

## Drugs and devices – A better way

Current mechanisms for approving, advertising, prescribing, financing, and monitoring *new* drugs and devices are costly and contentious. Many current “oversight” activities allegedly initiated to address these issues simply add to the confusion and waste. They focus more upon indicting a “token” scapegoat than seeking consensual, constructive, societal solutions. They also encourage increased personal injury litigation.

A few recent examples include actions regarding the lipid lowering drugs, Vytorin and Zetia, diabetes drug, Avandia, cancer drug, Avastin, anemia drug, Epogen, and fibromyalgia drug, Lyrica. Absent clear evidence of fraud, other criminal behavior, unscrupulous profiteering, and unethical behavior (actions that should be aggressively investigated and prosecuted), we need to discourage a “prosecutorial” approach. Most drug and device makers and medical practitioners act responsibly. Problems usually occur not because of intentionally malicious or negligent behavior but a lack of general understanding of the limitations of scientific knowledge and the current mechanisms – as a society – we have elected to address the consequences of scientific discovery, both *positive* and *negative*.

Few of us would opt to limit our medical armamentarium to the drugs and devices that were available 50-100 years ago. We live longer, higher quality lives free of major disability because of the new drugs and devices available. Many of us have had certain body parts, e.g., eyes, hips, knees, restored to a functional level we enjoyed as young adults. We appreciate these *positive* advances and support development of additional ones, especially for those who still suffer from pain and/or functional limitations, as well as those who die prematurely.

However, whenever a drug or device touches or enters the human body, there is the potential for *negative* consequences and adverse events. During development and limited clinical trials of these drugs and devices, there is occasionally clear evidence of the overwhelmingly *positive* consequences of their use in certain individuals and equal evidence of the highly unlikely probability of any serious *negative* consequences. Unfortunately, in many situations, the “trade-off” ratio is closer to 50:50 or unclear.

Part of the difficulty is that although a therapeutic *positive* effect may be evident in many of the relatively few individuals with a targeted affliction studied during a clinical trial, thousands of individuals might have to receive the treatment before certain *negative* or adverse effects become obvious. (In some situations this is also true as regards *positive* gains, where some “intermediate” measure, e.g. decrease in low density lipid levels, tumor shrinkage, prostate cancer detection, anemia correction, - that one would expect would result in less suffering and death - fails to demonstrate this expected outcome when subsequently used by the thousands of patients necessary statistically to demonstrate such definitive gains.) It would be very expensive and could take decades to amass enough individual results to discover such adverse (or positive) consequences if the drug and device remained as part of a limited controlled, clinical trial. Furthermore, in

the interim many individuals might be deprived the positive gains such treatment could potentially afford.

Thus, to the cheers of many physicians, patients and patient advocates - and protestations of others - many *new* drugs and devices are approved for broader “monitored” use and their use often covered by third party insurers. Many subsequently live up to their expectations and have few serious side effects. Others fail to do so and/or demonstrate adverse consequences much greater than anticipated. When the latter occurs, the day after the “disappointment” is announced a congressional committee announces a costly “hearing” and a group of lawyers appear on TV soliciting patients for a class action lawsuit. If the legal action is successful, some patients (or patients’ families) receive monetary compensation and the attorney condominium markets in Florida and Dubai flourish at the expense of the U.S. health care system. Seldom is negligence the true problem, although one can always question any decision with crafty rhetoric and twenty-twenty hindsight.

One possible explanation for such “disappointments” is that there often are certain “sub-populations” within the overall study population (and general population) who – because of yet unknown genetic, environmental, or other factors – will respond very *positive* or very *negative* to the treatment. If we knew who they were, we would only give the treatment to the *positive* responders and avoid giving it to the *negative* responders, greatly increasing the efficacy of the treatment and decreasing the adverse consequences. Everyday, we are gaining new scientific tools to assist in this regard but, unfortunately, we often lack such knowledge at the time a treatment is approved for broader use. In fact, often during broader use, and the accompanying monitoring, we might elucidate the previous undetected characteristics of such sub-populations and we can adjust the use of the drug or device accordingly. It is a catch 22 in that we might not discover such knowledge for decades without such broader use but some patients will suffer because of it.

To add to the problem is the direct advertising to consumers of such new drugs and devices. Over the objections of many medical groups, patient advocacy groups and civil libertarians defend such advertising based upon the concept of patient autonomy and the right of consumers to pursue whatever treatments might help them, including prodding their physicians to explore the use of such treatments. The difficulty is that such advertising can be very “suggestive” resulting in patients fixating upon – or exaggerating - symptoms and linking them to the condition for which the advertised drug or device was approved. When patients approach their doctor in this manner, studies show up to 80% of patients often will get a drug to treat the condition, although it is the advertised drug only about half the time. Before indicting physicians, one must remember that the diagnoses of many conditions rely on the description of subjective symptoms and there are no good objective measures, e.g., blood sugar, available to definitively confirm or dispel the diagnoses. In fact, many have criticized physicians for “not listening to the patient” or suggesting the symptoms “are in the patient’s head.” Such patients are not likely to experience positive gains (since they are not likely to suffer from the targeted condition) but are likely to experience the *negative* consequences. Also, if we restrict

broader U. S. use of a “promising” treatment (that individuals will readily learn about through the World Wide Web), many patients will obtain it from foreign sources or the black market, with the quality and authenticity potentially suspect.

If we want to continue to enjoy the extraordinary medical progress new drugs and devices have provided us, there are various options to explore, each with their own tradeoffs. Many are currently under discussion. These include limiting the direct advertising of new drugs and devices until broad release monitoring affords us a better fix on efficacy and adverse reactions. We might consider reducing approvals for broader use based upon “intermediate” measures, requiring the actual demonstration of increased survival or reduced suffering. We might explore revising our approach to liability during the broad introduction period, compensating those who suffer an adverse event through a structured liability fund, much as we do children with adverse reactions to vaccines. We might approve broader use but deny insurance coverage until the evidence gathered from the broad release phase has further elucidated efficacy and risk. This would favor the rich to receive the benefits of the new treatment but they would also suffer the undetected adverse consequences. However, if we do not find a way to contain “scapegoat” hearings and “knee jerk” liability actions, we will stifle the medical advances we have enjoyed.

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