COMPLEX CONSIDERATIONS

'Right to Try' Laws Raise Ethical Concerns

NICHOLAS J. KOCKLER, PhD, MS

In 2015, the Oregon legislature passed a "Right to Try" law allowing a qualified patient to use an investigational product, meaning one that has not been approved by the U.S. Food and Drug Administration, when the product is offered by a lawfully authorized health care practitioner for the purposes of treating a terminal illness.[1] To date, 38 states have passed Right to Try laws, and in 2017 the U.S. Senate passed a Right to Try bill, S.204, that awaits approval in the House of Representatives.

It would appear that passage of Right to Try laws at the federal and state levels is inevitable. For the Catholic health care ministry, the question now for patients, providers and health care organizations is whether — and to what extent — a request for a Right to Try care plan raises ethical concerns.

Using the Oregon statute as an example, a qualified patient may request the use of a non-approved investigational product. A qualified patient is an adult (18 years old or older) who is capable of making his or her own decisions, is a resident of Oregon and who has a terminal diagnosis. A non-approved investigational product may be a "drug, biological product, or device" that has successfully completed the FDA's investigational phase assessing the product's minimal safety, but not its efficacy, so the product is being used in clinical trials but is not on the market.

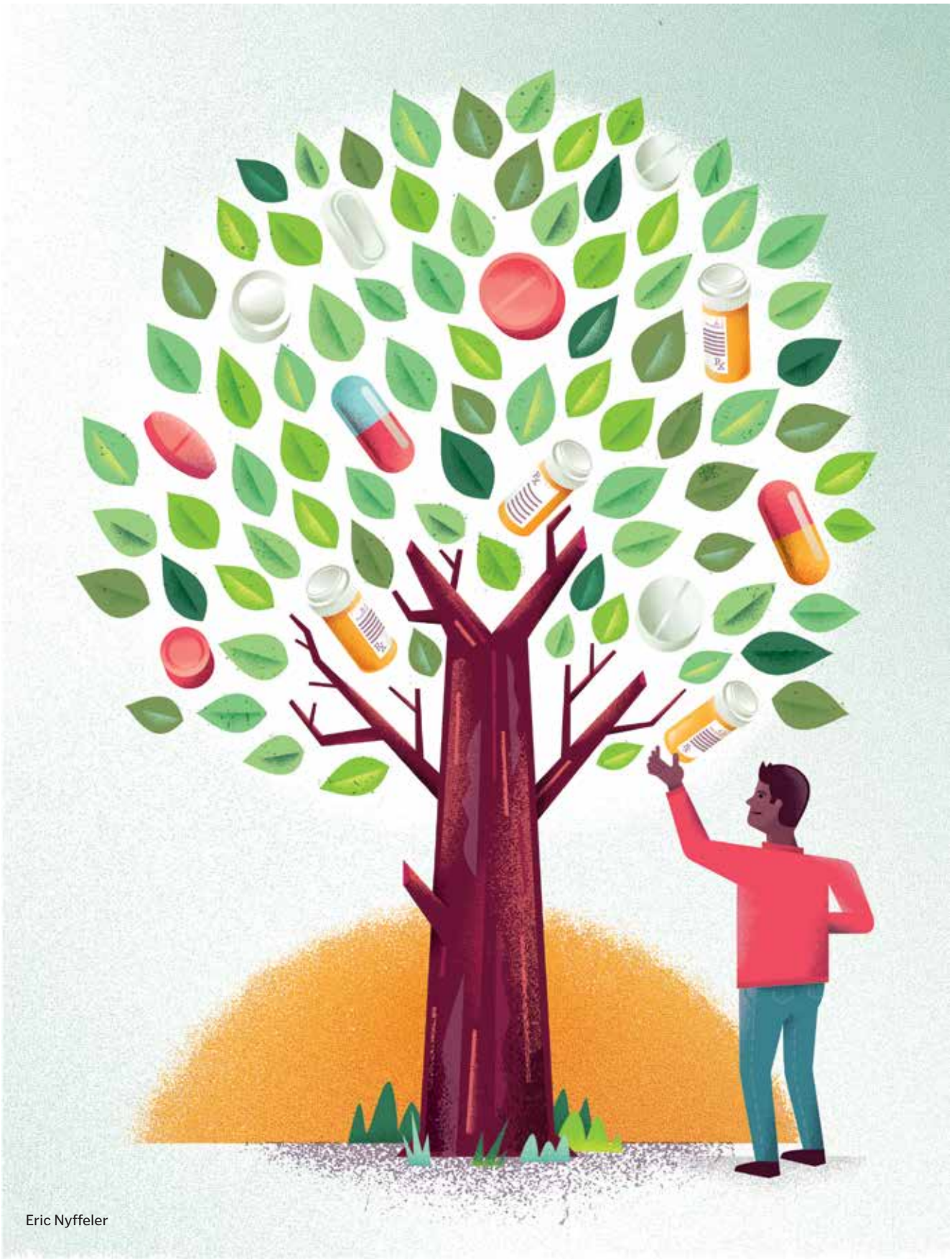
The Oregon Right to Try law is like others in that it restricts the range of clinically relevant scenarios to treatment of an adult with terminal illness. However, the law is distinct from others in that it specifies "terminal" as "an illness or medical or surgical condition that, in a physician's reasonable medical judgment, will result in the patient's death within six months."

Readers should note that the six-month time frame means such patients theoretically would be eligible for hospice care, as well as for physician-assisted suicide, known in Oregon law as "Death with Dignity."

During the state legislative process, leaders in the Oregon Region of Providence Health & Services (now Providence St. Joseph Health) offered testimony based on ethical thinking supplied by the Providence Center for Health Care Ethics. Having ethicists integrated across the continuum of care and within leadership provided the opportunity for close collaboration between the government affairs team, executive leadership, clinical leaders and the center's ethicists.

As Right to Try laws proliferate, the health care ministry's caregivers are likely to be confronted with requests from patients in a broad range of settings, including but not limited to cancer care (chemotherapy or immunotherapy requests, for example) and heart and vascular care (valvular devices).

The Oregon experience readied us at the Center for Health Care Ethics to emphasize the complexity of Right to Try requests, the challenges of



Eric Nyffeler

public discourse on the applicable issues, and the broader issues that may not be addressed by Right to Try laws.

A Right to Try law presents two ethical questions: (1) Whether our health care ministries shall permit their providers to respond affirmatively to Right to Try requests and therefore prescribe or administer such interventions; and (2) whether our health care ministries shall implement policies or guidelines pertaining to Right to Try requests.

DYNAMICS AT WORK

To help frame an ethical analysis of Right to Try care plans, it may be helpful to describe several different dynamics operating in these cases and in the dialogue about the issues. To begin, commentators note several relevant social dynamics, including the following:

- Racial and other disparities in access to clinical trials in general
- Socioeconomic disparities reinforced by Right to Try legislation
- Public interest in biomedical and scientific innovation
- Public discourse and the unscientific, yet compelling nature of tragic anecdotes[2]

Next, there also are important psychological factors to take into consideration when patients inquire or request to exercise a Right to Try:

- Self-preservation as motivation to seek a "right" to try an investigational product
- Duress from desperation, or need for hope, at the end of one's life
- Therapeutic misconception[3]
- Health and science literacy rates in general[4]

WHAT ADVOCATES AND CRITICS SAY

Development and approval of drugs, biologics and devices to be marketed in the United States can be a lengthy process. The Food and Drug Administration established an expanded access (commonly known as "compassionate use") paradigm that allows individual patients to apply for access to an investigational drug for treatment, under certain circumstances.[5]

The Goldwater Institute, a Phoenix-based think tank that, among its interests, advocates for Right to Try legislation, cites five reasons for the Right to Try paradigm:[6]

1. Most terminal patients are not able to participate in clinical trials

2. Right to Try is necessary because dying patients do not have access to promising treatments once clinical trials are over, "even if the drug was successful and will be approved."

3. The FDA "compassionate use" process doesn't help enough people because the application process is complicated, time-consuming and expensive

4. It takes too long for promising treatments to be approved by the FDA

5. Patients should not have to ask the federal government for permission to try to save their own lives

Critics of Right to Try argue that advocates are relying on two myths:[7] that the FDA's expanded access process is long and complicated, and that Right to Try laws will eliminate the bureaucracy between terminally ill patients and the drugs they desire to try.

Regarding expanded access, commentators reply,

> ... it is hard to envision how the [FDA] could provide a faster turnaround time on expanded access requests while still conducting a thorough review of a patient's medical history and proposed treatment plan. The form that physicians must submit to the FDA for review after a company agrees to supply a patient with an experimental drug requires less than one hour to complete. The FDA approves more than 99 percent of these requests, and it does so, on average, within four days. For emergency requests, the agency responds in one day or less.[8]

Regarding elimination of bureaucracy, commentators express worry that doing so would "expose the patients to exploitation without guaranteeing access to the drugs they seek. And weakening the FDA puts everyone else who takes drugs or uses medical devices or vaccines at grave risk."[9]

Furthermore, critics of Right to Try have observed that there are other ways Congress can help patients gain access. A May 3, 2017, entry on the *Health Affairs* blog proposes six alternative ways lawmakers could help patients who desire to use an experimental product:

- Investigate, with drug manufacturers, incentives to make the FDA expanded access process

more appealing to drug and device companies

- Continue to improve and enhance the FDA's expanded access program
- Allow FDA protocols to require physicians to report additional data from expanded access requests
- Support targeted educational activities to help better inform health care professionals and researchers on the expanded access process
- Eliminate local institutional review board oversight for individual expanded access requests
- Develop laws and other means to address access to and equity in clinical trial enrollment[10]

ETHICAL ANALYSIS OF CARE PLANS

To help frame an ethical analysis of a care plan that results from a Right to Try process, one may turn to the Catholic tradition's extensive teaching and theological discourse on issues in decision-making when facing a life-limiting illness. The Vatican addresses decision-making at the end of life in the 1980 *Declaration on Euthanasia* as follows: "In any case, it will be possible to make a correct judgment as to the means by studying the type of treatment used, its degree of complexity or risk, its cost and the possibilities of using it... and comparing these elements with the results that can be expected, taking into account the state of the sick person and his or her physical and moral resources. (#IV)."[11]

"What a sick person needs, besides medical care, is love, the human and supernatural warmth with which the sick person can and ought to be surrounded by all those close to him or her, parents and children, doctors and nurses."

— DECLARATION ON EUTHANASIA

The *Declaration* continues, "What a sick person needs, besides medical care, is love, the human and supernatural warmth with which the sick person can and ought to be surrounded by all those close to him or her, parents and children, doctors and nurses."

In part flowing from this *Declaration*, the *Ethical and Religious Directives for Catholic Health Care Services* include several relevant directives. Especially pertinent are Directives 4, 9, 26, 31, 32, 55, 56 and 57.[12] It helps to review Directives 56 and 57 together to capture the spectrum that patients and caregivers must navigate in considering a Right to Try care plan:

> 56. A person has a moral obligation to use ordinary or proportionate means of preserving his or her life. Proportionate means are those that in the judgment of the patient offer reasonable hope of benefit and do not entail an excessive burden or impose excessive expense on the family or the community.
>
> 57. A person may forgo extraordinary or disproportionate means of preserving life. Disproportionate means are those that in the patient's judgment do not offer a reasonable hope of benefit or entail an excessive burden, or impose excessive expense on the family or the community."

Somewhat hidden in these directives is this fundamental clinical and ethical question: Is it medically reasonable, based on sound professional judgment, to offer a particular treatment, whatever the circumstances?

Although professional judgment is alluded to in Directive 55,[13] it is not obvious. Requests for medically inappropriate treatment[14] impose on the professional autonomy of clinicians, who, based on a traditional understanding of the medical profession, are entrusted with the healing arts to fulfill a fiduciary responsibility to people who are sick or at risk of being sick. This concept is reflected in the passage from *Gaudium et Spes* that reinforces the importance and autonomy of science in faithful living:

> Therefore if methodical investigation within every branch of learning is carried out in a genuinely scientific manner and in accord with moral norms, it never truly conflicts with faith, for earthly matters and the concerns of faith derive from the same God. Indeed whoever labors to penetrate the

secrets of reality with a humble and steady mind, even though he is unaware of the fact, is nevertheless being led by the hand of God, who holds all things in existence, and gives them their identity. Consequently, we cannot but deplore certain habits of mind, which are sometimes found too among Christians, which do not sufficiently attend to the rightful independence of science and which, from the arguments and controversies they spark, lead many minds to conclude that faith and science are mutually opposed.[15]

Furthermore, requests for Right to Try interventions may further impose on drug companies, in that the request means releasing a drug before adequate biomedical research is completed, which may expose the company and its drug development to liability issues should harm result. It forces a company to release, or provide access to, its products before the company may be ready to distribute them, without due process and other risk-monitoring strategies.

While drug and device manufacturers navigate the process to bring products to market, they also are demonstrating scientific validity of benefit and safety. This would be bypassed and potentially undermined by widespread use of Right to Try. It also would restrict the ability of health care professionals and institutions to exercise their professional duties with integrity.

The Catholic tradition suggests guidance that seeks a middle ground in discerning what medical interventions are proportionate versus those that may be disproportionate. Furthermore, as St. John Paul II teaches, biological life is not an ultimate good; we are called to respect it from conception to natural death: "After all, life on earth is not an 'ultimate' but a 'penultimate' reality; even so, it remains a sacred reality entrusted to us, to be preserved with a sense of responsibility and brought to perfection in love and in the gift of ourselves to God and to our brothers and sisters."[16]

When ethicists consider the moral character of participating in a patient's request to exercise his or her right to try a drug, biological product or device, they may frame the question as whether such participation would demonstrate integrity in the therapeutic relationship. That is, according to the model for ethical decision-making in the clinical setting, whether the participation demonstrates *honesty* in the delivery of quality care (clinical integrity), *dependability* in manifesting beneficial outcomes (beneficence), *fairness* to the patient in his or her context (autonomy), and *accountability* for other obligations (justice/nonmaleficence).[17]

To begin, three fundamental components of the therapeutic relationship provide a critical prism through which to analyze the Right to Try paradigm and its social and psychological dimensions. Those three components are (1) the bond between professionals and patients in clinical encounters, (2) the goals shared between professionals and patients and (3) the care mutually agreed to and engaged by professionals and patients.

The Catholic tradition suggests guidance that seeks a middle ground in discerning what medical interventions are proportionate versus those that may be disproportionate.

In considering the bond between professionals and patients or their decision-makers, one may ask:

- Is informed consent (i.e., the permission given by a patient to a provider) possible and present?
- What are the bases for requests, demands and "rights to try"?[18]
- What influence may emotional distress and anticipatory grief (compassion and clinical empathy) have on decision-making?
- Is the general and specific trust in the medical profession and biomedical sciences in jeopardy?

For shared goals between decision-makers and clinicians, one may ask:

- Are desired outcomes nonfeasible, feasible but not probable to help and may be likely to harm (disproportionately), or feasible and probable to help and not probable to harm?
- Has the full range of alternatives been considered, including expanded use access, hospice

care in the setting of terminal illness, or other alternatives?

Lastly, as the clinician — perhaps in consultation with an ethicist — undertakes creating an appropriate Right to Try care plan, one may inquire:

- Are other treatment options demonstrably exhausted?
- Is there a legitimate rationale for excluding the patient from clinical trials?
- What is the clinician's confidence in safety data?
- What reasonable expectations of effectiveness (biological plausibility, for example) are there?

Finally, looking through this lens at participation in Right to Try care plans, one may observe the following insights, which we submitted in our testimony to the Oregon legislature:

BENEFICENCE: Beneficence (dependability) may be at risk if there is little to no reliable data on clinical efficacy and appropriateness. That is, Right to Try establishes a "bar we believe is too low for patients to be offered safely with reasonable hope of benefit."

NONMALEFICENCE: Without reasonable hope of benefit and assurances of safety, our commitment to protecting patients from potential harm (nonmaleficence) is also at risk in so far as we may expose them to such risks without a reasonable hope of benefit.

AUTONOMY: Attention to fairness to patients in their contexts demands that we recognize the vulnerability of patients requesting Right to Try treatment — the request may occur in circumstances in which "they are running out of options to manage their disease and may, in desperation, find themselves willing to consent to interventions for which there is insufficient evidence of benefit to ethically offer it to them." Desperation and related emotional distress in these cases may reflect a less-than-free choice and, as a result, patient autonomy is not advanced in this context.

CLINICAL INTEGRITY: Patient requests for Right to Try treatment may expose caregivers to several moral hazards, putting their professional integrity at risk. Although there is a zone of professional discretion whereby a provider could offer a treatment that is not approved for a given medical indication, the Right to Try paradigm exposes providers to requests that may be medically incoherent.

One important feature of the Right to Try paradigm, especially as it is defined by the Oregon statute, is the role of financial implications in the consent process. In most cases, insurance may not cover the cost of the investigational product, and the patient would be responsible for the costs of the product itself, the administration of the product and the care necessary for any adverse events that may result from trying the product. This financial responsibility exposes them to the risk of medical bankruptcy. Such risk may be avoided if the patient pursues an expanded-access application to the FDA rather than Right to Try.

CONCLUSION

In summary, based on our analysis, it would appear that the Right to Try paradigm in general and Right to Try care plans in particular are ethically problematic. However, our health care ministries within the Oregon region entrust such decision-making on a provider-by-provider basis.

Whether an organization should institute a policy that categorically permits or prohibits participation in Right to Try requires further dialogue. There are legitimate alternatives to enable patients greater access to investigational products that have, in the clinical judgment of a provider, a medically coherent rationale and that may be reasonably safe. The question now for patients, providers and health care organizations is whether — and to what extent — a Right to Try care plan request can be accommodated.

NICHOLAS J. KOCKLER holds the Endowed Chair in Applied Health Care Ethics and is regional director of Providence Center for Health Care Ethics, Providence St. Joseph Health, Portland, Oregon.

NOTES

1. See www.oregonlegislature.gov/bills_laws/lawsstatutes/2015orLaw0819.pdf.
2. For example, see Rebecca Dresser, "'Right to Try' Laws: The Gap between Experts and Advocates," *Hastings Center Report* (May-June 2015): 9-10. Also, see Arthur Caplan and Alison Bateman-House, "Should Patients in Need Be Given Access To Experimental Drugs?" *Expert Opinion in Pharmacotherapy* 16, no. 9 (2015): 1275-79; and Elizabeth Weeks Leonard, "Right

to Experimental Treatment: FDA New Drug Approval, Constitutional Rights, and the Public's Health," *Journal of Law, Medicine, & Ethics* 37, no. 2 (Summer 2009): 269-79.
3. For example, see Gail Henderson et al., "Clinical Trials and Medical Care: Defining the Therapeutic Misconception," *PLOS Medicine* 4, no. 11 (2007): e324.
4. See Nancy Morris, et al., "Prevalence of Limited Health Literacy and Compensatory Strategies Used by Hospitalized Patients," *Nursing Research* 60, no. 5 (September 2011): 361-66.
5. Julie A. Jacob, "Questions of Safety and Fairness Raised as Right-to-Try Movement Gains Steam," *JAMA* 314, no. 8, (Aug. 5, 2015): 1-3.
Also: https://www.fda.gov/downloads/drugs/guidances/ucm351261.pdf.
6. Goldwater Institute, website righttotry.org/about-right-to-try/.
7. Alison Bateman-House, Kelly McBride Folkers and Arthur Caplan, "'Right To Try' Won't Give Patients Access to Experimental Drugs. Here's What Will," *Health Affairs* blog, May 3, 2017, www.healthaffairs.org/do/10.1377/hblog20170503.059926/full/.
8. Bateman-House, Folkers and Caplan, *Health Affairs* blog (May 3, 2017).
9. Bateman-House, Folkers and Caplan, *Health Affairs* blog (May 3, 2017).
10. Bateman-House, Folkers and Caplan, *Health Affair*s blog (May 3, 2017).
11. Congregation for the Doctrine of the Faith, *Declaration on Euthanasia*, May 5, 1980. www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_19800505_euthanasia_en.html.
12. United States Conference of Catholic Bishops, *Ethical and Religious Directives for Catholic Health Care Services*, 5th ed. (Washington, D.C.: USCCB, 2009). www.usccb.org/issues-and-action/human-life-and-dignity/health-care/upload/Ethical-Religious-Directives-Catholic-Health-Care-Services-fifth-edition-2009.pdf. (accessed January 13, 2017).
13. *ERDs*, Directive 55, in part, states, "Persons in danger of death *should be provided with whatever information is necessary to help them understand their condition* and have the opportunity to discuss their condition with their family members and care providers. *They should also be offered the appropriate medical information* that would make it possible to address the morally legitimate choices available to them." (emphasis added).
14. Gabriel Bosslet et al., "An Official ATS/AACN/ACCP/ESICM/SCCM Policy Statement: Responding to Requests for Potentially Inappropriate Treatments in Intensive Care Units," *American Journal of Respiratory and Critical Care Medicine* 191, no. 11 (June 1, 2015): 1318-30.
15. Second Vatican Council, *Gaudium et Spes*, para. 36.
16. John Paul II, *Evangelium Vitae*, para. 2.
17. For background on this, see Nicholas Kockler and Kevin Dirksen, "Integrating Ethics Services in Contemporary Catholic Health Care: The Providence Experience in Oregon," *National Catholic Bioethics Quarterly*, forthcoming. See also, Laura Nash, *Good Intentions Aside: A Manager's Guide to Resolving Ethical Problems* (Boston: Harvard Business School Press, 1993).
18. See Daniel P. Sulmasy, "*Exousia*: Healing with Authority in the Christian Tradition," in *On Moral Medicine: Theological Perspectives on Medical Ethics*, 3rd ed., eds. M. Therese Lysaught, Joseph Kotva and Stephen E. Lammers (Grand Rapids, Michigan: Wm. B. Eerdmans Publishing Co., 2012) 300-12.

JOURNAL OF THE CATHOLIC HEALTH ASSOCIATION OF THE UNITED STATES www.chausa.org

HEALTH PROGRESS®

Reprinted from *Health Progress*, March - April 2018