

## When Caring for Critically Ill Patients, Do Clinicians Have a Responsibility to Be Innovative and Try Unproven Approaches When Accepted Approaches Are Failing?

Bruce K Rubin MEngr MD MBA FAARC and Kenneth P Steinberg MD

### Introduction

#### The Arguments: Pro and Con

#### Accepted Mechanisms for Obtaining Experimental Products for Therapy

#### Summary

As the first paper in this Journal Conference on intensive care unit controversies, the editors wished us to set the tone for the debate by discussing the ethics of medical “adventurism” in the intensive care unit. More life-or-death decisions are made in the intensive care unit than elsewhere in the hospital, and the critical care specialist often sees himself or herself as a warrior in a battle with death. This adrenaline-charged calling attracts highly intelligent, hard-working, and compassionate caregivers, as well as fiercely independent clinicians. The result of this is that critical care specialists passionately debate about the meaning and application of published “evidence” and this leads to thoughtful debate, as exemplified by the papers in this and the next issue of *RESPIRATORY CARE*, as well as thoughtless and often dangerous disregard for evidence-based medicine. Physicians are morally obligated to provide the best and most appropriate care possible for their patients, but when accepted approaches are failing and a critically ill patient is getting worse, the critical care physician must make a decision regarding innovative therapy, based on the patient’s prognosis, the available evidence, the resources on hand, the expertise of the physicians, and the values of the patient and the physician. This decision may lead, at times, to trying unproven and innovative strategies to achieve a clinical goal. In such cases, it is to be hoped that this can be done in such a way that data are formally and prospectively collected to increase our knowledge. *Key words: ethics, adventurism, Food and Drug Administration, FDA, patient safety, clinical research, investigational drugs, evidence-based medicine, clinical trials.* [Respir Care 2007;52(4):408–413. © 2007 Daedalus Enterprises]

### Introduction

Do not go gentle into that good night,  
Old age should burn and rave at close of day;  
Rage, rage against the dying of the light.

—Dylan Thomas, 1951

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Bruce K Rubin MEngr MD MBA FAARC is affiliated with the Department of Pediatrics, Wake Forest University School of Medicine, Winston Salem, North Carolina. Kenneth P Steinberg MD is affiliated with the Department of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, Washington.

Our role as clinicians is to provide the best and most expert care at all times, to relieve suffering, and, when

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Correspondence: Bruce K Rubin MEngr MD MBA FAARC, Department of Pediatrics, Wake Forest University School of Medicine, Winston Salem NC 27157-1081. E-mail: brubin@wfubmc.edu.

possible, to heal our patients. Ethically, when proven and accepted approaches are failing a critically ill and suffering patient, and there is a promising experimental therapy, it is our duty as compassionate caregivers to do our best to obtain that therapy for our patient.

As part of the Hippocratic oath we are taught *primum non nocere* (first, do no harm). Philosophically, it is clear that this means to avoid taking harmful actions, but it also implies the obligation to avoid not taking actions that could benefit a patient. Morally, acting and failing to act are equivalent under these circumstances. The ethics of this is acknowledged by government agencies, such as the Food and Drug Administration (FDA). In the January/February 2000 issue of *FDA Consumer* magazine, the article “Experimental Treatments? Unapproved But Not Always Unavailable”<sup>1</sup> detailed both the barriers that prevent patients from getting investigational new drugs (INDs) and the appropriate way for patients to obtain these experimental therapies. In that article the FDA spokesperson stated that “The FDA institutional philosophy is supportive of thoughtful risk taking by seriously ill persons with no effective options available, to have the earliest access to unapproved products that could be the best therapy for them.”<sup>1</sup>

It is often beneficial for a patient to get access to experimental medications. It can make a profound difference to the patient, and society may also benefit from the additional safety and efficacy information that can be collected when the patient gets the drug. For example, people with acquired immune deficiency syndrome who participated in clinical trials for protease inhibitors benefited because these medications were dramatically effective. Even if increased access does not change survival, it can empower patients and their families to believe that they are not simply victims of a serious disease. However, the unthinking application of unproven therapies in an uncontrolled manner carries many risks and few benefits.

### The Arguments: Pro and Con

Tens of thousands of lives are lost each year in the United States and billions of health-care dollars are squandered because of unsafe medical care. In *Crossing the Quality Chasm: A New Health System for the 21st Century*, the Institute of Medicine recommended that health care should be patient-centered, timely, equitable, efficient, safe, and effective, and that “patients should receive care based on the best available scientific knowledge. Care should not vary illogically from clinician to clinician or from place to place.”<sup>2</sup>

Evidence-based medicine has been described as “conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.”<sup>3</sup> Thus, the evidence-based practice of medicine is not about doing the same thing for all patients, which is

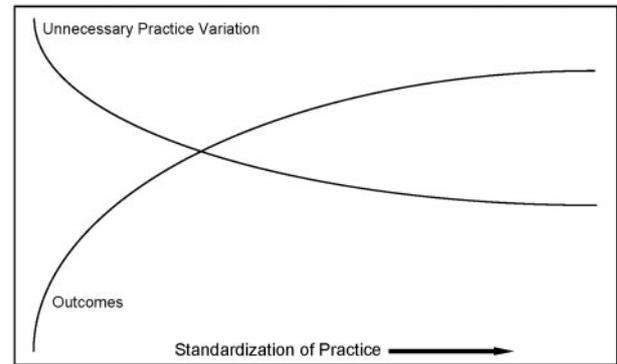


Fig. 1. Theoretical relationship between unnecessary clinical practice variability and outcomes. As unnecessary variability in practice (defined in the text) increases, outcome variability increases, and this increases the probability of serious adverse events. We acknowledge that this is a theoretical construct, because in practice it is impossible to completely eliminate unnecessary variation.

often derisively called “cookbook medicine”; rather, it describes a decision-making practice that integrates the best research evidence with clinical expertise and patient values.<sup>4</sup> Access to experimental therapy under the specific circumstances detailed below should not be confused with “adventurism.” Innovation is part of the process of research. Adventurism often entails wearing “evidence blinders,” to the potential detriment of the patient, the physician, and the health-care system.

In the North American health-care system there is a reliance on the autonomy of health-care providers, and the physician is often seen as a highly skilled and independent craftsman. This autonomous attitude can lead to unnecessary variability in health-care practice.<sup>5</sup> *Unnecessary variation* describes illogical differences in practice between providers who, without good reason, provide different care to similar types of patients. It is true there are times when a provider cannot safely use the standard or recommended therapy for a specific patient, due to patient intolerance of a medication, lack of access to a therapy, or circumstances that prevent the timely application of a recommended therapy. In these circumstances, the use of an alternative therapy is referred to as *necessary variation*. Stated another way, necessary variation is therapy based on the patient’s individual needs and situation. Theoretically, there is an inverse relationship between unnecessary practice variation and health-care outcomes (Fig. 1). As unnecessary variation decreases, more patients receive care based on current best evidence, and, in general, outcomes improve. There will always be necessary variation as clinicians integrate the best evidence with clinical expertise and the patient’s values.

Critical care is a high-intensity, high-risk specialty, and for many conditions there are few high-quality studies to provide strong evidence about safe and effective practice.

The practice of critical care attracts physicians, therapists, nurses, and other health-care personnel who value the ability to rapidly and independently come to important, often life-saving, decisions on behalf of their patients. Some have used the American cowboy as a metaphor for the fiercely independent, hard-working critical care specialist. But these traits, so valuable in a crisis, can also be the source of great harm. Intensive care unit (ICU) adventurism increases unnecessary variability in care, increases the cost to the patient and the health-care system, increases confusion among caregivers, adds to the complexity of care, and thus increases the chances of harm to the patient.

Many therapies that were once embraced in the ICU proved useless or even harmful to the ICU patient when studied in appropriately-controlled clinical trials. Sadly, despite clear evidence of lack of efficacy or worse, all too often the critical care “cowboy” will continue to use these therapies, to the detriment of all. Examples of this illogical and unnecessary variation in care include the use of pressure-controlled inverse-ratio ventilation, calcium for cardiopulmonary resuscitation, theophylline infusions for asthma, and pulmonary artery catheters for monitoring. The continued use of readily available, approved therapy that has been shown to be harmful is a far more pervasive and pernicious problem than the occasional use of truly experimental “off-label” therapy.

Beyond the personality traits that attract a caregiver to an ICU specialty while potentially encouraging adventurism, there are other pressures to engage in ICU adventurism. Organizationally, there may be financial incentives for the physician or institution, a perception of liability if not “everything” is tried, and there are patient and peer expectations to do all that is possible before accepting a poor patient outcome. Clinicians are also subject to prevailing opinions based on local standards of care, local or national opinion leaders who disagree with the evidence (sometimes called “eminence-based medicine”), and their level of training, confidence, and expertise. Paradoxically, it is often the most confident practitioners who are most open to engaging the evidence and changing practice accordingly. The level of clinical uncertainty is high in the ICU; physicians have to deal with their own sense of competence, a sense of compulsion to act (“Don’t just stand there, *do something!*”), and information overload that sometimes makes it hard to clearly recognize and accept research-based evidence.<sup>6</sup>

Clinical decisions are made by considering the evidence in context of the resources available, the expertise of the clinician and the institution, and the values of the patient and the provider.<sup>7</sup> Fear of litigation or the heroic notion of rescuing someone from imminent death may motivate providers to apply unproven therapies, while the egalitarian belief that costs and benefits should be distributed equally

Table 1. Research Versus “Adventurism”

Research	Adventurism
Distinguishes helpful from unhelpful, or even harmful, therapies	Fails to advance knowledge Unable to distinguish benefit from harm
Vital to improving care	Often leads to false conclusions
Advances knowledge, even if it doesn’t help the individual patient	Ignores evidence
Generates evidence	

in society may cause a clinician to avoid the consideration of innovative experimental therapies.<sup>8</sup>

Research is very different in intent from ICU adventurism (Table 1). Research is vital to improving care. It distinguishes helpful from nonhelpful, or even harmful, therapies and advances knowledge, even if it does not directly benefit an individual patient.

### Accepted Mechanisms for Obtaining Experimental Products for Therapy

The FDA has established regulatory mechanisms and worked with manufacturers to ensure that seriously ill patients can get access to promising but not fully evaluated products. “Treatment IND” regulations were established in 1987, and mechanisms were put in place to make experimental drugs available to seriously ill patients earlier in the development process. The treatment IND allows a patient with a serious and life-threatening illness to take an investigational drug while being tested in a clinical trial, based on the recognition that that such IND treatments can generate useful information about how a drug might affect larger segments of the patient population than would receive it in a clinical study.

If enough is known about a drug’s safety and there is some clinical evidence of effectiveness, the FDA may allow a patient to become his or her own study. This so called “single-patient IND” or “compassionate use IND” increases patient access to INDs. The FDA requirements for a single-patient IND are relatively simple (Table 2), but the actual process of enabling the individual patient to obtain the drug is not. Barriers to access beyond the FDA include:

- The drug company must be willing to provide the drug to the patient. This can be expensive and time-consuming, because, in addition to providing the drug, the company must track shipments of the drug, create patient-specific instructions for its use, and create a way of collecting safety data and a mechanism for tracking outcomes for each patient. This greatly increases medication costs.
- If a serious safety problem is found with an individual

Table 2. Food and Drug Administration Requirements for Obtaining Permission to Use an Investigational New Drug With a Single Patient

To obtain Food and Drug Administration (FDA) permission to use an investigational new drug (IND) with a single patient, the treating physician must submit a "Physician Request for a Single-Patient Investigational New Drug for Compassionate or Emergency Use of an Unapproved Drug or Device." The first step is to obtain permission from the manufacturer. Without the manufacturer's consent the product will not be available to the patient, regardless of the FDA's position. After the manufacturer agrees to provide the product, the procedure is to submit the following information to the appropriate review division of the FDA's Center for Drug Evaluation and Research. The request may be made via facsimile, with a letter to follow.

The correspondence must include:

1. The phrase "Request for a Single-Patient Investigational New Drug for Compassionate or Emergency Use" at the top of the letter.
2. A brief clinical history of the patient, including the diagnosis, disease status, prior therapy, response to prior therapy, and the rationale for requesting the proposed treatment.
3. A proposed treatment plan, including the dose, route, planned duration, monitoring procedures, and modifications (eg, dose reduction or treatment delay) for toxicity. Reference a published protocol or journal article if appropriate.
4. A "drug supply reference statement," which names the drug supplier and/or manufacturer and a statement that a "letter of authorization" to cross reference an appropriate IND of the supplier or "drug master file" of the manufacturer is included. The treating physician must contact the supplier or manufacturer for that statement.
5. An "informed consent statement" that states that informed consent and approval of the appropriate institutional review board will be obtained prior to initiating treatment. Some institutional review boards have specific procedures for approving emergency requests.
6. An "investigator qualification statement" that specifies the training, experience, and licensure of the treatment physician. The first 2 pages of the physician's curriculum vitae are usually sufficient.
7. FDA Form 1571, completed, with the treating physician listed as the sponsor. Obtain Form 1571 at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>.
8. The physician's contact telephone number and facsimile number. If the request is approved, an IND number will be issued by the FDA and the treating physician will be contacted by phone or facsimile, with a letter to follow. The IND is considered active upon issuance of the number. The IND sponsor (treating sponsor) will then contact the drug supplier and provide the IND number. The supplier may then ship the drug directly to the treating physician.

(Adapted from the FDA Center for Drug Evaluation and Research Web site, <http://www.fda.gov/cder/cancer/singleIND.htm>, which also lists the phone numbers for the divisions of the Center for Drug Evaluation and Research.)

patient IND, it may hinder the approval process for the broader use of the medication.

- The patient must give full informed consent and understand that the drug is not approved and may cause adverse effects that could range from mild to fatal. Patients must be aware of all the known potential benefits and risks from the treatment. They must be told what animal

and/or human studies have shown about the effectiveness of the drug, and the known dangers and adverse effects found in those studies.

- The patient's physician must be willing to take responsibility for treating the patient and agree to collect the information about the effects of the drug.
- Usually, the patient's family must pay all costs for the medication and necessary monitoring, as these costs are rarely covered by insurance.

If a drug is frequently used as a single-patient IND, the FDA can streamline the process for obtaining permission. An example of this is thalidomide, which was associated with birth defects in the 1950s but is now experimentally used to treat cancer.

For patients in search of novel treatments today, there are many opportunities. There are many clinical studies underway, and there are mechanisms to permit expanded access to investigational drugs outside of controlled clinical trials. The FDA will permit an investigational drug to be used as a treatment IND if there is preliminary evidence of efficacy and the drug is intended to treat a serious or life-threatening disease, or if there is no comparable alternative drug or therapy available to treat that stage of the disease in a specific patient who is not eligible to participate in the definitive clinical trial.

There are some things that the FDA cannot do. The FDA cannot give out the name of a drug in development, and, unless a company publicly releases information, the FDA is forbidden to even acknowledge that it knows about the drug. The FDA has no authority to make the drug available to individual patients or physicians. The FDA cannot require a company to make its drug available outside of a clinical trial. The FDA does not conduct any clinical trials or drug studies. The FDA will not give advice to physicians or patients.

To comply with federal regulations on the emergency use of unapproved drugs, biologics, and devices, the following 5 criteria must be met:

- The tested item (drug, biologic, or device) is used one time per institution to treat a single patient.
- The patient has a condition that is life-threatening or severely disabling.
- No standard treatment is available.
- There is not sufficient time to obtain a peer review of an experimental study.
- The FDA is fully informed of this experimental use.

Access to experimental therapy under these specific circumstances should never be used as a cloak to protect the

marketing and sales of unproven or fraudulent therapy. In 1979, as a result of the importation and sale of laetrile to cancer patients, the Supreme Court upheld the FDA's right to withhold experimental drugs from patients. The court held that the FDA has the authority to require a showing of safety and effectiveness in every drug, including those used to treat the terminally ill. The court construed that Congress intended to shield even those patients from fraudulent products.<sup>9</sup> This case established that the FDA can constitutionally prevent patients from having a choice in their drug therapy. However, in response to a petition from the Abigail Alliance (an advocacy group for terminally ill patients and their families), some portions of that ruling were overturned in May 2006 by a 3-judge panel of the United States Court of Appeals, District of Columbia Circuit. Two members of that panel ruled that patients with life-threatening diseases and otherwise untreatable diseases have a *constitutional right* to seek experimental treatments for which efficacy is not established, and the government cannot interfere unless it provides compelling interest. Judge Judith Rogers wrote, "The prerogative asserted by the FDA—to prevent a terminally ill patient from using potentially life-saving medication to which those in Phase II clinical trials have access. . . impinges upon an individual liberty deeply rooted in our Nation's history and tradition of self-preservation."<sup>10</sup> In mid-June 2006, federal officials filed an appeal, seeking to have the case reheard by the full 9-judge panel of the Appeals Court. This appeal was strongly supported by the Society for Clinical Trials Board of Directors.<sup>11</sup> In the August 3, 2006, issue of *The New England Journal of Medicine*, Susan Okie wrote an editorial<sup>10</sup> on that ruling, in which she emphasized that the FDA has a responsibility to protect the critical scientific studies that must be carried out to determine which drugs are truly safe and effective and how they can best be used. The FDA is concerned that if the drug is made available to patients earlier, it will be harder to obtain data on safety and efficacy, because patients may seek treatment directly rather than enrolling in trials.<sup>12</sup> Thus, the interests of society must be balanced against the rights of individual patients.

### Summary

To make informed decisions we must first know and acknowledge the evidence regarding specific therapies, as well as the limitations to that evidence. It is essential that we also assess the values and goals of the patient and his or her family, and the values that we bring to the situation, and that we consider the resources available. We are never ethically obliged to provide futile therapies. In deciding whether to implement an unproven therapy, we believe that ICU adventurism and futility medicine should be condemned and avoided. There is no room in the modern ICU

Table 3. Sources of Information About Investigational New Drugs

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Information Program on Clinical Trials ( <a href="http://www.lhncbc.nlm.nih.gov/clin">http://www.lhncbc.nlm.nih.gov/clin</a> ) mandated by the Food and Drug Administration (FDA) Modernization Act of 1997, is a joint FDA/National Institutes of Health (NIH) resource. Though initially it contained only NIH studies, it will eventually include all federally and privately financed clinical studies.
CancerNet ( <a href="http://cancer.net.nci.nih.gov">http://cancer.net.nci.nih.gov</a> ) is run by NIH's National Cancer Institute. It provides information on clinical trials. Information is also available through the National Cancer Institute's Cancer Information Service, at 800-4-CANCER.
ACTIS ( <a href="http://www.actis.org">http://www.actis.org</a> ), the AIDS Clinical Trials Information Service, provides a wide range of information on current AIDS (acquired immune deficiency syndrome) research, including drug trials, vaccine trials, and other educational material. Sponsored by the United States Public Health Service, including FDA, National Institute of Allergy and Infectious Diseases, Centers for Disease Control and Prevention, and the National Library of Medicine. ACTIS can be reached at 1-800-TRIALS-A.
Information on clinical trials for rare diseases can be found at <a href="http://rarediseases.info.nih.gov">http://rarediseases.info.nih.gov</a> , which is a database compiled by NIH's Office of Rare Diseases.
CenterWatch Clinical Trials Listing Service ( <a href="http://www.centerwatch.com">http://www.centerwatch.com</a> ) is published on the Internet by CenterWatch Inc, which is a multimedia publishing company in Boston, Massachusetts. It provides information on more than 5,000 active clinical trials, and other information.
When a clinical trial is not an option, FDA facilitates access to an investigational new drug or an investigational medical device through other programs. For information on programs for, or access to, an unapproved investigational new drug, call FDA's Office of Special Health Initiatives at 301-827-4460.

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for medical "cowboys," either in trying approaches that have little physiologic or pharmacologic support or in applying therapies in a situation beyond hope.

We also must be aware of how to enroll our patients in appropriate clinical trials when they qualify, as this is by far the best way for us to develop the evidence base needed for optimal clinical care (Table 3). When a patient is ineligible to join a clinical trial but there is evidence for potential benefit from an experimental therapy for a life-altering or life-threatening condition, the above-described mechanisms and processes must be followed.

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## Discussion

**MacIntyre:** You made very cogent arguments about “*n*-of-1” trials [in which the patient acts as his or her own control and is the only patient in the trial]. In trying to learn each time we do something new, does it always require a placebo trial? Bruce Rubin made a very interesting point about patients having to go into a trial where they might receive a placebo, but is that always required?

**Rubin:** According to the District of Columbia Circuit Court's decision in March 2006, the answer is no, because the patient has a constitutional right to receive experimental therapies. Patients are dying and they want anything that might help. I think our positions are fairly close. I am a stickler for evidence-based medicine. I always think it is far better to not “just do something,” but to make the time to think about what you are doing. But the answer to your question is that you don't need placebo control. What you do need when you design these IND studies is to collect the data—and you can usually get approval for treatment with an IND within 30 minutes of phoning the FDA and giving them the information.

It takes time to do everything necessary to get the drug, but we are obliged, if we are going to do a non-placebo-controlled test, to collect the information, to monitor for safety, to monitor outcomes, and to get that information to the FDA and the manufacturer, to assist with informed decisions. But this may change: the appeal

went in June of 2006. It will probably be heard by the Court of Appeals in 2007.

**Kallet:** Bruce, I am disturbed by the Court of Appeals decision, because it essentially violates the ethical code of social justice. What it says is the very bourgeois position that (pardon my leftist take) if you have money, you can throw it away on a therapy that is unproven but may help. but if you are middle-class or poor, then you may need to go into financial ruin to do this, or be cut off from access to the treatment. The decision automatically cuts off the vast majority of citizens of this country from that type of treatment.

**Rubin:** How many millions of Americans are uninsured and underinsured right now? We are on the same page here. Yes, that's exactly what it's doing, and it is very costly. But it may be an opportunity if it is used to collect additional data, as long as it doesn't risk torpedoing potentially useful therapies by using them on the wrong patient, at the wrong time, for the wrong reasons.

**MacIntyre:** Is it fair to say that any time an unproven therapy is used it ought to be given in the context of collecting information for research? It doesn't necessarily have to be a placebo trial, but is that a fair statement, Ken?

**Steinberg:** Yes, I think it is a pretty fair statement. I agree that not every trial has to have a placebo arm. And in an

*n*-of-1 trial I didn't mean in the strictest sense that it has to be compared to placebo, but rather that you have to have a period of time of placebo and a period of time of intervention. When you try something new or unproven, you need to try to learn as much as you can from that experience, while trying to help—and not harm—the patient. Collecting data can help you do that—starting a therapy and measuring, as best you can, whether the patient is benefiting, and of course stopping if they are not benefiting.

**MacIntyre:** There are people who want to try new ventilation modes all the time, and I used to be one of those adventurers. But as I've gotten older and, hopefully a little bit wiser, I am trying to restrict that. Not that we shouldn't try new modes, but we should do it with a systematic set of rules on whom we try it on and how we do it, and collect specific information on it, so we learn something from it and hopefully improve our practice. That reduces confusion and provides consistency, so the day shift is applying the mode in exactly the same way the night shift does. If the mode is applied in different ways by different clinicians, it can harm patients.

**Rubin:** Data, however, are worthless if they are only in your head. Data need to be disseminated. Since this is a Journal Conference, and, partly because we have David Pierson\* and

\* David J Pierson MD FAARC, Editor in Chief, RESPIRATORY CARE.

Katherine Kreilkamp<sup>†</sup> here, I want to mention that there is a tremendous publication bias in all journals to publish data that show that something is better or improved, rather than that there is no difference. Such positive findings are considered more exciting and more interesting. It gets on the news if you've got a new therapy, rather than showing that a new therapy doesn't work. And there is frequently the criticism that if you found that something doesn't work, your research might have suffered a type-2 [false negative] error and/or the study was insufficiently powered to identify a difference. It is tremendously difficult to publish negative data. Reviewers and editors don't like negative findings, because they don't get attention, but negative data are as important as positive data, so I think it goes beyond the obligation to *collect* information; we must also *share* the information so it can be useful to practitioners and patients.

**Hess:** The problem that I have with *n*-of-1 trials in the ICU is that the outcome we are really interested in is survival, and the outcome that researchers usually choose in an *n*-of-1 trial is some physiologic outcome, such as improvement in P<sub>O<sub>2</sub></sub>. We now have a lot of evidence that some therapies that improve P<sub>O<sub>2</sub></sub>, such as inhaled nitric oxide, large tidal volume, prone position, and so forth, do not affect important outcomes such as survival. So I have not known quite what to do with *n*-of-1 trials in the ICU, where the outcome that we really want is improved survival.

**Deem:** Ken, I want to come to the defense of anesthesiologists and pathologists with regard to your comment that we are interchangeable. I think that is an incorrect and unfortu-

nate public perception. There is a lot of independence in practice, and a good example was at a hospital in Seattle, where about half the faculty recently left because the hospital instituted the Toyota method of standardizing approaches to care, and there was a lot of disgruntlement about that. The anesthesiology faculty left in droves. And with regard to pathologists being interchangeable, I think that among pathologists there is 100% concordance on interpretation of tissue samples only about half the time. So I don't think it's true that they are interchangeable.

I have a question about practice variability being harmful. Are there data to support that assertion? There's quite a lot of evidence from other fields, such as business, the stock market, and studies of gambling, that variability, diversity, and independence in a group are very important, and that better decisions are made when there is a lot of variability in thought, and perhaps in practice, as opposed to a standardized approach. In other words, a large group of individuals with a lot of diversity will come to a better decision than a small group of experts, or one single expert. What are the data regarding the benefits of uniformity in health care?

**Steinberg:** About your first point, just because anesthesiologists left that hospital because they were unhappy about having to behave like airline pilots doesn't mean that standardization didn't improve patient care. About your second point, by "variability" I don't mean individualizing care when it's dictated by clinical circumstances. I am not arguing for "cookbook medicine" on everything. Decision making is based on more than just evidence.

But I think there are a lot of data, not just in health care but in other industries, that variability in practice can lead to harm. I'm not sure you want an airline pilot to say, "I'm going to ignore these usual steps that I

go through to get ready for landing the plane, because I know how to do it better." I think there is a role for standardizing our approaches to certain problems, and then, of course, if there's wind shear, for instance, the pilot has to adapt to those conditions.

I think that minimizing unnecessary variability while allowing individualized decision making is probably the best way to go. It doesn't mean that you'll make the right decision in every case, but for the majority of patients I believe the quality of care tends to rise with standardized procedures.

**Deem:** I think that analogy to airline pilots is a bit misguided, because airline pilots are faced with a fairly fixed number of problems that have a fixed number of solutions, whereas in medicine, particularly in critical care, we have an almost infinite variety of problems and possible solutions. So I don't think that's a very fair comparison.

**Steinberg:** Our brains can't handle an infinite number of solutions! We have to have a way to approach a problem, I think. I agree that the analogy with the airline industry is a little stale, but I think we can learn a lot from other industries that have standardized their approaches to common problems.

**Hurford:** Just to show that anesthesiologists aren't interchangeable, Steve, I disagree. The airline analogy is really quite a good one. They have a way of dealing with the unexpected situation. They say "Let's see what happens if we move all the controls to the right." They do this in flight simulators, with lots of training for the unexpected. We don't do that in medicine.

**MacIntyre:** Because we don't have simulators!

**Steinberg:** Not yet.

**Rubin:** Because all airplanes are pretty much the same, whereas all pa-

<sup>†</sup> Katherine Kreilkamp, Assistant Editor, RESPIRATORY CARE.

tients are not. One of the reasons Airbus has been successful over Boeing is that the controls are so similar on every Airbus, and that makes it easier to train pilots. You train on one, you've trained on all. And what we need to be thinking about as anesthesiologists and critical care physicians is standardizing our patients, making them all the same, and then we can use a simulator.

**Hurford:** They are more the same than you think, and there are gains to be made. My question is whether it is reasonable to try to do that and spend time figuring out, How *do* we standardize our patients, rather than saying, "I read this idea in a journal; let's try it. Even though it didn't work the last 5 times I tried it, maybe this time it will." There's an intellectual defeatism in saying that the patients are too variable and we can't figure it out, so we must let randomness control our practice.

**Fessler:** Steve, you indicated that groups often come to better decisions than individuals, and that may be true when groups are reaching the decision. But an individual physician taking care of an individual patient is just making his own decision. If you have 10 anesthesiologists taking care of the same patient who come to 10 different conclusions, only one or two of those conclusions will be the right thing to do. We as scientists ought to figure out which is the one right pathway, and then make sure that the other 9 anesthesiologists do that.

**Deem:** I don't know if that's true. There may be multiple right pathways, and in the global context it may be that as a group, the group will come to correct decisions overall, even though there may be some wrong individual decisions. And overall outcomes will be better if made by a group with diversity and independence than they

will be if the approach is standardized. That's my point, I think.

**Cheifetz:** I take a slightly different slant on this. If a group of clinicians makes a decision for an individual patient, I agree that they are probably more likely to come to a better therapeutic plan than one physician acting alone. And hopefully the group's decision is based on the medical literature.

But an important problem can occur when there is a change in the attending physician between the day and night shift. If the attending changes the group plan, then things may go astray. You end up with a concerning situation if each attending physician independently individualizes the plan. Management can start to wax and wane, leading to a deterioration in the quality of patient care. So data-driven clinical pathways (or at least guidelines) may help minimize variability among attending physicians.