

REPORT 2 OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS (A-14)
Ethically Sound Innovation in Medical Practice
(Reference Committee on Amendments to Constitution and Bylaws)

EXECUTIVE SUMMARY

The word “innovation” can refer to many things in medicine—from improving an existing intervention, to introducing an innovation into one’s own clinical practice for the first time, to using an existing intervention in a novel way or translating knowledge and skill from one clinical context into a new one. Innovation shares features with both research and clinical care but is distinct from both. Physicians’ obligations to advance knowledge and to enhance the quality and safety of patient care argue for a general obligation to participate in innovation. This report by the Council on Ethical and Judicial Affairs examines the conditions for ethical innovations and the ethical responsibilities of physicians who participate in designing, developing, disseminating, or adopting innovative and as yet unproven modalities.

Ethically sound innovation is based on good scientific evidence and principles, is developed with input from peers, minimizes risks to patients while maximizing benefits for patient populations, and is sensitive to cost implications as well as potential for conflicts of interest. When physicians offer innovative diagnostic or therapeutic interventions to individual patients, ethical practice requires that physicians be transparent about the status of the innovation in the profession and their own experience with it and their rationale for offering the innovation, in addition to informing the patient about anticipated risks and benefits, and any conflicts of interest the physician may have with respect to the innovation.

Physicians collectively have a responsibility to promote appropriate knowledge, skills, and experience; ensure meaningful professional oversight of innovation; and promote innovation that will result in higher quality, more affordable, and more accessible care for patients.

REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS*

CEJA Report 2-A-14

Subject: Ethically Sound Innovation in Medical Practice

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Referred to: Reference Committee on Amendments to Constitution and Bylaws
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1 The AMA's *Code of Medical Ethics* provides extensive guidance for physicians in various contexts
2 of clinical practice and in clinical research. In its review of the *Code*, however, the Council on
3 Ethical and Judicial Affairs (CEJA) realized that the *Code* provides little if any guidance with
4 respect to innovation in medicine. The present report identifies key issues relevant to innovation
5 and provides guidance for ethically sound practice in this area.

6 7 CHARACTERIZING INNOVATION IN MEDICINE

8
9 The term “innovation” can refer to many things in medicine. For example, it can refer to improving
10 an existing intervention or introducing an intervention into one’s own clinical practice for the first
11 time. Or it can refer to using an existing intervention in a novel way (e.g., off-label use of an
12 approved drug), or to applying concepts associated with a particular condition to a different
13 condition or bodily system.

14
15 Some have sought to define innovation by distinguishing it from research, focusing on seeming
16 contrasts in their respective focus and goals, methods, risks, outcomes, or effects on clinical
17 practice. For example, where research focuses on benefits for populations of patients, innovation
18 often targets individual patients, such as patients with a particular rare disease or for whom a
19 standard therapy is ineffective (such as “n-of-1” trials).[1,2] Where research adheres to protocols
20 with established methods, criteria for selecting specific participant populations, and specific,
21 clearly defined outcome measures, innovation often modifies techniques as it progresses, may
22 select different participants over time, or may redefine goals.[3] Research is characterized as
23 drawing conclusions that are generalizable to large populations of patients, while innovation
24 typically draws conclusions that are confined to a single patient or small subset of patients,[3]
25 though innovations may generalize to larger patient populations over time, and may or may not
26 require formal research protocols to justify widespread clinical adoption.[3,4].

27
28 Others have noted similarities between research and innovation in order to distinguish innovation
29 from clinical practice (i.e., in shared aims of learning and improving treatments,[4] or as being
30 riskier or more burdensome than clinical treatment) [5,6].

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1 Still others define innovation as being typically evolutionary, building incrementally on new
2 knowledge,[7] which nonetheless over time may come to seem like a revolutionary change in
3 practice.

4
5 Finally, some view innovation as falling on a continuum between clinical practice and clinical
6 research.[8] For example, the Belmont Report, the foundation for research ethics in the United
7 States, characterizes innovation as activity that departs in a “significant way from standard or
8 accepted practice” yet does not automatically qualify as research just because it is “new, untested
9 or different.”[9]

10
11 However, as Kass and colleagues note, “a growing number of activities in health care cannot be
12 comfortably classified as either research or therapy, the one excluding the other.”[5] For example,
13 the distinction between seeking to benefit the individual patient versus seeking generalizable
14 knowledge to benefit populations is critiqued for being overly subjective,[6] and for under-
15 appreciating how both research and clinical practice can contribute to learning.[5]

16
17 Both research and innovation have been distinguished from clinical treatment as carrying greater
18 risk, in part because they involve unproven interventions. However, both research and clinical
19 practice carry risks and burdens.[2] Nor are outcomes always better for patients in clinical practice
20 than for research participants.[10,11] In fact as many as 50 percent of interventions in clinical
21 practice lack adequate evidence of effectiveness,[5,12] while both research and clinical practice
22 impose burdens beyond those of interventions themselves that are not related to outcomes—for
23 research, the requirements of the protocol, for example; for clinical practice, repeat office visits,
24 wait time, or paperwork.[13,6] In some areas of medicine, enrolling a patient in a research protocol
25 is considered the standard of care—for example, pediatric cancers. Likewise, although research
26 typically involves specific and discrete protocols that dictate the course of action, under the rubric
27 of evidence-based medicine clinical practice is also increasingly expected to conform to
28 guidelines.[5]

29 30 ETHICS & INNOVATION

31
32 Physicians’ obligations to advance knowledge [14] and to enhance the quality and safety of health
33 care [15–17] argue for a general obligation to participate in innovation. The fact that the boundaries
34 among research, innovation, and clinical practice are increasingly blurred does not mean that
35 characteristics of ethically sound innovation cannot be identified. Indeed, identifying such
36 characteristics will help clarify expectations for physicians’ professional conduct to inform
37 physicians’ judgments about their own innovative activities.

38
39 Activities across the research-innovation-clinical care continuum share a common ethical
40 foundation in physicians’ professional commitments to safeguard patient well-being and ensure
41 that the interests of current and future patients are not compromised.

42 43 *Conditions for Sound Innovation*

44
45 More than 20 years ago, Moore identified critical aspects for responsible innovation in
46 surgery.[18,cf.19,3] First, innovation must be scientifically well grounded—there must be
47 reasonable evidence from animal studies or other sources that a proposed innovation is feasible and
48 likely to be effective. Second, innovators must have appropriate skills and knowledge. Third,
49 innovation should focus on the interests of patients, not the interests of innovators or their
50 institutions. Lastly, innovation should be reviewed and discussed openly with peers. This analysis
51 of aspects of responsible surgical innovation generalizes to medical innovation, as well.

1 Evidence Base. Requiring that a proposed innovation have a scientific justification protects the
 2 interests of patients, helps to ensure that the innovation is medically credible and amplifies the
 3 chance that other physicians will be able to introduce the innovation successfully in their own
 4 practices. Further, while innovation often relies on intuition and incremental advances in
 5 knowledge, making it difficult to reduce innovation to specific, discrete protocols, it is desirable to
 6 structure innovation in a way that maximizes objectivity, helps enable others to replicate it, and
 7 enhances the chance to gain meaningful knowledge.[5,13] For example, a proposed innovation
 8 could identify and clarify the types of patients who might benefit most, standardize the process or
 9 procedures used, and resolve technical problems in applying the procedure.[20]

10
 11 Knowledge, Skill & Experience. Requiring that innovators have—or acquire—appropriate
 12 knowledge, skill, and experience is also in the interests of patients. There is a “learning curve”
 13 associated with any innovation, whether an innovation is new to medicine or simply new to an
 14 individual physician’s practice, and until physicians develop competence, outcomes may be
 15 uncertain, while morbidity and mortality may be significant.[23] Laparoscopic cholecystectomy
 16 provides an example of the importance of the learning curve and the necessity of having a
 17 mechanism to gather data about the outcome of innovation.[21] The procedure was touted as
 18 offering shorter hospital stays and lower discomfort for patients. The randomized trials that were
 19 carried out were not large enough to detect any relevant concerns. However, as the procedure
 20 became widespread it was not until a state health department established a clinical registry to track
 21 data that it became clear the surgery led to severe complications.[21] When there is unresolved
 22 controversy about an innovation or its value, physicians must make difficult choices before
 23 introducing it into their own practice, and the balance of harm and benefit may shift over the course
 24 of introducing the innovation.[22]

25
 26 Identifying strategies to limit the harms associated with the learning curve is important for
 27 protecting patients. For example, using simulations when possible can enable physicians to develop
 28 needed expertise without exposing patients to undue risk.[23,24] Physicians can collaborate with
 29 colleagues to manage the learning process through institutional credentialing mechanisms to reduce
 30 the likelihood that a physician will inappropriately use an innovative intervention with patients
 31 before he or she has acquired the skill to do so safely.[23,3,25] (The pathway of credentialing and
 32 privileging may also be appropriate where the innovation as such is not novel, but is new to the
 33 physician.)

34
 35 Professional societies can play a significant role by helping to define the minimum skills and
 36 baseline competence physicians must demonstrate before introducing an innovation into their
 37 practices.[23] Professional societies can also contribute by creating “hands on” courses for new
 38 techniques,[24] and can organize and support mentorship programs where individuals with
 39 experience with a particular method or procedure teach new users.[22,24] In some cases,
 40 physicians might rely on industry representatives to demonstrate proper use of an innovative
 41 device. Industry representatives, in this capacity, play an important role in patient safety and
 42 quality of care, but physicians have an ethical responsibility to maintain patient privacy,
 43 confidentiality, and quality patient care,[26] and should exercise due diligence in adopting
 44 innovations marketed by manufacturers.

45
 46 Focus on Patient Benefit. Requiring that efforts to innovate be directed first and foremost toward
 47 benefit for the patient(s), not benefit for the innovator, is in keeping with physicians’ core fiduciary
 48 responsibilities as professionals.[14,28] Physician-innovators may gain personal financial benefits,
 49 advance their careers, or garner prestige or create a competition edge for themselves or their
 50 institutions but that should not be the primary impetus to innovate [18,cf.6,7,29,30].

1 Entrepreneurship, career development, and financial gain undoubtedly can drive individual and
2 institutional efforts to develop and market innovations, and to the extent that these increase
3 innovation and progress in medicine, they should be supported—for example, by granting patents
4 on devices.[29] Yet because the physician’s primary responsibility is always to the patient,
5 physicians have an obligation at minimum to disclose conflicts of interest to patients, and more
6 broadly to resolve conflicts in favor of the patient.[31,32]

7
8 Physicians should be sensitive to the outside forces that might drive the creation and adoption of
9 innovative practices for reasons other than patient benefit. For example, in the 1990s, physicians
10 and payers faced political pressures from breast cancer patients, lobbyists, and patient advocate
11 groups to provide (and pay for) high-dose chemotherapy and autologous bone marrow transplant
12 (ABMT) to treat advanced stage cancer, despite lack of evidence for its efficacy.[33] Over 41,000
13 patients were exposed to expensive and very toxic treatment before ABMT was proven in formal
14 clinical trials to be no better than existing, proven treatments.[33]

15
16 Consultation & Oversight. Consulting with colleagues or other professionals in relevant specialties
17 before innovating in patient care can help ensure that a proposed innovation has been objectively
18 considered, is well grounded and minimizes risk. The value of consultation is reflected in the
19 Declaration of Helsinki, which recommends that physicians seek expert advice before using an
20 unproven intervention in patient care.[2] But what form of oversight or consultation, if any, is
21 appropriate for activities that fall somewhere between research and clinical care?

22
23 At its simplest, “consultation” can mean seeking input from a colleague before modifying an
24 accepted intervention during the course of caring for an individual patient. Or it can mean
25 discussing a new idea for improving an accepted intervention with another physician in the local
26 community or a colleague in a different specialty who might be able to offer insight. At its most
27 complex, “consultation” might involve formal review by an institutional body charged with
28 overseeing innovation in patient care, such as Stanford University’s practice of convening an
29 “innovative care committee” to review proposed innovations.[25]

30
31 Formal review has value insofar as it calls for well-thought out description of and justification for a
32 proposed innovation, systematically brings multiple perspectives to bear, and emphasizes balancing
33 anticipated benefits and risks to protect patients. However, Institutional Review Board (IRB)
34 review as such has also been criticized for causing “delays, confusion, and frustrations” at the
35 boundaries of clinical care and research and for overprotecting patients from low risk interventions
36 that could contribute to health care safety and quality.[5] Striking a balance between supporting
37 robust innovation and protecting the well-being of patients is key. The greater the departure from
38 accepted treatment or the more serious the foreseeable risks for the patient, the stronger is the
39 argument that physician-innovators should seek input from [colleagues and other](#) knowledgeable
40 professionals before pursuing an innovation

41
42 Institutions can contribute by creating clear strategies for pursuing innovation and policies to help
43 guide their individual physicians as they introduce innovation into practice. For example, Stanford
44 University’s “Innovative Care Guidelines” provide guidance for physicians on the level of review
45 appropriate for a specific innovative practice. A variety of outcomes are possible: the innovation
46 may be judged more akin to research and require IRB review; the risk-benefit ratio may be deemed
47 not to support proceeding with the proposed care as research or innovation; or the proposed
48 practice may be determined not to be truly innovative and thus can be handled through the
49 institution’s privileging process. If the proposed care is innovative and reasonable, Stanford
50 recommends the treatment be restricted to a small number of patients (1–5), from whom the
51 physician obtains informed consent (which includes discussing the innovative nature of the

1 treatment, risks, and alternatives), and that implementation of the innovation be monitored. If a
2 successful innovation is to be offered to a larger patient population, systematic study with a formal
3 research protocol and IRB review might then be required.[25]

4
5 Colleagues, other professionals in relevant areas of practice, professional societies, and health care
6 institutions can all play a role in providing meaningful consultation, guidance, and oversight in
7 order to facilitate innovation while protecting patients.

8
9 Sharing Knowledge Gained. Physicians' responsibility to share knowledge is well
10 recognized.[14,35,2] This responsibility is fulfilled when physician-innovators publish, present, or
11 otherwise make available knowledge they have gained during the course of innovation. This might
12 include sharing outcomes data from short- and long-term follow-up of patients who received an
13 innovative therapy, sharing information about relative risks and benefits (especially unanticipated
14 risks), and disclosing both positive and negative findings.

15
16 Intentionally withholding new knowledge, skills, or techniques for personal gain is "detrimental to
17 the medical profession and to society and is to be condemned." [35] Conversely, innovation
18 introduced prematurely or without significant evidence of its benefit can be both harmful to
19 patients and costly. [36] While it might not be feasible to carry out cost-effectiveness analysis in the
20 context of innovation, especially at the earliest stages of an innovation, physicians do have a
21 responsibility to be wise stewards of societal resources. Thus they have some measure of
22 responsibility for collecting and sharing information that can help assess the cost implications of an
23 innovative therapy. Gathering information about the resources needed to implement an innovation
24 effectively over the lifecycle of its development, as well as about risks and patient outcomes, can
25 lay the foundation for subsequent societal decisions about the relative value of an innovative
26 therapy.

27 28 IMPLICATIONS FOR PATIENT CARE

29
30 In addition to these broad considerations, long-standing ethical obligations in the realm of patient
31 care, as well as expectations for the responsible conduct of research, offer insight into issues that
32 physicians must address when they recommend innovative treatment for a particular patient.
33 Prominent considerations include obligations to minimize risk and to obtain the individual's
34 informed consent.

35 36 *Minimizing Risk*

37
38 When a physician recommends an innovative intervention to a patient, a key concern is whether,
39 and to what extent, a departure from standard therapy poses distinctive risks for the patient [20] and
40 the extent to which that risk can be minimized. The implication is that a decision to innovate in the
41 clinical care of a patient must rest on a physician's well-considered judgment that it is in the best
42 interest of the patient, given his or her clinical circumstances and the anticipated risks and benefits
43 of the innovation, to depart from established therapy in the way the physician proposes. This is in
44 keeping with physicians' general obligation to base treatment recommendations on patients'
45 medical needs.[14,28,38,13]. The physician must also have a scientifically grounded reason to
46 believe that the proposed departure from standard care will provide benefit to the patient
47 [18,cf.19,38], in keeping with the obligation to avoid recommending (or providing) an intervention
48 that is unlikely to achieve identified goals for care [39]. Physicians should not engage in medical
49 practices that have no scientific basis [40].

1 Depending on what specific innovation is contemplated and how much is or is not already known,
 2 it may be more or less challenging to assess whether the proposed benefits of a proposed
 3 intervention will exceed its risks. For example, the side effects of an approved drug are likely to be
 4 known (or to be reasonably predictable), while its effectiveness in an off-label use has not been
 5 demonstrated. It may be more difficult to predict the relative risks of a never-before-used surgical
 6 technique, such as different complications or longer healing time.

7 8 *Transparency & Informed Consent*

9
10 As for any medical intervention or enrollment in clinical research, the patient's informed consent is
 11 required before the use of an innovative therapy. The obligation to respect patient self-
 12 determination cuts across the continuum of research, innovation, and patient care. It requires both
 13 researchers and practicing clinicians to ensure that patients can have a meaningful role in making
 14 decisions about whether to participate in research or what care plans best addresses their values,
 15 preferences, and medical needs [41,42,28,43].

16
17 Brody argues that informed consent is best achieved when physicians are transparent about why
 18 they recommend a specific course of action.[44] In the context of innovation, transparency entails,
 19 at a minimum, informing the patient that the physician proposes to use an innovative therapy and
 20 how the innovation differs from standard therapy for the patient's condition, as well as explaining
 21 why the physician believes the particular innovative therapy is appropriate in the patient's
 22 circumstances. Just as the physician should inform a patient about the anticipated risks of standard
 23 therapy, the patient should be advised of the known risks posed by an innovative therapy.
 24 However, in the context of innovation, transparency also requires that the patient be informed that
 25 the innovative therapy may pose other, as-yet-unknown risks and medical uncertainties.[45]

26
27 Transparency is also best served when physicians provide other information patients can
 28 reasonably be expected to want to make informed decisions about health care. In the context of
 29 innovation, research suggests that patients want to know how much experience a physician has
 30 with a proposed innovation. For example, in one survey of 383 surgical patients, approximately 80
 31 percent indicated they wanted to know a surgeon's level of experience with a procedure before
 32 making decision about whether to have surgery.[46] Patients also wanted information about
 33 outcomes.[46] Physicians can enhance transparency and address patients' preferences for
 34 information by disclosing their level of experience with an innovative practice and the outcomes
 35 they have had when they introduce an innovation into their practice. For example, they can tell the
 36 patient that "To date, I have completed 4 surgeries, one of which required an extra day of
 37 hospitalization compared to the standard surgery." [47] Determining when such disclosure is no
 38 longer required because a physician has attained sufficient expertise will likely vary with the nature
 39 of the intervention and associated risks.

40
41 The responsibility to be transparent and candid is fundamentally no different when a physician
 42 seeks a patient's consent to try a novel intervention for the first time than at a later stage in the
 43 evolution of a particular innovative therapy. Informed consent still requires that the patient be made
 44 aware that a previously untried approach is proposed, what it entails (to the best of the physician's
 45 ability to predict), and why the physician recommends it.

46 47 BROADER IMPLICATIONS OF INNOVATION

48
49 Innovation carries implications for the health care system, and the wider community, as well as for
 50 individual patients. Among the most important are the possible influences of innovation on health

1 care costs and access to care. For example, how should considerations of responsible stewardship
2 influence decisions to innovate or disseminate particular innovations?
3

4 Innovation is double edged, insofar as it can both be a path to containing costs and a driver of cost
5 increases. “Technological innovation is believed to be responsible for the rise of the cost of health
6 care at 2 to 3 times the rate of inflation.”[3]
7

8 Nor is all innovation equally necessary—innovation for the sake of innovation alone is hard to
9 justify. As Callahan notes, “[u]nrestrained and cost-insensitive innovation needs to be stifled. In its
10 place must be put a prudent, priority-oriented, vision based on prevention, primary care medicine,
11 and low-cost technologies.”[48] Like Callahan, Fuchs argues that an environment of constrained
12 resources in health care, requires a “shift to value-conscious innovation instead of fostering the
13 ‘progress at any price’ attitude that has dominated biomedical innovation.”[49] Rather, innovation
14 must be reviewed for its effects on three areas: quality of care, cost and value.[49] Iserson similarly
15 argues that before an innovation is adopted into practice, consideration should be given to whether
16 it is safer, quicker, more effective, and cheaper or more cosmetic than standard care.[7]
17

18 Physicians’ responsibility to be prudent stewards of health care resources and to support access to
19 medical care for all people require that physicians take such considerations into account before
20 adopting or promoting innovative and as yet unproven therapies individually in their own practices
21 and collectively as a profession.[14,51,13,38]
22

23 RECOMMENDATION

24

25 In light of the foregoing considerations, the Council on Ethical and Judicial Affairs recommends
26 that the following be adopted and the remainder of this report be filed:
27

28 Innovation in medicine can range from improving an existing intervention, to introducing an
29 innovation in one’s own clinical practice for the first time, to using an existing intervention in a
30 novel way or translating knowledge from one clinical context into another. Innovation shares
31 features with both research and patient care, but is distinct from both.
32

33 When physicians participate in developing and disseminating innovative practices, they act in
34 accord with professional responsibilities to advance medical knowledge, improve quality of
35 care, and promote the well-being of individual patients and the larger community. Similarly,
36 these responsibilities are honored when physicians enhance their own practices by expanding
37 the range of techniques and interventions they offer to patients.
38

39 Individually, physicians who are involved in designing, developing, disseminating, or adopting
40 innovative modalities should:
41

- 42 (a) Innovate on the basis of sound scientific evidence and appropriate clinical expertise;
- 43
- 44 (b) Seek input from colleagues or other medical professionals in advance or as early as
45 possible in the course of innovation;
- 46
- 47 (c) Design innovations so as to minimize risks to individual patients and maximize the
48 likelihood of application and benefit for populations of patients; and
- 49
- 50 (d) Be sensitive to the cost implications of innovation;

- 1 (e) Be aware of influences that may drive the creation and adoption of innovative practices
2 for reasons other than patient or public benefit.
3

4 When they offer existing innovative diagnostic or therapeutic services to individual patients,
5 physicians must:
6

- 7 (f) Base recommendations on patients' medical needs;
8
9 (g) Refrain from offering such services until they have acquired appropriate knowledge
10 and skills;
11
12 (h) Recognize that in this context informed decision making requires the physician to
13 disclose:
14
15 i) how a recommended diagnostic or therapeutic service differs from the standard
16 therapeutic approach if one exists;
17
18 ii) why the physician is recommending the innovative modality;
19
20 iii) what the known or anticipated risks, benefits, and burdens of the recommended
21 therapy and alternatives are;
22
23 iv) what experience the professional community in general and the physician
24 individually has had to date with the innovative therapy; and
25
26 v) what conflicts of interest the physician may have with respect to the
27 recommended therapy.
28
29 (i) Discontinue any innovative therapies that are not benefiting the patient; and
30
31 (j) Be transparent and share findings from their use of innovative therapies with peers in
32 some manner. To promote patient safety and quality, physicians should share both
33 immediate or delayed positive and negative outcomes.
34

35 To promote responsible innovation, the medical profession should:
36

- 37 (k) Require that physicians who adopt innovative treatment or diagnostic techniques into
38 their practice have appropriate knowledge and skills;
39
40 (l) Provide meaningful professional oversight of innovation in patient care; and
41
42 (m) Encourage physician-innovators to collect and share information about the resources
43 needed to implement their innovative therapies effectively.
44

45 (New HOD/CEJA Policy)

Fiscal Note: Less than \$500.

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