penetrant genetic mutations that predictably result in disease, clinical sequencing will enable individual screening, monitoring, prevention, and treatment of medically actionable conditions. On the other hand, there will be a large proportion of potentially deleterious variants associated with medium-sized odds ratios for disease and variable phenotypic predictive power. In keeping with evidence-based clinical decision making, such biomarkers should be used in conjunction with clinical observation, laboratory tests, and empirical treatment to refine estimates of the probability of disease and treatment prognoses. For example, knowledge about *CYP2C9* mutations in cytochrome P-450 should lead to the development of decision-support tools that influence the administration of warfarin and other drugs that use the same metabolic pathways.

Ultimately, clinical use of sequencing data should reduce the cost of care. If genetic information can be stored, analyzed, and disseminated in a private, cost-effective, and timely manner, precise and affordable molecular and genetic diagnoses should result in more specific treatment guidelines and avoidance of costly diagnostic and therapeutic procedures. Furthermore, supplementing clinical intuition with molecular diagnoses in syndromes with overlapping symptoms may reduce variance in diagnosis and treatment outcomes between academic medical centers and community hospitals and clinics. Although additional molecular and informatics research is needed, we are confident that NGS will eventually revolutionize clinical care just as it is revolutionizing the scientific endeavor.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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DOI: 10.1056/NEJMp1400788

When Religious Freedom Clashes with Access to Care

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At the tail end of this year's Supreme Court term, religious freedom came into sharp conflict with the government's interest in providing affordable access to health care. In a consolidated opinion in *Burwell v. Hobby Lobby Stores* and *Conestoga Wood Specialties Corp. v. Burwell* (collectively known as *Hobby Lobby*) delivered on June 30, the Court sided with religious freedom, highlighting the limitations of our employment-based health insurance system.

Hobby Lobby centered on the contraceptives-coverage mandate, which derived from the Affordable Care Act (ACA) mandate that many employers offer insurance coverage of certain "essential" health benefits, including coverage of "preventive" services without patient copayments or deductibles. The ACA authorized the Department of Health and Human Services (HHS) to define the scope of those preventive services, a task it delegated to the Institute of Medicine, whose list included all 20 contraceptive agents approved by the Food and Drug Administration. HHS articulated various justifications for the resulting mandate, including the fact that many Americans have difficulty affording contraceptives despite their widespread use and the goal of avoiding a disproportionate financial burden on women. Under the regulation, churches are exempt from covering contraception for their employees, and nonprofit religious organizations may apply for an

"accommodation," which shifts to their insurance companies (or other third parties) the responsibility for providing free access. However, HHS made no exception for for-profit, secular businesses with religious owners.

Hobby Lobby, a craft-store chain with more than 13,000 employees, is a closely held, for-profit corporation owned by a Protestant family that operates the business in accordance with its Christian principles — for example, donating a portion of proceeds to Christian missions and remaining closed on Sundays. The family does not object to providing coverage for some contraceptives, but it challenged the mandate because it includes contraceptive methods that the family believes cause abortion by preventing implantation of a fertilized egg. The Mennonite owners of Conestoga Wood Specialties raised a similar challenge.

The challenge in *Hobby Lobby* was not about the Constitution or its First Amendment. Rather, it hinged on the Religious Freedom Restoration Act of 1993 (RFRA), which was Congress's response to a Supreme Court decision holding that even if a law in fact burdened religion, it could stand as long as it was not intended to burden religion (was "neutral"), applied without regard to religious beliefs or practices (was "generally applicable"), and was rationally related to a legitimate government interest — a low bar. RFRA was meant to give greater protection to religion.

RFRA applies when a federal law is deemed to "substantially" burden a person's exercise of religion, even if it is neutral and generally applicable. Such laws may be enforced against religious objectors only when they further a compelling government interest using the least restrictive means available. This is the most demanding standard of judicial review, and few laws meet its re-

Buffer Zones, Bubble Zones, and Abortion Clinics — Another Women's Health Case

In 2000, concerned about clashes between antiabortion protesters and women seeking abortions, the Massachusetts legislature established an 18-ft radius around the entrances and driveways of facilities providing abortions and specified that within that area, no person could, without consent, approach within 6 ft of another person (a so-called "bubble zone") for the purpose of protesting, leafleting, counseling, or education. In 2007, the legislature concluded that law was not effective enough and increased its stringency, imposing a 35-ft fixed buffer zone with few exceptions. The law was challenged on free-speech grounds in a case called *McCullen v. Coakley,* and on June 26, 2014, the U.S. Supreme Court unanimously struck it down as unconstitutional.

The lead opinion by Chief Justice John Roberts, joined by four other justices, noted that sidewalks and public ways hold a "special position in terms of First Amendment protection because of their historic role as sites for discussion and debate." Although it was abortion that had motivated the statute, the Court held that the law was content- and viewpoint-neutral: it did not focus on what was said but on where it was said, and it burdened all speech, not merely disfavored speech. On this point, the four remaining justices disagreed. Nevertheless, the Court held that the statute failed the second part of the relevant constitutional test because it was not "narrowly tailored to serve a significant governmental interest." In particular, though the Court recognized that the buffer zones furthered the state's interests in "ensuring public safety" on streets and sidewalks and in "preserving access to adjacent healthcare facilities," it determined that the law problematically criminalized not only protests, but also sidewalk counseling, which could not be done at a distance of 35 ft. It also found that the buffer zones burdened "substantially more speech than necessary to achieve" the state's interest and suggested a plethora of less intrusive means the state could have used instead, some of which are used in other states.

Although the decision deals another blow to abortion rights, that blow is not as substantial as some had feared: the finding that the law was content- and viewpoint-neutral allows for the possibility that Massachusetts and other states could pass similar but narrower laws. Moreover, the Court left open the future of the floating "bubble zone" around women approaching clinics for abortions — the strategy that Massachusetts had used from 2000 to 2007 and one that the Court upheld in a Colorado case in 2000. Several justices, however, indicated a willingness to revisit that decision in future litigation.

quirements. In a 5-to-4 decision, the Court found that the contraceptives-coverage mandate did not.

In its RFRA analysis, the Court had to address several key questions: Are closely held, for-profit corporations "persons" for the purposes of RFRA protection? Can corporations exercise religion? Does the contraceptives-coverage mandate substantially burden religion? Does the mandate advance a compelling government interest? And are there less restrictive alternatives that would achieve the same result?

In a ruling in which Justice Samuel Alito wrote for the majority (joined by Chief Justice John Roberts and Justices Antonin Scalia, Anthony Kennedy, and Clarence Thomas), the mandate came up short. The majority concluded that RFRA was intended to protect even for-profit corporations and that corporations may exercise religion, rejecting as unreasonable any definition of "person" that would include some but not all corporations.

The majority also concluded that the mandate did place a substantial burden on the companies' religious beliefs, given the dramatic financial consequences of noncompliance (for example, Hobby Lobby would have faced a fine of $475 million per year) and the fact that the government had extended other exemptions and accommodations in recognition of that burden. The majority assumed that the government has a compelling interest in promoting free access to contraceptive agents, but it held that the government had failed to advance that interest in the least restrictive way, given the possibility of extending its existing exemptions and accommodations to for-profit corporations.

Thus, the Court held that as applied to closely held, for-profit corporations with religious objections, the mandate violates RFRA. It was careful, however, to restrict the decision to the case before it, refraining from opining on the implications for other types of employers or objections to other health care services, which it cautioned must be addressed on a case-by-case basis. Nonetheless, the case may have broad practical impact, since approximately 90% of all U.S. companies are closely held, and "closely held" is not synonymous with "small."

Justice Ruth Bader Ginsburg issued a sharp dissent, in which she was joined by Justice Sonia Sotomayor and in large part by Justices Elena Kagan and Stephen Breyer. Delivering her opinion from the bench, Justice Ginsburg underscored the burden that the majority decision would allow to be placed on women in favor of religious objectors: "Today's potentially sweeping decision . . . discounts the disadvantages religion-based opt outs impose on others, in particular, employees who do not share their employer's religious beliefs."

Hobby Lobby's outcome is of concern to U.S. health care professionals because our health insurance system is still largely dependent on employers. Employers and employees may have fundamentally different perspectives on which medical interventions are acceptable, particularly when the employer's fundamental mission is not to advance specific religious beliefs and its employees are therefore unlikely to be drawn exclusively from its own religious group. The Court's decision allows the beliefs of employers of various sizes and corporate forms to trump the beliefs and needs of their employees, potentially influencing the types of care that will be affordable and accessible to individuals and permitting employers to intrude on clinician–patient relationships.

The case also has important implications for efforts to achieve compromise between religious freedom and health care access. The Obama administration's attempts to compromise on the contraceptives-coverage mandate ultimately backfired, since its efforts were used to demonstrate that applying the mandate even to secular employers was not necessarily the only way to achieve the government's interests. In the future, regulators may be less willing to seek compromise lest their efforts be similarly used against them — and it is bad news for all of us if health policy can be made only through polarization and rancor rather than compromise. On the other hand, in other contraceptives-mandate cases working their way through the courts, nonprofit religious employers argue that the government's accommodations do not go far enough in protecting their religious freedom, essentially requiring them to deputize a third party to commit what they think is a sin on their behalf.

Finally, in the wake of *Hobby Lobby*, we may anticipate challenges to other medical services that some religions find objectionable, such as vaccinations, infertility treatments, blood transfusions, certain psychiatric treatments, and even hospice care. *Hobby Lobby*'s implications may

also extend into civil rights law, with employers asking to "opt out" of laws intended to protect people from employment and housing discrimination based on religion, race, sex, national origin, or pregnancy status. Although the majority deemed these slippery-slope concerns unrealistic, the dissent expressed serious concerns.

Though the decision applies only to closely held, for-profit corporations, it sets a precedent for religious exemptions that could have sweeping implications — and reflects the Supreme Court's great potential impact on U.S. health care. Yet the Court was applying Congress's statute, and Congress could, if it chose, scale back the protection offered to religious objectors — a good reason to share public reactions to the decision with our elected representatives.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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This article was published on July 2, 2014, at NEJM.org.

DOI: 10.1056/NEJMp1407965