HOW VALID ARE YOUR CLINICAL TRIALS DATA?

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It is widely accepted that patients participating in clinical trials are less than perfectly compliant with their medication regimens. The extent to which non-compliance affects the results of clinical trials is unknown. Several factors mitigate against the assessment of this phenomenon, principal of which is the lack of a methodology to monitor patient compliance in a non-invasive (ie: unbiased) way.

Compliance with prescribed medication is thought to decrease with duration of therapy, the number of times a day the medication must be taken, side effects, and break-through of clinical signs and symptoms. It is also over selected in certain populations such as the elderly and psychiatric patients.

Clinical research has depended largely on pill counts and the use of medication diaries. Participating patients are interviewed at intervals and their remaining pills are counted. Strategies may involve giving patients extra pills to assess their compliance. However, patients are known to not be forthcoming about non-compliance, generally from embarrassment or a desire to please the researcher. They are also known to fill out medication diaries retrospectively just before their interviews, often with less-than-perfect recollection.

Even patients who have interviews and correct pill counts may be non-compliant. With most medication trials the aim is to keep plasma levels within a therapeutic window. Not taking medication on time, taking extra medication, missing one dose and doubling up on the next can all result in plasma levels dropping below or exceeding the therapeutic window. The result may be ineffectiveness of the therapy due to inadequate plasma levels, or side effects due to increased levels. Both have serious implications for the clinical trials decision-making process.

Until recently, mechanical devices used to assess non-compliance were all flawed for a variety of reasons. They tended to interfere with the process of medication-taking by requiring the patient to behave differently when using them, and by their bulk and resultant inconvenience. They also affected the clinical trials process by their cost. For these reasons, they were not very useful in clarifying the non-compliance issue.

The newer generations of Electronic Compliance Monitor (ECM©) allow for monitoring a patient's compliance without additional patient input. They integrate seamlessly with the dispensing / manufacturing process and are reasonably priced.

If the ultimate goal of a clinical trial is to demonstrate efficacy and safety, this should clearly not be left to data of questionable accuracy. Accurate measurement of patient compliance during clinical trials is the key to better decision-making regarding investigational new drugs.