# PHARMACY AS A SIGNAL-TO-NOISE RATIO

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All research, including pharmacotherapy, may be viewed in terms of a signal to noise ratio (S/N). In administering a medication, the aim is to maximize the S/N. The signal is the desired clinical effect; the noise comprises a multitude of factors that interfere with, or obscure, the clinical effect. The clinical effect might be reduction in pain, control of seizures, reduction in white cell count, etc. Most of the myriad noise factors come under the category of 'individual differences' in response to medication. Gastrointestinal differences ranging from malabsorption to eating habits, differences in metabolism, concomitant use of alcohol and street drugs, body mass, level of activity, use of herbal remedies, and many other noise factors conspire to obscure the therapeutic effect (signal).

The importance of maximizing the S/N is obvious in the area of clinical trials. Clinical trials are designed to determine if the therapeutic effect (S) of an investigational new drug (IND) stands out from all the detracting effects (N) at a significant enough level to warrant approval of the new drug application (NDA) by the regulatory body for clinical pharmacy (general use by practitioners).

Analysis of variance, a widely used test of this significance, is simply a ratio of the variability between treatment groups (sum of squares between) to the variability within groups (sum of squares within) – the F ratio. This is a S/N, where SS between groups is the desired therapeutic effect (S) and the SS within the obscuring noise (N).

It follows that, in clinical trials, anything that increases the S/N ratio (F ratio) will speed up recognition of the therapeutic effect of an IND. Higher F ratios in essence result in more rapid approval of INDs. They can also have more subtle positive effects such as increasing the accuracy of the dosing regimens developed for a new drug and influencing contraindication profiles.

The idea of S/N extends to general clinical pharmacy - the widespread use of medications that have received regulatory approval. In practice, the physician prescribes a medication for a clinical indication and watches for the anticipated therapeutic response (signal). For example, a child with an ear infection might be prescribed an antibiotic to be taken three times daily for 10 days. At the follow-up visit the physician looks for the signal (a cured infection). If the infection is still present, the physician might reasonably assume that the organism responsible is resistant to the antibiotic prescribed and switch the patient to a broader spectrum or more potent antibiotic with more potential for toxicity (side effects).

In this example, there are two reasons for the lack of a signal: first, the physician's assumption may be correct - the infection is caused by an organism that cannot be eradicated by the antibiotic used so there is no signal. The second reason is that there really is a therapeutic effect but it is obscured by noise.

**Patient Non-compliance with Prescribed Medication as a Source of Noise**

Patient noncompliance with prescribed medication has long been identified as interfering with the therapeutic effect of prescribed medication. This source of noise has been estimated to cost the U.S. health care system upwards of $100B annually, to be responsible for over 125,000 deaths, and to account for over 10 percent of hospitalizations (est. for 1996). These statistics are well-known and widely accepted to be conservative. It is also known that 50 percent of patients with chronic illnesses are non-compliant with their prescribed medications and that over 20 percent of medication prescriptions never get filled. Within this model, removal of non-compliance-generated noise would have a significant beneficial effect on health care costs.

Efforts to improve patient compliance with prescribed medication are designed to do this. The oral contraceptive wheel was devised as a means of increasing the therapeutic effect (S) in a clinical setting where non-compliance could have obvious and devastating consequences. Other strategies have been devised to address noncompliance. In clinical trials the medication diary and pill count have been widely used to assess this problem. Blister packaging has evolved at least partially in response to this problem.

The general assumption is that non-compliant patients are so because they forget to take their medication, not because they have an agenda to confound the therapeutic process. The corollary is that making medication-taking easier will increase patient compliance. Although electronic means of monitoring patient compliance have been on the market for the last decade, they have not gained widespread acceptance due to a number of factors including cost, size, and especially the fact they do not integrate seamlessly in the medication-taking process.

More recently, seamless means of monitoring patient compliance electronically, such as the Med-ic® Electronic Compliance Monitor (ECM©), have come to market. It is now possible to track patient compliance accurately. Initially, these devices are proving invaluable in clinical trial applications, where their ability to increase the S/N by reducing noncompliance can be translated into quantifiable cost savings through speeding up the approval process for INDs. The advantage of the new generation of ECMs is that they can be integrated seamlessly into standard blister packages and require no extra effort on the part of the patient.