Lay titles for clinical trials: A balancing act

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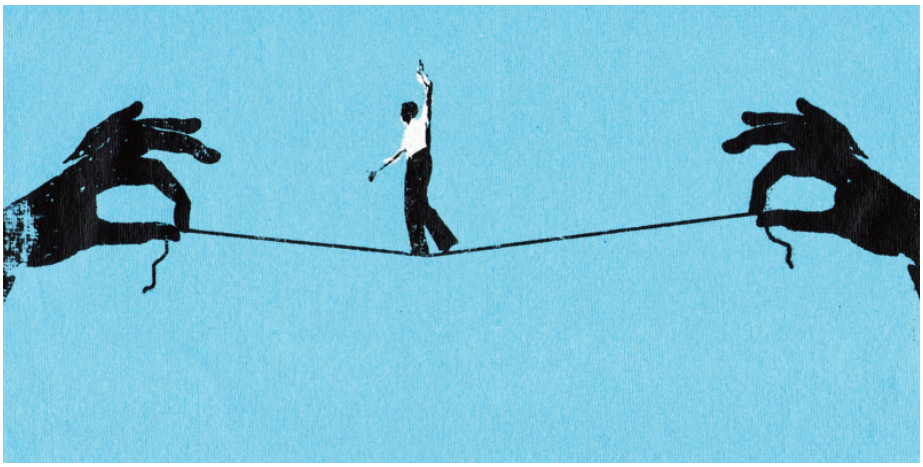
Abstract
With increasing transparency demands and the new legal requirements for providing clinical trial information to lay readers, clinical trials need to be given titles that patients can understand and recognise. Trial titles inform the readers what the trial is about, what substances are studied, and who the target population is. Devising a lay title is challenging as it needs to be understandable to lay readers, fully identify the trial, meet registry requirements, and also be translatable into different languages. Lay titles also need to fit different types of documents, e.g. trial protocols, trial advertisements, informed consent forms, and lay summaries. As the lay title is one of the first pieces of information that is displayed, good lay titles help patients searching clinical trial registries for trial participation. For sponsors, informative and understandable lay titles increase the chances of attracting the target patient populations for clinical trials.



Every clinical trial protocol needs a title to define and identify the trial. This title serves as a point of reference within the sponsor organisation, with ethics committees, institutional review boards, and regulatory authorities. The scientific title is developed by the trial sponsor and is primarily written for medical experts who read the protocol and may become investigators in the trial. The scientific title therefore needs to provide a considerable amount of detail. It informs investigators about the objective of the trial, its main design features, the key characteristics of the trial participants, the medical procedures to be performed, and other information considered important. This results in trial titles that are complex and highly condensed, aiming to convey a maximum of information using technical language, sometimes with abbreviations and acronyms only familiar to medical specialists. The title usually includes specific trial features (e.g. randomisation, blinding, placebo, or active controls) to help identification within electronic databases. The CONSORT 2010 statement[1] recommends including the word "randomised" in the trial title to ensure that the trial is identified as a randomised trial. Scientific trial titles, written for the scientific community, are usually too complex to provide insightful information to patients and the general public.

Increasing transparency demands and legal requirements for the provision of clinical trial information to the public, as well as the need to demonstrate scientific integrity, have led to the mandatory registration of clinical trials in public registries. In general, all clinical trials involving human subjects need to be registered before trial start.[2,4] Many major medical journals will not publish results of trials that have not been registered.[3] In addition to the scientific title, many registries require trials to have a version of the title that is understandable for the lay public.[4] Most importantly, ClinicalTrials.gov requires that every trial posted must have a brief title "written in language intended for the lay public".[5,6] However, the terminology used by ClinicalTrials.gov is confusing as the word *brief* only addresses length restrictions and does not convey the notion of lay-friendliness that is required according to ClinicalTrials.gov instructions.[6] We will therefore use the term "lay title". Trial registries are searchable by patients and the title is usually the first and most prominent piece of information about a trial they will encounter. Attractive and understandable titles help lay readers decide whether they should continue reading or focus on other registry entries.

Trial titles that are understandable for lay readers are needed for several trial-related documents (see Figure 1). These include informed consent forms, trial advertisements, and lay summaries of clinical trial results.[7] For the public, the lay title is the main identifier of a trial. Therefore it is important that each trial has only a single lay title that is used across all documents.

Lay titles and patient engagement
Depending on the disease, clinical trials are an important option for patients to receive innovative treatment. Patients who are searching for clinical trials need to be able to readily determine whether any given trial is of interest to them. For sponsors, it is important to inform potential participants about available trials as this supports recruitment and hence accelerates clinical development. The lay title is often the first element of contact between the patient and the

trial. Sponsors of clinical trials have several ways to inform patients about trials they could participate in. In addition to large registries such as ClinicalTrials.gov, information about clinical trials is available via local and national trial finders and databases of hospitals, charities, and patient advocacy groups. Most of these databases include a lay title in addition to the scientific title, while some only include a lay title without providing the scientific title at all. Many databases import their data, including the lay title, directly from ClinicalTrials.gov. The words used in the lay title will therefore determine how likely a patient is to find the trial. As a consequence, the lay title might be the single most important sentence of a trial's public posting. By ensuring that the lay title is informative and understandable, sponsors can attract the appropriate target patient population. This can be done not only via registry entries but also in trial-specific advertisements either online, in print media, or via other channels. To help potential trial participants understand the purpose of a trial, lay titles should also be used on informed consent forms or trial information leaflets.

In addition to the many uses of lay titles at the outset of clinical trials, lay trial titles are also relevant after completion of a trial. A good lay title will help sponsors to ensure that patients and their doctors can find the results of clinical trials they participated in or of other trials that are also relevant for them. Therefore, the lay title should also be mentioned on the lay summary detailing the clinical trial results.

What are the challenges in writing lay titles?

As mentioned above, trials should have a single lay title in all documents for trial participants and the general public. The most stringent requirements for lay titles seem to be those of ClinicalTrials.gov (see Table 1). The requirements of ClinicalTrials.gov concern both technical and content aspects for lay titles. Apart from the formal requirements, our experience is that ClinicalTrials.gov reviewers may sometimes have additional requests. Examples of such requests are that titles comprise a single sentence, that they should not have a full stop at the end, and that trial acronyms are included only at the end of the title.

Lay titles on ClinicalTrials.gov need to be unique.[8] This is important when searching for trials in order to differentiate between similar trials. However, it is more difficult to provide unique lay titles than unique scientific titles because lay titles mention fewer distinguishing features of a trial. Especially in the early stages of clinical development, individual trials may not differ much from one another and subtle differences between trials may be difficult to convey with their lay titles. Examples include the single rising dose and multiple rising dose Phase

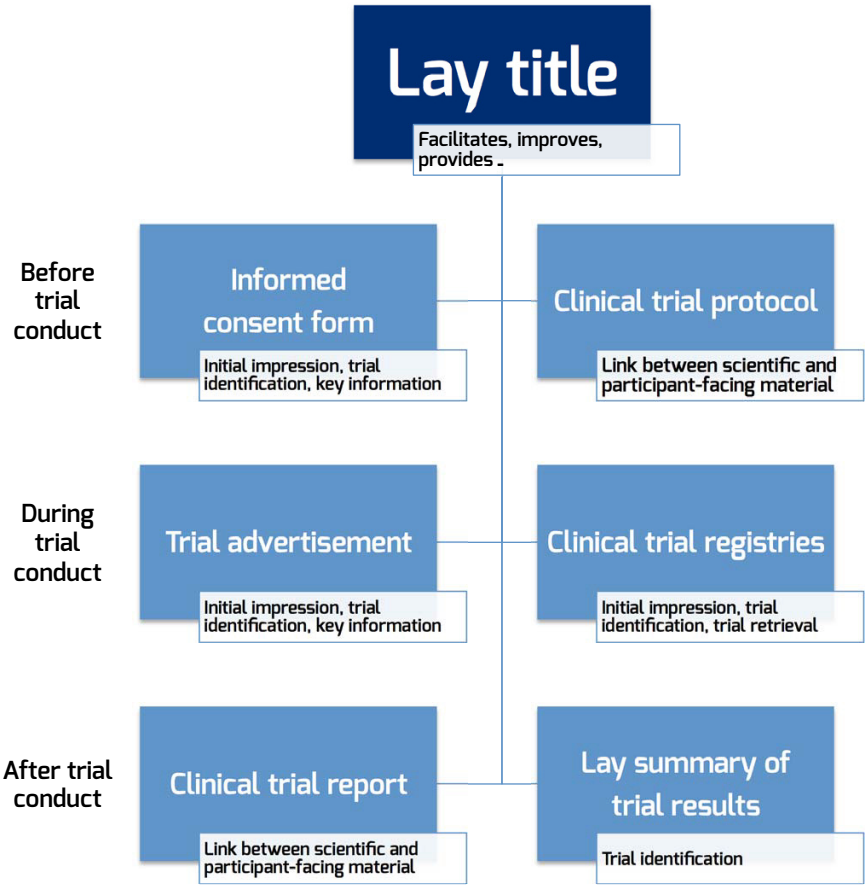


Figure 1. The need for a harmonised lay title across a range of clinical trial documents and the information it provides for each document.
"Trial identification" means that the lay title serves as the key identifier for the participant-facing material for a particular trial. "Trial retrieval" refers to the importance of the lay title for the identification of trials using a given search term.

Table 1. Lay title requirements by ClinicalTrials.gov

Requirements for the brief title in ClinicalTrials.gov[5,6,8]		**Our experience based on frequent interactions with Clinicaltrials.gov reviewers***	
Technical requirements	*Content*	*Content not to be included*	*Possible other format items*
Maximum of 300 characters including spaces	Intervention	Phase	Need to explain abbreviations
Has to be biunique	Condition	Randomisation	Should only be 1 sentence
	Target population	Blinding	Should not have a full stop at the end
	Scientific aim		Trial acronym should be at the end

*These are expectations that have occasionally been provided as feedback from ClinicalTrials.gov reviewers. As this did not happen for all lay titles, these items seem to depend on the individual ClinicalTrials.gov reviewer.

Table 2. Examples for lay titles for different trials

Type of title	
Example trial 1	
Scientific title	Safety, tolerability, pharmacokinetics and pharmacodynamics of single rising intravenous doses of Testdrug in healthy male subjects (single-blind, partially randomised, placebo-controlled design)
Sentence	This study in healthy men tests how different doses of Testdrug are taken up in the body and how well Testdrug is tolerated.
Title format	A study to find a suitable dose of Testdrug in healthy men and to test how different doses of Testdrug are taken up in the body
Example trial 2	
Scientific title	A randomised, double-masked, double dummy, placebo and active controlled study to evaluate the efficacy, safety and tolerability of orally administered Testdrug for 52 weeks in patients with mild visual impairment due to center-involved diabetic macular edema (DME). ACRONYM1
Sentence	This study tests how well Testdrug is tolerated and how effective it is. This is studied in patients with mild eye problems because of diabetic macular edema. ACRONYM1
Title format	Effects of Testdrug in patients with mild eye problems because of diabetic macular edema – ACRONYM1

I trials, where the only distinguishing feature is how often the substance is taken.

Because of length and content restrictions, as well as the need to translate medical concepts into lay language, it is inevitable that lay titles deviate from the scientific title. The translation of complex medical or technical concepts into lay terms often increases word count and is one reason why a lay title can only provide a limited amount of detail about the trial. It may be difficult to include specific details on trial design, procedures, or patient population while adhering to requirements for length and lay language. As a result, some ethics committees might find that a lay title provided on the patient information or informed consent form does not include all important information, or that it is not consistent with the scientific title. The challenge for the sponsor is to find the appropriate balance between adhering to registry requirements, making the title understandable for the lay reader, and staying as close as possible to the scientific title.

How can sponsors write a good lay title?

A well-written lay title is not only easy to read but also informs the reader what the trial is about, what interventions are studied, and who the target population is. A poorly written lay title could mean that patients miss the opportunity to participate in clinical trials that could be of benefit to them.

There are a few general considerations when it comes to writing a good title. The title should be informative to the reader and as specific as possible.[9,10] It should also be concise – not only to meet formal requirements, but also because short titles are more likely to make an impression with readers and to be remembered.[9,10] Titles also need to be accurate and care must be taken not to be misleading about potential benefits of the intervention being investigated.[11] Including details on the research design in the title may be informative but this usually comes as the expense of conciseness.[9]

To ensure consistency and quality, lay titles should ideally be written by a single function. We believe that medical writers are best suited to writing lay titles. Medical writers as language experts can balance the competing aims of providing a title that is informative, compliant with regulations and guidelines, and understandable for patients. A key role of medical writers is to develop consistent standards and messages across a range of different documents. This also applies to lay titles. A good tool to ensure consistency across lay titles is a continuously updated repository of all lay titles that have already been provided by the sponsor. Collecting information about the trial, such as the scientific title, the clinical phase, or the indication can help immensely in the development of standards and in harmonisation across trial designs and therapeutic areas.

Content of a lay title

The lay title gives patients an immediate impression of what the trial is about. At a minimum, the lay title should include the name of the substance or intervention, the target population, and ideally the aim of the trial. For the name of the substance, the choice is between the international nonproprietary name (INN), the lab code, and the tradename. The advantage of the tradename is that it is most likely to be recognised by patients. However, tradenames can differ by country and region and might also change over time. Our recommendation therefore is to use the INN, but if no INN is available, the lab code could also be used.

The description of the target population usually means including the name of a specific disease or subtype of a disease. The names of common diseases (e.g. diabetes, asthma) are often well known to the general public and are therefore likely to be understood if included in lay titles. Rarer diseases and those with complicated medical names (e.g. palmoplantar pustulosis, non-valvular atrial fibrillation) will not be understood by members of the wider public but are likely to be known to patients with that particular diagnosis. To make the lay title meaningful for the wider population but specific enough for the target population, it can be helpful that the title includes both the wider concept of the disease as well as the medical name, for example "… in patients with the skin disease palmoplantar pustulosis". If length permits, we recommend including additional details about the patient population. Including information on sex, required age range, or required background medication can all help the title address the relevant patient population.

Describing the aim of the trial within the constraints of a lay title can be challenging. We recommend focusing the lay title on the primary objective of the trial, even if that means losing some information that is provided in the scientific title. It is also useful to define standard phrases for specific scientific terms. For example, "pharmacokinetics" in the scientific title can be written as "how [substance X] is taken up by the body" for

the lay title. Such an approach also helps to achieve harmonisation across different trials. It might also be useful to consider how frequently certain words are used in everyday language.

To keep the lay titles for similar trials unique, adding the trial acronym is recommended, provided one is available.[8] The disadvantage is that trial acronyms might be cryptic, difficult to read, and thus likely to cause confusion for a lay reader.[11]

The use of abbreviations in titles has both advantages and disadvantages. Abbreviations in lay titles could be perceived as helpful by laypersons because they reduce the number of complicated, technical words and might in some cases be more common than the long form (e.g. HIV). On the other hand, ClinicalTrials.gov requires abbreviations to be explained at first occurrence,[12] which is technically the lay title.

Format and structure of a lay title

There are several structure and format considerations that authors need to think about when writing lay titles. One is whether to use a classic title format or a sentence (see Table 2). A sentence format might be easier to read for laypersons because complex information can be divided over two short sentences. The sentence format allows adding more specific details about the trial, which may help patients identify relevant trials and also helps keep titles unique. However, titles over two sentences or more are not always accepted by ClinicalTrials.gov reviewers (see Table 1). Furthermore, readers are often not familiar with a sentence format for titles and may even not recognise it as a title. The reason for this is that we are all trained to recognise a line of text as a title because of its location and its structure. In everyday life, titles do not follow the conventional sentence structure of subject, verb, and object. Instead, they are fragments of text that anticipate the subsequent content.

As the lay title will be used on documents at any time during the conduct of the clinical trial, it should be in the present tense. Titles should be written in the active rather than the passive voice because active voice is clearer and easier to understand.[13]

Lay titles often need to be translated to other languages. Some words and phrases are hard to translate into certain languages. In some cases a word for word translation might lead to a misleading description of the trial. As the translator might not be familiar with the medical content, it is important to use language that is as clear as possible.

Conclusions

Clinical trials need to have titles that can be easily understood by laypersons. A good lay title can help patients find an appropriate trial for their condition, and sponsors in the recruitment of the relevant target population for clinical trials. The lay title is the link between different trial-related documents from trial registration to the provision of trial results. Writing a lay title is a balancing act between registry requirements, readability for lay audiences, level of detail required and permitted, and reflecting the trial design and objective.

Conflicts of interest

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

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