

**CENTERS FOR EDUCATION AND RESEARCH
ON THERAPEUTICS (CERTs)
“BENEFIT THE PATIENT, MANAGE THE RISK”
RISK SERIES THINK TANKs**

Risk Communication

“Improving Communication of Drug Risk Information to Prevent Injury”
April 29 - May 1, 2001

Risk Assessment

“Postmarketing Assessments of Pharmaceutical Risk”
May 29 - 31, 2002

Benefit Assessment

“Overcoming Difficult Issues in Characterizing Therapeutic Benefit”
September 17 - 19, 2002

Risk Communication and the Media

“The Importance of the Media in Pharmaceutical Risk Communications”
January 7 - 8, 2003

Risk Management

“Managing the Risks of Therapeutic Products”
January 12 - 14, 2003

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RISK COMMUNICATION THINK TANK

SUMMARY

In recent years, a number of drugs have been removed from the market. In most cases, these drugs were removed because the medical system could not appropriately manage their known, preventable side effects. Amidst considerable media attention, the question arose: How can we improve communication about the appropriate use of prescription drugs?

The current communication methods between the government, medical products industry, and caregivers must improve to change the behaviors that lead to preventable patient injury. The Risk Communication Workshop was organized to determine the current status of risk communication and to develop a research agenda for improvement. “Despite all of the recent emphasis placed on the risk of therapeutics, very little research has focused on the optimal ways to communicate risk, whether to health care providers or patients,” said Dr. Robert M. Califf, director of the CERTs Coordinating Center.

The workshop participants agreed that current methods of risk communication are inadequate, and expressed the desire to collaborate more in developing new approaches to risk communication. Participants agreed that several important factors should guide the development of risk communication methods:

- Current medical environments, such as physicians’ offices, are not well-suited for traditional communication methods to be effective.
- Single methods of communication (such as product labeling) are ineffective when used alone, and should be integrated into a multi-tiered approach.
- Messages about risk should be personalized and tailored to the unique practice situations of a variety of caregivers.
- Current technology provides an attractive but unproven avenue for extending the reach of risk information while individualizing it.
- The education of caregivers needs improvement and should provide the vocabulary and background for effective risk communication.
- Consumers receive massive amounts of information about effectiveness, but only the minimum about risk. If the former can be effective, so can the latter.

The group submitted a manuscript for publication in the journal *Pharmacoepidemiology and Drug Safety* which summarizes the workshop proceedings. It identified three major categories for research: descriptive research (what is working and what is not), etiological research (what is influencing risk communication now), and interventional research (what will change risk communication as it is now).

“This clearly is an opportunity for CERTs leadership to contribute to improved pharmacotherapy and health outcomes at a national level,” said Dr. William Campbell, principal investigator of the UNC CERTs. “It is sobering because there are so few research data to guide decisions, but also stimulating because all stakeholders agree on the critical importance of developing more effective methods of risk communication.”

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RISK ASSESSMENT THINK TANK

SUMMARY

Rapid advances in medicine have led to more effective therapies for patient care. But more effective tools carry the increased potential to do harm when they are not used optimally. Thus, understanding the risk of adverse drug reactions, which cause an estimated 100,000 deaths and 1.5 million hospitalizations in the US each year, should be a national priority.

Clearly, with this number of adverse reactions occurring each year, the current system for detecting and preventing them is less than ideal. Workshop participants set out to determine how to mend the flaws in the current system while laying the groundwork for a new system that would assess the risks of a particular drug or device and weigh them against its benefits. Considerable effort is now spent on detecting rare adverse reactions from newly marketed drugs, yet most adverse reactions are from the inappropriate use of older drugs, an area subject to very little effort.

Workshop participants discussed the flaws in the current system—flaws which emerge from the focus of the current system on the need to meet regulatory requirements, resulting in occasional crisis-driven problems. These problems occur after marketing, with inadequate attention paid to important measures needed to inform clinical decision makers about the balance of benefit and risk. Given the many barriers to the collection of reliable data, such as the expense of data collection, the incompatibility of various databases, and various legal and privacy issues, it is not surprising that we rely too heavily on the FDA Adverse Event Reporting System (AERS). AERS, while necessary, is outmoded, failing to capture many events, and lacking in the consideration of the true numerator or denominator needed to calculate risk. Claims and medical records databases are useful, but are lacking in breadth or depth or both. Factors such as a lack of a single organization responsible for the funding and development of the nation's risk assessment methods, and an overall lack of personnel trained in pharmacoepidemiology are central to the list of problems. The participants agreed that efforts to improve the system should be governed by these principles:

- AERS must continue, though it must be made more efficient and accurate; merely increasing event reporting will not solve the problem.
- New efforts must be truly national and must inter-relate with global efforts; availability of the data is as important as compatibility.
- Various old (meta-analysis and subgroup analysis) and new tools (computer learning and data mining techniques) for analyzing data can be brought to bear on existing datasets.
- A new mindset is necessary at the time of drug marketing. Manufacturers must be proactive in anticipating risks rather than reacting to crises.
- More focus is needed on the risks associated with inappropriate use of older drugs.
- The study of acceptable risk—how society determines whether the benefit of a treatment outweighs its risks—needs greater emphasis.

The ambitious goal of improving our nationwide system will require funding and constituency building. The full, detailed discussion of these issues has been submitted for publication in the journal *Pharmacoepidemiology and Drug Safety*.

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BENEFIT ASSESSMENT THINK TANK

SUMMARY

Any discussion of risk management should have a firm grounding in the benefit side of the consideration. Indeed, the concept of a Benefit Assessment Workshop arose from discussions about risk management. Assessing and managing risk without a quantitative assessment of benefit leaves decision-makers in a difficult quandary. Unfortunately, for many medical products, benefit is not directly measured; rather, “surrogate” outcomes often are accepted for placing products on the market. For many others, the most appropriate outcome for clinical practice has not been assessed directly, so that the relative choices to be made about balancing risk and benefit lack important quantitative information. In many cases, directly comparative clinical trials are not available to assess the benefits of a proposed therapy relative to an alternative treatment.

Workshop participants considered benefit assessment during the pre-approval and post-approval phases in the life cycle of medical products. The Workshop focused on the type of information that would be most useful to decision-makers; the limits to measurement of benefit; the limits to nonrandomized, post-approval assessments of benefit; and the interaction of the regulatory system with the clinical system in promoting appropriate studies.

“To think about risk management without a clear understanding of the benefits of a therapeutic approach would be like looking at the offensive statistics of a basketball player without considering turnovers or defensive abilities. In the end, it’s the balance of benefits and risks that should dictate the risk management strategy,” said Robert M. Califf, MD, director of the CERTs Coordinating Center.

Workshop participants identified many problematic areas, leading to consensus about multiple gaps in our system of benefit assessment. Many of the specific gaps are subsumed under the basic concept that the science of understanding therapeutic benefit has evolved dramatically in recent years, but our system of clinical trials and outcomes assessment has not been able to keep pace. A second fundamental gap is that we do not have a national approach to matching clinical studies with the most pressing national needs.

Consensus was reached that a relatively modest investment in research could result in substantial progress. A detailed report of the Workshop will be submitted for publication in the journal *Pharmacoepidemiology and Drug Safety*.

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RISK COMMUNICATION AND THE MEDIA THINK TANK

SUMMARY

The media has an enormous impact on public perceptions and can directly influence individual decision-making. Recent national discussions about anthrax and smallpox vaccines have reinforced the importance of this issue. Despite the enormous influence of the media on the public's perception of risk and how to manage it and the implications of policies related to the media, little research has been done in this area.

The Risk Communication and Media Workshop brought together a small representative group from the media, academic researchers, consumers, government agencies and the medical products industry to review the role of the media and how to communicate the risks and benefits of drugs, devices, and biological products.

The media represented included newspapers, television, magazines, the Internet, medical journals, and other vehicles. The various approaches used by government, medical products industry, and academia to tell their "stories" to the media were reviewed. What constitutes a "story" and the role of the media were also discussed. And finally, the effect of the media on public policy and individual behavior was assessed.

Of note, only four schools of journalism in the U.S. offer an advanced degree program in health journalism. "Despite the fact that we are dependent on the media for the transmission of risk information to the public and we are all fascinated by the way the press handles risk information, remarkably little research has been done on this subject," said Dr. Tom Linden, who directs the Master's degree program at the University of North Carolina at Chapel Hill School of Journalism.

The Workshop reviewed several case studies where participants explored how government, industry, and academia interact with the media to communicate the risks and benefits of medical therapies.

The management of risk should take into account the effect of the media on the knowledge and actions of all those with a stake in risk management. The development of strategies to work with the media will play an increasing role in medical research. A product of the Workshop was the development of an agenda for research on risk communication and the media. Resulting research will provide a resource for those interested in communicating broadly about the risks and benefits of proposed therapies.

CERTs RISK MANAGEMENT THINK TANK SUMMARY

When our own doctor prescribes a new therapeutic agent, most of us would like to think that it will benefit us immensely. We are less likely to think about the unintended side effects it may cause. As research has given us more potent and effective therapies, there is, unfortunately, no “risk-free” treatment.

In this fifth and final workshop of the CERTs Risk Series, experts from academia, government, industry, healthcare, and consumer groups grappled with the ways to assure that the benefits of therapeutic agents outweigh their risks.

Current methods of risk management for therapeutic agents with identified *serious* risks involve both education (of health professionals and patients) and restrictions on the distribution of the product (e.g. dispensing contingent on physician qualifications, required registration, or certification via a sticker on the prescription). In this two-day meeting the workshop participants recommended on the following principles to guide the future development of risk management approaches for therapeutic agents:

- All new products should have a risk management plan.
- Evaluation of both the processes and outcomes of risk management programs is essential; these evaluations should be in the public domain.
- The primary objective of risk management programs should be protecting the public health.
- Risk management programs should be evidence-based, science-driven, and patient-focused.
- Risk management programs should avoid barriers and complexity for health care professionals and patients.
- Risk management should be integrated into a broader system of medical quality assurance activities.

After jointly developing the above principles, the meeting participants identified and prioritized research and policy gaps related to risk management. They also brainstormed innovative ideas for risk management solutions, including, for example:

1. Use of personal digital assistants with electronic prescribing to drive good therapeutics; the content for prescribing alerts must be improved to increase the “signal to noise ratio”.
2. (Pro) Active surveillance—leveraging electronic databases and establishing targets in advance of product release.
3. Testing of educational tools prior to “launch” of a product and before deployment in a risk management program.

A detailed report will be submitted for publication to the journal *Pharmacoepidemiology and Drug Safety*. Steering Committee chair, Dr. Hugh H. Tilson, who led the consensus development activities in the meeting, observed, “There is an impressive level of agreement among these diverse participants.”