Is basic science disappearing from medicine? The decline of biomedical research in the medical literature

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ABSTRACT **Explosive growth in our understanding of genomics and molecular biology have fueled calls for the pursuit of personalized medicine, the notion of harnessing biologic variability to provide patient-specific care. This vision will necessitate a deep understanding of the underlying pathophysiology in each patient. Medical journals play a pivotal role in the education of trainees and clinicians, yet we suspected that the amount of basic science in the top medical journals has been in decline. We conducted an automated search strategy in PubMed to identify basic science articles and calculated the proportion of articles dealing with basic science in the highest impact journals for 8 different medical specialties from 1994 to 2013. We observed a steep decline (40–60%) in such articles over time in almost all of the journals examined. This rapid decline in basic science from medical journals is likely to affect practitioners' understanding of and interest in the basic mechanisms of disease and therapy. In this Life Sciences Forum, we discuss why this decline may be occurring and what it means for the future of science and medicine.—Steinberg, B. E., Goldenberg, N. M., Fairn, G. D., Kuebler, W. M., Slutsky, A. S., Lee, W. L. Is basic science disappearing from medicine? The decline of biomedical research in the medical literature.** ***FASEB J.*** **30, 515–518 (2016). www.fasebj.org**

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For centuries, clinicians have maintained their competency and kept abreast of scientific advances by regularly consulting medical journals. This practice persists; reading of peer-reviewed journals remains one of the top sources of information for clinicians (1).

One area of medicine that has undergone rapid change is our understanding of the molecular basis of disease. In fact, advances brought by the molecular and genomic eras have led to the possibility of personalized medicine; for example, the recently announced Precision Medicine Initiative (2) focuses on individual biologic variability with the goal of providing tailored, patient-specific care. This ambitious vision will require an exceptionally integrated understanding of genomic, biochemical, and bioinformatic information. Because it is ultimately clinicians who will be tasked with delivering personalized medicine, it is reasonable to expect medical journals to keep them abreast of advances in our understanding of the mechanisms of disease and of human biology.

As scientists and clinicians at an academic center, we have anecdotally noted fewer basic science advances being presented in widely read, high-impact medical journals. This is mirrored by a decreased emphasis on basic research and the mechanisms of disease within North American clinical and academic programs (3, 4). Indeed, medical trainees perceive biomedical sciences as being less relevant to clinical care (5), paralleling a long-standing concern in medical education over the retention of basic science knowledge (6). We considered the possibility that a decline in the profile of basic science research might induce a self-fulfilling prophecy: if trainees and clinicians never see such research, would it be surprising that they come to perceive it as relatively unimportant?

To test whether our impression about the decline in the representation of basic science in the medical literature was correct, we quantified the prevalence of basic science articles in specialty medical journals over the last 20 years. We hypothesized that over the past 20 years, medical journals have been reporting progressively less fundamental research despite an exponential increase in basic scientific knowledge.

MATERIALS AND METHODS

Using a bibliometric approach, we devised a search strategy for the National Center for Biotechnology Information PubMed database to identify basic science articles for the 20-year period spanning 1994–2013; we omitted 2014 and 2015 to avoid inclusion of incomplete PubMed records. The search was run with the following terms: (Journal Title[journal]) AND (cellular* [Title/Abstract] OR cell[Title/Abstract] OR animals[Title/Abstract] OR Biologic Markers[mh] OR mice OR Polymorphism[mh] OR pathway[Title/Abstract] OR mechanism[Title/Abstract] OR cytokine[Title/Abstract] OR signal transduction [mh] OR animal[mh] NOT clinical trial[Publication Type] NOT editorial[Publication Type] NOT Case Reports[Publication Type] NOT Practice Guideline[Publication Type] NOT Comment[Publication Type]).

To avoid selection bias, we surveyed the highest-impact specialty medical journals in cardiology, endocrinology, gastroenterology,

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infectious diseases, nephrology, neurology, oncology, and pulmonology (**Table 1**). As a control, we identified the prevalence of basic science articles in the *Journal of Biological Chemistry*, the *Journal of Clinical Investigation*, and *Cell*, 3 well-known nonclinical journals dealing with biologic sciences.

Our search strategy intentionally defined basic science articles broadly, including any article involving cell culture or animal models. We specifically included publications dealing with disease pathogenesis, human physiology, biologic markers of disease, and genetic polymorphisms. For comprehensiveness, the search included review articles that presented or compiled basic science data. Clinical trials, case reports, practice guidelines, editorials and commentary, letters to the editor, clinical case and image presentations, and book reviews were all excluded from the search for basic science content; conversely, the *total* number of articles for the given journal and year was used as the denominator. To calculate the sensitivity of the search strategy, we manually identified the first 25 basic science articles from the tables of contents, abstracts, and full text of individual journals and determined what proportion of the identified articles was detected by the automated search. The specificity of the automated search was determined by manually reviewing the first 25 articles identified by our search and adjudicating which constituted basic science. This process was repeated independently by the authors for the years 1994 and 2013; disagreements were resolved by consensus. The sensitivity and specificity for the surveyed journals are provided in Table 1. As a control, clinical trials were identified using the Medical Subject Heading "Clinical trial."

The fold change in the proportion of journal articles made up by basic science from 1994 to 2013 was calculated by subtracting the figure for 2013 from the corresponding number for 1994, then dividing by the proportion for 1994. For journals that began publication after 1994, the first year of publication was used instead.

For comparison, we also considered the 3 highest-impact general medical journals: *Lancet*, *JAMA*, and the *New England Journal of Medicine*. Although the automated search performed well in the specialty journals, its specificity was very low in these journals as they publish few basic science articles. Accordingly, we manually determined the number of basic science articles in these 3 journals at the beginning and at the end of the 20-year period. To do so, we manually reviewed the first, fourth, and sixth issues of each journal for the years 1994, 1996, 2012, and 2014. The proportion of articles dealing with basic science was then averaged for each year.

RESULTS

We observed a marked decline in the frequency of basic science articles from 1994 to 2013 in 6 of 8 medical specialty journals (**Fig. 1*A***). When the results for the 8 journals were pooled, 73.3 ± 7.2% (means ± SD) of articles in 1994 were classified as relating to basic science. This proportion fell to 51.1 ± 11.6% by 2013, reflecting a relative decline of 30%. For the 6 journals in which the proportion of basic science fell, the decline ranged from approximately 40–60% and was highly statistically significant (Table 1). In contrast, the *Journal of Biological Chemistry*, *Journal of Clinical Investigation*, and *Cell* demonstrated no change in the proportion of basic science articles over time (Fig. 1*B*). This indicates that the observed decrease within medical specialty journals is not an artifact of our search strategy. As an additional control, the proportion of articles dealing with clinical trials did not change over the same period (Fig. 1*B*). Although the total number of articles published by the specialty journals increased over time, the magnitude of the increase was highly variable between journals and was not statistically significant in some cases (Fig. 1*C* and not shown), which indicates that the decline in basic science in the specialty journals reflects both an increase in nonbasic science content and an absolute decline in the number of basic science articles in some of the journals.

Our automated search strategy was deliberately designed for high sensitivity, which exceeded 80–90% in most cases. Not surprisingly, the specificity of our search was lower, ranging from approximately 40–98% across all journals and years (Table 1). The manual search of the top general medical journals revealed little basic science content at both the beginning and the end of the 20-year period (**Fig. 2**).

DISCUSSION

Our data demonstrate a steep decline in the frequency of basic science articles over the last 20 years**;** its consistency across 6 of 8 of the highest impact medical specialty journals suggests that the trend is widespread and not due to selection

TABLE 1. *Operating characteristics of the automated PubMed search*

Journal	Sensitivity		Specificity		Fold change in the proportion of basic science articles, 1994–2013	*P* value[a]
	1994	2013	1994	2013		
American Journal of Respiratory and Critical Care Medicine	0.8	1.0	0.88	0.7	0.53	0.00001
Diabetes Care	0.89	0.86	0.71	0.56	1.01	0.62
Gastroenterology	0.96	0.88	0.98	0.8	0.49	0.0003
The Lancet Neurology	1.0	0.76	0.48	0.8	0.55	0.00004
Journal of American College of Cardiology	0.84	0.83	0.88	0.62	0.55	0.000001
The Lancet Infectious Diseases	1.0	0.96	0.34	0.4	0.41	0.004
Journal of the American Society of Nephrology	0.84	0.92	0.64	0.78	0.97	0.28
The Lancet Oncology	1.0	0.92	0.62	0.36	0.50	0.00004

For the first and last year examined (1994 and 2013), sensitivity and specificity of the search was calculated for each journal. For journals that began publication after 1994, the first year of publication was used. The second column from the right shows the fold change in the frequency (proportion) of basic science articles in the last year compared with the first year of the search period. [a]A 2-tailed Student's *t* test was performed to compare the proportion of articles dealing with basic science in the periods 1994–1998 to 2009–2013. For journals in which publication started after 1994, the first 5 years of publication were used instead.

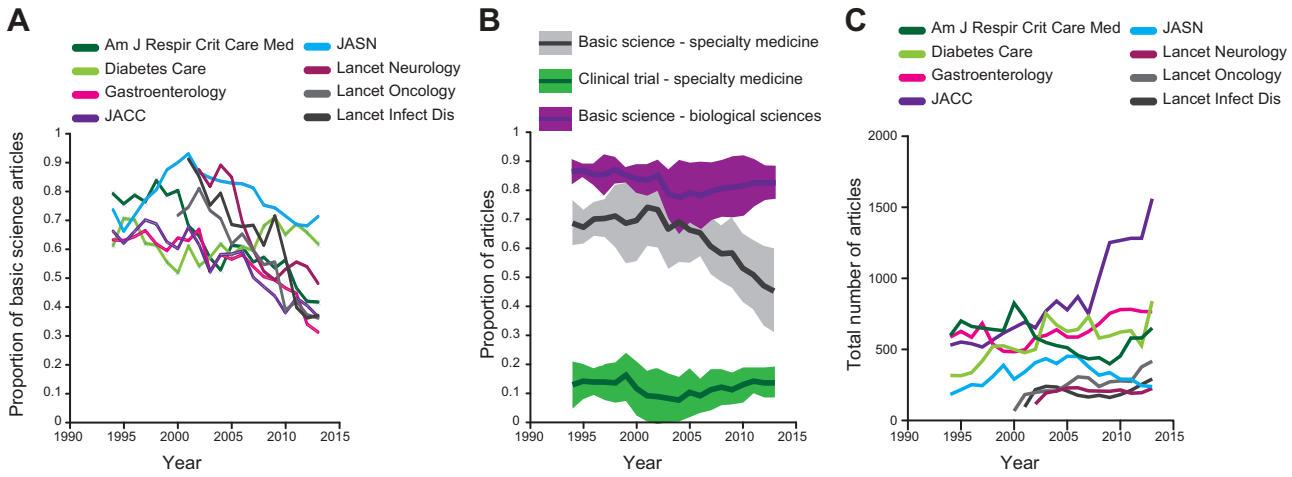

Figure 1. *A*) Changing proportion of basic science articles in the top journals from 8 medical specialties from 1994 to 2013. Data are presented as the number of basic science articles divided by the total number of publications listed in PubMed for the given journal and year. *B*) The same search strategy was applied to the *Journal of Biological Chemistry*, *Journal of Clinical Investigation*, and *Cell*, 3 well-known nonclinical biologic science journals. The proportion of basic science articles in these 3 journals was averaged (purple line) and compared with the average proportion of basic science articles in the 8 medical specialty journals (black line). Data are plotted as average (line) ± SD (shaded area). As another control, the proportion of articles comprising clinical trials in the 8 medical specialty journals is shown (green line). Am J Respir Crit Care Med, *American Journal of Respiratory and Critical Care Medicine*; JACC, *Journal of the American College of Cardiology*; JASN, *Journal of the American Society of Nephrology*; Lancet Infect Dis, *The Lancet Infectious Diseases*. Data are plotted as average (line) ± SD (shaded area). *C*) Total number of articles published by the medical specialty journals over the same period.

bias. A baseline and consistent paucity of basic science content is also apparent within general medical journals.

The robustness of our automated search strategy was established in a number of ways. First, we determined the sensitivity and specificity of our strategy for each journal at both the beginning and the end of the 20-year period. Second, as a control, we demonstrated that there was no decline in the proportion of basic science articles published by 3 well-known nonclinical biologic science journals. Third, as an additional control, we demonstrated that the proportion of articles dealing with clinical trials in the same 8 journals did not decline over the 20-year period (Fig. 1*B*).

Of note, our search strategy was sensitive (Table 1), meaning that relatively few basic science articles were likely to have been missed; furthermore, our specificity was lower, suggesting that the true frequency of basic science articles is likely to be lower. Taken together, our data indicate that the number of basic science articles being presented to clinicians through the top specialty medical journals is in sharp decline.

The reasons for this drop are unclear, but may reflect an editorial preference away from basic science research. We speculate that this may be in part due to the higher citation frequency of clinical papers compared with those presenting basic scientific discovery (7), as citations contribute directly to a journal's impact factor. The fading of basic science from medical journals also parallels the rise of clinical epidemiology and more recently the emphasis on quality of care, medical education, health systems, and ethics. Indeed, the total number of articles published by some of the journals increased over the 20-year period, likely reflecting this change in content (Fig. 1*C*). However, it is instructive that the proportion of studies made up by clinical trials has remained constant, while the fraction representing basic science is plummeting.

Some may argue that the proliferation of journals dedicated solely to basic science accounts for its disappearance from medical journals. In fact, some clinical journals have largely assigned basic science manuscripts to associated biomedical journals. It is worth noting, however, that these journals typically have lower impact factors than medical journals. Thus, preferential selection of these specialized journals by authors is unlikely to account for the decline we observed. More to the point, these basic science specialty journals are less likely to be read by medical trainees and by practicing clinicians than medical journals, even if published by clinical societies.

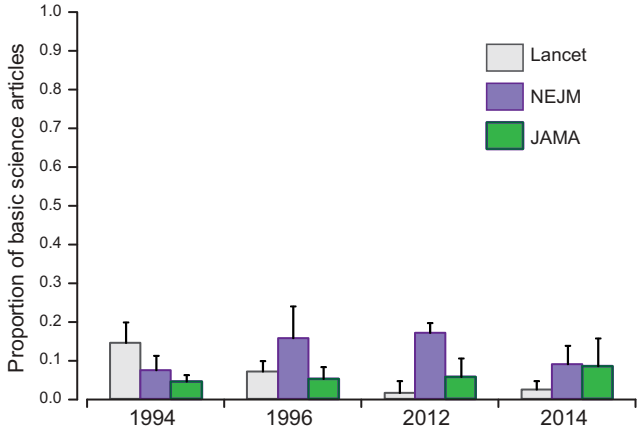

Figure 2. Proportion of basic science articles in the 3 highest impact general medical journals during the years indicated. Data are mean and SD. JAMA, *Journal of the American Medical Association*; NEJM, *New England Journal of Medicine*.

What are the implications of this trend? If the decline continues, could basic science actually disappear from the pages of specialty medical journals? Are there any consequences to decreasing exposure of clinicians to basic science? One possibility is that clinicians have diminished experience with the pathogenesis of disease and mechanisms of therapy, and thus will have less understanding of or interest in these concepts. The paucity of basic science in the top medical specialty journals may send a subconscious message to trainees and practitioners that basic science research is either irrelevant to clinical medicine or simply uninteresting. This decreased exposure could also contribute to medical trainees being less likely to pursue careers as physician-scientists performing fundamental research (8).

At a broader level, our results are perhaps only the latest symptom of a growing disconnect between science and clinical medicine. This chasm bodes ill for the development of personalized medicine, which depends on an exquisite understanding of the molecular and physiologic milieu of each patient. With the Precision Medicine Initiative, the medical community sits on the threshold of a new era in health care. Will clinicians continue to lead these scientific and technological advances from bench to bedside? If scientific discovery is to represent the "future of medicine" (9), don't medical practitioners have to be exposed to these discoveries?

In 1910, the now-famous Flexner report called for American medical schools to emphasize the importance of scientific principles and research to enhance medical education (10). The report's emphasis on the scientific method was intended to fortify medicine against the lure of quackery and anecdotal cures. Modern-day clinicians are bombarded by new biomedical discoveries; however, the relevance and validity of these discoveries can be difficult to judge. The modern medical journal thus has a critical role to play in helping clinicians make sense of ongoing advances in human biology and pathophysiology, which represent the cornerstone of knowledge required by physicians. It is hard to argue with Robert Tjian, the president of the Howard Hughes Medical Institute, when he writes that "fundamental discovery research . . . has proven to be the foundation of modern medicine" (p. 134, ref. 11). We would extend the argument even further and assert that an understanding of the basis of disease is one of the key qualities distinguishing clinicians from technicians. There is even some evidence that exposure to basic science content enhances both learning and diagnostic skills by clinicians (12–14). In our opinion, in this era of molecular medicine, exposure of clinicians to basic scientific research is even more important now than it was a century ago. FJ

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