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Third Parties in the Clinical Encounter

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FROM THE EDITOR
Outside Influences on Medical Practice

In an ideal world, physicians and patients would be able to make treatment choices in patients' best interest without having to consider extraneous factors, but that is far from the way medicine is practiced in this day and age. Instead, physicians must operate within a scheme of regulations imposed by numerous third parties that impose a host of constraints, ranging from what physicians can say to what medical procedures they must perform. This past November, the DEA published a long-anticipated notice of proposed rulemaking that seeks to schedule the drug Tramadol [1]. This notice came with little fanfare in the medical community and, like most such decisions, went almost entirely unnoticed by medical students. It is easy to wonder why medical students would care about such a technical and minor government action, but it does matter. Many free student-run clinics, including ours at the University of Florida, have adopted voluntary policies of not prescribing controlled substances. For clinics like these, Tramadol, a currently unscheduled prescription painkiller, has been a mainstay in treating patients with refractive pain. With this decision to schedule Tramadol, we need to be prepared to replace one of our most relied-on tools. That is not to say that Tramadol should not be scheduled, but merely that these things matter to medical professionals, students included.

This issue of *Virtual Mentor* explores the various ways third parties, be they legislators, government agencies, or nongovernmental organizations, affect how physicians are able to care for their patients and the ethical dilemmas that arise when these rules are at odds with how we may prefer to act.

Regulations that affect the physician-patient relationship can be broadly grouped into three categories: those that compel or restrict actions during patient encounters, those that affect access to drugs, and those that carve out the rights of patients.

The first category is that in which the most obvious ethical dilemmas arise. Bahareh Keith, DO, and Kimberly B. Handley, MSW, LCSW, discuss how to navigate mandatory reporting statutes, such as those that govern child abuse, in the context of an asthmatic child repeatedly exposed to secondhand smoke, a situation which touches but does not necessarily cross the line of child abuse. In a second case commentary, Jen Russo, MD, MPH, explores the conflicts between ethical medical practice and laws that require doctors to show an ultrasound to a woman before proceeding with an abortion. This issue is particularly timely; it was just a few weeks ago that a federal judge struck down a North Carolina statute that went one step further, requiring physicians to describe the results of the mandatory ultrasound to patients in addition to requiring them to show it [2]. Jody Steinauer, MD, MAS, and

Carolyn Sufrin, MD, MA, further discuss legislative interference with abortion provision, including the problems caused for patients by legally protected conscientious refusals to refer them for abortion care.

On the flip side of mandatory actions are prohibited actions. Mobeen H. Rathore, MD, CPE, discusses gag laws that prohibit physicians' asking patients about gun ownership. This law thwarts our ability to protect children by promoting gun safety at home. At the same time, it forces us to contemplate the nonmedical rights of our patients.

The second category concerns the effects of third-party decisions on the access our patients have to essential drugs. When third parties make rules restricting drug use or artificially inflate prices to astronomical levels, our patients' access to necessary drugs is severely curtailed. Susan Wood, PhD, recounts the Food and Drug Administration's abnormal handling of the application to sell emergency contraception over the counter, which obstructed appropriate access to levonorgestrel for over a decade for what appeared to be politically motivated rather than scientific reasons. Gary M. Reisfield, MD, explains how the FDA's decision to withdraw approval for generic versions of OxyContin after approving a new abuse-deterring formula, OxyContin OP, has delayed the long-anticipated appearance of cheaper generic versions of the drug.

On the other hand, when access to drugs is expanded, our patients stand to benefit greatly and our ability to fulfill our obligation to care is enhanced. In the podcast, Gary Wang, MD, PhD, discusses how the FDA's expanded indications for Truvada granted our patients improved access to the drug and allowed physicians to serve our HIV-positive patients better. It is a telling example of how a simple regulatory move regarding a drug that was already on the market was able to improve patient care. In her case commentary, Ly Le Tran, MD, JD, explores the arguments for and against accepting free samples from pharmaceutical companies to dispense to patients, in the context of the Sunshine Act, designed to make relationships between physicians and the pharmaceutical industry more transparent. An excerpt from the AMA *Code of Medical Ethics* takes up questions of drug-related cost containment and physicians' relationships with industry.

Finally, this issue tackles the subject of protections for patients. Collin O'Neil, PhD, examines the ethical implications of proposed changes to the Common Rule that would allow doctors to conduct certain forms of low-risk research on their patients without patient consent. He concludes that such research cannot be done ethically without the explicit consent of the participants. Another excerpt from the AMA *Code of Medical Ethics* discusses physicians' participation in clinical trials and the avoidance of related conflicts of interest. William D. White, PhD, reviews the concepts underlying mixed self- and third-party regulation in medicine and the concerns raised by some critics about whether self-regulation is sufficient to protect patients' and society's interests. Lauren B. Solberg, JD, MTS, introduces online

medical communities, membership in which can pose certain privacy risks that are only partly mitigated by legal protections against health-based discrimination.

Third-party decisions influence everything physicians do, from the mundane activities of daily practice to the most innovative advances our field is making. It is my hope that this issue illustrates the important issues that arise when medicine interacts with third parties and that it will encourage medical students and physicians to stay abreast of these topics as they continue their careers.

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ETHICS CASE
Mandated Ultrasound Prior to Abortion
Commentary by Jen Russo, MD, MPH

Amy sits in the waiting room by herself, bouncing her leg nervously. Four weeks ago she found out she was pregnant, and today she visits Dr. Robbins' office to ask what her options are. She is strongly considering having an abortion. After 20 minutes pass, Kathy, a fourth-year medical student starting an externship, leads Amy to an examination room. Picking up on her anxiety, Kathy asks Amy if she is all right.

"I've always been uncomfortable with gynecologists," Amy says, fidgeting on the examination table.

"I understand," Kathy says, preparing the transvaginal probe as Amy stares wide-eyed.

"The first step in this process is to perform an ultrasound to determine how far along you are. According to our state law, I must show you the ultrasound and you must hear the fetal heartbeat, if there is one. I know this might be uncomfortable, and I apologize."

"I don't want to see the ultrasound," Amy says. "What the baby looks like doesn't make a difference to me—I am having this abortion because I'm not financially able to support a child right now. Having to see this ultrasound isn't going to change my mind."

"I understand your frustration. Although an ultrasound is often an important part of the process in abortion care, I don't think women should have to view the ultrasound if they don't want to. Unfortunately, this was a law that was passed last year and we can lose our license if we do not provide the ultrasound and have you view it. I can't proceed with your visit until we have completed this part."

Amy concedes to the ultrasound.

Later, Kathy talks with Dr. Robbins. "I think the patient made a valid point about the ultrasound. I'm really struggling to understand how forcing her to look at the ultrasound is acceptable. At my medical school, we don't have to force the patient to look at the ultrasound. Some women want to look and some don't. It doesn't usually seem to change their decision." Heat floods Kathy's cheeks. "Amy's already in a really vulnerable position. Why is the legislature allowed to dictate how we practice medicine?"

Commentary

This case brings up several clinical and ethical questions. Is there evidence suggesting that ultrasound viewing has an impact on patient decision making about abortion? Should there be legislation intended to influence women's decisions about abortion? What role should legislation play in the patient-physician relationship? What role should legislation play in physician decision making?

Kathy struggles with a question that has become more frequent in the past decade, as those who oppose abortion advocate limitations on abortion care. Medical education prepares a medical student or a physician to counsel a patient on reproductive health care decisions, but sometimes clinicians must comply with legal obligations that directly contradict the findings of medical research.

Clinical Evidence: Ultrasound Viewing

Ultrasound, either abdominal or transvaginal, prior to an abortion procedure is common practice to assure appropriate dating of the pregnancy. However, it is not medically necessary and can add to the cost of the abortion procedure [1].

Do women undergoing abortion want to view the ultrasound? A recent study of patients at a large urban US abortion center found that 42.6 percent of women desired to view their ultrasounds [2]. The authors found that patients with low-to-moderate certainty about their decisions to have abortions were more likely to choose to view the ultrasound. No studies have examined the impact of *mandated* ultrasound viewing, but, given that 57 percent of patients in a recent large study did not want to view the ultrasound, one might conclude that required viewing interferes with the shared decision making model typical in the patient-physician relationship [2].

The literature on the impact of *optional* ultrasound viewing in abortion care is limited to a small pool of studies. Two small studies examine first-trimester ultrasound viewing [3, 4]. Both demonstrate that women appreciate having the option of ultrasound viewing. Women who viewed their ultrasounds before first-trimester abortions continued with abortion at the same rate as women who did not view the ultrasound. More recently, a large study found that women who are less certain of their decision to have an abortion might be more likely to continue their pregnancies after ultrasound, but that the majority of women opt to terminate after viewing the ultrasound [5]. Most of the literature on ultrasound viewing demonstrates that women would like to have a choice about whether to view the ultrasound and that ultrasound viewing is not conclusively linked to the decision to continue a pregnancy [5].

Legislation: Ultrasound Viewing

Kathy and Dr. Robbins resemble nearly half of all abortion providers in that the law regulates all or some aspects of their practices. The number of overall abortion restrictions has increased dramatically in recent years. According to the Guttmacher Institute, "205 abortion restrictions were enacted over the past three years (2011–

2013), but just 189 were enacted during the entire previous decade (2001–2010)" [6]. And, despite the lack of evidence that ultrasound viewing influences abortion decision making, a number of laws require the practice. The Guttmacher Institute cites 22 states that regulate the provision of ultrasounds by abortion providers [1]. In 2013, two states, Wisconsin and Indiana, added laws mandating that a clinician perform and describe the ultrasound and offer the patient the opportunity to view it and listen to the fetal heartbeat [6]. Three states—Louisiana, Texas, and Wisconsin—require clinicians to show and describe the ultrasound to the patient [1]. In two other states, North Carolina and Oklahoma, laws requiring ultrasound viewing are on the books but not currently enforceable [1].

Legislative Interference

The American Congress of Obstetricians and Gynecologists (ACOG) recently addressed the role of government in the patient-physician relationship:

> Absent a substantial public health justification, government should not interfere with individual patient-physician encounters…. Laws that require physicians to give, or withhold, specific information when counseling patients, or that mandate which tests, procedures, treatment alternatives or medicines physicians can perform, prescribe, or administer are ill-advised. Examples of such problematic legislation include laws that prohibit physicians from speaking to their patients about firearms and gun safety; laws that require medically unnecessary ultrasounds before abortion and force a patient to view the ultrasound image; laws that mandate an outdated treatment protocol for medical abortion; and laws that prescribe what must be communicated to patients about breast density and cancer risk, contrary to current evidence-based scientific data and medical consensus [7].

Kathy is legally required to tell Amy that she cannot decline an ultrasound if she wishes to proceed with her medical care in this setting [8]. Amy does not want to view her ultrasound but must. This legislation forces physicians to violate the ethical principle of respect for patient autonomy, which entails that patients be able to choose which treatments they receive and that they be able to make treatment decisions without coercion [9]. Laws requiring that a patient be offered an ultrasound and the opportunity to view the results might be consistent with both the medical evidence on ultrasound viewing in abortion care and ethical medical practice, but laws that require it are not. Furthermore, forcing patients to have unwanted procedures—especially invasive procedures—or to view results against their will may in fact cause harm, violating the ethical principle of nonmaleficence [8]. Moreover, while ultrasound may be beneficial in pregnancy, viewing the ultrasound has little proven effect as demonstrated in the current literature [3-5]. Therefore, requiring mandatory ultrasound violates the principle of beneficence, or performing only those procedures that have a benefit to the patient.

Abortion is a contentious area of medicine, but, as noted by ACOG above, this precedent of legislative interference in abortion care has important implications for other areas of medicine that may be less contentious but equally important to the trusting relationship between patient and physician.

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ETHICS CASE
Drug Samples: Why Not?
Commentary by Ly Le Tran, MD, JD

Dr. Williams, the medical director of a large clinic, announces to her staff, "As of next month, we will no longer be offering free drug samples to patients here." Over the immediate dissent of the doctors, she continues, "I am concerned that, with our limited supply, we are often starting patients on drug regimens that we know we cannot continue to provide for free and that they will not be able to afford once their samples run out."

"This is the only way some of our patients can get their medication!" protests one physician.

Dr. Williams explains that the office has stopped accepting gifts such as dinners from pharmaceutical companies and says she thinks that this is really just in keeping with those policies.

Dr. Silverstein points out that, under the new Physician Payments Sunshine Act, drug samples are exempt from mandatory reporting, unlike material goods, stock options, grants, consulting fees, travel, and other perks. He insists that this is clear evidence that drug samples are unlike these other things the clinic has stopped accepting and that Dr. Williams ought to reconsider her position. In turn, she asks him, are drug samples really helping their patients if they can't receive the full regimen without financial hardship?

Commentary
This case narrative illustrates a common scenario: a doctor tries to find ways to reduce financial burdens to a patient, and one way to do that is to provide drug samples. The case then asks whether drug samples are really helping patients if they can't receive the full regimen without financial hardship. I think the answer is yes, and I provide my reasons for thinking so in this commentary.

The rising cost of health care in the US has resulted, in part, from the price of drugs [1]. To market their new products effectively, pharmaceutical companies spend enormous amounts on promotion efforts aimed at physicians, such as gifts, free samples, educational seminars, entertainment, and consulting arrangements. Free drug samples constitute a large portion of pharmaceutical companies' marketing budgets—between 1996 and 2000, slightly more than half of all dollars spent by the pharmaceutical industry went toward promotion [2]. An estimate of the retail value of samples provided to doctors in 2004 puts the value at approximately $16 billion

[2]. Critics of this expenditure [3] have concluded that drug samples raise the cost of health care, as companies recoup marketing costs through higher prices and increased sales volume.

Regulatory Context

In 2003 the Office of the Inspector General of the Department of Health and Human Services (OIG) published the Compliance Program Guidance for Pharmaceutical Manufacturers [4], urging pharmaceutical companies to review their existing policies for complying with guidelines aimed at reducing fraud and abuse in federal health care programs. As outlined by the OIG, many instances of giving gifts or free samples, putting on educational seminars, or forming entertainment and consulting arrangements risk criminal liability under the federal anti-kickback statute [5] whenever the intent of the activity is to increase business. If an activity provides a benefit to the physician with the intent to "induce or reward referrals" of federal health care business to the sponsoring company, that activity violates the anti-kickback statute, even if it has a legitimate purpose.

In addition to the federal anti-kickback statute and the voluntary guidelines, many states have their own anti-kickback statutes and Medicaid fraud statutes that include anti-kickback provisions [6-8]. The federal Physician Payments Sunshine Act requires that drug and device companies report any compensation or payment to individual physicians that has a value of $100 or more [9], and some states also require pharmaceutical companies to report the amount they spend on specified marketing activities each year [6-8]. Clearly the laws prohibit marketing activities that induce "kickback" responses on the part of physicians. But these marketing activities do not include drug sampling.

For over a decade some medical centers, hospitals, clinics, and group practices have banned the receipt of drug samples [10]. Many have banned interactions with pharmaceutical representatives (commonly known as "drug reps") or severely restricted their visits [11]. For fear of the appearance of "kickbacks," many medical group practices also restricted their acceptance of promotional materials [12, 13].

In compliance with the FDA rules and state statutes, the pharmaceutical industry as a whole has changed its marketing practices; many companies have stopped such promotional activities as gifts, meals, and various types of entertainment and have limited their drug sample programs [14]. With these restrictions and limited interactions with pharmaceutical reps, followed by a controlled free drug sampling program nationwide [15, 16], the cost of health care is still rising as the costs of medical services and drugs continues to increase [17]. A study conducted at Madras Medical Group, a rural family practice clinic in Madras, Oregon, where the authors examined the effects of restricting pharmaceutical industry detailing and sampling, found that curbing or removing drug sampling programs did not reduce drug cost [18]. Arguments for and against drug samples can be summed up as follows:

Table 1. Arguments for and against free drug samples from pharmaceutical companies

Drug samples are harmful	Drug samples are helpful
Can pose a risk to patients due to lack of pharmacist's input/assistance	Can replace expensive prescriptions for acute problems
Can encourage or enable misuse due to unregulated handling and use or resale	Lowers medication cost for patients
Inappropriate disposal of unused/expired samples	Allows patients to try out new medications: to establish efficacy and tolerance before expensive purchase
Can influence prescribing behavior	Can increase adherence by starting therapy right away
Supply can be unreliable or inconsistent	Physicians can counsel patients about sample use rather than leaving education to pharmacists dispensing prescriptions

Arguments in Favor

Free samples may allow trials before purchase [19], provide an immediate start to treatment rather than the delay of filling a prescription, and give doctors an opportunity to gain experience with new drugs. Alikhan et al. [20] concluded that, in dermatology in particular, where new drugs appear with greater frequency than in other specialties, the benefits of drug sampling outweigh the risks because they help dermatologists avoid wasteful spending with short-term trials (evaluating preference, efficacy, and tolerability). Advantages of using drug samples was also reported in geriatric care: after an extensive evaluation of 13,847 Medicare beneficiaries, Tjia et al. concluded that "policies restricting or prohibiting drug sample distribution may adversely impact access to medications among patients in high-risk groups" [21]. The authors also maintained that use of prescription drug samples is especially common among people "with cost-related medication non-adherence and poor health status" [21].

Arguments Against

The sampled drugs provided free are branded products that cost more than generics; once the sample is exhausted, doctors tend to prescribe the branded product previously introduced as a free sample [22, 23], and, in some cases, this leads to interruptions in therapy for those who cannot afford full courses of the brand-name drug [24, 25]. Opponents contend, further, that drug samples influence physicians' and residents' prescribing habits [22, 23], more specifically that physicians with access to free samples are more likely to prescribe the brand-name medication than equivalent generic medications [26]. The Madras Medical Group study showed reductions in branded drug use in certain categories [18]. Another study, conducted at Lakeview Internal Medicine, a private clinic in West Des Moines, Iowa, showed an increase in generic prescriptions following a 90-day removal of drug samples [27].

Furthermore, a lack of explanation, written instructions, or understandable language on sample packages may lead to misuse [28-30]. Some commentators point to the lack of safety reporting infrastructure to alert dispensers or recipients of sample drugs in the event of a drug recall [31]. Others have raised concerns about storage and accountability systems for drug samples; samples tend to be stored in open shelves and dispensed without detailed documentation, which could enable misuse or diversion [32]. Finally, critics have cited misuse of drug samples, including dispensation to physicians' relatives and purported "trading" or "resale" of samples [33]. Some consider the dispensing of samples to "non-poor" patients inappropriate [33], though this enables the useful trials of therapy described above.

Conclusion

There are ways to dispense samples that address some of the concerns about drug sampling. Physicians who choose to dispense free drug samples should plan for and reserve adequate time for patient counseling. A standard reporting practice such as detailed documentation in a patient's chart and maintaining up-to-date medical records can resolve handling and accountability concerns; requirement of such practices would be even more effective. Drug sampling need not be prohibited to prevent these potential problems.

As for the question of influence on prescribing practices, the reduction in brand-name prescriptions in the Madras study was, when all categories of prescribing were included, insignificant [26]. Furthermore, hospitals' formulary committees constrain what can be prescribed by doctors within a given system; insurance companies' formulary lists constrain which medications will be covered by patients' insurance (and therefore, in many cases, what they can afford) [34, 35]. Cost-reducing measures undertaken by both hospitals and insurers may have a chilling effect on the prescribing of expensive drugs that counters influence from pharmaceutical companies. Furthermore, the influence of samples on prescribing may not always be inappropriate or harmful to patients. If a patient's condition responds positively to a sampled drug and the doctor prescribes it rather than putting the patient through a trial of another therapy, clearly the patient benefits.

Ultimately, I believe that, with the proper safeguards and physician awareness, the benefits of drug sampling outweigh the harms. Dispensing free drug samples to indigent patients helps to defray individual health care costs (albeit in the short term) and provides the opportunity for patients and doctors to evaluate tolerance and preference prior to spending money on a costly treatment.

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A Crash Course? What Happens When a Patient's Medical and Economic Best Interests Collide? March 2006

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ETHICS CASE
Is Parental Smoking Neglect of an Asthmatic Child?
Commentary by Bahareh Keith, DO, and Kimberly B. Handley, MSW, LCSW

A mother carrying a coughing child walks into the emergency room. She hysterically flags down a triage nurse and tells her that her daughter, Rose, is having trouble breathing. The nurse directs mother and child to a bed in the emergency room cordoned off by a light blue curtain. Less than five minutes later, Tricia, a third-year medical student on her pediatrics rotation, shows up to do a thorough history and physical of the patient. The first thing Tricia notices is that both mother and daughter are saturated in the scent of cigarettes. Upon questioning, the mother admits to smoking two packs a day in the house.

"Have you tried quitting?" Tricia asks.

The mother scowls. "The smoking's not a problem. I keep all the windows open." At that moment, her daughter has a severe coughing fit. She scoops Rose into her arms, and rubs soothing circles on her back. "My daughter has asthma. That's why we're here," she tells the student.

Tricia jots a note in the patient's record and sees Rose has been admitted multiple times in the past for asthma. After flipping through these notes, Tricia sees that the mother has been counseled repeatedly about the need to stop smoking for the sake of Rose's health. Tricia goes to find her attending and presents Rose's case, highlighting signs of neglect. She then asks whether or not this would be grounds to notify child protective services.

Commentary
Neglect is failure to satisfy a child's basic needs, not only those for food, clothing, and shelter but also those for appropriate and timely medical care and shielding from exposure to family violence and substance abuse in the home, among other things. Implicit in these is the classification of lack of parental supervision or failure to protect a child from harm as neglect. In considering whether Rose's mother's behavior is neglectful, we must ask whether Rose's asthma exacerbations can be tied solely to the mother's smoking or whether other factors that could contribute to the problem, such as allergens or other environmental triggers, are present.

Neglect can be categorized as mild, moderate, or severe depending on the degree of harm (or risk of harm) to the child and the frequency and length of time of the neglectful behavior. The Children and Families Safe Act of 2003 defines child maltreatment as "any recent act or failure to act on the part of a parent or caregiver

which results in death, serious physical or emotional harm, sexual abuse or exploitation, or an act or failure to act which presents an imminent risk of serious harm" [1]. So we must consider: what is the effect of Rose's mother's smoking on her health, safety, and well-being?

Studies are now demonstrating that secondhand smoke (SHS) can exacerbate or cause children to develop asthma. In a metaregression review, Vork et al. demonstrated that the duration of secondhand smoke exposure can incite asthma. After adjusting for confounding factors they found a 33 percent higher incidence of asthma among those exposed to secondhand smoke [2]. In a recent large meta-analysis Burke et al. found that there may be a 28-70 percent increased risk of incidence of wheezing due to SHS [3]. This is also supported by findings that anti-SHS legislation has resulted in an overall decrease in asthma-related visits to local emergency rooms [4].

The US Department of Health and Human Services includes asthmatic children exposed to secondhand smoke as an example of exposure to hazard, which can be categorized as inadequate supervision and neglect [5]. This means HHS considers secondhand smoke to belong to the same category as poisons, loaded guns, unsanitary living conditions, and lack of vehicle safety restraints. It also means that parents' failure to follow a physician's instructions can be defined as medical neglect according to some state laws [6]. Family courts, too, have been receptive to information about SHS exposure, particularly when a child suffers from a chronic respiratory illness such as asthma [7]. In *Lizzio v. Lizzio* [8], the Supreme Court of New York reversed a custody decision and assigned physical custody to one parent because the other parent refused to provide a smoke-free environment for him. Ultimately, then, the scenario of Rose and her mother is a recognized example of neglect.

Interventions

So what should we do? First and foremost, we must remember that we are in a partnership with the families that we care for. When the care of a child is suboptimal, we must first look at ourselves to ensure that we have done our best to provide families with the tools they need to keep their children healthy. We must summon the optimist in ourselves and assume that the parents are doing what they feel is best for their children. If what they are doing does not appear to be adequate care, then perhaps we have not done our best to educate them or give them the tools to be successful.

Next we must do our part in a noncritical and helpful manner and record what we have done so that the caregivers who follow us have an accurate record of the situation.

In this case, the mother clearly does not believe there is a connection between her child's asthma and her smoking, a not-uncommon misperception. Fifty-eight percent of parents surveyed by Farber et al. who smoked and had asthmatic children reported

that tobacco smoke exposure had little or no negative effect on their child's asthma [9]. The medical student's review of Rose's record reveals that the mother has been told this before, but our duty is to be certain that she understands it. On the other hand, preaching at our patients and families is not always the most effective tactic. We must meet them where they are in terms of education level, with consideration of psychosocial factors and readiness to stop smoking.

Lack of resources or psychosocial burdens may contribute to this mother's behavior [10]. Suppose, for example, that she is a single mother who lives in an apartment complex that does not allow smoking in public spaces and has a high crime rate. She may have decided that smoking inside with the window open is safer for her and her child than taking the risk of going across the street from her apartment to smoke.

A second place we may have failed this mother is by not giving her feasible options. Smoking is an addiction and, if she is unable to quit, merely counseling her to do so is not an effective way to reduce Rose's secondhand smoke exposure. If a parent is not ready to quit, then other solutions should be offered. Hennessey et al. found that many families intend to ban smoking in their homes but encounter obstacles to doing so [11]. They concluded that it may be more effective to focus on considering alternative locations to smoke. Having the smoker take small steps—focusing on eliminating or reducing smoke exposure—could be more feasible and better received. For example, we may ask if it is possible for the mother to smoke outside. Other concrete practical instructions would include no smoking in the car, using a smoking jacket that is left outside, and washing hands after smoking.

It is also important to discern whether there are other neglectful actions—such as failure to fill the child's prescriptions regularly or missed medical appointments—that could be contributing to Rose's frequent exacerbations.

Once all this is done, if the child is still repeatedly harmed by the parent's behavior then we must involve others to ensure that the child is safe. Reporting to child welfare authorities is mandatory if the effects on the child are severe. The state child welfare agency is more likely to provide services if the harm to the child is severe or if there is a pattern of neglect; e.g., the mother is not keeping doctor's appointments or not filling the child's medications. If there is uncertainty, then we must consider whether it would be beneficial to report. Reporting may cause a family to feel accused, become uncomfortable disclosing pertinent information accurately in the future for fear of repercussions, or even sever the therapeutic relationship. The essential and difficult question that physicians must ultimately answer is whether exposure to secondhand smoke is more harmful to Rose than being removed from her home would be.

Conclusion

Overall, employing supportive measures that augment parents' natural tendency to protect their children may be the most effective approach to reducing secondhand smoke exposure in children. We must begin by providing parents with adequate,

timely, and easily understandable education. Next we need to give them palatable options for decreasing their children's smoke exposure. If we have helped the mother troubleshoot obstacles to reducing Rose's smoke exposure and the child continues to be harmed by SHS, then we are ethically and legally bound to report that Rose is being neglected.

On a larger scale we can protect children by advocating for policy change; for example, a ban on smoking in cars and homes. Smoking in a vehicle in the presence of children is already banned in numerous areas of the world, including Australia, the United Arab Emirates, South Africa, and 5 American states [12]. Physicians could, for example, advocate for smoke-free laws governing all indoor spaces where children may be exposed.

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THE CODE SAYS
The AMA *Code of Medical Ethics*' Opinions on Physicians' Participation in Clinical Research

Opinion 2.07 - Clinical Investigation
The following guidelines are intended to aid physicians in fulfilling their ethical responsibilities when they engage in the clinical investigation of new drugs and procedures.

(1) A physician may participate in clinical investigation only to the extent that those activities are a part of a systematic program competently designed, under accepted standards of scientific research, to produce data which are scientifically valid and significant.

(2) In conducting clinical investigation, the investigator should demonstrate the same concern and caution for the welfare, safety, and comfort of the person involved as is required of a physician who is furnishing medical care to a patient independent of any clinical investigation.

(3) Minors or mentally incompetent persons may be used as subjects in clinical investigation only if:

(a) The nature of the investigation is such that mentally competent adults would not be suitable subjects.

(b) Consent, in writing, is given by a legally authorized representative of the subject under circumstances in which informed and prudent adults would reasonably be expected to volunteer themselves or their children as subjects.

(4) In clinical investigation primarily for treatment:

(a) The physician must recognize that the patient-physician relationship exists and that professional judgment and skill must be exercised in the best interest of the patient.

(b) Voluntary written consent must be obtained from the patient, or from the patient's legally authorized representative if the patient lacks the capacity to consent, following: (i) disclosure that the physician intends to use an investigational drug or experimental procedure, (ii) a reasonable explanation of the nature of the drug or procedure to be used, risks to be expected, and possible therapeutic benefits, (iii) an offer to answer any inquiries concerning the drug or procedure, and (iv) a disclosure of alternative drugs or procedures that may be available. Physicians should be completely objective in discussing the details of the drug or procedure to be employed, the pain and discomfort that may be

anticipated, known risks and possible hazards, the quality of life to be expected, and particularly the alternatives. Especially, physicians should not use persuasion to obtain consent which otherwise might not be forthcoming, nor should expectations be encouraged beyond those which the circumstances reasonably and realistically justify.

(i) In exceptional circumstances, where the experimental treatment is the only potential treatment for the patient and full disclosure of information concerning the nature of the drug or experimental procedure or risks would pose such a serious psychological threat of detriment to the patient as to be medically contraindicated, such information may be withheld from the patient. In these circumstances, such information should be disclosed to a responsible relative or friend of the patient where possible. (ii) Ordinarily, consent should be in writing, except where the physician deems it necessary to rely upon consent in other than written form because of the physical or emotional state of the patient.

(5) In clinical investigation primarily for the accumulation of scientific knowledge: (a) Adequate safeguards must be provided for the welfare, safety, and comfort of the subject. It is fundamental social policy that the advancement of scientific knowledge must always be secondary to primary concern for the individual. (b) Consent, in writing, should be obtained from the subject, or from a legally authorized representative if the subject lacks the capacity to consent, following: (i) disclosure of the fact that an investigational drug or procedure is to be used, (ii) a reasonable explanation of the nature of the procedure to be used and risks to be expected, and (iii) an offer to answer any inquiries concerning the drug or procedure.

(6) No person may be used as a subject in clinical investigation against his or her will.

(7) The overuse of institutionalized persons in research is an unfair distribution of research risks. Participation is coercive and not voluntary if the participant is subjected to powerful incentives and persuasion.

(8) The ultimate responsibility for the ethical conduct of science resides within the institution (academic, industrial, public, or private) which conducts scientific research and with the individual scientist. Research institutions should assure that rigorous scientific standards are upheld by each of their faculty, staff, and students and should extend these standards to all reports, publications, and databases produced by the institution. All medical schools and biomedical research institutions should implement guidelines for a review process for dealing with allegations of fraud. These guidelines should ensure that (a) the process used to resolve allegations of fraud does not damage science, (b) all parties are treated fairly and justly with a sensitivity to reputations and vulnerabilities, (c) the highest degree of confidentiality is maintained, (d) the integrity of the process is maintained by an avoidance of real

or apparent conflicts of interest, (e) resolution of charges is expeditious, (f) accurate and detailed documentation is kept throughout the process, and (g) responsibilities to all involved individuals, the public, research sponsors, the scientific literature, and the scientific community is met after resolution of charges. Academic institutions must be capable of, and committed to, implementing effective procedures for examining allegations of scientific fraud. No system of external monitoring should replace the efforts of an institution to set its own standards which fulfill its responsibility for the proper conduct of science and the training of scientists.

(9) With the approval of the patient or the patient's lawful representative, physicians should cooperate with the press and media to ensure that medical news concerning the progress of clinical investigation or the patient's condition is available more promptly and more accurately than would be possible without their assistance. On the other hand, the Council does not approve of practices designed to create fanfare, sensationalism to attract media attention, and unwarranted expressions of optimism because of short-term progress, even though longer range prognosis is known from the beginning to be precarious. With the approval of the patient or the patient's family, the Council, however, encourages the objective disclosure to the press and media of pertinent information. If at all possible, the identity of the patient should remain confidential if the patient or the patient's family so desires. The situation should not be used for the commercial ends of participating physicians or the institutions involved.

Issued prior to April 1977; updated June 1994 and June 1998.

Opinion 8.0315 - Managing Conflicts of Interest in the Conduct of Clinical Trials

As the biotechnology and pharmaceutical industries continue to expand research activities and funding of clinical trials, and as increasing numbers of physicians both within and outside academic health centers become involved in partnerships with industry to perform these activities, greater safeguards against conflicts of interest are needed to ensure the integrity of the research and to protect the welfare of human subjects. Physicians should be mindful of the conflicting roles of investigator and clinician and of the financial conflicts of interest that arise from incentives to conduct trials and to recruit subjects. In particular, physicians involved in clinical research should heed the following guidelines:

(1) Physicians should agree to participate as investigators in clinical trials only when it relates to their scope of practice and area of medical expertise. They should have adequate training in the conduct of research and should participate only in protocols which they are satisfied are scientifically sound.

(2) Physicians should be familiar with the ethics of research and should agree to participate in trials only if they are satisfied that an Institutional Review Board has reviewed the protocol, that the research does not impose undue risks upon research subjects, and that the research conforms to government regulations.

(3) When a physician has treated or continues to treat a patient who is eligible to enroll as a subject in a clinical trial that the physician is conducting, the informed consent process must differentiate between the physician's roles as clinician and investigator. This is best achieved when someone other than the treating physician obtains the participant's informed consent to participate in the trial. This individual should be protected from the pressures of financial incentives, as described in the following section.

(4) Any financial compensation received from trial sponsors must be commensurate with the efforts of the physician performing the research. Financial compensation should be at fair market value and the rate of compensation per patient should not vary according to the volume of subjects enrolled by the physician, and should meet other existing legal requirements. Furthermore, according to Opinion 6.03, "Fee Splitting: Referral to Health Care Facilities," it is unethical for physicians to accept payment solely for referring patients to research studies.

(5) Physicians should ensure that protocols include provisions for the funding of subjects' medical care in the event of complications associated with the research. Also, a physician should not bill a third party payer when he or she has received funds from a sponsor to cover the additional expenses related to conducting the trial.

(6) The nature and source of funding and financial incentives offered to the investigators must be disclosed to a potential participant as part of the informed consent process. Disclosure to participants also should include information on uncertainties that may exist regarding funding of treatment for possible complications that may arise during the course of the trial. Physicians should ensure that such disclosure is included in any written informed consent.

(7) When entering into a contract to perform research, physicians should ensure themselves that the presentation or publication of results will not be unduly delayed or otherwise obstructed by the sponsoring company.

Issued June 2001 based on the report "Managing Conflicts of Interest in the Conduct of Clinical Trials," adopted December 2000.

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THE CODE SAYS
The AMA *Code of Medical Ethics*' Opinions on Physicians' Relationships with Drug Companies and Duty to Assist in Containing Drug Costs

Opinion 8.061 - Gifts to Physicians from Industry
Many gifts given to physicians by companies in the pharmaceutical, device, and medical equipment industries serve an important and socially beneficial function. For example, companies have long provided funds for educational seminars and conferences. However, there has been growing concern about certain gifts from industry to physicians. Some gifts that reflect customary practices of industry may not be consistent with the Principles of Medical Ethics. To avoid the acceptance of inappropriate gifts, physicians should observe the following guidelines:

(1) Any gifts accepted by physicians individually should primarily entail a benefit to patients and should not be of substantial value. Accordingly, textbooks, modest meals, and other gifts are appropriate if they serve a genuine educational function. Cash payments should not be accepted. The use of drug samples for personal or family use is permissible as long as these practices do not interfere with patient access to drug samples. It would not be acceptable for non-retired physicians to request free pharmaceuticals for personal use or use by family members.

(2) Individual gifts of minimal value are permissible as long as the gifts are related to the physician's work (e.g., pens and notepads).

(3) The Council on Ethical and Judicial Affairs defines a legitimate "conference" or "meeting" as any activity, held at an appropriate location, where (a) the gathering is primarily dedicated, in both time and effort, to promoting objective scientific and educational activities and discourse (one or more educational presentation(s) should be the highlight of the gathering), and (b) the main incentive for bringing attendees together is to further their knowledge on the topic(s) being presented. An appropriate disclosure of financial support or conflict of interest should be made.

(4) Subsidies to underwrite the costs of continuing medical education conferences or professional meetings can contribute to the improvement of patient care and therefore are permissible. Since the giving of a subsidy directly to a physician by a company's representative may create a relationship that could influence the use of the company's products, any subsidy should be accepted by the conference's sponsor who in turn can use the money to reduce the conference's registration fee. Payments to defray the costs of a conference should not be accepted directly from the company by the physicians attending the conference.

(5) Subsidies from industry should not be accepted directly or indirectly to pay for the costs of travel, lodging, or other personal expenses of physicians attending conferences or meetings, nor should subsidies be accepted to compensate for the physicians' time. Subsidies for hospitality should not be accepted outside of modest meals or social events held as a part of a conference or meeting. It is appropriate for faculty at conferences or meetings to accept reasonable honoraria and to accept reimbursement for reasonable travel, lodging, and meal expenses. It is also appropriate for consultants who provide genuine services to receive reasonable compensation and to accept reimbursement for reasonable travel, lodging, and meal expenses. Token consulting or advisory arrangements cannot be used to justify the compensation of physicians for their time or their travel, lodging, and other out-of-pocket expenses.

(6) Scholarship or other special funds to permit medical students, residents, and fellows to attend carefully selected educational conferences may be permissible as long as the selection of students, residents, or fellows who will receive the funds is made by the academic or training institution. Carefully selected educational conferences are generally defined as the major educational, scientific or policy-making meetings of national, regional, or specialty medical associations.

(7) No gifts should be accepted if there are strings attached. For example, physicians should not accept gifts given in relation to the physician's prescribing practices. In addition, when companies underwrite medical conferences or lectures other than their own, responsibility for and control over the selection of content, faculty, educational methods, and materials should belong to the organizers of the conferences or lectures.

Issued June 1992 based on the report "Gifts to Physicians from Industry," adopted December 1990; updated June 1996 and June 1998.

Opinion 8.135 - Cost Containment Involving Prescription Drugs in Health Care Plans

When health care plans, whether publicly or privately financed, establish drug formulary systems, physicians are obligated to advocate for formularies that meet the medical needs of their patients.

(1) Physicians should maintain awareness of plan decisions about drug selection by staying informed, where appropriate, about pharmacy and therapeutics (P&T) committee actions and by ongoing personal review of formulary composition. P&T committee members should include independent physician representatives. Mechanisms should be established for ongoing peer review of formulary policy. Physicians who perceive inappropriate influences on formulary development should notify the proper regulatory authorities.

(2) When scientifically based evidence is available, physicians are ethically required to advocate for changes to the formulary that would benefit the patient. Physicians

also should advocate for exceptions to the formulary on a case-by-case basis when justified by the health care needs of particular patients. Mechanisms to appeal formulary exclusions should be established. Other cost-containment mechanisms, including prescription caps and prior authorization, should not unduly burden physicians or patients in accessing optimal drug therapy. Quality improvement rather than cost containment should be the primary determinant for formulary exclusions. In order to be cost efficient, however, physicians should select the lowest cost medication of equal efficacy for their patients.

(3) Physicians should advocate that limits be placed on the extent to which health care plans use incentives or pressures to lower prescription drug costs. Financial incentives are permissible when they promote cost-effectiveness, not when they require withholding medically necessary care. Physicians should not be made to feel that they jeopardize their compensation or participation in a health care plan if they prescribe drugs that are necessary for their patients but that may also be costly. There should be limits on the magnitude of financial incentives, which should be calculated according to the practices of a sizeable group of physicians rather than on an individual basis, and incentives based on quality of care rather than cost of care should be used. Prescriptions should not be changed without the physician's knowledge and authorization. This affords the physician the opportunity to discuss the change with the patient.

(4) Physicians should encourage health care plans to develop mechanisms to educate and assist physicians in cost-effective prescribing practices, including the availability of clinical pharmacists. Such initiatives are preferable to financial incentives or pressures by health care plans or hospitals, which can be ethically problematic.

(5) Physicians should advocate that methods to limit prescription drug costs within health care plans in which they participate be disclosed to patients. In particular, they should encourage health care plans to inform patients upon enrollment concerning:

(a) the existence of formularies,
(b) provisions for cases in which the physician prescribes a drug that is not included in the formulary,
(c) incentives or other mechanisms used to encourage formulary compliance by physicians,
(d) relationships with pharmaceutical benefit management companies or pharmaceutical companies that could influence the composition of the formulary.

If physicians exhaust all avenues to secure a formulary exception for a significantly advantageous drug, they are still obligated to disclose the option of the more beneficial drug to the patient, so that the patient can consider whether to obtain the medication out-of-plan. Under circumstances in which the health care program will not subsidize the drug, physicians should help patients by identifying alternative forms of financial assistance, such as those available through pharmaceutical companies' assistance programs.

Issued June 1996 based on the report "Managed Care Cost Containment Involving Prescription Drugs," adopted June 1995; updated June 2002

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JOURNAL DISCUSSION
Legislating Abortion Care
Jody Steinauer, MD, MAS, and Carolyn Sufrin, MD, MA

One Hundred Professors of Obstetrics and Gynecology. A statement on abortion by 100 professors of obstetrics: 40 years later. *Am J Obstet Gynecol*. 2013;209(3):193-199.

Minkoff H, Ecker J. When legislators play doctor: the ethics of mandatory preabortion ultrasound examinations. *Obstet Gynecol*. 2012;120(3):647-649.

Abortion is one of the most common medical procedures in the United States, with 1.1 million performed in 2011 [1]. It is also an aspect of medicine that greatly interests the public and politicians: in 2011, 24 states passed 92 legislative restrictions on abortion [2]. No other medical practice has invited such broad and detailed regulation of the patient-clinician relationship. It is essential for trainees, who are learning how to cultivate relationships with patients, to recognize the ethical and patient care implications of such laws. Two recent editorials published in obstetrics and gynecology journals highlight the harmful effects of such legislation on the practice of ethical and evidence-based medicine [3, 4].

The authors of "A Statement on Abortion by 100 Professors of Obstetrics: 40 Years Later" [3] reflect on a statement published just before the *Roe v. Wade* decision. The original 1972 article, also signed by 100 professors, envisioned a future of legal abortion and defined the responsibilities of obstetrician-gynecologists in ensuring access to safe abortion for women. Their optimistic 1972 vision centered on the anticipated positive public health impact of safe abortion and their certainty that the previously common complications of unsafe abortion would disappear. They discussed a number of medical points such as the importance of hospitals' including abortions in the scope of caring for women and the need for physicians in training to be taught the skills of uterine evacuation. They envisioned that academic medical centers would be key in ensuring access to abortion services. The authors also discussed broader societal issues, such as their strong opinion that "abortion should be made equally available to the rich and the poor" [5].

The current 100 professors praise the predictions of the earlier authors and write with disappointment about the ways in which legislation has kept those predictions from being realized. For example, the Hyde Amendment, passed soon after the *Roe v. Wade* decision, prohibits federal financial support for abortion, and only 17 states use their own funds to pay for abortions [6]. This lack of funds makes abortion distinctly less accessible for poor women. The current 100 professors also note that

39 states now require parental involvement in a minor's decision to have an abortion, contradicting the original professors' hope that a pregnant teen would have the "freedom to determine the fate of her pregnancies" [7].

The current authors identify two types of legislative abortion restriction that directly and negatively impinge upon the patient-clinician relationship. The first relates to a clinician's ability to refuse to provide abortion care to patients on the basis of his or her beliefs. "Conscience clauses" supported by a number of federal and state laws protect clinicians from being forced to provide or being discriminated against for not providing abortion services [8]. While the original 100 professors recognized that some would be unwilling to provide abortion care, they expected that these doctors would refer their patients to others. However, as the current 100 professors note, current conscience clause legislation does not require the declining physician to refer patients.

In its practice bulletin "The Limits of Conscientious Refusal in Reproductive Medicine" [9], the American Congress of Obstetricians and Gynecologists states that professional ethics requires that health care delivery be respectful of patient autonomy and that it be timely, effective, evidence-based, and nondiscriminatory. It also states that physicians who cannot in good conscience provide a service must refer patients in a timely manner to another physician who can. Laws that protect conscientious refusal, however, do not uniformly stipulate referral. The interpretation that conscientious refusal need not include a referral is not limited to legislators. A study of 1,200 physicians in 2007 found that 29 percent believed that a physician is not ethically obligated to refer a patient for a desired, safe, legal procedure with which he or she disagrees [10]. Timely referral is especially important for abortion care, since delay in care is associated with an increase in morbidity [11]. Furthermore, the current 100 professors name five states that *prohibit* referral for abortion services by physicians who work in institutions that receive state funding. Such legal support for physician refusal to refer patients for abortion on conscience grounds obscures the fact that *providing* abortion is, for many, also a conscience and values-based decision [12].

The second category of abortion legislation that encroaches on the ethical dimensions of the patient-clinician relationship is regulation of the informed consent process. Learning the skill of providing unbiased, scientifically accurate information to guide patients as they make health care decisions is a critical part of medical trainees' professional development. The original 100 professors envisioned that women would be free to consent to abortion without impediment. However, 17 states now mandate that clinicians provide women seeking abortions with scripted counseling that includes false information on at least one of the following topics: a link between abortion and breast cancer, the ability of a fetus to feel pain, and long-term mental health consequences for women who have abortions [6]. These statements are not evidence-based and have been countered in the literature [13-15]. To require that clinicians give inaccurate information to patients is, to say the least, unethical.

The ethical violations of laws that interfere with informed consent are also addressed in a second editorial, "When Legislators Play Doctor: The Ethics of Mandatory Preabortion Ultrasound Examinations" [4]. Minkoff and Ecker review the recently proposed or enacted laws in North Carolina, Oklahoma, Louisiana, Texas, and Wisconsin that require women to view their fetuses on ultrasound before their abortions [2, 16]. The authors argue that this requirement violates the principle of respect for patient autonomy by introducing coercion into the informed consent process. Some may suggest that physicians routinely use ultrasound to date a pregnancy and that requiring it before an abortion is not an additional diagnostic procedure. But there are scenarios—for example when a patient has already had a dating ultrasound—in which a pre-abortion ultrasound is not necessary. Ultimately, Minkoff and Ecker argue that the decision to perform a diagnostic test before an abortion is the responsibility of the physicians and not the government, just as the decision to perform an angiogram before placing a cardiac stent is a clinical one, not something that should be codified in law.

Further, there is no medical reason to require that the patient look at the ultrasound results whether she wants to or not. It is not a necessary component of informed consent, as it does not familiarize the patient with the risks to herself, benefits, and alternatives of the procedure, and it does not affect her health. The authors offer the analogy that patients who choose to continue a pregnancy affected by fetal anomalies are not required to view a video depicting children with disabilities. Thus, Minkoff and Ecker argue, an ultrasound may be appropriate in the preabortion care of a particular patient, but the patient and doctor should decide "its timing, context, and the way in which it is used and viewed" [17]; this decision should not be scripted by law.

As Minkoff and Ecker acknowledge, the informed consent process is not a value-free exchange, but the physician's role is to assist patients in making choices congruent with their own—that is, the patient's own—values. Clinicians' values, the authors emphasize, should not enter into the conversation, nor should the values of lawmakers. We would add that in medical education it is critical to help trainees assess their own values so that they can more effectively guide patients through the informed consent process in a value-neutral or unbiased manner.

Legislative policies that require a physician to misrepresent the risks of abortion to patients, and to show the patient an ultrasound and those that allow physicians not to provide referral for abortion create a "conflict between the physician's obligation to the patient and to the law" [17]. Professionalism requires physicians to place the patient's welfare first, and "market forces, societal pressures, and administrative exigencies must not compromise this principle" [18]. Legislative micromanagement of the content of patient-clinician interactions in abortion care, which exists to no comparable degree anywhere else in medicine, violate medical ethics, which oblige physicians to be truthful and respectful of patients' right to self-determination.

It is crucial for medical students and residents to recognize the far-reaching implications of the political regulation of the practice of medicine through abortion legislation. Not only do these laws affect a woman's access to abortion, they also threaten the sanctity of the patient-clinician relationship, one that is ideally based on trust, truth, and adherence to ethical principles of respect for autonomy. These two editorials elucidate the ethical problems caused by legislative interference in this relationship.

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STATE OF THE ART AND SCIENCE

The Benefits of Online Health Communities

Lauren B. Solberg, JD, MTS

The number of users of online health communities such as PatientsLikeMe [1] and Inspire [2] is growing. PatientsLikeMe, for example, has approximately 220,000 registered users—about double the number of users it had in 2011 [3]. Although this is far below the numbers of more general social networking sites like Facebook (which has more than one billion registered users) [4], online health communities offer patients the opportunity to interact with others who have been diagnosed with a variety of diseases and conditions, track their health information on the site, and become involved in research. And, at least one online health community—PatientsLikeMe—includes a networking feature and a "real-time research" platform [5].

Some of the disparities in membership between sites like Facebook and online health communities can be explained by the amount of advertising that Facebook does, the media coverage that the company receives, and its general—rather than health care-specific—social networking purpose. In short, people have heard of Facebook, and they can use it to talk about more than just their health.

Benefits of Participation

The American public has realized that it can find an abundance of information online about health and health care. According to a 2013 Pew Research Center report, of the 85 percent of adults in the US who use the Internet, 72 percent (or about 61 percent of *all* US adults) reported using it to find information about their health, whether seeking a possible diagnosis for themselves or others, a recommendation for a clinician, or other information [6]. A 2011 Pew report found that of the 74 percent of adults who used the Internet, 80 percent (or about 59 percent of *all* US adults) looked for information on a specific disease or treatment [7].

Online health communities offer an abundance of information for patients and their caregivers, family members, and friends. More than half of PatientsLikeMe members said that the site was either moderately or very helpful for learning about their symptoms, more than half said it helped them manage symptoms and understand treatments, and almost half said that they connected with another member who helped them learn more about a medical treatment [8].

The opportunity to become a part of a support system is significant. Users of online health communities cited the emotional support received from other members, the accountability the sites provided them for reaching their health-related goals, the

motivation they got from other members, and the advice they received from other members as reasons for their membership in the community [9]. They pointed to advantages of online health communities over other social networking sites—such as Facebook—for achieving these goals because Facebook's purpose is "to communicate the impression of being interesting people who [are] in control, positive, and not struggling" [9].

In addition to offering information and support, online health communities can serve as the birthplace for beneficial social movements, such as "participant-led research," in which "participants are the leading force in the initiation or conduct of research projects" [10]. For example, as a group, Inspire members with spontaneous coronary artery disease (SCAD) convinced a researcher at the Mayo Clinic to initiate research that led to the creation of a SCAD registry [11], an important step in conducting more research on this rare disease. Without an online forum, these women might never have been able to connect with each other and galvanize support for such a project.

Drawbacks of Participation

Despite the benefits, there are drawbacks to online health communities that should be acknowledged. It can be difficult to control the quality of the information shared on these sites, causing concern about dissemination of inaccurate information. The FDA, for example, encourages people to carefully evaluate health information found online because of the possibility that it may not be accurate [12].

In the research context, concerns have been raised that clinical trial participants use online forums to try to figure out whether they are randomized to the placebo or study drug [13]. Site users have also encouraged prospective study participants to falsify information provided during screening to appear eligible to enroll or to withdraw from studies early [13]. Such influences could ultimately bias study results and compromise the progress of research.

Potentially inaccurate health information and biased study results, of course, exist outside the online world, but the widespread access to information that the Internet provides essentially guarantees that posted information will reach a large audience.

Despite these drawbacks, I believe that medicine and public health benefit when patients who are willing and able are encouraged to share their health information online. Patients' ability to receive emotional support is good for their health [14], active and informed patients may have better outcomes [15], and new research results may translate into practice (though that is often easier said than done) [16]. Unfortunately, the US does not yet have a perfect mechanism for reducing or eliminating the risk of sharing such information online.

Potential Privacy Risks

People who only search for health information online face fewer risks than those who provide information about themselves to other Internet users, but many benefits

of online health community membership stem only from fully engaging in the site, which involves sharing information. Out of almost 1,800 people surveyed recently, 30-40 percent said they had used social networking sites to consume health-related information, but less than 15 percent reported posting information online [17]. Admittedly, more research is needed to attempt to explain this discrepancy, but privacy concerns could contribute to it.

Privacy concerns associated with sharing health information online include possible discrimination by the employers, insurance companies, friends, or family of those who post [8]. There are also concerns about "potential 'data intruders'…with motivations ranging from personal research, genealogy, ancestry, forensic purposes or use in marketing, insurance, or employment decisions" [8]. In the research context, institutional review boards (IRBs) may be concerned about how information from online health communities is being collected and used as they strive to protect research participants from invasion of privacy [18].

Although the Genetic Information Nondiscrimination Act of 2008 (GINA) prohibits employers and health insurance companies from discriminating on the basis of genetic information [19], the act's scope is limited. People are not protected under federal law from possible discrimination when applying for life, long-term care, or disability insurance, and GINA's employer and health insurance protections cover genetic test results and family medical history but not the patient's own medical history. The Affordable Care Act (ACA) now, in most cases, protects against higher health insurance premiums for people with preexisting conditions, but some grandfathered plans will not offer this protection [20]. Neither GINA nor the ACA addresses the problem of social stigma against people with certain diseases or conditions.

Online health communities take measures to protect the privacy and security of the information shared by their members, such as using "commercially reasonable" methods to protect the security of information that users provide and supplying details in their privacy policies about how the information users share with the site may be disclosed to and used by third parties, including pharmaceutical companies [21, 22]. Privacy is never guaranteed, however; any information posted could be redisclosed either within or outside the site, and these sites are careful to remind their users about this possibility [21, 22]. Furthermore, an important purpose of social networking sites is to share information, and online health communities are no exception. Indeed PatientsLikeMe has—in addition to a privacy policy—an openness philosophy that says the company encourages the sharing of information [23].

Conclusions

I offer the following suggestions for encouraging patient use of online health communities. First, physicians should educate themselves about the different purposes for which their patients use—or could use—social networking sites and online health communities in particular. They should pass this information on to their patients to facilitate shared decision making. Second, IRBs should become

comfortable with their researchers using online health communities to recruit participants and collect data, and they should ensure that they have the appropriate expertise on their committees to be able to conduct thoughtful, thorough reviews of studies that use such methods. Third, we should consider enacting new legislation that will provide additional protections beyond what GINA and the ACA currently offer, so that patients and their friends and families can share their information with others and get the support they seek without fear of repercussions. Social stigma surrounding illness is likely to be reduced when information is shared openly and we become more educated about these issues.

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HEALTH LAW

Professional Self-Regulation in Medicine

William D. White, PhD

Any time a physician sees a patient or provides a treatment, he or she enters into a complex web of interlocking systems of public and private professional regulation. These systems delineate scope of work and restrict who can do what tasks, regulate conduct, and set entry qualifications and ongoing educational standards for physicians. Because of the ubiquitous nature of systems of professional regulation and their role in defining and enforcing standards of professional conduct, it is important for young medical professionals to understand how they work and the challenges they pose. Moreover, self-regulation is a key component in medicine, and during their careers many physicians may be involved in setting, implementing, and possibly enforcing professional standards.

Rationale for Professional Regulation

From a public policy perspective, the rationale for professional regulation of medicine is patient protection [1]. Patients generally lack the knowledge, skills, or judgment to diagnose or treat disease and, thus, have strong incentives to rely on caregivers with specialized expertise, such as physicians, to assist them. Entrusting their care to physicians can yield large benefits, but, if it is difficult to evaluate physicians' qualifications or performance, patients may be hesitant to place trust in them. As a consequence, regulating their behavior and preventing physicians from, for instance, misrepresenting their qualifications, making unfounded claims for cures, failing to exercise due diligence in providing care, or engaging in other forms of malfeasance, may yield large benefits. A key question, however, is how to regulate physician behavior and at what cost?

Eliot Friedson describes the role of professions in society as a "third logic"; they serve as an alternative to individualistic competitive markets and bureaucratic administrative systems [2]. Based on their expertise and willingness to accept professional values, physicians are charged with overseeing the profession collectively while retaining monopoly power over their area of work, an arrangement that can be viewed as a compact between medicine and society. Professionalism in medicine involves much more than simply formal regulatory oversight. Important dimensions include the creation of institutions for professional education, the exchange of knowledge, and the promotion of social norms supporting autonomous, knowledge-based decision making and professional behavior [3]. However, the focus here will be on formal systems of regulation.

Overview of Systems of Professional Regulation in Medicine

Underpinning systems of professional self-regulation in medicine in the US are occupational licensure laws, which grant medicine a monopoly over the practice of medicine. Historically, physicians were subject to guild-style regulations, but these were largely swept away in the Jacksonian era [4]. Modern occupational licensure laws were introduce in the late nineteenth century and are the foundation for increasingly complex interlocking systems of voluntary certification.

In order to practice medicine in a state, a physician must be licensed in that state. State practice laws set standards for entry and regulate conduct. The primary mechanisms for assuring the competence of those who enter the profession are testing and requirements for minimum levels of education and training. While periodic reregistration is required, recertification requirements are usually limited to participation in continuing education. Regulation of conduct has focused on ethical issues (e.g., unprofessional or criminal behavior), but there has been a longstanding reluctance to try to evaluate clinical performance.

Although state licensure boards are public rather than professional bodies, their membership comprises predominantly physicians. Licensure standards routinely incorporate standards set by professional bodies within medicine for accrediting medical schools and approving postgraduate programs, and rules on conduct typically draw on professional codes of ethics [5].

Specialty Board Regulation

Overlying licensure laws are systems of private certification directly governed by medical specialty boards. These systems began to emerge in the early twentieth century and have proliferated rapidly. There are now more than 150 recognized specialties and subspecialties, and it is not uncommon for physicians to have multiple certifications.

Legally, board certification restricts the use of occupational titles. Like licensure boards, certification boards set standards for entry, recredentialing, and conduct, and they may also regulate the scope of medical practice [6]. At least nominally, however, certification is voluntary; legally, any physician can provide any specialty service as long as he or she does not claim to be board certified. In practice, hospitals and public and private payers regularly use board certification as a criterion for determining who can have privileges and be paid for services. Reflecting the importance of private certification, more than 800,000 physicians are board certified as specialists and subspecialists by 24 specialty boards associated with the American Board of Medical Specialties (ABMS), [7] and, in a 2008 national survey [8], 90 percent of US physicians reported some form of board certification [9].

Professional Regulation and Public Policy

Professional regulation in medicine intersects with public policy at a number of levels. Continued reliance on existing state licensure laws creates barriers to geographic mobility in an era when physicians are moving more frequently and

health systems may span multiple states, and the growing use of the Internet and telemedicine compounds these problems [10]. Specialty boards have moved more rapidly than licensure boards towards rigorous standards for recredentialing, and ABMS maintenance of certification (MOC) programs seek to encourage continuous professional development [11], but arguably standards still focus on assessing qualifications, not clinical performance.

More generally, it is unclear whether current systems of governance best serve the public interest in several respects. While less pronounced than in the past, one longstanding concern is that medicine may abuse self-regulation at the expense of patients and payers [12]. Critics argue, for example, that entry to the profession may be constrained to drive up physician incomes [2]. Likewise, as we know from experience, efforts to constrain market-oriented behavior on the grounds that it undermines professionalism may also constrain competition in ways that benefit the profession. In this context, as Friedson notes [13], there may be inherent tensions between professionalism and reliance on markets to promote efficiency [14].

A more immediate concern is that systems of professional regulation are not keeping pace with recent industry trends and public need and are creating barriers to innovation. For example, licensure laws may hinder the use of nurse practitioners, physician assistants, and multidisciplinary teams, when maldistribution of the physician workforce demands innovative uses of these professionals and teams, and at least one proposal has been made to consider licensing teams rather than individuals [15]. More broadly, given that the primary rationale for licensure and board certification is quality assurance, how will improvements in the ability to assess quality through process and outcome affect the future of credentialing systems?

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POLICY FORUM
OxyContin, the FDA, and Drug Control
Gary M. Reisfield, MD

"One percent of people will always be honest and never steal," the locksmith said. "Another one percent will always be dishonest and always try to pick your lock and steal your television. And the rest will be honest as long as the conditions are right—but if they are tempted enough, they'll be dishonest too. Locks won't protect you from the thieves, who can get in your house if they really want to. They will only protect you from the mostly honest people who might be tempted to try your door if it had no lock."
—*Dan Ariely*, The Honest Truth About Dishonesty: How We Lie to Everyone—Especially Ourselves

In 2010, 16,651 Americans died from prescription opioid overdoses [1]. For each death there were 15 drug-treatment center admissions, 26 prescription opioid-related emergency room visits, 115 people who met criteria for prescription opioid abuse or addiction, and 733 people who used these medications nonmedically (that is, for the feeling that the drug provided) [2].

Access to prescription opioids—and the morbidity and mortality associated with their abuse—are not limited to the patients for whom they are prescribed. Indeed, according to the National Survey on Drug Use and Health, of the more than 12 million Americans who used prescription opioids nonmedically in 2010, 54 percent of respondents had most recently obtained their opioids from a friend or relative for free, and 17 percent had bought or stolen them from a friend or relative. Of note, 85 percent of respondents who obtained their opioids from a friend or relative for free indicated that the opioid originated from one or more physicians' prescriptions [3].

Normally, the FDA grants brand-name drugs five years of market exclusivity before allowing generic versions to be sold. The United States Food and Drug Administration (FDA) made the unusual decision to withdraw its approval for generic versions of OxyContin after a new, abuse-resistant formulation, OxyContin OP, was patented and approved. Critics have argued that efforts to create abuse-resistant opioids and restrict access to easily abused formulations place the interests of public health or law enforcement over the financial or clinical interests of patients with chronic pain (for whom the cost of a branded abuse-resistant formulation may be a barrier to appropriate opioid therapy) [4]. From a clinical perspective, the border between patients' interests and public health is an invisible one. The FDA's decision

is a reasonable, incremental step toward making long-term opioid therapy safer for everyone.

The Role of Tamper-Resistant and Abuse-Deterrent Opioids

The epigraph to this article is an apt metaphor for why "locks," that is, abuse-deterrent features on potent, controlled-release opioids, have a potentially important role in mitigating the harms associated with this indispensible class of analgesics. Some of our patients who are prescribed opioids always use their medications as prescribed, always keep them stored in a safe place, and never give away, trade, or sell them. For these patients, locks on opioids are unnecessary. Some of our patients are addicted to opioids and will do whatever is necessary to get them. For these patients, locks on opioids will not deter them: they will attempt to subvert ("pick the lock" on) the abuse-deterrent features of the opioid; they will insist on receiving "unlocked" (non-abuse-deterrent) opioids; or they will seek out other sources of opioids that can be smoked, snorted, or injected.

The remainder of our patients comprise a vast and heterogeneous middle ground. Some abuse prescription opioids by a variety of means and out of a variety of motivations, including boredom, curiosity, impulsivity, or the desire to get high. Some well-intentioned patients give opioids to friends or family members. Many, because of unsafe households or neighborhoods, are at risk of having their medications stolen. A small percentage criminally diverts some or all of their opioids—for cash, sex, or other drugs. It is for all of these patients—and for their families and friends and others who gain access to their medications—that abuse-deterrent opioids can play a role in mitigating the harms associated with these drugs.

Physicians would like to believe that every patient for whom they prescribe opioids is a patient who has a medical need for opioid pain relief. But things are not nearly so simple. There are no laboratory tests or imaging studies that prove the presence of pain. Nor are there such tests or studies to diagnose abuse or addiction. It is nearly impossible to detect the 84-year-old patient who sells part of his opioid prescription to a neighborhood drug dealer in order to pay his utility bill, or the 78-year-old patient whose grandson makes an interesting find in her medicine cabinet. Complicating the picture further, chronic pain, substance use disorders, and diversion can, and often do, coexist in the same patient.

Knowledgeable and conscientious physicians screen for substance use disorders and assess for risk factors associated with the future development of opioid-related problems. They tailor their pain treatments to the risk posed by each patient. If they prescribe opioid therapy, they monitor for problems by speaking with their patients about the effects of these medications on their pain and on their lives, by querying state prescription drug monitoring databases for evidence of "doctor shopping," and by performing random drug testing.

Yet, each of these measures is imperfect. Every patient poses some finite degree of opioid-related risk. And every physician who prescribes opioid analgesics, no matter

how experienced, sometimes gets fooled. At the end of each office visit, the physician sends her patient out into the world with an opioid prescription and little knowledge of what will become of it. Thus, from a clinical perspective, the division between the welfare of the patient and the welfare of the public is nebulous.

OxyContin and the Role of the FDA in Mitigating the Abuse of Controlled-Release Opioids

Oxycodone—particularly in the original controlled-release formulation OxyContin—holds a place of ignominy in the current prescription opioid epidemic. First marketed in the US in 1996, it was the most abused prescription opioid in the country within a decade [5]. In Florida—the epicenter of the problem—prescription drug overdoses increased by 84 percent from 2003 to 2009. During this period, the greatest increase in death rate was observed for oxycodone (265 percent), followed distantly by methadone (79 percent), hydrocodone (35 percent), and morphine (26 percent) [6].

The original OxyContin was reformulated with abuse-deterrent properties in 2010 [7], and there is evidence that it has reduced the abuse of the drug. For example, according to the National Poison Data System, in the two years following its reformulation, poison center reports for OxyContin-related intentional events (i.e., abuse, suspected suicide, and misuse) and unintentional events (i.e. misuse, general, and therapeutic errors) each declined by 25 percent. In contrast, reports for each of these events increased for other single-entity oxycodone products [8]. On the basis of data such as this, the FDA approved abuse-deterrent labeling for the reformulated OxyContin—the only C-II opioid ever to receive such approval. The agency also determined that the risk-benefit ratio of the original OxyContin tilted in favor of risk, and announced that it would not accept applications for generic versions of the original OxyContin [7]. Thus, generic competitors to OxyContin are likely years away [9].

The suggestion that the FDA's decision, which is likely to keep the costs of controlled-release oxycodone high, will limit access to opioids for some patients who do not abuse the drug may be legitimate, but it is not compelling. We are awash in prescription opioids. Comprising less than 5 percent of the world's population, the US now consumes more than 99 percent of the world's hydrocodone, 82 percent of its oxycodone, 59 percent of its morphine, 53 percent of its methadone, 52 percent of its hydromorphone, and 48 percent of its fentanyl [10].

Moreover, OxyContin is only one of several controlled-release or long-acting opioids available on the US market. The group comprises buprenorphine (Butrans), fentanyl (Duragesic and generic), hydromorphone (Exalgo), morphine (Avinza, Kadian, MSContin, and generic), oxymorphone (Opana ER), and methadone (Dolophine and generic). The FDA has approved an eighth controlled-release opioid, hydrocodone (Zohydro ER), which will probably reach the market in the first half of 2014. Moreover, immediate-release oxycodone is available in combination with acetaminophen (e.g., Percocet, Tylox, and generic), aspirin (Percodan and generic),

and ibuprofen (Combunox and generic), and as a single entity (Roxicodone and generic).

The FDA has taken other steps to mitigate the harms associated with controlled-release opioids. First, they recently adopted the Risk Evaluation and Mitigation Strategy (REMS) for these medications [11], which requires drug companies to provide physicians with educational materials on the safe prescribing of these drugs. Second, they have mandated labeling changes to these opioids that address correct prescribing, risks, and alternatives [12]. Third, they now require drug companies to conduct longer-term and more comprehensive post-marketing studies to assess the long-term risks associated with the use of this class of medications [12].

Conclusions

The US is at once in the midst of a prescription opioid epidemic [13] and a chronic pain crisis [14]. The FDA plays a vital role in ensuring appropriate access to the most powerful analgesics while helping to mitigate the harms associated with their abuse.

The development of abuse-deterrent formulations of controlled-release opioids has been described by the FDA as an agency priority [7]. For pharmaceutical manufacturers, the process of designing and producing these opioid formulations can take years and involves enormous expense, all without any guarantee of success. Purdue Pharma, the manufacturer of OxyContin, seems to have produced a success, and the FDA's decision to not accept abbreviated new drug applications for generics based on the original OxyContin formula appears to have rewarded Purdue's effort. Perhaps the OxyContin decision will serve as an incentive for other opioid manufacturers to pursue abuse-deterrent features for their most powerful opioids.

Ideally, all controlled-release opioids would have abuse-deterrent features. It would not solve the problem of prescription opioid abuse, but it would be an incremental step toward the goal of providing safer long-term opioid therapy in an unsafe world.

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POLICY FORUM
Physician "Gag Laws" and Gun Safety
Mobeen H. Rathore, MD, CPE

Gun violence has become an epidemic in the United States. While mass shootings such as those in Newtown and Columbine receive most of the attention, firearm-related deaths in the home are a far more common event in the United States. Often the victims of these shootings are "innocent bystanders," especially children. Physicians can and should play an important role in efforts to stem this epidemic—by advising their patients about the dangers posed by firearms in the home and counseling them about best safety practices.

Unfortunately, in recent years many states have attempted to regulate such physician-patient conversations between physicians and their patients. These attempts by the states to curtail physicians' ability to ask their patients about firearms in the home infringe a basic constitutional right to free speech protected by the First Amendment. Moreover, these state efforts are fraught with danger, not only because they place patients and their families at risk of serious injury or death, but also because they would set a precedent that could lead to restrictions on other essential conversations physicians must have with their patients about sensitive topics. It is a dangerous precedent if politicians and policymakers are able to outlaw lines of questioning that do not meet their own ideological standards.

Since Florida passed the "physician gag law" in 2011, twelve other states have introduced similar legislation. Bills limiting physicians' free speech right to communicate with their patients were introduced but defeated in Virginia and West Virginia [1]. Similar gag law bills died in the legislatures of Alabama, Missouri, North Carolina, South Carolina, and Tennessee [2, 3], but they remain pending in Oklahoma, Wisconsin, and Ohio [3, 4]. A speech-restricting bill was enacted in Minnesota [2, 5].

The Florida Chapter of the American Academy of Pediatrics, other professional associations, and several individual Florida physicians sued the state in federal court to stop enforcement of the physician gag law, and Judge Marcia Cooke issued an injunction barring its enforcement [6]. Florida has appealed the ruling, and in July 2013 arguments were heard by the US Court of Appeals for the 11th Circuit [7]. The results of the appeal are pending at the time of this article's publication.

From the onset the gun lobby has pushed for physician gag laws in the belief that the physicians gather information about gun safety in the home to dissuade their patients from or attempt to interfere with gun ownership. The state of Florida has suggested

that physicians will communicate gun ownership information to the federal government to create databases, even though federal law strongly protects the privacy of patient medical records and specifically prohibits the creation of such a database of gun owners [8].

The American Medical Association is on record opposing physician gag laws [9]. Other professional organizations including the American Academy of Family Physicians [10], the American College of Physicians [11], the American College of Emergency Physicians [12] and the American Academy of Pediatrics [13] support physicians' ability to counsel their patients and families about firearm safety in an effort to make firearm ownership safer.

While the politicians and lobbyists for each side continue to debate the constitutional dimensions of these laws, preventable firearm-related deaths continue to occur and continue to increase at alarming rates [14, 15]. Although physicians subscribe to varying viewpoints and political and social value systems, we stand firmly on the side of the patient on every issue.

Any time a physician's ability to practice the best possible medicine is challenged, the medical profession should join together to thwart the attacks. Physicians value their relationships with their patients and their patients' families. They provide patients with a secure and safe place during their interaction in order to obtain accurate information, make the correct diagnosis, and provide invaluable preventive and anticipatory counseling. This dialogue between the patient and physician is sacred, confidential, and protected by law. Patient confidentiality is a hallmark of the practice of medicine and breaches of such confidentiality are not only unethical but have severe repercussions under current federal law.

First Amendment Rights

The First Amendment right to free speech is cherished in the United States. Clearly free speech has some limits, but the right is undeniable. A legislated restriction on a physician's right to free speech by legislation that should be a cause for concern to all Americans. It is a physician's professional duty to ask questions even if the patient may find them uncomfortable. The patient's interest in privacy is adequately protected by his or her right not to answer the question. Indeed, the Florida physician groups did not challenge the law's provision that protects a patient's right to decline to answer questions about gun ownership [16].

In the unique patient-physician relationship, physicians are able to ask patients about sensitive and private information, and the patients can answer with complete confidence that the answers will be kept confidential. In fact, HIPAA laws should provide additional confidence that the age-old confidentiality of the patient-physician relationship is enshrined in law, with stiff civil and in some cases criminal penalties. Even a broad interpretation of the right to own firearms would not in any way limit the First Amendment rights of physicians and their patients to ask and answer

questions and engage in follow-up counseling about the dangers that firearms in the home pose to children or the critical need for safe storage practices.

The Patient-Physician Relationship

A visit to the physician's office is an important time for the patient. Patients visit their physicians for treatment of their ailments, but also to keep healthy and out of harm's way. Preventive medicine and health education are key to a healthy American population. As a matter of routine, physicians bring up subjects critical to health, illness prevention, and safety [17]. The information obtained by the physician during history taking forms the basis for management of problems the patient is facing and an opportunity for the physician to provide anticipatory guidance to the patient for things that are potentially harmful to health. Firearms at home is one such topic. Patients may not be aware that the presence of firearms in a home can have dangerous and unintended consequences, especially if there are children in the house. The risk of accidental and unintentional firearm-related injury and death are real but preventable. Physicians can provide preventive guidance about the importance of using trigger and gun case locks, keeping firearms unloaded, and storing ammunition and firearms in separate places. These simple and proven tips do not guarantee safety, but they can decrease firearm-related morbidity and mortality and make the home safer. And, if the patient does not welcome this advice, he or she has the right to stop seeking care form that physician for any reason or no reason at all.

Protecting Children

Since children are often not decision makers and are particularly vulnerable, civilized societies have laid out special principles for their protection. Parents are not allowed to abuse their children; in fact, no one is. We all want children to live in a safe environment, minors are required to go to school, and under certain circumstances children can be provided lifesaving treatments without their parents' consent.

Children are at particular risk for firearm-related injuries and often die from injuries inflicted by firearms in the house. If we take steps to protect children from living in homes with lead-based paint or abusive parents, why would we not take steps to inform parents about the risks of having firearms in the house and give information about how to make it safer for children.

According to the Centers for Disease Control and Prevention data from 2007, 25 percent of deaths among children 15 to 19 years of age were firearm-related, and firearms accounted for 17 percent of all injury-related deaths in children. American children between the ages of 5 and 14 years are 10 times more likely to die from unintentional firearm-related injuries than children of similar ages in other developed countries [18]. To protect children, physicians must be able to educate gun-owning parents and guardians about safe gun storage.

Conclusion

While the horrible tragedies of mass gun-related murders such as Sandy Hook,

Aurora, Virginia Tech, and Columbine get most of the media attention and rightly the outrage of the nation, many people, especially children, die of senseless accidental shootings every day [19]. It is simply unacceptable for those caring for children not to know that if they have firearms in their homes there are simple steps that can make their homes safer. When more Americans die from firearm injuries than terrorist attacks, we have a lot to answer for to our fellow Americans. Therefore, it is of paramount importance that determination of the content of patient-physician conversations remains outside the halls of politics and legislatures and in physicians' offices. Optimal health care can only be delivered when physicians and patients feel free to discuss relevant issues openly.

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MEDICINE AND SOCIETY

Consent and Rights in Comparative Effectiveness Trials

Collin O'Neil, PhD

Since the FDA usually requires only that a new treatment be proven superior to placebo for approval, physicians must often choose between two or more approved therapies for a given condition without good evidence to guide them. Comparative effectiveness research on existing treatments has the potential to rectify this situation, and randomized controlled trials are often the most reliable method of determining the relative merits of different treatments. Although nothing experimental is administered to the patients in a randomized controlled trial comparing approved therapies, such a trial still counts as human subjects research and is covered by the federal regulations governing such research. These regulations, known as the "Common Rule," require that institutional review boards (IRBs) review these trials to ensure that the rights and interests of the subjects are adequately protected. In particular, IRBs are charged with ensuring that the researchers obtain consent to participation in research from the subjects [1].

Some commentators have identified these trials as an area of low-risk research that is overburdened by the current regulations. The most provocative recommendation they have made is that, in at least the most innocuous of these trials, the regulations should no longer require researchers to obtain explicit consent for research from the patients [2-5]. Underlying this recommendation is a moral claim, namely, that even though the subjects are involved in research, the consent obtained in ordinary clinical practice suffices for respecting the rights of the subjects against the interventions in these trials. On one interpretation these commentators are merely claiming that, so long as the health care system adequately publicizes the fact that treatment within the system will be offered in the context of randomized controlled trials, the physicians themselves need not disclose to patients that they are involved in research. My criticism will be directed against the more radical interpretation of the recommendation, namely, that in at least some of these trials the research purpose need not be disclosed to the patients at all [6-8].

I will begin by examining two rights-based reasons for disclosing the research purpose in these trials. The first is that, unless the patients are made aware of the research purpose, they are liable to be mistaken about the risks and benefits of the interventions because they differ from what one would expect to receive in clinical care. The second, more broadly applicable reason is that, even when there is no difference between the risks and benefits of the trial interventions and those of clinical care, unless the research purpose is disclosed, the trial may enroll some patients who have objections to serving particular research purposes or to

participating in research altogether. Both rationales for disclosing the research purpose are concerned with avoiding the same danger, namely, that patients may be accepting interventions they would not have accepted had they been more fully informed and that, consequently, their rights are infringed despite their consent. But there may be RCTs that avoid this danger without disclosing the research purpose, and neither of these two rationales would apply in such cases. I will sketch a new rights-based argument that requires disclosing the research purpose in all RCTs, even when there is no danger that the patients would not have accepted the interventions had they been informed of the research purpose [9].

Consent Based on Ignorance or Mistake about the Risks and Benefits

The kind of trial at issue is a randomized controlled trial (RCT) designed to evaluate the relative merits of two FDA-approved treatments, X and Y. In such a trial the physician recommends X to the patient, not because he or she believes it is better than Y for the patient, but because this is what the randomizing device instructs. The physician follows this instruction for the purpose of generating information of benefit to future patients.

Treatment X is an intervention, and it is widely acknowledged that people have a moral right against being intervened upon, a right against physical interference. This does not mean of course that physicians may never administer interventions. The patient may waive his or her right against being intervened upon by giving consent: the function of consent is to waive rights. But it is a familiar point that consent is not always successful in waiving whatever right needs to be waived—i.e., that consent is not always "valid." One reason consent may be invalid is that it is *based* on ignorance or mistake about the intervention; if the patient had been better informed, he or she would not have consented to it. One argument for disclosing the research purpose in at least certain RCTs is that, unless it is disclosed, there is a danger that the patients' consent to the interventions will be based on a mistaken assessment of the relevant risks and benefits.

Patients have different expectations of clinical care than of research participation. Among other things, a patient expects of clinical care that (a) any interventions the physician proposes will be necessary for her care, and (b) if there is more than one proven treatment for her condition and the physician believes one would be better for her than the other, the physician will recommend the treatment she believes to be superior. Clinical trials sometimes disappoint these expectations. They may, unlike standard clinical care, include nontherapeutic interventions, such as blood draws conducted for purely research purposes, disappointing (a). And a trial may assign a patient a treatment at random even when the physician believes one treatment would be better for the patient, disappointing (b). Although, in the kind of trial under consideration, X and Y are both approved treatments and neither has been proven superior to the other, a physician might still have reason to believe that one would be more effective for a patient or that a patient might find the side-effect profile of one more acceptable. If the patient is to contribute meaningful data to the study,

however, the treatment cannot be assigned on the basis of what the physician or the patient might prefer, but must be assigned randomly [10].

If a patient consents to a nontherapeutic blood draw under the false impression that it is necessary for her care, she is significantly mistaken about its risks and benefits and, insofar as her consent is based on this mistake, her consent is invalid. Since X is, unlike the blood draw, a proven treatment, she may not be mistaken about its risks and benefits. But her consent to X may be based on the mistaken belief that, since the physician only recommended X, there must not be any alternative treatment available that in the physician's judgment would be better for her or might be more acceptable to her. In theory, a patient could understand how these clinical care expectations are disappointed without knowing why. But it would be far easier for her to comprehend these deviations if the research purpose underlying them were disclosed.

Consent Based on Ignorance or Mistake about the Purpose Underlying the Intervention

The reason just given for disclosing the research purpose applies only when the trial violates the clinical care expectations mentioned above. But some RCTs will not violate those expectations. Consider a trial that involves no nontherapeutic interventions and that enrolls patients only with the physician's assent, so that patients are randomized only when the physician is truly indifferent between X and Y. Assume as well that X and Y do not differ along any dimensions, such as side-effect profiles, that might give a patient reason to prefer one or the other. In this case, ignorance of the underlying research purpose would not lead to mistakes about the risks and benefits of the interventions relative to clinical care. Is there still a danger of invalid consent if the research purpose is not disclosed?

The fact that in accepting the treatment the patient would thereby be contributing to a research goal is in itself a departure from clinical care. The research purpose may not cause the risks and benefits to differ from those of clinical care, but some patients might have conscientious objections to playing a role in promoting particular types of research goals. Other patients might be inclined to refuse to consent to the treatment if they knew there was a research purpose underlying the assignment just because they are suspicious of research and fear that their interests will be compromised. Even if these fears are unwarranted and they would in no respect be better off receiving standard clinical care, it would still be true of these patients that, had they been informed of the research purpose, they would not have consented.

Certainly the most reliable way to ensure that no patients who would refuse to participate if they were informed that it was research are enrolled in the trial is to disclose the research purpose to everyone. But when the goal of the research is uncontroversial, as it is in these RCTs comparing two FDA-approved drugs, conscientious objections would be unlikely. Mistrust of research may be more common, but there might, at least in principle, be other means adequate to ensure that patients who mistrust research are not enrolled in the trial, e.g., careful subject

selection. Let's suppose, for the sake of argument, that the researchers can somehow be sure that none of the patients enrolled in the trial would have refused the interventions had they been made aware of the research purpose. Although such patients are ignorant of the research purpose, their consent to the interventions is not *due* to this ignorance. In such an idealized situation, would there still be any rights-based reason to disclose the research purpose to the patients?

Consent In Ignorance of the Right that Needs to be Waived

To successfully waive a right against an intervention, the consent to the intervention must not be based on ignorance or mistake. But more is required. To waive a particular right via consent, it must be waived intentionally. This means that one must know which right or rights one needs to waive. Even if one would have attempted to waive a certain right had one known it was the right one needed to waive, so that one's consent is not *based* on ignorance of which right one needs to waive, that right is not waived unless one actually attempts to waive it and not some other right.

So it is important to ask: which right or rights does a participant in an RCT need to waive? The patient knows that X is a bodily intervention, and so knows that the right against physical interference is the general kind of right she needs to waive. But we possess a variety of distinct rights against bodily interventions, such as a right against unintended interventions and (much stronger) rights against intended interventions. Within the class of rights against intended interventions, there is another significant division. We have rights against interventions that are intended for our own benefit and rights against interventions intended for the benefit of others. These are not merely different specifications of one general right against physical interference. These are distinct rights, with distinct (though partly overlapping) rationales. We mark the infringement of the distinct right against interventions intended for the benefit of others by saying that the person subject to the intervention was "used" or "exploited," not merely that they were interfered with.

When a physician proposes to administer a blood draw for purely research purposes to a patient, this is an especially clear case in which the right against interventions intended for the benefit of others needs to be waived. But even when an intervention is a treatment, as X is, this same right needs to be waived when the reason one treatment is administered rather than another is in order to achieve a research purpose, as in RCTs. To waive this right via consent, patients must know that this is the right they need to waive, something they can know only if they know that there is a research purpose behind the choice of intervention. Thus, on pain of failing to respect the patients' rights, research consent must be obtained even in those RCTs in which there is no reason to believe that, if patients were made aware of the underlying research purpose, they would not have consented to the intervention [11]. Explicit consent to treatment plus merely presumed consent to research does not suffice to waive the right against being intervened upon for the benefit of others, because successfully waiving this distinct right requires actually knowing that it is the right one needs to waive.

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11. It is important to note that this argument for obtaining research consent in RCTs does not extend to all research. Consider research that merely collects data on the outcomes of clinical care that is not itself motivated by a research purpose. Although the patients are contributing to research, their right against being intervened upon for the benefit of others does not need to be waived, since the only interventions that are performed on them are for their own benefit, not for the benefit of others. The same is true of research on samples or specimens that were originally extracted for therapeutic purposes. Again, the subjects are contributing to research, but it is only their samples that are being used, not the patients themselves. If patients had a right not to contribute to research purposes, even indirectly, then research consent would be required in these cases as well. But I do not believe they possess such a right, although I will not argue for this here. (This is not to say that there are no other rights that might need to be waived in research on medical records and stored samples.)

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OP-ED

Inappropriate Obstructions to Access: The FDA's Handling of Plan B

Susan F. Wood, PhD

When prescribing or purchasing a medication or medical device in the US, most people assume that the product has been reviewed and, based on good evidence, approved as safe and effective by medical experts. This assumption is accurate in most cases; the Food and Drug Administration (FDA) is charged with the oversight, approval, and regulation of most (though not all) of these products [1, 2].

While scientific evidence and processes do not always trump nonscientific policy priorities—in such matters as job creation, transportation funding, and even grant funding by federal research agencies—in governmental decision making, they do drive decisions at the FDA. According to the 1938 Food, Drug and Cosmetic Act, the secretary of the US Department of Health and Human Services (HHS) or her delegate, the commissioner of food and drugs, is to base drug approval decisions on evidence of safety and effectiveness, quality of manufacturing and processing, and accuracy of labeling [3]. In this law, Congress specifically did not give the secretary broad latitude to base decisions on other policy considerations. The process for approving emergency contraception (levonorgestrel) to be sold "over the counter" (OTC) without a prescription marked a major departure from standard FDA procedure, with alterations to the usual approval process and obstruction of access to a safe and effective drug. That departure could set a dangerous precedent for future decisions.

Background

Prevention of unintended pregnancy is the most effective way to avoid the need for abortion [4]. Furthermore, recent data confirm that levonorgestrel-based emergency contraception does not affect what happens after implantation of a fertilized ovum but works prior to ovulation [5, 6] and thus is not an abortifacient. Hence, Plan B should not be subject to restrictions on or objections to abortion.

A very safe medication—safer, in fact, than many other OTC products [7]—Plan B and other levonorgestrel-based emergency contraceptives are more effective when used promptly (as early as possible within 72 hours after unprotected intercourse), so that the delays and hurdles involved in obtaining and filling a prescription (including limitations in doctors' schedules and pharmacy opening hours) can lessen or obviate its effectiveness. This makes the drug an obvious candidate for over-the-counter sale. Since the 2003 application for Plan B emergency contraception to become a nonprescription drug, the FDA's scientific and medical reviewers recommended full

OTC status with no age restrictions. It was ideological and political interference that made what should have been a straightforward approval process a contested one.

An Unusual Age Restriction

The saga of bringing Plan B (and now Plan B One-Step) fully over-the-counter can be broken in to three phases over ten years. As assistant commissioner for women's health at the FDA and director of the Office of Women's Health from 2000 to 2005, I observed the first few years of the tortuous, and indeed politicized, process of approving a safe and effective, but time-sensitive, contraceptive product for over-the-counter sale [8]. During the Bush Administration, approval of Plan B for over-the-counter sale was delayed several times, despite recommendations in favor of OTC status for all ages from both the FDA reviewers and its outside advisory committee [9]. As the US Government Accountability Office's (GAO) report on this decision process explains,

> The Plan B decision was not typical of the other 67 proposed prescription-to-OTC switch decisions made by FDA from 1994 through 2004. The Plan B OTC switch application was the only one during this period that was not approved after the advisory committees recommended approval. The Plan B action letter was the only one signed by someone other than the officials who would normally sign the letter [10].

The FDA leadership overruled the recommendation of the reviewers and the advisory committee and proposed an age restriction—initially age 16, then age 17—based on the premise that the studies required for an "OTC switch" application had not included enough young women under the age of 16 to determine whether they could accurately comprehend the drug's label and use it as directed. The FDA had never before required such age-specific studies before on label comprehension and "actual use" to approve a prescription drug for over-the-counter sale [9]. The GAO's report continues,

> There are no age-related marketing restrictions for any [other] prescription or OTC contraceptives that FDA has approved, and FDA has not required pediatric studies for them....GAO found that high-level management's involvement for the Plan B decision was unusual for an OTC switch application....The Acting Director acknowledged to GAO that considering adolescents' cognitive development as a rationale for a not-approvable decision was unprecedented for an OTC application, and other FDA officials told GAO that the rationale differed from FDA's traditional practices **[**10].

When the manufacturer responded by submitting an application for the dual status proposed—over-the-counter sale to adult women, but prescriptions required for younger people—FDA leadership delayed approval again and started a regulatory process to determine whether a federal regulation was needed to establish such a

dual-label approval, despite the fact that other products, like nicotine patches, had been given this age-related dual status in the past [11].

This was the point, in late 2005, at which I resigned my position as assistant commissioner of women's health. It was clear to me at the time that, even with an unwarranted age restriction, FDA leadership was going to continue to block unfettered access to this safe and effective drug for reasons unrelated to safety and effectiveness. Though it was difficult to leave my excellent and dedicated colleagues at the FDA, it was better for me to move outside of the agency and to be able to voice my concerns in public. I spent the next year speaking and writing about how science and evidence must drive our health policy decisions, particularly at the FDA. Little did I know that this was just the beginning of the story.

Half Measures

Beginning in 2005, *Tummino v. Von Eschenbach*, a lawsuit against the FDA, had been filed by a number of plaintiffs including individual women, organizations, and health professionals, based on an original petition that they had filed asking the FDA to approve all levonorgestrel-based emergency contraceptive methods for OTC status [12]. This lawsuit, with the plaintiffs represented by lawyers at the Center for Reproductive Rights, would later play a major role in leading to FDA approval of OTC status.

In August 2006, the acting FDA commissioner, who was seeking Senate confirmation as permanent commissioner, concluded that no federal regulation was needed for age-restricted OTC approval, but that the age restriction should be 18 rather than 17 [13]. He announced this decision the day before his Senate confirmation hearing, where he was to face senators, including Patty Murray (D-WA), Hillary Clinton (D-NY), and Barbara Mikulski (D-MD), who had been calling for a science-based decision on Plan B since 2004. The commissioner's announcement cleared the way for approval with an age restriction of 18, and this approval came remarkably quickly, within less than a month [14], as did his confirmation as commissioner.

From 2006 to 2009, no further regulatory actions occurred. Plan B was available in pharmacies for sale without a prescription for women 18 or older or with a prescription for women younger than 18, with little controversy. Though this constituted progress, it was certainly not ideal: these age restrictions have real consequences for women seeking emergency contraception. Because of the age restriction, levonorgestrel is held behind the counter, so that only an open pharmacy can dispense it, even to women "old enough." This may mean waiting until pharmacies open for business, and showing an ID prior to purchase can be intimidating in such a sensitive situation.

Further Obstructions

In March of 2009, the federal judge hearing the *Tummino* case issued his first ruling, ordering the FDA to immediately roll back the age restriction to 17 (on the grounds

that the change to 18 was clearly arbitrary) and to reevaluate the need for any age restriction through the usual FDA review and approval processes [15]. The FDA did roll back the age restriction to 17, but took no further action on lifting the age restrictions as directed by the court.

In late 2010, the Center for Reproductive Rights and the plaintiffs in the *Tummino* lawsuit filed new legal motions against the FDA. The FDA responded that the manufacturer had now started new studies on younger teens and that, therefore, it was waiting for a new application for over-the-counter sales rather than considering the previous 2003 application. This is an important point. The FDA did not need new research studies to have enough information to approve Plan B (or Plan B One-Step, the current formulation); the reviewers and advisory committee had recommended full approval back in 2003 and 2004 based on the previously provided data. The request for additional data on teens had been made through inappropriate interference by political leadership in 2004, not by the original reviewers or the advisory committee. FDA management was now making the same inappropriate request of the manufacturer.

More Politically Motivated Interference

The manufacturer submitted a new application with new data on younger teens in 2011. The FDA was prepared to approve the application for full OTC status of Plan B One-Step [16], but then a new and unexpected roadblock appeared. The secretary of HHS, Kathleen Sebelius, overruled the FDA commissioner and blocked approval for OTC status, stating that there was inadequate data on the ability of 11- and 12-year old girls to understand the label or use the product as directed [17]. President Obama supported her decision, stating his concern as a parent about access to emergency contraception without a prescription by young girls [18]. These last-minute concerns echoed those raised previously by the Bush Administration and by opponents of access to emergency contraception in general, but moved the age concerns even earlier to preteens—a logical leap the Guttmacher Institute described as "specious," given data showing that fewer than 1 percent of 11-year-old girls in the United States are sexually active [19]. I joined many in speaking out against the decision [20].

This was truly unprecedented: *never before* had an HHS Secretary overruled the FDA on a medical product approval [21]. Because this decision occurred in a presidential election year, it seems likely that full OTC approval was blocked to avoid political controversy. When the secretary overruled the FDA commissioner, she set a new and troubling precedent for future decisions that might be deemed politically sensitive.

Resolution

This new denial led to new legal action. The Center for Reproductive Rights renewed its lawsuit, adding Sebelius as a defendant in early 2012. By spring of 2013, US District Court Judge Edward Korman issued his ruling [22]: all levonorgestrel-based emergency contraception was to be made available over the counter within 30

days, and the FDA's decisions around Plan B were described as "arbitrary, capricious, and unreasonable" [23].

The Obama administration appealed the decision and asked the United States Court of Appeals for the Second Circuit to delay FDA action, pending the appeal. Within days the appeals court denied the request for delay, noting that the age restriction on the brand-name drug Plan B One-Step could remain if the FDA so chose, but that generic products should immediately be available without a prescription for all ages [24]. The administration promptly withdrew its appeal and approved Plan B One-Step as an OTC product without age restrictions [25]. Plan B One-Step came onto the shelves during the summer of 2013, to little fanfare or controversy. Those who had raised objections can see that the sky did not fall.

Conclusion

Now that levonorgestrel is finally approved for OTC sale without age restrictions, we have added a valuable tool to our constellation of reproductive health efforts to reduce unintended pregnancies, but it's not a magic bullet. Furthermore, new scientific questions have emerged about its efficacy for overweight or obese women. Clarification is needed on the product label to accurately reflect updated information on its mechanism of action. However, these concerns can be addressed appropriately within the scientific research community, the FDA and health care delivery systems, not in the political arena.

New debates about contraception have arisen, both in the political arena and in the courts, concerning the requirement for insurance coverage of contraception under the Affordable Care Act [26]. The scientific and medical communities must defend the clear evidence of the health benefits to women and to families of access to family planning tools, including emergency contraception. While women's reproductive health has been the focus of centuries-long political, religious, and moral debates, we must ensure that safe, effective, and beneficial drugs are made as available as possible.

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CORRESPONDENCE

American Society for Reproductive Medicine Updates Consent Forms for Egg Donation

Response to "Fully Informed Consent for Prospective Egg Donors"

To the editors:

In "Fully Informed Consent for Prospective Egg Donors," co-authors Cahn and Collins identify and recommend addressing five significant "points" in counseling and informed consent protocols for reproductive egg donors: (1) detailed medical risks; (2) subsequent use of donated eggs for research purposes; (3) the risks of both multiple donations (health) and donation at multiple IVF programs (consanguinity); (4) confidentiality issues; and (5) compensation.

The authors suggest that current professional standards and guidelines are inadequate in meeting these needs and urge the adoption of "legal regulation" to "ensure uniform implementation." We would like readers to be aware of new model consent forms that address virtually all of the concerns raised by the article.

The same month this article was published, model consent forms for egg donation were released by the American Society of Reproductive Medicine (ASRM) through its affiliated professional society, the Society of Assisted Reproductive Technologies (SART) [1]. These comprehensive model consents were the result of two years' work by a multidisciplinary committee [2] and address, both explicitly and in detail, four of the five "points" suggested in the article. In particular, the model consents include: explanatory figures and illustrations detailing the medical procedure; descriptions of and statistics for multiple risks; opportunities to grant or withhold consent to use of donated tissues in subsequent research, explicitly including embryonic stem cell research; and information about compensation. Consistent with established informed consent principles (and in contrast to the article's fictional "Eggs R Us" vignette), we planned for these consent forms to be provided to, and reviewed in person with, any prospective donor well in advance of any donation decision and procedure. We also anticipate that with the rapid rise of egg freezing, egg donor recruitment will increasingly be put back into the hands of medical programs with a correspondingly diminished role for nonmedical recruiting programs. As members of this committee, we participated in months of discussions, debates, drafts, and revisions on many of the points raised by the article's authors.

The fifth issue raised by Cahn and Collins—multiple donations and consanguinity—was addressed by ASRM in a 2008 practice guideline [3], and a number of other

donor issues noted by the authors have been addressed in ASRM Ethics Committee opinions that were not referenced in the article. The 2008 guideline specifically disqualifies prospective donors after six donations, an issue that should be picked up with counseling and candid egg donors, although a national egg donor registry would more effectively address this issue.

We anticipate the model consent forms will, as intended, provide the type of uniform disclosure of information and risks and promote the fully informed consent for egg donors that the authors call for. We also believe the authors' call for "legal regulation" would not necessarily ensure uniform implementation of any legislated disclosure protocol, given that the law on informed consent varies from state to state. We hope the model consents will be a valuable addition to the informed consent process, enabling clinicians to provide donors valuable and material information about the donation process in an effective and timely manner. We appreciate the authors raising these important informed consent issues for egg donation, and we believe the model consents we have described reflect a critical crossdisciplinary understanding and approach and have done much to address these issues and many more.

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CORRESPONDENCE
Decision on Mandating Coverage for ART Must Begin with Accurate Data

Response to: "Who Pays? Mandated Insurance Coverage for Assisted Reproductive Technology"

We read the above-named article with great interest. While this article addresses many relevant issues, clarification of certain points is warranted.

One of the authors' primary arguments against mandated insurance coverage for in vitro fertilization (IVF) is the "low success rate." As evidence, they cite a per-cycle implantation rate (IR) of 4-36 percent. Implantation rate is defined as the number of fetuses with cardiac activity found on ultrasound divided by the number of embryos transferred. Although IR is used in research, it is considered a surrogate outcome and not typically clinically relevant [1-4]. For example, a patient who receives one embryo and miscarries at 10 weeks, after cardiac activity has been detected, has an IR of 100 percent, while a patient who receives three embryos and has only one identifiable pregnancy on ultrasound has an IR of 33 percent, even if she subsequently delivers a live infant. Therefore, IR does not truly reflect IVF "success."

The authors subsequently reference data from the 2011 Society for Assisted Reproductive Technology (SART) registry, which reports live birth rates of 4-40 percent per cycle. The use of this data to support the authors' claim of "low success rates" is problematic for several reasons. First, the live birth rates published by SART are age-specific. The 4 percent live birth rate per cycle cited by the authors is applicable to women over age 42, comprising only 6 percent of all cycles performed in the United States (US). In reality, more than half of autologous IVF cycles reported to SART are performed in women younger than 38, a group with a live birth rate of 30-40 percent per cycle [5]. Second, cumulative live birth rates, although not reported by SART, are more clinically relevant than per-cycle data. Studies have demonstrated a cumulative live birth rate for young women exceeding 80 percent after three IVF cycles, effectively surpassing rates achieved through natural fecundity [6-9].

Clarification is also needed regarding the advantages and disadvantages of adoption and assisted reproductive technology (ART). The authors fail to highlight the various treatment options available to the infertile couple and, in fact, make no mention of donor-oocyte therapy. This is especially troublesome since patients considering IVF with donor oocytes are frequently the same women contemplating adoption. The lack of comment on this group is especially conspicuous during the authors' endorsement

of adoption over IVF, when they claim that adoption "boasts a 'success' rate much higher" than an IVF cycle and is "more accessible and affordable than ART."

These claims are inaccurate. First, patients who receive donor oocytes experience relatively high success rates. Donor-oocyte IVF cycles are associated with a live birth rate of 55 percent per fresh embryo transfer, with cumulative live birth rates as high as 85 percent [5-7, 10]. Next, oocyte donation may offer a faster path to parenthood than the 9- to 18-month waiting period advertised by some US adoption agencies, since patients with access to frozen donor oocytes can initiate IVF and achieve pregnancy within a few weeks [11, 12].

Also, the authors do not provide any data to support their claim that adoption is "more affordable" than IVF. In fact, adoption is incredibly expensive. The average cost of a domestic newborn adoption through an agency in the US is nearly $40,000, and international adoptions can be far more costly [13-16]. While we agree that IVF is also expensive, we feel that the authors' failure to disclose the high cost of adoption is misleading. Furthermore, the authors did not consider the fact that IVF provides the opportunity for embryo cryopreservation and additional children. Patients with excess cryopreserved embryos after conceiving with IVF have the opportunity to have a second or even third child in the future at a substantially lower cost.

Finally, during their objection regarding the expense of mandated coverage, the authors claim that "arguments about cost effectiveness remain unconvincing" and "more stringent enforcement of ASRM guidelines [limiting the number of embryos transferred] could prove just as effective." Here, there is no mention of costs generated by non-ART treatments. Too often, patients who cannot afford IVF are treated with controlled ovarian hyperstimulation with intrauterine insemination (COH-IUI) because it is cheaper on a per-cycle basis [17]. Although the number of COH-IUI cycles performed in the US is unknown, estimates suggest that these cycles produce four times more births than IVF, or about 4.6 percent of newborns [18]. Each cycle of COH-IUI carries a 25-30 percent multiple pregnancy rate and a 7-11.6 percent triplet-and-higher-order-multiple (HOM) pregnancy rate [19]. A recent publication from the CDC estimated that non-IVF fertility treatments such as COH-IUI were responsible for 45 percent of HOM births in the US in 2011, compared to 32 percent for IVF [20]. Finally, expedited treatment with IVF rather than COH-IUI is associated with a shorter time to pregnancy and lower cost per delivery [17]. Improving access to IVF could, therefore, theoretically limit the number of COH-IUI cycles performed, improve the cost-effectiveness of treatment, and reduce the substantial costs associated with HOM pregnancies.

Determining what "a reasonably just state should offer" is the fundamental basis of any discussion regarding medical resource allocation, but the authors' misinformed use of certain facts and lack of comment on key areas led them to oversimplify the discussion on both sides. The decision for a society to support a citizen's right to reproduce is a complex one, and both perspectives have valid and substantial

evidence to support their arguments. While we applaud Falloon and Rosoff for raising this issue in a public forum, we encourage readers to recognize that the discussion has already been carried far beyond what was presented in their article.

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