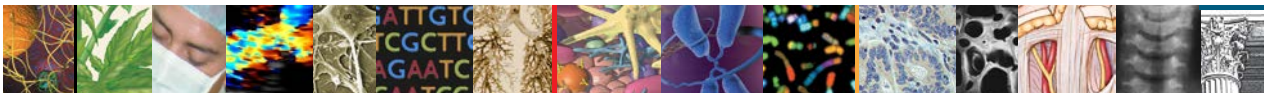

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Perspective

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HISTORY OF MEDICINE

Regulating Homeopathic Products — A Century of Dilute Interest

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Homeopathic drugs made several regulation-related headlines in 2015. First, in March, the Food and Drug Administration (FDA) filed a request for public comments to learn what the public and physicians think about homeopathic drugs and whether its limited regulatory oversight of these products was "appropriate to protect and promote public health."[1] The agency then held a 2-day public hearing featuring homeopathic care providers and representatives of the homeopathic drug industry, as well as drug-safety experts. Then in September, the Federal Trade Commission (FTC) held its own public workshop on the advertising of homeopathic products and whether it might violate section 5 of the FTC Act, which prohibits deceptive acts or practices affecting commerce.

These actions came after more than a century of missed opportunities to regulate homeopathic medicines. Founded by Samuel Hahnemann in Germany around the turn of the 19th century and introduced into the United States shortly thereafter, homeopathy was predicated on such notions as "like cures like" and the "law of infinitesimals," whereby extraordinarily diluted products that in their original form might have caused symptoms resembling those of the illness in question are administered to patients in a highly individualized fashion.

In the competitive U.S. medical marketplace of the 1830s and 1840s, orthodox physicians took notice and drew attention to the biologic implausibility of homeopathic remedies. The most caustic critique was voiced by Oliver Wendell Holmes, who declared homeopathy a "mingled mass of perverse ingenuity, of tinsel erudition, or imbecile credulity, and of artful misrepresentation," while noting the potential therapeutic effect on patients of "the strong impression made upon their minds by this novel and marvelous method of treatment." But Holmes similarly criticized the orthodox "heroic" medicine of his day (which was grounded in bleeding and emetics), and homeopathy continued to attract adherents, including some conventional physicians.

Throughout the 19th century, homeopaths founded hospitals, societies, and medical schools and developed a complicated relationship with orthodox medicine: conventional physicians (whom homeopaths dubbed "allopaths" because of their emphasis on treating or suppressing symptoms) could incorporate homeopathic remedies into their practice, and homeopaths could perform certain procedures, such as surgeries, normally performed by conventional physicians.

In the aftermath of the 1910

Flexner report on medical education, however, medicine's increasingly self-conscious grounding in laboratory science rendered homeopathy academically suspect.[2] Its base of support shifted in subsequent decades, as "lay" practitioners increasingly spoke for the field, and popular interest intensified from the 1960s onward in the context of counterculturalism, antiauthoritarianism, and growing disillusionment with the reductionism of conventional medicine.

By the 1990s, homeopathy was well represented in the armamentarium of alternative healers, whose appeal flummoxed members of the medical establishment. For example, lamenting the consumption of enormous quantities of alternative remedies, *Journal* editors Marcia Angell and Jerome Kassirer noted, "There cannot be two kinds of medicine — conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work."[3]

By testing, they explained, "we mean the marshaling of rigorous evidence of safety and efficacy as required by the . . . FDA for the approval of [conventional] drugs." This definition was ironic, however, given the FDA's historical accommodation of homeopathy. The Pure Food and Drug Act of 1906, which had endowed the agency with its initial regulatory power and mandated that drug products actually contain the ingredients on their labels, governed drugs recognized in the U.S. Pharmacopeia and the National Formulary, as well as any product intended to cure, mitigate, or prevent disease. This scope would clearly have covered homeopathic remedies, which were largely administered by clinicians at the time, but regulators had been focused on stemming the tide of truly dangerous quack products containing cocaine, heroin, and chloroform, among other harmful substances.[4]

The next major piece of legislation that could have restricted homeopathic products was the 1938 Food, Drug, and Cosmetic Act. That law, however, focused on the safety, rather than efficacy, of new drugs, and remedies listed in the Homeopathic Pharmacopeia were considered to have met the new quality standards. The inclusion in the Act of a reference to the Homeopathic Pharmacopoeia appears to have resulted not only from the efforts of Senator Royal Copeland (D-NY), a homeopathic practitioner and sponsor of the bill, to differentiate homeopathy from quackery, but also from the belief among such prominent leaders of academic medicine as Morris Fishbein (editor of *JAMA*) that the distinctions between conventional medicine and homeopathy would continue to dissolve in the crucible of scientific investigation.[4]

When the 1962 Kefauver–Harris Amendments mandated that the efficacy of conventional drugs be proven through "well-controlled investigations," homeopathic remedies remained under the regulatory radar, protected by the amendments' failure to change the status of products in the Homeopathic Pharmacopeia. Moreover, both the subsequent Drug Efficacy Study Implementation (DESI) process, by which all drugs approved between 1938 and 1962 were retrospectively evaluated, and the FDA's review of over-the-counter remedies, excluded homeopathic products, in the latter case with the intention that they would be reviewed "at a later time" (they weren't).[4]

In 1988, recognizing the increasing size of the homeopathic-drug market, the FDA issued a Compliance Policy Guide mandating conformity with good manufacturing practices and appropriate labeling regarding ingredients and directions for use. Homeopathic drugs used for "serious" conditions were to be prescribed by clinicians, whereas those offered for self-limited conditions could be sold over the counter. Thus, the FDA not only recused itself from evaluating the efficacy of remedies prescribed by homeopathic clinicians but also allowed over-the-counter homeopathic drugs to be marketed as therapeutic.

Homeopathic remedies have enjoyed continued popularity over the past three decades. According to the 2012 National Health Interview Survey, about 5 million U.S. adults and 1 million children had used a homeopathic treatment in the previous year. Although homeopathic drugs are generally considered to be safe — they consist of preparations so diluted that no trace of the original active ingredients may even remain — some physicians worry that even inert homeopathic remedies will redirect patients away from effective conventional remedies or clinicians. In addition, dangerous examples have emerged; for instance, the purportedly homeopathic Zicam Cold Remedy actually contained high doses of zinc gluconate, and in 2009 it was pulled from the market because its intranasal use was linked to anosmia.

Unlike dietary supplements, which were explicitly excluded from rigorous FDA regulation in 1994, homeopathic products can actually be substantially regulated by the FDA, since the Food, Drug, and Cosmetic Act allows

them to be sold as "therapeutic." We believe that, at minimum, regulators should reconsider the way homeopathic drugs are marketed, so that consumers who are seeking conventional medicines at pharmacies don't become confused. In August, the FTC submitted comments to the FDA recommending that the agencies better harmonize their approaches to regulating homeopathic products and their advertising.[5] Reconsidering the over-the-counter sale of homeopathic remedies entirely would be an even more drastic step and would require the FDA to take on the entire industry for propagating remedies that don't meet the same standards of scientific proof applied to conventional medicines. The recent actions by the FDA and FTC may finally signal the end of homeopathic drugs' century-long evasion of regulatory scrutiny.

An audio interview with Dr. Podolsky is available at NEJM.org

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

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ACOs and High-Cost Patients

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Managing the care of high-cost patients is a key concern of physicians and health systems that are forming accountable care organizations (ACOs) and entering into alternative payment contracts tying reimbursement to performance on cost trends and quality measures.[1] The logic is simple: given that a small percentage of patients (often those with complex or multiple medical conditions) account for the majority of health care spending,[2] directing additional resources and services toward patients who are likely to incur high costs and experience poor outcomes — a strategy known as high-risk care management — could substantially reduce costs and improve quality. Faith in this proposition has led to widespread adoption of high-risk care-management programs by ACOs.[2]

Successfully structuring these programs requires targeting the particular drivers of excess care utilization by high-cost patients; only programs that closely match delivery interventions to specific clinical needs have succeeded.[3] Prevailing approaches for managing the care of high-cost patients focus on improving adherence and disease management for multiple co-occurring conditions — a strategy developed and tested among Medicare patients.[1] Can tactics honed among the elderly be successfully applied to other high-cost populations?

Health services researchers have documented that across populations covered by different health care payers, small groups of patients are responsible for outsized portions of health care costs.[2] Less is known, however, about variation in clinical characteristics and care-utilization patterns among payer-defined groups. To further characterize this variation, we analyzed 2014 claims data for the costliest 1% of patients in each payer category whose care is managed by Partners HealthCare, a large integrated delivery system in Massachusetts (see table). Because of the structure of U.S. health care financing, these payer-defined populations are helpful surrogates for clinically distinct subgroups of patients and reflect the locus at which alternative payment contracts are negotiated.

The costliest 1% of Medicare patients had an average of eight co-occurring chronic conditions. Most had cardiovascular risk factors, and more than half had end-stage sequelae of ischemic heart disease, congestive heart failure, or chronic kidney disease. These patterns argue for the use of disease management and care coordination to improve care and