are the key contact points between readers and authors, and they are the most read part of any article, book, posting, or trial registry entry. Based on the title, readers will decide whether they want to retrieve further information. A title should direct attention, be easy to read, and comprehensively and clearly describe what the main document is about. A title should also be informative to the reader and as specific as possible.

This is also true for clinical trials. Titles of clinical trials may directly influence whether patients, caretakers, or healthcare professionals will want to obtain more information about the trial. Because most clinical trial registries return a list of trial titles in response to a search query, the title is the key element in identifying clinical trials that are of interest for patients, caregivers, and healthcare providers.

All registries that contribute to the World Health Organization International Clinical Trials Registry Platform (ICTRP) are required to provide both a scientific title and a lay title for each clinical trial. In many registries, the title displayed in response to a search query is the lay title, referred to as the “public title” by the ICTRP and the “brief title” by ClinicalTrials.gov.

The requirement to provide a lay title was originally introduced with the initial release of ClinicalTrials.gov (2008) and with the launch of the ICTRP (2005). Although the requirement has been around for more than 15 years, many sponsors still do not appear to provide easy-to-read and understandable trial titles in their trial registrations. For example, an assessment of patient focus in a representative sample of ClinicalTrials.gov records from 2017 to 2018 showed that brief titles achieved only 52% of the maximum score, indicating that patient focus was underdeveloped.

By providing a plain language checklist, ClinicalTrials.gov recently (September 2022) bolstered the use of lay language in trial registry entries such as brief summaries, which intend to provide high-level overviews of clinical trials.

Previously, we analysed the challenges in generating lay titles for clinical trials that are effective at both informing the readers and complying with ClinicalTrials.gov requirements.

A well-written lay title is not only easy to read but will also inform the reader about the topic of the
It should also be concise so that it meets formal requirements and increases the likelihood that it will be remembered. Titles also need to be accurate and not mislead the reader about potential benefits of the intervention being investigated.

Lay titles need to be written in language that is understandable for non-specialists, that is, the lay public. This is stated in the ClinicalTrials.gov Protocol Registration Data Element Definitions, which explain that the brief title should be “a short title of the clinical trial written in language intended for the lay public. The title should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied.” The limit for brief titles on ClinicalTrials.gov is 300 characters including spaces.

In the current study, we assessed the quality of lay titles for late-phase clinical trials registered in ClinicalTrials.gov in 2021. We focused on late-phase clinical trials because we assumed that they are of particular interest to patients, mainly because they tend to be large, multinational trials that offer a realistic opportunity for participation. Furthermore, late-phase trials often compare an investigational drug with established treatments that patients may already be familiar with. We also considered that late-phase trials would be of particular interest to patients because the safety profile of the investigational substances has already been explored more comprehensively than in earlier-phase trials.

Methods

Data extraction

In February 2022, we extracted lay titles of trials posted on ClinicalTrials.gov during 2021. We focused on industry-sponsored interventional clinical trials in Phase II/III or Phase III. To limit the total number of lay titles to be analysed, we further narrowed the scope to the following therapeutic areas: bowel disease, dementia, chronic kidney disease, and breast cancer. These four search terms were entered in the ClinicalTrials.gov search field. This resulted in a list of 74 lay titles.

Analysis of lay titles

Four experts (i.e. the authors of this article) with 2–7 years (median 6.5 years) of experience in lay language writing and creating lay titles were randomly assigned to rate the lay titles so that each title would be rated by two different experts. The analysis included three categories: presence of recommended elements, presence of technical terms, and an expert assessment on adequacy and informativeness. After completing the assessment, individual scores were compared, with differences resolved by discussion among the experts to achieve a single harmonised score.

Assessment of the presence of recommended elements

The presence of the following recommended elements was assessed: intervention, target population, scientific aim, and condition. Members of the expert panel scored the presence of each required element in the lay title from 0 to 4.

Assessment of the presence of technical terms

It was assessed whether the lay titles included any technical terms. For example, words in Latin language like “versus” or specialised terms like receptor names or mode of action details were considered technical. However, substance name and disease name were not considered to be technical terms (see Table 1). Titles were categorised into the following groups: titles

All registries that contribute to the ICTRP are required to provide both a scientific title and a lay title for each clinical trial.
without technical terms, those including one technical term, and titles with two or more technical terms.

**Expert assessment of adequacy and informativeness**
Titles were assessed based on the experts’ previous experience in the field and were scored as “adequate” or “needs improvement”. Titles could be assigned a score of “needs improvement” if they lacked important information, were very complicated, included cryptic terminology, or had grammar problems like unclear pronoun references or unclear sentence structure.

**Other assessments**
The length of the titles was determined based on the number of characters with spaces and descriptive statistics were calculated. Thereafter, the inclusion of technical terms and recommended elements as well as the expert assessment were analysed for short titles with fewer than 100 characters and longer titles with 100 characters or more. In addition, the use of trial acronyms was investigated. Lay titles with and without trial acronyms were compared with regards to inclusion of recommended elements, use of technical terms, overall adequacy, and length.

**Statistical analysis**
Only descriptive analyses were performed. Calculations were made using Microsoft Excel (Version 2202; Microsoft Corporation, Redmond, WA, USA), and figures were prepared using GraphPad Prism (Version 9; GraphPad Software LLC, San Diego, CA, USA).

**Results and discussion**

**Recommended elements**
Only 28% of the 74 lay titles included all four recommended elements (intervention, target population, scientific aim, and condition; Figure 1). In other words, 72% of titles were not in line with recommendations. Almost a quarter of the lay titles only included two recommended elements (23%), while another 47% included three recommended elements.

**Technical terms**
Only 27% of lay titles were free of technical terms, 31% had one technical term, and 42% included two or more technical terms (Figure 1). The abundance of technical terms is not surprising because they are shorthand for complex content. Lay-friendly expressions are usually longer and do not always cover all aspects of the technical term. However, the inclusion of technical expressions may drastically limit understanding and, hence, the usefulness of a title, particularly for the general public.

It can be challenging for authors of lay titles to determine whether certain terms are “technical” or not. For example, the meaning of some technical terms may be well known to people living with a disease but not to the wider population. Table 1 lists some frequently occurring words and phrases together with the rationale for the experts’ assessments of whether they were considered technical terms.

**Expert assessment**
Each lay title was assessed individually based on the experts’ impression and given an overall score. The aim was to have an experience-based assessment of the adequacy and informativeness of the titles. For example, a title with poor grammar would be assessed as not adequate, as would a title that comprised many technical terms or a title with an unclear or missing aim. Based on the experts’ assessment, only about half of the analysed lay titles (49%) were considered adequate (Figure 1).

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**Table 1. Frequently occurring terms in lay titles and whether they are considered technical terms**

<table>
<thead>
<tr>
<th>Term</th>
<th>Frequency</th>
<th>Considered a technical term?</th>
<th>Rationale for assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic/Metastasis</td>
<td>26%</td>
<td>No</td>
<td>Likely to be well known to people living with cancer</td>
</tr>
<tr>
<td>Safety and efficacy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>26%</td>
<td>Yes</td>
<td>Non-informative; technical terminology whose full meaning is unlikely to be known to non-specialists</td>
</tr>
<tr>
<td>Placebo</td>
<td>14%</td>
<td>No</td>
<td>Term is widely known; it is important for potential trial participants to know they may receive placebo</td>
</tr>
<tr>
<td>Moderate to severe&lt;sup&gt;b&lt;/sup&gt;</td>
<td>9%</td>
<td>Yes</td>
<td>Grading of disease severity is usually conducted by investigators. Their assessment may or may not coincide with that of patients living with a disease, hence, this is a specialist’s assessment whose rationale is unclear to most patients.</td>
</tr>
<tr>
<td>Versus</td>
<td>8%</td>
<td>Yes</td>
<td>Latin term with confrontational connotations that does not fully reflect the comparison intended by the trial design.</td>
</tr>
<tr>
<td>Trial phase</td>
<td>7%</td>
<td>Yes</td>
<td>Unlikely to be understood by non-specialists</td>
</tr>
</tbody>
</table>

<sup>a</sup> Or “efficacy and safety”  
<sup>b</sup> Or variation of this phrase
Length
Sentence length in plain language writing is an important consideration. Various guidelines recommend using short sentences because they are easier to understand. To investigate whether this applies also to lay titles, we asked whether short titles are as effective as longer titles at fulfilling the requirements.

All titles analysed were within the ClinicalTrials.gov-specified maximum of 300 characters including spaces. The longest title was 283 characters and the shortest was 56 characters. The majority of titles (89%) had fewer than 200 characters (Figure 2), while 41% had fewer than 100 characters. The median title length was 118 characters, and the mean length was 127 characters. Our overall analysis of lay titles suggests that an emphasis on brevity comes at the cost of inclusion of recommended elements. All four recommended elements were included in 41% of the titles with 100 characters or more but only 10% of those with fewer than 100 characters. Expert assessment was “adequate” for just over half (55%) of titles with 100 characters or more but for only 40% of those with fewer than 100 characters. Interestingly, titles shorter than 100 characters were more likely to be free of technical terms (37%) than those with 100 characters or more (20%) (Figure 2).

Acronyms
When communicating about a particular trial, it is not very practical to use the full trial title. A shorthand notation or acronym facilitates trial-specific communication and outreach to both healthcare providers and patients. That is one of the reasons why sponsors create trial acronyms to make communication easier and more memorable. Further reasons may be that the trial acronym is an element of branding as some trial acronyms are also used for follow-up trials (e.g. EASE SBS 3, EASE SBS 4). Trial acronyms convey cohesion across the different communication channels, for example, through scientific publications, posters, flyers, and regulatory
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A. Number of recommended elements

![Bar chart showing the percentage of titles with different numbers of recommended elements for lay titles of fewer than 100 and 100 characters or more.]

B. Number of technical terms

![Bar chart showing the percentage of titles with different numbers of technical terms for lay titles of fewer than 100 and 100 characters or more.]

C. Expert assessment

![Bar chart showing the percentage of titles assessed as adequate or needing improvement for lay titles of fewer than 100 and 100 characters or more.]

Figure 2. Analysis of lay titles according to length in characters

Lay titles of fewer than 100 and 100 characters or more (including spaces) are compared for the (A) number of recommended elements, (B) number of technical terms, and (C) expert assessment. Due to rounding, percentages may not add up to 100%.

documents such as the Informed Consent Form, Clinical Trial Report, and Lay Summary. However, the use of acronyms is contentious. Positive-sounding acronyms or those that suggest a positive trial outcome can be manipulative and may unduly influence patients’ decisions about participation. Currently, there is no regulation on the use of acronyms in clinical trial titles.

In our sample of 74 late-phase lay titles, 43 (58%) contained a title acronym. Overall, seven trials did not enter the acronym into the appropriate field, while 84% of the acronyms were correctly entered. We found that lay titles with an acronym were on average longer, had fewer technical terms, had more recommended elements, and were more likely to be assessed as adequate than those without (Figure 3). One possible reason is that sponsors that choose to develop a trial acronym may be exercising greater care for other trial title attributes and therefore design more lay-friendly titles. Some of the acronyms in our sample imply a positive outcome of the trial, such as PRESERVE 2, STABILIZE-CKD, EASE SBS 3,
CORRECTION, CONVERSION, ELEVAT UC 40 JAPAN, and TRAILBLAZER-ALZ 4. In addition to acronyms that suggest a positive outcome, there are those that can be associated with strength or other positive qualities, such as ENIGMA-SC, ZEUS, EPIK-B5, STARS extend, DESTINY-B12, and ARTEST. Some acronyms seemed to resemble women's names, such as EMBER-3, SERENA-6, KATE3, Astrafenia, and OVELIA, potentially with the objective of conveying qualities traditionally associated with women: caring, loving, and healing. In OVELIA, the two connotations are even combined, as the name "velia" in Greek means "help".

In some cases, the acronyms are constructed so that they phonetically resemble a familiar word or expression but with a different spelling. For example, ARTEST is pronounced as “artist”, and EPIK-B5 is pronounced as “epic”. Both are associated with positive-sounding, familiar terms. But the different spelling could also cause problems and confusion when searching for a particular trial.

Many acronyms lack a direct link to the disease or the trial. From the acronym alone, it is difficult to know what the trial is about. However, some acronyms include the abbreviation of the disease, the affected organ, or an important gene mutation, such as TROPION-Breast01, STABILIZE-CKD, FIND-CKD, HER2CLIMB-05, TRAILBLAZER-ALZ 3, and TransportNPC. However, the abbreviations included might only be meaningful for people with a certain disease.

Figure 3. Comparison of lay titles
With and without acronyms for the (A) number of recommended elements, (In the group without acronym, there were no titles with 1 recommended element, and in the group with acronyms, there were no titles with 0 or 1 recommended elements.) (B) number of technical terms, (C) expert assessment, and (D) length. Due to rounding, percentages may not add up to 100%.
or for healthcare professionals and not for the general public. To be truly helpful, an acronym should relate to the trial, be easy to pronounce and remember, and not be misleading or coercive.

Conclusion
Our analysis suggests that industry sponsors have not yet realised the potential of good, comprehensive, and understandable lay titles for their clinical trials. While many titles are very short (<100 characters), this brevity comes at the cost of important details about the trial. Lay titles often include technical terms that may not be understood by potential trial participants. Furthermore, well-designed acronyms may be helpful for trial identification and communication. Overall, industry sponsors are yet to achieve the optimal balance between length, level of detail, and readability in trial titles for lay audiences.

Disclosures and conflicts of interest
The authors are employed by Boehringer Ingelheim Pharma GmbH & Co. KG or BioNTech SE. However, the views expressed in this article are those of the authors and do not necessarily reflect those of their employer or EMWA.

Data availability statement
For inquiries about data and other supplemental information, please contact the corresponding author.

References

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