

Coherence and correspondence in medicine

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Abstract

Many controversies in medical science can be framed as tension between a coherence approach (which seeks logic and explanation) and a correspondence approach (which emphasizes empirical correctness). In many instances, a coherence-based theory leads to an understanding of disease that is not supported by empirical evidence. Physicians and patients alike tend to favor the coherence approach even in the face of strong, contradictory correspondence evidence. Examples include the management of atrial fibrillation, treatment of acute bronchitis, and the use of Vitamin E to prevent heart disease. Despite the frequent occurrence of controversy stemming from coherence-correspondence conflicts, medical professionals are generally unaware of these terms and the philosophical traditions that underlie them. Learning about the coherence-correspondence distinction and using the best of both approaches could not only help reconcile controversy but also lead to striking advances in medical science.

Keywords: philosophy of science, theories of truth, medical decision making, coherence, correspondence.

1 Introduction

Theories of truth have been debated since the time of Aristotle. More recently in the twentieth century, philosophical discussion has focused on the distinction between “coherence” and “correspondence” theories of truth (Kirkham, 1992). The coherence approach seeks logic and explanation, often through the application of a scientific theory. The correspondence approach ignores theory in favor of empirical correctness. For example, the quality of a weather forecast predicting rain might be judged either with regard to a state-of-the-art forecast model (coherence) or whether it actually rained (correspondence).

Hammond (1996 & 2007) has argued that the concepts of coherence and correspondence are necessary for understanding and organizing research findings in the field of judgment and decision making. Likewise, I argue that they are necessary to understand conflicts in medicine. Although these concepts provide the foundation for medical research, the terms “coherence” and “correspondence” are virtually unknown to medical investigators and physicians alike. The distinction between science “making logical sense” (coherence) and being “empirically correct” (correspondence) seldom appears in the medical literature. This paper examines a number of medical controversies using the framework of coherence and correspondence and hypothesizes that fail-

ure to appreciate the differences between coherence and correspondence is the underlying cause of the controversies. Furthermore, reframing the disagreement in terms of two different, but equally useful, approaches may reduce or eliminate the controversies. Several illustrations of medical controversies show both the tension between the approaches as well as the explicit lack of awareness of these concepts. The paper concludes by illustrating how a unified approach that incorporates both philosophies can provide a useful framework to advance the field of medicine.

2 The origins of coherence and correspondence approaches in medicine

The development of coherence and correspondence approaches in medicine differs from its development in human activity in general. Hammond asserts that correspondence is the oldest strategy for assessing accuracy (Hammond, 2007, p. 29). For example, the success of hunting in the prehistoric world would have been assessed by correspondence accuracy (was food obtained) rather than by coherence standards (the quality of hunting techniques). In contrast, the field of medicine historically focused on coherence arguments, and only recently has attention been focused on correspondence approaches. For example, the original rationale for bloodletting was based

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on the notion that disease stems from an imbalance of humors. Hundreds of years elapsed before correspondence-based studies showed that bloodletting lacked efficacy (Morabia, 1996). From the present point of view, it seems surprising that physicians historically paid less attention to studying patient outcomes than on practicing medicine according to prevailing theories. However, given the large uncertainty in patient outcome (regardless of treatment) a correspondence approach would be difficult without modern statistical techniques.

Even today, coherence arguments carry enormous weight in justifying medical therapies. An important goal of biomedical research is the understanding of mechanisms of disease so that treatments can be specifically targeted to restore the normal state of affairs. Practicing physicians often use coherence arguments to explain their judgments. For example, physicians usually attribute tension headaches to spasm in the muscles of the scalp and neck even though this plausible explanation is incorrect based on the best available evidence (Rollnik, 2001). Furthermore, when diseases lack coherent explanations, physicians tend to doubt their validity. Examples include chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome (Goldenberg, 1999; Barsky, 1999; Prins, 2006).

The correspondence approach to medical research has gained visibility in the past several decades. This approach involves the systematic acquisition and statistical analysis of patient data in which outcomes are related to clinical cues (risk factors) and/or treatments. The Framingham study of heart disease (Kannel, 1961) produced the most famous, early correspondence results. Those investigators identified the now-familiar cardiac risk factors such as hypertension, smoking and hypercholesterolemia by observing a cohort of people over their adult lives. Later studies showed reduced cardiac disease and death among patients who successfully lowered their modifiable cardiac risk factors.

This correspondence approach made no effort to explain *why* the risk factors were associated with cardiac disease. Hypertension proved particularly problematic in this regard. For many years it was not clear that hypertension could even be called a disease (Jennings, 1991). The concept of essential (unexplained) hypertension lacks coherence. Early theories postulated that artery narrowing and loss of elasticity from atherosclerosis “necessitated a hypertension of the blood to compensate for the circulatory interference” (Ambard, 1904, p. 308). It would take years for the medical profession and the public to accept the importance of treating mild degrees of hypertension. For example, George Pickering, a highly respected hypertension specialist, wrote: “Essential hypertension represents no more than that section of the population having arterial pressures above a certain level, selected on arbi-

trary grounds, and having no disease to account for these arterial pressures” (Pickering, 1955, p. 130). He later advises no specific treatment for patients without symptoms unless their pressure is high enough to “seriously endanger life” (Pickering, 1955, p. 337). In 1970, correspondence data finally provided convincing evidence that lowering moderate elevations in blood pressure improved morbidity (VA Cooperative Study Group, 1970).

In the 1990s, the correspondence approach gained momentum in the form of the evidence-based medicine (EBM) movement. Its proponents define EBM as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research” (Sackett, 1996, p. 71). EBM represented a new attention to correspondence. An EBM working group convened and published their philosophy: “Evidence-based medicine de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research” (Guyatt, 1992, p. 2420). However, EBM does allow for coherence to play a role in medical judgment in cases where correspondence evidence bearing on patients’ problems is sparse.

3 Atrial fibrillation as a model of coherence-correspondence conflict

The current controversy about how to manage atrial fibrillation illustrates the tension between coherence and correspondence competence in medicine. Atrial fibrillation is the most common sustained cardiac rhythm disturbance (Fuster, 2006). It is characterized by irregular, chaotic electrical activity of the atria, the upper chambers of the heart, which leads to an irregular and often rapid heartbeat. The decreased cardiac output and irregular rhythm can cause fatigue, shortness of breath, and palpitations.

Historically, recommendations for treating atrial fibrillation were correspondence-based. When first described about 100 years ago, atrial fibrillation was generally managed with rest and digitalis (Stevens, 1922, p. 640). These measures slowed the heart rate and ameliorated the symptoms but did not correct the underlying rhythm disturbance. Later, the development of effective antiarrhythmic treatments led to a shift in therapy based on coherence arguments. The “new” approach sought to restore normal sinus rhythm (“rhythm control”) by means of electric shock, anti-arrhythmic drugs, or both. Indeed, there are

strong coherence arguments in favor of the rhythm control strategy. A slow, regular rhythm produced by normal heart action:

1. moves blood more efficiently by allowing adequate filling time for each beat;
2. restores the “atrial kick,” whereby the atria help complete ventricular filling before the main pumping action; and
3. avoids clot formation in the left atrium and also prevents strokes caused by dislodged clots.

Some cardiologists have returned to the older correspondence approach by suggesting that simply slowing the heart rate (“rate control”), without restoring a regular rhythm, might be good enough to control symptoms and would avoid the side effects of anti-arrhythmic drugs. Thus, the controversy hinges on whether the goal should be to restore normal cardiac rhythm (coherence) or control the heart rate to relieve symptoms (correspondence).

Since 2002, several teams of investigators have addressed this controversy by directly comparing the rhythm control and rate control strategies. The AFFIRM study randomized 4060 patients with atrial fibrillation to either rhythm-control or rate-control strategies and compared rates of death, hospitalization, and adverse drug effects (AFFIRM Investigators, 2002). The investigators reported: “The strategy of restoring and maintaining sinus rhythm had no clear advantage over the strategy of controlling the ventricular rate and allowing atrial fibrillation to persist. There was a trend toward increased mortality in association with the rhythm-control strategy” (p. 1829). The rhythm-control group had more subsequent hospitalizations and many more adverse drug effects. There was no difference in stroke rates between the two groups. The authors concluded: “None of the presumed benefits of rhythm control . . . were confirmed in this study. The implication is that rate control should be considered a primary approach to therapy . . .” (p. 1832). A European study with very similar findings was published in the same journal issue (Van Gelder, 2002). These two studies provided strong evidence that rate control leads to better outcomes than rhythm control.

Some cardiologists, however, discount this correspondence data in favor of the coherence arguments for rhythm control. For example, the editorial published with the AFFIRM and European trials questioned the generalizability of the findings, noting that most of the study patients had recurrent atrial fibrillation which might indicate a “propensity for recurrent arrhythmia” (Falk, 2002). Regarding a first episode of atrial fibrillation, the editorial states, “An attempt to restore sinus rhythm is appropriate, although it can no longer be deemed imperative” (p. 1884). In essence, the editorial questions the newly published correspondence data, and using coherence argu-

ments, suggests that the rhythm control strategy may be preferable. Even with the publication of additional well-designed trials showing better outcomes with rate control (Carlsson, 2003; Opolski, 2004), the controversy continues. A recent paper on antiarrhythmic therapy states: “The hemodynamic consequences of atrial fibrillation result primarily from the loss of atrioventricular synchrony but also from the rapid rate and irregularity of the ventricular response” (Zimetbaum, 2007, p. 936). The proponents of these differing points of view do not appear to realize that the disagreement stems from using different means to evaluate truth.

The compelling logic that a normal rhythm should be optimal has led to a randomized trial targeting patients expected to particularly benefit from rhythm control: those with both atrial fibrillation and heart failure (Roy, 2008). The study findings, however, again favored rate control and continued to surprise cardiologists advocating a coherence-based approach. An accompanying editorial articulates their disappointment: “Nature has equipped the human heart with a complex electrical system for the purpose of coordinated propulsion of blood under a variety of physiologic conditions. Considerable effort is expended by the heart to maintain sinus rhythm. Cardiac electrophysiologists . . . are frustrated by the conundrum that atrial fibrillation is associated with increased morbidity and mortality, yet attempts to prove that a strategy to maintain nature’s rhythm has a favorable effect on patients have been met with one setback after another” (Cain, 2008, p. 2725).

4 Physicians lack insight about the coherence-correspondence distinction

Although many past and current controversies in medicine stem from the tension between coherence and correspondence approaches, the field of medicine is generally unaware of the philosophical concepts of coherence and correspondence. Thus, physicians fail to understand why their points of view differ. Table 1 lists a number of other examples of recent controversies from various medical specialties. Usually, the coherence view comes first, followed later by contradictory correspondence evidence from clinical trials. Physicians are drawn to explanations that “make sense” or using Kuhn’s terminology, conform to the “paradigm” (Kuhn, 1962). The compelling nature of coherence arguments causes physicians to resist evidence-based recommendations that contradict their notions of disease mechanisms. For example, many physicians still prescribe antibiotics for otherwise

Table 1: Examples of controversies based on coherence/correspondence differences

Topic	Coherence view	Correspondence view	References
Antibiotics for acute bronchitis	Since bronchitis involves infection of the airways in the lungs, antibiotics should help.	Studies of antibiotics for bronchitis fail to show a benefit for most patients.	Braman, 2006 Wenzel, 2006
High dose chemotherapy for breast cancer	More chemotherapy should lead to better outcomes.	High dose chemotherapy with bone marrow transplantation has been shown not to be beneficial in breast cancer.	Lippman, 2000 Mello, 2001 Stadtmauer, 2000
Long-acting bronchodilators for asthma	Asthma is reversible airways obstruction. Bronchodilators reduce the degree of obstruction.	Long-acting bronchodilators are associated with severe exacerbations and increased asthma mortality	Nelson, 2006
Weight loss diets	High-fat foods should be avoided if the goal is to reduce fat.	Evidence points to carbohydrate restriction as being as effective as fat restriction for long-term weight loss.	Bonow, 2003 Foster, 2003 Stern, 2004 La Berge, 2008
Vitamin E to prevent heart disease	Anti-oxidants such as vitamin E thought to prevent cell damage.	Large clinical trials show no evidence of benefit.	Tatsioni, 2007
Cancer-related anemia	Use a blood forming hormone (erythropoietin) to treat anemia.	Evidence shows worse outcome with erythropoietin.	Tefferi, 2007

healthy patients with acute bronchitis despite considerable evidence that antibiotics don't help (Braman, 2006; Fowler, 2006). Many rationalize the decision based on perceived patient demand, but that too has its origins in coherence: "If antibiotics cure pneumonia, and bronchitis is another type of lung infection, antibiotics must good for bronchitis, too." The EBM working group implicitly recognized the allure of coherence when it stated: "The study and understanding of basic mechanisms of disease are necessary but insufficient guides for clinical practice. The rationales for diagnosis and treatment, which follow from basic pathophysiologic principles, may in fact be incorrect . . ." (Guyatt, 1992, p. 2421).

A recent publication titled "Persistence of contradicted claims in the literature" explicitly discussed the reluctance to change behavior even when strong, contradictory evidence-based data appear (Tatsioni, 2007). The authors specifically focused on claims that Vitamin E, acting as an antioxidant, decreased cardiovascular disease. By 2004, the authors reported, published randomized trials, meta-analyses, and practice guidelines all provided correspondence evidence against any benefit of Vitamin E. Nevertheless, Tatsioni and colleagues found numerous arguments in the literature that tended to discredit

the correspondence evidence and defend the effectiveness of Vitamin E. The arguments included purported biases in study design, diversity of participants, issues with bioavailability of Vitamin E, co-interventions, and inadequate duration of follow-up before assessing outcomes. The authors reported similar findings for claims of beta-carotene for cancer prevention and estrogen for dementia prevention. In discussing these findings, the authors state: "The defense of the observational associations was persistent, despite the availability of very strong contradicting randomized evidence on the same topic. Thus, one wonders whether any contradicted associations may ever be entirely abandoned, if such strong randomized evidence is not considered as much stronger evidence on the topic." They go on to suggest: ". . . better communication between research specialists and evidence-based clinical science may improve this situation and may lead to more rational and concerted translational efforts in basic, pre-clinical, and clinical research" (p. 2525). Interestingly, the terms "coherence" and "correspondence" never appear in the paper despite the obvious application of the concepts. Reframing the controversy in terms of the competing meta-theories of truth clarifies the reasons for the persistence of the coherence-based views.

5 Coherence and correspondence approaches to medical research

Traditional medical research tends to be coherence-oriented and driven by theory. The ultimate test of a theory, however, is confirmation with correspondence-based observations. When observations contradict coherence theory, investigators may be tempted to either discard the theory or question the validity of the observational data. However, paying attention to the coherence-correspondence conflict and searching for the underlying causes of unexpected findings has led to some important therapeutic advances. A particularly striking example is the drug sildenafil (Viagra™). Scientists at the Pfizer pharmaceutical company initially applied a coherence approach to develop a new drug for hypertension and angina based on its theoretical relaxation of smooth muscle in blood vessels. The drug development process was called “rational drug design” (Kling, 1998). The investigators then proceeded with correspondence-based clinical trials. The drug failed to lower blood pressure, but investigators had noted that subjects reported erections as a side effect. By doing further coherence-based research, the company was able to demonstrate how the drug could plausibly treat erectile dysfunction. A change in our understanding of the disease from being a psychological problem to a blood vessel problem was also needed for the coherence approach to succeed.

The dramatic success of this medication illustrates the value of applying both coherence and correspondence standards in research. Had the investigators focused only on the coherence-driven approach, they would have interpreted sildenafil as a failure because the drug was not effective for hypertension. Paying attention to the correspondence evidence led to the scientific advance.

The recent influence of EBM with its emphasis on correspondence through clinical trials may lead to the impression that to evaluate truth by coherence in medicine is an unscientific approach. However, this is not the case. Much of current medical knowledge is coherence-based and has stood the test of time as well as being confirmed by correspondence-based methods. The recent advances in immunology and cytogenetics, which have led to novel biological treatments for cancer and autoimmune diseases, illustrate the importance of the coherence approach to modern medicine. For example, research on the genetic abnormalities in chronic myelogenous leukemia has found an abnormal protein made in tumor cells. The drug imatinib was specifically developed to inhibit this protein and in clinical trials has produced striking improvements in patient outcomes (Savage, 2002). As with

the sildenafil story, both coherence and correspondence methods contributed to the imatinib breakthrough.

6 Conclusions

Classifying medical research methods according to their use of either coherence or correspondence approaches provides considerable insight. The historical emphasis on coherence-based theory has shifted to correspondence-based outcomes research and evidence-based medicine. Both coherence and correspondence approaches have advantages and disadvantages — neither is always the “correct” standard of truth. Medical scientists’ and practitioners’ lack of familiarity with these philosophical traditions has produced many instances of controversy in which the source of disagreement simply stems from different methods of evaluating truth.

Teaching physicians about the value of each of the two approaches may not only help reduce controversy but can also identify fruitful avenues for further research. Physicians could gain considerable insight by recognizing situations in which correspondence-based outcomes data conflict with prevailing coherence-based theories. The historical tendency to discount the correspondence data in favor of prevailing theory should be replaced by a search for truth guided by both philosophical traditions together. Coherence and correspondence should become part of the standard medical lexicon. Familiarity with these concepts could provide a useful framework for understanding and resolving medical controversies. As the sildenafil and imatinib stories illustrate, the resulting medical advances can be striking.

References

- AFFIRM Investigators. (2002). A comparison of rate control and rhythm control in patients with atrial fibrillation. *The New England Journal of Medicine*, 347, 1825–1833.
- Ambard, L. & Beaujard, E. (1904). Causes of arterial hypertension. In A. Ruskin (Ed.), (1956), *Classics in arterial hypertension*. pp. 297–310. Springfield, IL: Charles Thomas Press.
- Barsky, A. J., & Borus, J. F. (1999). Functional somatic syndromes. *Annals of Internal Medicine*, 130, 910–921.
- Bonow, R. O., & Eckel, R. H. (2003). Diet, obesity and cardiovascular risk. *The New England Journal of Medicine*, 248, 2057–2058.

- Braman, S. S. (2006). Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines. *Chest*, *129*, 95–103.
- Cain, M. E. (2008). Rhythm control in atrial fibrillation—one setback after another. *The New England Journal of Medicine*, *258*, 2725–2727.
- Carlsson, J., Miketic, S., Windeler, J., Cuneo, A., Huan, S., Micus, S., Walter, S., & Tebbe, U., for the STAF investigators. (2003). Randomized trial of rate-control versus rhythm-control in persistent atrial fibrillation: The strategies of treatment of atrial fibrillation (STAF) study. *Journal of the American College of Cardiology*, *41*, 1690–1696.
- Falk, R. H. (2002). Management of atrial fibrillation — radical reform or modest modification? *The New England Journal of Medicine*, *347*, 1883–1884.
- Foster, G. D., Wyatt, H. R., Hill, J. O., McGuckin, B. G., Brill, C., Mohammed, B. S., Szapary, P. O., Rader, D. J., Edman, J. S., & Klein, S. (2003). A randomized trial of a low-carbohydrate diet for obesity. *The New England Journal of Medicine*, *248*, 2082–2090.
- Fuster, V., Ryden, L. E., Cannom, D. S., Crijns, H. J., Curtis, A. B., Ellenbogen, K. A., Halperin, J. L., Le Heuzey, J., Kay, G. N., Lowe, J. E., Olsson, S. B., Prystowsky, E. N., Tamargo, J. L., & Wann, S. (2006). ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. *Circulation*, *114*, e257–e354.
- Goldenberg, D. L. (1999). Fibromyalgia syndrome a decade later: What have we learned? *Archives of Internal Medicine*, *159*, 777–785.
- Guyatt, G. for The evidence-based medicine working group. (1992). Evidence-based medicine: a new approach to teaching the practice of medicine. *JAMA* *268*, 2420–2425.
- Hammond, K. R. (1996). *Human judgment and social policy: Irreducible uncertainty, inevitable error, unavoidable injustice*, pp. 103–110. New York, NY: Oxford University Press.
- Hammond, K. R. (2007). *Beyond rationality: the search for wisdom in a troubled time*. New York, NY: Oxford University Press.
- Jennings, D., & Netsky, M. G. (1991). Essential hypertension: a sign in search of a disease. *Canadian Medical Association Journal*, *144*, 973–979.
- Kannel, W. B., Dawber, T. R., Kagan, A., Revotskie, N., & Stokes, J. I. (1961). Factors of risk in the development of coronary heart disease — six year follow-up experience; the Framingham study. *Annals of Internal Medicine*, *55*, 33–50.
- Kirkham, R. L. (1992). *Theories of truth: A critical introduction*. Cambridge, MA: MIT Press.
- Kling, J. (1998). From hypertension to Viagra. *Modern Drug Discovery* *1*, 31–38.
- Kuhn, T. S. (1962). *The structure of scientific revolutions*. Chicago, IL: University of Chicago Press.
- La Berge, A. F. (2008). How the ideology of low fat conquered America. *Journal of the History of Medicine and Allied Sciences*, *63*, 139–177.
- Lippman, M. E. (2000). High-dose chemotherapy plus autologous bone marrow transplantation for metastatic breast cancer. *The New England Journal of Medicine*, *342*, 1119–1120.
- Mello, M. M., & Brennan, T. A. (2001). The controversy over high-dose chemotherapy with autologous bone marrow transplant for breast cancer. *Health Affairs*, *20*, 101–117.
- Morabia, A. (1996). P. C. A. Louis and the birth of clinical epidemiology. *Journal of Clinical Epidemiology*, *49*, 1327–1333.
- Nelson, H. S., Weiss, S. T., Bleecker, E. R., Yancey, S. W., & Dorinsky, P. M. (2006). The Salmeterol multicenter asthma research trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. *Chest*, *129*, 15–26.
- Opolski, G., Torbicki, A., Kosior, D. A., Szulc, M., Wozakowska-Kaplon, B., Kolodziej, P., & Achremczyk, P., for the Investigators of the Polish HOT CAFÉ trial. (2004). Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish how to treat chronic atrial fibrillation (HOT CAFÉ) Study. *Chest*, *126*, 476–486.
- Pickering, G. W. (1955). *High blood pressure*. New York, NY: Grune & Stratton.
- Prins, J. B., Van der Meer, J. W. M., & Bleijenberg, G. (2006). Chronic fatigue syndrome. *Lancet* *267*, 346–355.
- Rollnik, J. D., Karst, M., Fink, M., & Dengler, R. (2001). Botulinum toxin type A and EMG: A key to the understanding of chronic tension-type headaches? *Headache*, *41*, 985–989.
- Roy, D., Talajic, M., Nattel, S., Wyse, D. G., Dorian, P., Lee, K. L., Bourassa, M. G., Arnold, J. M. O., Buxton, A. E., Camm, A. J., Connolly, S. J., Dubuc, M., Ducharme, A., Guerra, P. G., Hohnloser, S. H., Lambert, J., Le Heuzey, J., G. O'Hara, Pedersen, O. D., Rouleau, J., Singh, B. N., Stevenson, L. W., Stevenson, W. G., Thibault, B., & Waldo, A. L., for the atrial fibrillation and congestive heart failure investigators. (2008). Rhythm control versus rate control for atrial fibrillation and heart failure. *The New England Journal of Medicine*, *358*, 2667–2677.

- Sackett, D. L., Rosenberg, W. M. C., Gray, J. A. M., & Haynes, R. B. (1996). Evidence based medicine: what it is and what it isn't. *British Medical Journal*, *312*, 71–72.
- Savage, D. G., & Antman, K. H. (2002). Imatinib mesylate — a new oral targeted therapy. *The New England Journal of Medicine*, *246*, 683–693.
- Stadmauer, E. A., O'Neill, A., Goldstein, L. J., Crilley, P. A., Mangan, K. F., Ingle, J. N., Brodsky, I., Martino, S., Lazarus, H. M., Erban, J. K., Sickles, C., Glick, J. H., and the Philadelphia bone marrow transplant group. (2000). Conventional-dose chemotherapy compared with high-dose chemotherapy plus autologous hematopoietic stem-cell transplantation for metastatic breast cancer. *The New England Journal of Medicine*, *342*, 1069–1076.
- Stern, L., Iqbal, N., Seshadri, P., Chicano, K. L., Daily, D. A., McGrory, J., Williams, M., Gracely, E. J., & Samaha, F. F. (2004). The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Annals of Internal Medicine*, *140*, 778–785.
- Stevens, A. A. (1922). *The practice of medicine*. Philadelphia: Saunders.
- Tatsioni, A., Bonitsis, N. G., & Ioannidis, J. P. A. (2007). Persistence of contradicted claims in the literature. *JAMA*, *298*, 2517–2526.
- Tefferi, A. (2007). Pharmaceutical erythropoietin use in patients with cancer: Is it time to abandon ship or just drop anchor? *Mayo Clinic Proceedings*, *82*, 1316–317.
- Van Gelder, I. C., Hagens, V. E., Bosker, H. A., Kingma, J. H., Kamp, O., Kingma, T., Said, S. A., Darmanata, J. I., Timmermans, A. J. M., Tijssen, J. G. P., & Crijns, H. J. G. M., for the rate control versus electrical cardioversion for persistent atrial fibrillation study group. (2002). A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *The New England Journal of Medicine*, *347*, 1834–1840.
- Veterans Administration Cooperative Study Group on Antihypertensive Agents: (1970) II. Effects of treatment on morbidity in hypertension: results in patient with diastolic blood pressures averaging 90 through 114 mm Hg. *JAMA*, *213*, 1143–52.
- Wenzel, R. P., & Fowler, A. A. (2006). Acute bronchitis. *The New England Journal of Medicine*, *355*, 2125–2130.
- Zimetbaum, P. (2007). Amiodarone for atrial fibrillation. *The New England Journal of Medicine*, *356*, 935–941.