PATIENT REPORTED OUTCOMES NEWSLETTER

METHODS

Patients First: Making Technology Easy to Use

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Keywords

COMPUTERIZED QUESTIONNAIRES, DATA COLLECTION, DATA MANAGEMENT, ELECTRONIC DATA, PROS

Introduction

Patient-Reported Outcomes (PROs) are an important focus in clinical trials. In some cases, such as pain or mood, the patient is the only possible source of the information. For other types of data, such as visits to the toilet, or measurements of lung function, the patient is essentially acting as an observer of objective data, but can record information in the context of normal life in a way that is not otherwise possible.

Electronic solutions are increasingly being used to collect PRO data in clinical research and drug development. These ePRO systems differ greatly from the data collection and management solutions used in other parts of the clinical trial process because patients, rather than research personnel, are the end users. Firstly, with patients, it is not possible to assume any degree of expertise or familiarity with computers. Patients are selected for a study on clinical criteria, not on their ability to use a particular system. Secondly, it is not possible to spend a great deal of time training patients to use such ePRO systems. Thirdly, the demands we make of patients must be reasonable, and patients must be comfortable with what is being asked of them, otherwise we cannot expect them to cooperate and be compliant with the ePRO data collection protocol.

All of these factors mean that the design of the ePRO user interface – the interface that the patient will be interacting with – is crucial to the successful use of these systems in drug and medical device development. A great deal of work has been done on user interface design, in particular, standardizing the conventions and tools used in different applications so that learning to use one application gives the user a head start in using another[1]. This model, however, implies that there is a considerable amount of initial training that is required to use systems effectively, and that if users are unfamiliar with the basic conventions, they can, and should, learn them. The time taken can be significant. For example, Rao and co-workers[2] introduced a Palm-based medical reference and database system to a residency program with four one-hour training modules for doctors. Clearly, such training is too long for use in a typical clinical trial and the interface must therefore be a great deal simpler. Fortunately the types of information being collected are relatively simple, and with careful attention to the details of design, it has been shown that it is possible to develop systems, which can be used by virtually all patients with a minimum of training[3,4]. Some of the main issues will be considered here, and examples given of how they may be put into practice in a handheld computer system. Finally evidence will be presented that such systems really are effective, both in terms of ease of use and quality of data.

Avoiding Bias

Any clinical trial is carried out on a sample of patients, but the results are designed to be applicable to a much broader cross-section of patients. If particular types of patients are less likely to participate in the study because they are unable to use the ePRO system (or are perceived as being unable to use it), the results may be biased in ways that will seriously reduce their usefulness. The most obvious potential bias here is the elderly, who form a very important group for most new treatments, because they use more medicines on average than other age groups, and they may react differently to drugs than do younger patients. Other groups to consider are those who are more seriously ill than others, or those who have high levels of anxiety. Thus the ePRO system must be designed to be suitable for all these groups to avoid biasing the subject sample.

Bias could also arise in the actual values that are collected. There are several ways in which this could occur. Firstly, if fields are initially set to default values, these may be presumed by the patient to be normal or acceptable values, or the patient may simply omit to make an entry, resulting in an inappropriate default value being used. Secondly, not all necessary information may be immediately available to the patient, for example definitions of meanings of terms. This usually results from the small size of the display screen compared to a paper form. Thus all necessary information must be available to the patient, and each item of data must be explicitly entered by the patient.

If patients are not comfortable with the system, compliance with the ePRO protocol is unlikely to be good. Non-compliance is another possible source of bias, since the missing entries are unlikely to be randomly distributed over time. They could, for example, be more likely to occur when symptoms are particularly bad and disruptive. Conversely, some patients might forget to comply with the ePRO data collection when they are feeling especially symptom free, and active with other tasks. Thus measures to enable high compliance with the protocol also help to ensure that data are representative of the patient's condition.

A practical Example: Multiple Choice Questions

Consider the question shown in Figure 1.

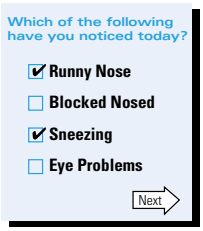

Figure 1

This display is clear, and there should be no problems in seeing which options are selected. However, there is a problem, at least for some patients, in making the selection. The tick box is rather small, and patients with poor eyesight or with a bit of tremor may have problems making a tap in the box. It is possible to set up the control so that tapping on the text will work as well as tapping on the box, which may help, but there is nothing to show that the text is tappable, and inexperienced users will still tend to try to tap just the box. A better option is to set up the display so that the area to be tapped is both as large as possible, and explicit, as in Figure 2.

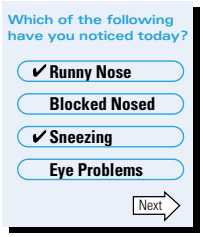

Figure 2

Now the patient can tap anywhere in the box surrounding the option test, and the display clearly indicates this tappable area, making it easier for an inexperienced user.

What if the patient has none of the symptoms? The starting screen will of course have no items checked. If the patient simply taps "Next" at this point, can we be sure that she had no symptoms? It is much better to have an explicit option for this, as shown in Figure 3.

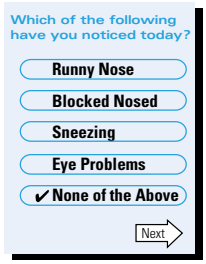

Figure 3

Now we can be sure that the patient has no symptoms, and a warning can be displayed if the patient taps "Next" without selecting at least one option from the response set.

This example illustrates the way in which careful design can help to make using a diary easier for a patient, and also make sure that data are reliable. It also illustrates a more general point — that design is likely to be improved if the application is thought through from the patient's point of view. It is helpful to think about the kind of patient who is most likely to have difficulties using the system. If we design with a patient with poor eyesight in mind, then a patient with 20/20 vision will not have any problems using the system. The reverse is not true. This idea, called inclusive design, is of the greatest importance where applications are intended for universal use.

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Compliance and Data Quality

High rates of completion of entries are not enough to prove good compliance, as with paper diaries patients may fill in entries at inappropriate times, for example filling in large amounts of data just before the clinic visit ("Parking Lot Compliance"). There is much evidence that this happens on a considerable scale. Most recently, Stone and co-workers[5,6] have used an instrumented paper diary to investigate compliance in a study of self-reports in pain. The diary recorded each occasion on which it was opened. Compliance with the paper diary was extremely poor. For example, only 11% of data were completed in accordance with the study schedule, although patients' own reports of compliance indicated that they were completing over 90% of entries on schedule. On about a third of the study days, the diary folder was not opened at all, although in most cases entries were made for these days. There was also evidence for forward filling of diaries (i.e. data entered before the scheduled completion time). By contrast, and in agreement with many earlier studies[7], compliance with electronic diaries was very good, above 90%.

There appear to be several reasons for the much better compliance with electronic diaries compared to paper. The use of signals or alarms to remind patients that entries are due is clearly helpful, but not the only reason. The use of signals with paper diaries leads to marked improvements in compliance, but not to the high levels seen with eDiaries[8]. Other mechanisms may include the patients' awareness that handheld devices include clocks that can record diary activity, and a feeling that has been reported in several studies that the use of ePRO systems conveys to the patient the importance and value being placed on their experiences[9]. In any case, it is clear that to obtain the high, documented, compliance figures with protocols which specify rather narrow schedules requires a combination of features: careful interface design, the use of behavioural-science based techniques to aid compliance, specific features such as alarms and feedback to patients, and effective training of patients.

There are a number of ways of assessing data quality in eDiaries as compared to paper, and all indicate that electronic methods have an advantage. One method is to look at data distributions in individual patients. Tiplady and co-workers[10] showed that several patients in their evaluation study had unexpectedly high numbers of entries of one particular value of a lung function measurement in their paper diaries, a pattern strongly suggesting retrospective entry. These patients showed normal distribution patterns with electronic entry, indicating that they were using the eDiaries appropriately.

Another approach is to determine the auto-correlation within the data, i.e. the tendency for a value to be correlated with the previously entered value. People are not good at generating random numbers, and if a retrospective entry is occurring, such correlations would be expected to result. Using scores for heartburn, degl' Innocenti and co-workers[11] showed that such correlations were significantly higher for paper diaries than for eDiaries, suggesting that patients may have been back-filling the diaries en masse. The electronic methods showed no such bias.

Finally, better data quality could result in greater reliability in the efficacy measures being studied in the clinical trial. One study has compared eDiary results with a similar previous study using paper diaries in over-active bladder clinical trials[12]. They showed a very substantial reduction in the error variance of the eDiary measures compared to paper, which suggests that the amount of "noise" introduced by poorly recalled or invented paper data is sufficient to seriously compromise the study outcome. The superior quality of eDiary data would allow future studies to be carried out with substantially smaller numbers of patients without loss of statistical power – in this case, allowing nearly a halving of the required patient numbers.

The Patients' View

The whole logic of collecting diary data is to obtain the patient's own perspective of the disease and its treatment. So it is equally important to get the patient's point of view of the way we collect the data, especially as the patient is likely to spend a considerable amount of time filling in the diary.

In studies comparing paper and electronic diaries, patients have in general preferred eDiaries[10,13,14]. Patients who were not comfortable with technology showed the same preference for eDiaries as other patients, and there was no evidence of differences related to gender or age. Where no direct comparison between paper and electronic was made, patients in general reported eDiaries to be easy to use, and did not have significant problems with them. For example in one study, over a third of patients had never used a PC – these patients also reported having no difficulty using eDiaries, showing that the goal of setting up an application that all patients can use is a realistic one[15].

Conclusions

Setting up ePRO solutions intended for use by a broad range of patients– not just those familiar with computers – requires careful attention to user interface design. The use of the application must be thought through from the patient's point of view, in particular keeping in mind those who are most likely to have difficulties. If this is done, eDiaries can be used successfully in a broadly based clinical trial program, without introducing biases or practical difficulties with recruitment, and patients will be able to use the system correctly and be comfortable with it. ●

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