Assessing participant adherence during clinical trials

What is adherence?

Participant adherence (also known as compliance) is an essential part of every clinical trial. However a participant in a particular trial may not be able to take the investigational medicinal product (IMP) in the way that is required. If that happened, any results collected from that participant would not be a valid assessment of how that medicine works.

Sometimes the word ‘adherence’ is used instead of compliance, but both words mean ‘the extent to which participants follow the instructions they have been given for participating in the clinical trial’.

Unlike in ordinary life, participants in clinical trials often need to do more than just take the medicine in the way they have been instructed – they may also be required to:

- Attend visits to the clinic at specific times to have tests carried out.
- Complete forms about how they feel between clinic visits.
- Record any possible side effects to report to the healthcare professional.

All of these activities help to measure participant adherence. This is later included in the clinical trial report.

There are often many things for a participant to remember when taking part in a clinical trial. It is important that they

fully understand everything they have been asked to do, they should be given the opportunity to ask as many questions as they desire.

What happens if participants do not adhere to the instructions?

The number of participants that need to take part in a clinical trial to allow drawing conclusions from the results is worked out using a calculation known as the ‘power calculation’.

A further important consideration for determining the adequate number of participants is to estimate how many participants in the trial will be able to complete all the trial activities.

Studies have shown that between 43% and 78% of participants receiving treatment during a clinical trial for chronic conditions can be classified as being compliant (1). The impact of participants not being compliant with their treatment during a clinical trial programme is significant:

- Missing data from participants who did not attend all the scheduled visits to the clinic means that an accurate safety and efficacy assessment of the IMP cannot be made. This can ultimately result in poor results for participants treated with the same medicine in the future.
- There is also a financial cost to the sponsors of the clinical trial if participants are not compliant with the trial protocol. If participants do not stay in the trial, or are not able to complete all the required sections of the trial, then the sponsor may have to recruit additional participants into the trial to ensure that the IMP is accurately assessed.

How is participant adherence assessed in clinical trials?

There are many different ways to measure how adherent a participant is with the clinical trial protocol. Below are examples of different methods to assess adherence.

Patient diaries

These can be paper or electronic records, and are designed to capture all the information needed from participants during a clinical trial such as the time when they took their medicine and how they felt at different times during the day.

Paper based diaries have traditionally been used and are generally easy to keep. However, participants may forget to complete them on a daily basis (2) and, it takes time for the clinical trial staff to transfer all the information in the diaries into an electronic form to be analysed.

Electronic diaries are preferred by many sponsors, as they are able to accurately capture the time and date when an entry was made and so provide a more reliable source of information. They are a way of preventing participants from completing their diary just before a clinic visit rather than in the prescribed manner (3).

Direct observation

This involves participants being observed taking their IMP or carrying out specific assessments that are part of the clinical trial. This method has the advantage of ensuring that participants are carrying out the required tasks. However, it is a time-consuming process for both the participant and the study staff. It is mainly used in trials where the IMP needs to be given by medical staff, e.g. by injection or infusion (drip).

Tablet counting

This method involves participants receiving more tablets at each clinical visit than is required. Participants are then asked to return any unused tablets at the next clinic visit. The clinician then calculates participant adherence based on the number of tablets that are returned. This is a relatively simple method of tracking adherence, but many studies have shown that it can be very unreliable (4).

Measuring medicine levels in blood or urine

For some trials it is critical that the level of the IMP found within the blood or urine is closely monitored. This process can also be used to assess adherence in some clinical trials. However, it should be noted that the way that a medicine is broken down by the body differs from participant to participant.

Smart packaging and smart pills

Smart packaging can be used to help the process of adherence by tracking when medicine is removed from the packaging. The data can then be downloaded during a clinic visit, or be sent to a central computer in real time.

Smart pills contain microchips that communicate with a patch on the participant’s body when the pill is swallowed. This provides information on when the medicine was taken. The patch can record measurements like heart rate and body angle (was the participant standing up or lying down) at the time the medicine was taken. The information can then be transmitted by phone to a central computer.

References

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