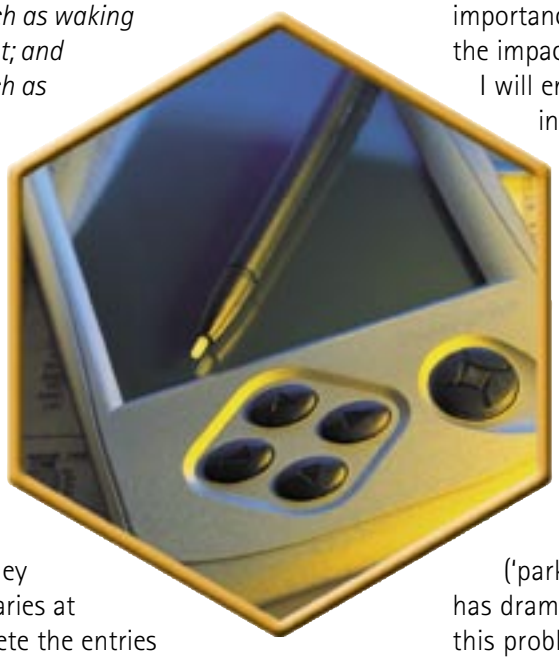
Electronic Patient Diaries

Trustworthy data from daily life

Brian Tiplady

Information collected directly from the patient (Patient Reported Outcomes, PRO) is an important part of many clinical trials. This includes symptoms, such as pain; events in the patient's everyday life, such as waking in the night, or going to the toilet; and physiological measurements such as peak expiratory flow or blood glucose readings. PRO data are often collected using patient diaries.



When such data are collected on paper, there are often problems. Patients may fill in diaries inappropriately, writing "Yes" against a symptom whose severity should be rated on a mild-severe scale, or entering their problems in their own words. They may forget to complete their diaries at the scheduled times, and complete the entries retrospectively,[1] thus losing one of the main benefits of diaries: the collection of data while the data are still fresh in the patient's mind.

Electronic diaries (eDiaries) can help eliminate or reduce these problems. Firstly, when a patient fills in a properly constructed eDiary, only valid entries can be made. Unlike paper, if the choices are "None", "Mild", "Moderate", and "Severe", it is not possible to make a mark between "Mild" and "Moderate", and the patient must choose one or the other. Thus in-range data are obtained and the need for editing eliminated. Secondly, eDiaries can both document and improve patient compliance with the clinical trial protocol. The device has a built in clock, which allows us to prevent or limit retrospective entry, and to mark every entry with its own time-stamp, so that compliance cannot be faked. The use of alarms, feedback, and features that help to integrate the diary into daily life can help patients comply with study schedules.[2,3] Provided care is taken in designing diaries, taking the needs of different types of patients (such as the elderly or those unfamiliar with computer technology) into account, patients find such systems easy to use, and in general prefer them to paper diaries.[4,5]

The use of electronic diaries is increasing[2] and is having a considerable impact on many areas of clinical trial management. I will deal here with two issues that are of current practical importance to researchers: data quality, and the impact of real-time availability of data.

I will end by considering developments in integrating eDiaries with other types of data collection systems.

How good are the data?

Data quality means much more than records being legible and consistent. Data must also be an accurate record of what is being measured. I remarked above that there are data about the poor quality of paper diary data based on the non-compliance of patients with study schedules, and back-filling of data ('parking lot compliance'). A recent study[1] has dramatically highlighted the extent of this problem, using a specially prepared paper diary in a folder equipped with light sensor circuitry, which recorded when the diary was opened. The patients were not aware of this, and recorded their entries along with a record of their compliance with the protocol. The researchers found that while the compliance claimed by the 40 patients who used the paper diary was 90%, only 11% of entries were actually made according to the study schedule. Many of these entries were not even made on the scheduled day: on 32% of days the dairy was not opened, but 90% of the entries for these days were recorded, with patients reporting they had been made at the scheduled times. By contrast, when another group of 40 patients used an electronic diary (set up on a Palm computer) the compliance was 94%, and because times of entries were recorded, we know exactly when these entries were made. So high compliance can be achieved with an electronic diary, and equally importantly, this compliance can be accurately documented by the eDiary application.

If a substantial proportion of paper diary data is at best recalled well after the scheduled assessment time, and at worst invented by the patient, this would be expected to show up in

the data obtained. This is indeed the case. In an early evaluation study,[6] we saw clear evidence of unreliable data. Two patients out of the 22 in the study showed an unusual pattern when they recorded their peak flow in the paper diary. About half the entries in each case were the same value. What was probably happening was that the patient filled in the missing entries at one time, and just entered, for example, "150" in every case. This was a crossover study, and all patients used both electronic and paper diaries, each for one month. You might expect that when these patients filled in electronic diaries, there would be a lot of missing data, because the eDiary did not allow retrospective entries to be made. Surprisingly, however, the electronic data showed good completeness, and a sensible, near-normal data distribution.

Another approach to data quality is to examine the correlation pattern within the data. People are not good at generating random numbers, and if retrospective entries are being made, then auto-correlation (that is a tendency for a given value to be correlated with the previously entered value) would be expected to result. Using scores for heartburn, degl' Innocenti *et al*[7] showed that such correlations were in fact significantly higher for paper diaries than for eDiaries, suggesting that patients may have been back-filling the paper diaries *en masse*. The electronic methods showed no such bias.

Finally, better quality data with eDiaries should show up in the reliability of the summary outcome measures obtained. In a recent study where an eDiary was used to assess overactive bladder,[8] similar previous studies with paper allowed a direct comparison between the two methods. It was found that while the mean values for number of micturitions were similar for the two trials the error variance for the diary outcome was reduced by about a third compared to paper diaries. This would allow an eDiary study to be run with about half the number of patients needed for a paper diary study, and have the same statistical power. Where diary data are the primary outcome measures for the study, this can represent a major saving in resources.

Data in real-time

When a patient uses a paper diary, the data are only available when the patient brings the diary into the clinic. With the first generation of eDiaries, the same limitation applied, but modems and (more recently) mobile phone technologies, now allow data to be transmitted directly to a central secure server, for example on a daily basis or after every entry. This transfer can be automated, so that the patient has no need to initiate transfer. For example if a modem is used, the patient will simply place the device in a docking station at night. This will both charge the batteries and transmit data automatically. If then patient forgets to do this one night, the accumulated data are still on the device, and will all be transferred the next time the device is docked.

Access to PRO data in real-time can be extremely useful for several reasons. Because the data flow is automated, neither the patient nor the clinic or monitoring staff need to be involved with data transfer, thus eliminating one of the ways in which eDiaries could potentially increase workload and the possibility of error. The speed of data transfer means that delays at the end of the study while the last diary data

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are located and checked are less likely. Also, any problems that do occur can be spotted quickly, and dealt with.

Real-time access to the data can be particularly useful where patients have problems. Data can be checked daily on a website, and if a particular patient is not filling in the diary entries, or not doing so correctly, this can be spotted, and action taken. For example the clinic could contact the patient and ask if there were problems, and offer encouragement or assistance. In a recent asthma study in Sweden,[9] two patients were helped in this way, and after a first week in which they had problems were able to complete the rest of the study satisfactorily.

Such real-time feedback can also be used to adjust patients' therapy. An example is a recent study in diabetes[10] in which diary information about blood glucose levels was uploaded nightly to a central server, and reviewed on the web. This information was used for adjustment during the dose-titration phase, thus allowing faster optimisation of treatment.

It may also be valuable to be able to detect exacerbations, or to monitor the number of end-points that are occurring to quickly determine eligibility for randomisation. For example, by tracking whether patients meet some minimum threshold of disease severity in the field, a determination can be made whether they qualify for randomisation or should be discontinued once enrolled in the clinical trial.

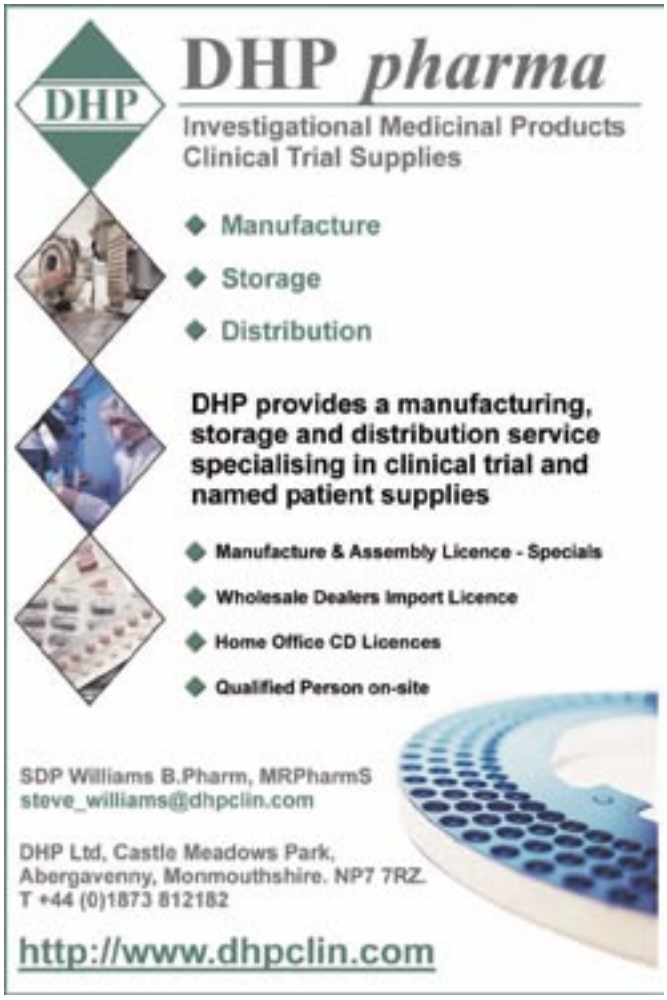
Future developments

One area of research that is under active development is integrating eDiary data collection methods with physiological data in the patient's natural, real world environments. For example, there are now electronic spirometers and blood-glucose meters that are small and simple enough for home use by patients. These devices can be integrated with an eDiary device to capture real-time physiological and PRO data. These integrated systems add another dimension to the richness of real-time data capture by allowing researchers to have parallel streams of data on patients objective and subjective experiences.

For example, in the case of lung function, the traditional method of data capture has been to assess peak flow at home using a simple mechanical flowmeter, with manual transfer of data to the diary card. Using an eDiary to replace the paper diary can certainly improve the trustworthiness of data by preventing retrospective entry,[11] but there is no guarantee that the patient followed instructions (for example by blowing three times and recording the highest value) nor that the value has been correctly recorded. Incorporating an electronic spirometer into the diary system can ensure that patients used the system in the intended manner, and also enable measurement of other aspects of lung function, including forced expiratory volume in one second (FEV1) that cannot be obtained from a simple flowmeter.

The composite system is rather more complex than a normal symptom or event diary, and Welin and co-workers carried out a pilot study[8] to evaluate the ability of patients to use this type of diary over a four-week period. They found good compliance with the protocol, and the data integration between the handheld and spirometer components worked as intended. Interestingly there was evidence from the study that peak flow gave more coherent data than FEV1, suggesting that the simpler method of evaluating lung function may be more robust in a field setting.

Electronic devices are in general becoming smaller, less expensive, and have better



communications. This allows many types of measurement that have in the past been only suitable for use in the laboratory, or in small patients samples, to be used in large scale monitoring of patients in their natural environments, and to be integrated with eDiary systems. One obvious example is ambulatory blood pressure.[12] Another is recording; patients' actual activity, either as an outcome measure in conditions where limitation of activity is one of the consequences, or to assess the amount of exercise people are doing.[13,14] Such integration will allow a much wider range of measurements to be made in the context of normal living.

Conclusions

A wide variety of patients can use eDiaries effectively. Being elderly, or unfamiliar with computer technology is not a problem if diaries are well-designed, and thought out from the patient's point of view. Data quality is improved by allowing only appropriate entries, and compliance can be enhanced and maintained by implementing a variety of features. The improved data quality and data integrity have been shown to improve trial power or fewer patients can be included to achieve the same power if diary measures comprise the primary endpoints. Real-time availability of data enables improved support to be given to patients and allows researchers to more carefully manage their trials.

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