7. Averting Conceptual Crisis – Semantic Stabilization of a Disciplinary Identity in the Twenty-First Century

The conceptual developments described in the previous chapter made biomedicine a broadly defined scientific discipline, which superseded the old categories of biological and medical research. But biomedicine was also bound to become a dominant and encompassing supercategory in the global science and policy discourses due to the high level of public health expectations associated with it. The term began to be understood much more broadly than only to justify the many efforts undertaken to tackle health care problems with the aid of basic research in the biosciences. Accordingly, there are references to "the biomedical research system, both basic and clinical", for example, thus indicating how biomedicine is currently the integrative concept for *all* the institutions of academic medicine (Heinig et al. 1999: 742). Similarly, in a systematic review of biomedical historiography, historian Nicolas Rasmussen understands biomedicine "as the areas of research supported and conducted by the NIH" (2018: 5). Obviously, the NIH harbors a far greater range of research types. As Edward Ahrens critically remarks: "'biomedical' is the inclusive word today for many kinds of research funded by the NIH and performed in our medical schools and medical research institutions by MDs, MD-PhDs, and others, and whose content runs the gamut from strictly biological to strictly clinical" (1992: 34).

These quotes suggest that the concept can also be viewed to comprise more than just the laboratory-based activities that I have identified as constituting the discipline. Rather, also other forms of research sponsored by the agency are subsumed under biomedicine as a supercategory – including clinical research at the bedside, which, as I showed, developed historically and institutionally distinct from the biomedical sciences. This is something to remember, when observing how biomedicine evolved into a vast research industry. The massive increase in spending for health care research and development (R&D) after World War II is a clear indication of the widespread belief in the biomedical model and its linear legacy – a belief that continues today. Additionally, a vast amount of communication on the topic has been spread through specialized publications over the past decades. A simple search for "biomed*" in publication abstracts and titles in the PubMed database, for instance, retrieves a total of 98,261 results

between 1965 (the date of the Woolridge Report's publication) and 2018. Displaying these results as publications relative to all releases per year listed in the database illustrates a steady increase of output referencing biomedicine (figure 7.1).

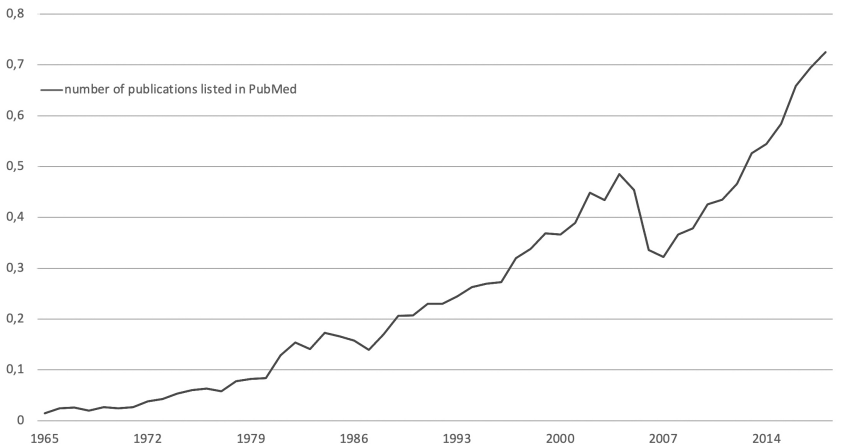

Figure 7.1: Graph showing relative number of publications per year with 'biomed' in title or abstract between 1965 and 2018. (Source: PubMed database, https://pubmed.ncbi.nlm.nih.gov/?term=%28biomed%2A%5BTitle%2FAbstract%5D%29&filter=years.1965-2018&sort=pubdate&sort_order=asc [Accessed November 15, 2020], my visualization).*

The history of the NIH budget is also taken as an indication of the growth of the enterprise in the second half of the twentieth century. It shows a massive inflation of biomedical research and reveals the NIH to be the largest single promotor of biomedicine in the world by far (Rasmussen 2018, see also Ahrens 1992). According to the figures Rasmussen presents in his review, the NIH's budget for scientific activities grew exponentially in the decades immediately following the war. Riding on the ideological wave of basic science, he states that the "life sciences as a whole" benefitted (ibid: 8). By the late 1960s, the NIH had hit the critical mark of $1 billion in research spending. In 1970, therefore, the institute's dramatic monetary inflation dwarfed the budget of the NFS's division of Biological and Medical Sciences, which was allocated at $49 million. This highlights the "overwhelming dominance of the NIH among all US funders of life science" (ibid: 3). In that same decade, the NIH accounted for 40 % of all "health R&D" expenditure in the United States, while all other govern-

ment agencies combined were investing 25 %, the industry was contributing roughly 30 %, and philanthropies accounted for less than 5 % (ibid., see also Ahrens 1992: 65–79). Although the budget of the agency plateaued in this period, funds for biomedical science began to increase again in the mid-1980s as the Cold War reached its second peak (ibid: 9). Today, the NIH continues to be the largest single funder in the field globally.[78] As stated on its homepage, the agency invests "about $41,7 billion annually in medical research for the American people".[79] Only in the mid-2000s, did the share of world health research and development conducted publicly by the United States fall beneath 50 %, although public and private spending combined at the time still accounted for more than half of the expenditure worldwide (ibid: 3).

That biomedicine had also become an accepted scientific discipline, however, can be taken from the imprints bearing its name. As I showed in the first chapters of my book, medical actors in the past used the founding of academic journals to arrange the medical discipline according to their ideals and interests. Journals can thus act as an indicator of how disciplines become integrated into the academic landscape since they represent a format through which actors within a scientific community communicate with each other and accordingly contribute to the growth of their field (Stichweh 2007). In wake of the recategorization from scientific medicine into biomedicine in the 1960s, specialized journals began appearing and contributed to the constitution of a biomedical discipline. It would require an extensive content analysis to see which of these journals represent the discipline genuinely and which have adopted the vocabulary more out of rhetorical reasons to connect themselves to the vastly growing biomedical enterprise under the supercategory – something that is beyond the scope of my investigation, though. Nevertheless, if we search the database Web of Science for publications in journals with "biomed*" in the title, it retrieves a total of 56,769 items between 1971 and 2019 (there appears to be no significant output before that timespan). The 1970s, moreover, appear to have been a critical time for establishing biomedical journals, launching at least four new journals bearing the category in its title (table 7.2).

78 In comparison to the NIH, the German Ministry of Education and Research (BMBF) spent more than 2.6 billion of its total 23 billion Euro research-budget on health-related investigations in 2017, with an increase of roughly 400 million Euros in budget and 100 million Euros in medical research spending in 2018. These figures were taken from the 2018 BMBF-report: https://www.bmbf.de/pub/Bufi_2018_Datenband.pdf (accesses August 20, 2020).

79 https://www.nih.gov/about-nih/what-we-do/budget (accessed August 20, 2020).

The ambiguity of biomedicine as a scientific discipline and a supercategory that exhibits the ability to subsume vast areas of heterogeneous activities in medicine has caused serious tensions between different actors in the academic system. Particularly practitioners in clinical fields soon began to perceive that the massive investments made in the name of biomedicine were unjustified. Especially molecular biology, with its stellar ascent in international science, was causing significant frictions. This "new biology" had evolved into a dominant discipline by the 1950s, coming from the collective work of chemists, physicists and biologists. The field emerged from studies relating to human physiology and pathology and was therefore present in many American medical schools, but it quickly transcended any immediate relevance to these areas (Kohler 1982: 324ff.). Nonetheless, its paradigm was seen to significantly relocate the study of processes of life and disease to the level of molecules, which could be investigated using microorganisms as models as well as with the aid of more and more sophisticated analytical techniques (Kay 1993, see also Rheinberger 2009).

first issue	journal title	ISSN
1967	*Journal of Biomedical Materials Research*	0021-9304
1970	*International Journal of Biomedical Computing*	1136-5056
1971*	*Biomedical Engineering / Biomedizinische Technik*	0013-5585
1972	*Annals of Biomedical Engineering*	0090-6964
1973	*Biomedicine: The European Journal of Clinical and Biological Research* *Biomédicine la Revue Européenne d'Études Cliniques et Biologiques*	0300-0893
1982*	*Biomedicine & Pharmacoptherapie / Biomédicine & Pharmacothérapie*	0753-3322
2001	*Journal of Biomedicine and Biotechnology*	1110-7251

Table 7.2: A selection of journals published since the 1960s bearing 'biomedical' or 'biomedicine' in the title. Asterisk (*) indicates that the journal was founded earlier but under a different name.

Molecular biology therefore implied that it was possible to study disease removed from the clinic and the patient, which made practical expertise in clinical medicine virtually obsolete.[80] The way molecular biology was performing "engendered a trend in which those undertaking research into disease were drawn increasingly to the laboratory bench" (Kraft 2013:

80 With respect to the "crisis" in clinical research see also the 2004 special issue of *Perspectives in Biology and Medicine* (Schechter/Perlman/Retting 2004).

28). As molecular biology research communities boarded the biomedical bandwagon, the field was receiving an ever-increasing share of funds from health care R&D-budgets, especially from the NIH, which acted as one of the major supporters of molecular biology during the Cold War Era (Appel 2000: 209–216). As a result, renown departments with apparently no clinical connection were built using NIH funds, like the "molecular biology hothouse" in Stanford University's biochemistry department (in the medical school!), "where luminaries like Paul Berg and Arthur Kornberg solved the riddles of gene expression in *E. coli* bacteria" (Rasmussen 2018: 6).

Molecular biology has strongly influenced the public image of what it means to do research in medicine after World War II (Strasser 2014: 12). But the dominant picture of molecular biology also entailed a superimposition of its cultural understanding onto the culture of clinical science. As is apparent throughout my book, medical scientists in preclinical as well as clinical departments have generally been physicians by training (even if they often refrained from any form of medical practice). While clinical departments remained dominated (and controlled) by medical doctors, the professional composition in preclinical departments began to change as sciences such as physiology or biochemistry started awarding their own graduate degrees by the start of the twentieth century. In 1992, Ahrens saw that also "the focus of clinical investigators" had "shifted dramatically" since the 1960s, from patient-oriented clinical research towards *in vivo* studies of disease using animal models and *in vitro* studies of human materials such as blood or tissue. He attributed this development to "a fascination with the power of the new reductionist technologies of molecular biology to reach new insights at the molecular level and to do so rapidly" (1992: 48).

At the same time, however, the conceptual contours of what it meant to do work in clinical science had themselves become critically unclear. In a 1999 review of clinical research in the United States, the authors detected that the collection of reliable data was hampered by a "wide discrepancy in the *definitions of clinical research*" and that the lack of a universally accepted definition "led to variability and contentiousness in accepting the designation of different kinds of research activities as 'clinical'" (Heinig et al. 1999: 727, see also Schechter/Perlman/Rettig 2004: 479f.). As I illustrated in chapter 5, clinical science evolved at the start of the twentieth century when actors adopted the scientific ideology of laboratory work but directed its methods to issues of clinical practice. In a current definition, therefore,

> "clinical investigations may encompass the whole gamut of research activities, including analyses of disease pathophysiology (for which sophisticated study of normal human biochemistry and physiology is necessary); of the prevention, cause, and course of disease; and of the effects of interventions (pharmacologic, surgical, behavioral, etc.) on human health" (Schechter/Perlman/Rettig 2004: 480).

Consequently, the activity describes an integrative approach to the study of disease in patients. This form of scientific activity, "synonymous with 'experimental medicine', 'clinical science', and 'clinical investigation'" (Ahrens 1992: 39), is aided by consultations with a clinical laboratory, but not reduced to it. Clinical science requires both proficiency in clinical care *and* basic research.

However, torn between the bedside and the bench, and subject to attempts in the early decades of the twentieth century to also widen the idea of clinical science towards population-based inquiries, it had become unclear what clinical science's methods and approaches to study the treatment of disease precisely entailed. Not the least has this ambiguity been accelerated by the overall success of molecular research under the wings of the supercategory biomedicine. According to historian Alison Kraft, clinical research constituted "a slippery term" by the end of the twentieth century, associated with a range of activities, "from patient-centered research at the bedside, to lab-based research into the molecular basis of disease, to the clinical trial" (2013: 33f., see also Borck 2020: 459). Accordingly, witnessing an increase in the numbers of non-medical doctors in clinical departments since the 1970s, Ahrens warned his readers that it would be a mistake to consider postdoctoral scientists "in clinical departments merely as individuals hired to perform laboratory work", which medical doctors have increasingly little time for, "or simply as supervisors of technicians in those laboratories" (1992: 25). Rather, the development indicated a colonization of clinical institutions by researchers in fields of the basic sciences. With biomedicine designating the whole complex of academic medicine and the concept of clinical science also comprising activities of basic laboratory research, therefore, the outlines of what were once deemed preclinical and clinical domains had faded. This induced a stronger reliance on the linear promises in the public understanding of biomedicine, while it also entailed a differentiation of the professional functions of actors in clinical medicine. An increasing divide between the practice of clinical medicine and clinical investigation on the one side and the research function of medical science was emerging in the institution, "and whilst some clinicians continued with clinical investigation in the

patient at the bedside, many others pursued a different kind of clinical research in the laboratory" (Kraft 2013: 30, see also Ahrens 1992: 48).

What were the consequences of such conceptual and professional ambiguities? And how did actors try to avert the looming crisis in medical research and clinical care? The shifting conceptions over roles and functions in the academic health care system meant that the idea of the physician as a scientific investigator in the historical sense was on the wane. At the same time, in its supercategorical dimension, biomedicine was assuming more direct responsibility for improvements in clinical medicine than its scientific discipline originally promised. This required clarifications, conceptually and institutionally, of what the relationship between the biomedical discipline and the system of clinical medicine comprised. I want to use this chapter to look at two recent categories that have not altered the meaning of biomedicine as such, but which have stabilized its general understanding by redefining the institutional structures of academic medicine with respect to clinical practice and research – evidence-based medicine (EBM) and translational research (TR). These categories emerged at the end of the twentieth and the start of the twenty-first century, respectively. If viewed from the perspective of conceptual and institutional history, they appear to have somewhat of an entangled semantic function. I argue that they work to recategorize the different areas of medical science by clarifying the position of clinical research and practice in face of the dominating biomedical concept.

On the one side, EBM corresponds mainly to biomedicine as a scientific discipline and acts to confirm its autonomy vis-à-vis clinical medicine. The concept is carried by a deep-seated dissatisfaction with the paradigm that bases practical medicine on explanations in knowledge of the biomedical laboratory. It therefore transitions the cultural foundation of clinical practice away from the lab to population-based reasoning and through the institutionalization of clinical guidelines. TR, on the other side, correspond to biomedicine as a supercategory and the vast research enterprise it harbors. The concept reinforces the idea of biomedicine's linear legacy by integrating into it a reinvented version of the historical ideal of the physician-researcher. This category, in other words, confirms the autonomy of the biomedical discipline through institutional distinction. But it also preserves its identity by confirming the linear legacy, connecting biomedicine semantically to the vague category of "clinical science".

I. Evidence-Based Medicine and the New Cultural Foundation of Clinical Practice

The debate about evidence-based medicine (EBM) is too vast and still ongoing as that it could be reasonably summarized here (see e.g., Cohen et al. 2004, Daly 2005: 102–127, 206–234, Knaapen 2014, Solomon 2011, also Borck 2020, Weisz 2005). Hence, I only want to show how the category was defined at its inception and point to its semantic function regarding the understanding of the relationship between biomedicine and clinical medicine. The main purpose of the category, in this respect, is to semantically remove practical medicine from a cultural foundation in the biomedical discipline, while maintaining a strictly scientific foundation for medical practice. Although EBM ostensibly brings a standardization to the practice of health care (Knaapen 2014, Timmermans/Berg 2003), the category can, in a sense, also be seen as the successful founding of clinical medicine on epidemiological instead of biomedical premises (Daly 2005).

I want to argue that this change of practical foundation confirmed the status of biomedicine as an autonomous discipline within the larger academic complex. Epidemiology had developed from an observation-based and dismissively treated approach for public health officials in the early decades of the twentieth century into a genuine scientific discipline in the post-war era. It incorporated the "experimental ideal" but transferred it to the study of disease in populations using statistical methods, thereby elevating itself to the same level scientifically as the laboratory sciences (Amsterdamska 2005). Epidemiology thus constituted an apt candidate for relocating practical medicine to a scientifically sound foundation, especially in an age that was anyhow increasingly adhering to the apparent soundness of statistical inference (Borck 2020: 455ff.).

Since about the 1960s, actors were making efforts to find ways to ensure that care was being delivered to patients according to clearly discernible and reproducible premises (as opposed to physicians' intuition or routine). The emergence of the discipline of clinical epidemiology in Canada and the United States at the time manifested this motivation to bring the population-based approaches characteristic of public health studies also to clinical medicine. Through its focus on quantitative methods for investigating clinical practice empirically, "clinical epidemiology represented a new way of thinking about clinical care that its proponents described as representing a paradigm shift" (Daly 2005: 4). Reminiscent of the developments in clinical science, which were illustrated in chapter 5, actors were

framing the discipline as a new "basic science for clinical medicine" (Borck 2020: 461).

Obviously, it was a difficult venture to simply shift the deeply rooted knowledge base of medical practice to the discipline of clinical epidemiology and its culture of statistical reasoning, given the historical tradition of socializing physicians in the habits of the laboratory sciences. A group of epidemiologists and clinicians from Canada and the United States formed the core of advocates for the new key medical concept of EBM. In 1992, they boldly proclaimed the advent of "A NEW paradigm for medical practice", in an article in the *Journal of the American Medical Association* that acts as the founding document for the movement:

> "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. Evidence-based medicine requires new skills of the physician, including efficient literature searching and the application of formal rules of evidence evaluating the clinical literature." (EBM Working Group 1992: 2420)

The proclaimed novelty of the movement deferred the attention away from the fact that, historically, clinical medicine and public health, from which the methods derived, were in fact institutionally divided. Very generally speaking, clinicians dealt with individual patients and their diseases, while public health had a far broader scope incorporating many perspectives onto the everyday lives of people and their relation to health. This division was of course a source of friction (Daly 2005: 121ff.).

The group of epidemiologists and clinicians promoting EBM therefore introduced it as "A New Approach to Teaching and the Practice of Medicine" (EBM Working Group 1992: 2420). Instead of merely transferring medical practice to an epidemiological basis, they thereby simply justified the change on the grounds of inserting new pedagogical ideals into medical practice, which nonetheless focused on statistical and epidemiological methods, including systematic ways to appraise the professional literature (Borck 2020: 462ff., Daly 2005: 75ff.). According to David Sackett, a leading proponent and practitioner of EBM, and his colleagues, the approach was defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett et al. 1996: 71). This meant that medical treatments were to be investigated in population-based clinical studies to generate such evidence for medical care, particularly using randomized controlled trials

(RCTs), which had emerged as the "gold standard" for evaluating drug safety and efficacy in the United States (Marks 1997). RCTs constituted a relatively simple but powerful transfer of the experimental design characteristic of investigations in the natural sciences to the study of clinical populations. "Its promise was that it would achieve the rigor, and certainty, of laboratory findings" (Daly 2005: 13). Together with the technique of meta-analysis, a way of statistically aggregating the results of various clinical studies of the same intervention, these methods were meant to continually update the "objective" basis for clinical care by invalidating "previously accepted diagnostic tests and treatments" and replacing them "with new ones that are more powerful, more accurate, more efficacious, and safer" (Sackett et al. 1996: 71).

Historian of medicine Cornelius Borck convincingly demonstrates how the category of EBM entailed a reorganization of the epistemic hierarchy governing clinical medicine. Not only did its advocates discard the "three historically most important ways of legitimising medicine" (i.e. as an art, an expertise and a science) (Borck 2020: 463); in their program, "theoretical knowledge and scientific explanations were downgraded epistemologically, from previously ranking as the highest form of knowledge in biomedicine to now functioning as a mere heuristic or useful strategy for identifying possible targets for new interventions (then to be evaluated by RCTs)" (ibid: 464). As with the case of emphasizing the scientific methodology in the medical curriculum to downgrade the epistemological place of clinical medicine in mid-nineteenth century Germany, in other words, the concept of EBM effectively meant that the foundation of the clinician's professional culture transitioned from being grounded foremost on experimental laboratory methods to epidemiological techniques.

According to this new ideology, knowledge of pathophysiology was still required but it was now also regarded as insufficient for practicing clinical medicine. "All pathophysiological inferences should be subordinated to the question of whether diagnostic or therapeutic interventions have been proven to be effective in sound empirical studies" (Timmermans/Kolker 2004: 183). While professional training of physicians still remains dominated by laboratory sciences, areas that proponents of EMB favored have also made it into today's curriculum. At the University of Bonn, for instance, students of medicine are required to take courses in "medical statistics", "epidemiology, biometry, and informatics", and "medical informatics", next to courses in pathology, clinical chemistry, and other medical

topics, in their first clinical semester (the fifth semester overall).[81] The original intention of the EBM movement was indeed to train doctors in the critical appraisal of the literature, that is, precisely in such fields. The idea was that clinicians should always be up to date with respect to the statistics of which treatments best applied to what cases. But this original ideal largely failed due to practical reasons: it conflicted with the busy workload of practicing clinicians. So, in contrast to the nineteenth century, where protagonists altered the cultural basis of medicine through changes in the curriculum, EBM has ended up changing the professional culture less through the explicit exposure to epidemiology at the student level, than through the introduction of guidelines into everyday clinical practice, which can be composed relatively easily based on meta-analytic studies (Weisz et al. 2007: 713).

II. Shifting the Basis of Clinical Medicine Through Guidelines

It is not my intention to go into any detail about the historical developments leading to the emergence of clinical guidelines (see Weisz et al. 2007); nor to engage in debates about the role of guidelines for the undermining or preserving of physicians' professional autonomy (Armstrong 2007, Timmermans/Kolker 2004, Vogd 2002). All I want to do here is shed a light on functional aspects of the category that serve the purpose of sustaining the argument that the biomedical discipline no longer constitutes the cultural foundation of practical medicine. But how can guidelines be seen as an indication of biomedicine's institutional autonomy?

Clinical guidelines have been presented as changing the way that the quality of medical practice is controlled. "Until the 1970s," according to George Weisz and his collaborators, "medical actions were indirectly regulated through the training and credentials guaranteed by both the organized profession and state authorities" (Weisz et al. 2007: 693). In the context of my elaboration, in other words, the quality of medical practices was guaranteed by the professional culture in which physicians were socialized during their studies. Self-governing bodies like medical associations made sure that the study courses providing the socialization upheld the required standards of medical practice. With the increasing

81 See the relevant information on the medical faculty's website: https://www.medfak.uni-bonn.de/de/lehre-studium/studiengaenge/humanmedizin/klinik/daten-und-plaene (accessed 15. November 2020).

importance of clinical guidelines since about the 1980s, however, this measure of control has been externalized from physicians, their experience and knowledge of pathophysiological processes to "*procedural standards* that specify the actions or protocols that must be followed in given situations" (ibid.).[82] The making of these standards, in turn, can be explained as a process of negotiated conventions, something Keating, Cambrosio and colleagues have conceptualized as "regulatory objectivity" (Cambrosio et al. 2006). A closer look at the idea of regulatory objectivity in the context of guidelines, which draws on the authors' preliminary work about biomedical platforms, will help answer this question.

The idea of regulatory objectivity describes a recursive procedure by which conventions guiding clinical practices are coordinated with those guiding the research process. In contrast to the concepts of objectivity of former times, the authors argue, "regulatory objectivity turns the focus away from objects towards collective forms of expertise combining people (clinicians, researchers, administrators, patients, etc.) and objects (entities, instruments, tools, techniques, etc.) connected by specific coordination regimes" (ibid: 194, see also Keating/Cambrosio 2012: 20f., 25ff.). The crucial point for my argument is that in the coordinated regime of RCTs, which lies at the heart of EBM, the correlation between the conventions of biomedical knowledge production and clinical action have been supplanted by that of the narrower focus of producing knowledge of effective interventions in the clinic. In face of this development, the EBM movement, as I explained, required that clinicians abandon intuition, clinical experience and pathophysiologic rationale and instead demanded that "evaluation be based on distinctions among levels of evidence" (Weisz et al. 2007: 713). Effectively, this meant a rejection of the confidence that scientific explanations can justify therapeutic interventions. Borck puts it most clearly, when he summarizes that, according to the fundamentals of EBM, "evidence suffices even in the absence of explanations, something which is absolutely unsatisfactory for science-based medicine" (2020: 466).

EBM thus infuses the basis of clinical practice with the priority for an epidemiological and not a biomedical understanding. An intervention

82 Reasons given for this development are "the increasing role of governments in every aspect of health care" and "the perceived need in nearly all Western nations to impose rational direction and coordination on an array of [health care] institutions […] that had been created incrementally and almost haphazardly over long periods of time that were increasing both in size and technological-functional complexity." (Weisz et al. 2007: 704f.).

is deemed legitimate not if the science says that it works, but if it has statistically been proven to work and if this "proof" is enshrined in clinical guidelines for best practice. Since RCTs form the single most important procedure for producing viable clinical evidence and meta-analysis is, in turn, the effective basis to produce guidelines: the actions of clinicians are no longer regulated primarily by biomedical explanations but by the coordinated conventions of population-based methods and clinical practice. In short, the introduction of EBM into academic discourses represents the climax of the differentiation between biomedical science and clinical care, which started in the Progressive Era. This does not mean that biomedicine and the clinic have nothing to do with each other anymore – far from it. But it does entail the fundamental restructuring of the epistemic hierarchies and research cultures that lay the foundations for medical practice. Like Virchow's program of scientific medicine, which moved the science of experimental physiology in the background to henceforth constitute the general framework in which medical science was performed, so, too, EBM has delegated biomedical science to constitute the general context in which clinical care is researched. But through the instruments of EBM, the conceptual basis for medical practice shifted away from the requirement of biomedical knowledge. In this constellation, clinical medicine has not only found a new scientific basis; EBM furthermore confirms the position of biomedicine as a discipline distinct from clinical responsibilities. Therefore, it stabilizes the original meaning of biomedical science – the post-war era basic research cultures in biology and medicine that hold the possibility to improve public health but cannot be pressed too hard on delivering that promise.

III. Confirming the Linear Legacy with Translational Science

If EBM targeted the concept of clinical practice, TR can be said to aim at reorganizing the idea of clinical science in the twenty-first century, especially in the wake of molecular biology and genetics. However, since EBM acts to confirm biomedicine in its remote contributions to the betterment of public health, TR offers a semantic correction that reinforces the linear legacy of the bench-bedside-connection. EBM functioned to differentiate clinical medicine from biomedicine by introducing its version of "clinical science", based on epidemiological reasoning, and removed from laboratory culture. TR also references "clinical science", however, framing it as an integral part of biomedicine to suggest its continued relevance for

health care. TR is also a concept that has received its deserved share of sociological investigations and the research landscape is increasing steadily (see Crabu 2018, also Mittra/Milne 2013). The purpose here is therefore again to only examine the category for its functional aspects in the current science and policy discourses with respect to the idea of biomedicine and the culture of clinical research.

The way the term TR is used can be distinguished roughly into a broader dimension, addressing a supposed breach in the biomedical innovation pipeline on the one side, and aiming more concretely at bridging the gap between basic research at the bench and patient treatment in the clinic on the other. Both meanings are interrelated, although commentators tend to find their underlying rationales to be contradictory. In most cases, TR is associated with the idea of a linear model of innovation or a continuum leading from the laboratory bench to clinical application. The implication is that the knowledge generated through basic biomedical research is meant to be translated into "ideas and knowledge about real (diseased) bodies and in[to] medical technologies", which then seek implementation in practical medicine (van der Laan/Boenink 2015: 39). The prevalence of this idea can be attributed to the ideological power of basic science, which in the case of biomedicine has been fueled by the dominance of molecular biology, leading to "an interpretation of the dynamic between the lab and the clinic as one in which, predominantly, information flowed from bench to bedside", as Kraft observes (2013: 29). Nonetheless, commentators on TR point out that the view of biomedical R&D as a linear and largely one-directional innovation process is "empirically inadequate" (van der Laan/Boenink 2015: 40f.) or "rarely reflects the reality on the ground" (Mittra 2016: 60).

My aim is not to prove or disprove the adequacy of the idea of a continuum between bench and bedside; just like I did not want to assess, in the conclusion to chapter 6, any kind of correspondence between the linearity engrained into the category of biomedicine and the empirical reality of biomedical research. Instead, I want to show how the underlying narrative of linearity was appropriated by protagonists in clinical science to stake out their professional turf by framing it as translation work regarding both spheres. Sociologists investigating the TR concept have shown that, as these clinician-scientists faced increasing incursions into their domain from pure laboratory-based research, the professional hierarchy within the biomedical system tilted to their disadvantage (Wilson-Kovacz/Hauskeller 2012, see also Mittra 2016: 96f.). To push back against the expanding boundary of the biomedical discipline, these actors aligned themselves

with other actors in the research policy front at the start of the twenty-first century, contributing to the formulation of the institutional requirements to pursue their professional interests (Vignola-Gagné 2014). Thus, rather than seeing the two understandings of the relation between laboratory and clinic enshrined into the category of TR as contradictory, we can regard it as a rhetorical strategy, in which both meanings are directed at two different discourses. These discourses emerged subsequently and relate to the professional culture of the clinician-scientist and health care R&D, respectively. More, we can observe that "translational research" was a prevalent category in the English-speaking world before "translational science" and "translational medicine" became important denotations (figure 7.3). As in the case of biomedicine, this indicates that we first had the description of the practices before they became used as a mark to distinguish a specific scientific culture, which was afterwards institutionalized in the academic system.

IV. The Character of Translation Practices

The term TR first emerged in the early 1990s in the field of cancer research, where it was associated with a bi-directional understanding of linking basic and clinical science but quickly spread to other biomedical fields after 2000 (van der Laan/Boenik 2015: 34f., see also Keating/Cambrosio 2012: 348). The meaning of TR "slightly shifted" after 2003, according to Anna Laura van der Laan and Marianne Boenink in a review of TR in the literature, from a "desire to finally see effective treatment for an awful disease [cancer]" to the assessment "that health improvements have not kept up with the increased speed of discovery in the life sciences", particularly in fields like genomics and molecular biology (2015: 36). In that year, the newly elected head of the NIH, Elias Zerhouni, initiated "The Roadmap" mentioned in the introduction, which aimed at reforming key processes of the institutes' biomedical R&D along the lines of three major themes – "New Pathways to Discovery, Research Teams of the Future, and Reengineering the Clinical Research Enterprise" (2003: 63). The policies of the NIH Roadmap were meant to address "today's pressing scientific challenges" and "roadblocks to progress" brought on especially through the sequencing of the human genome; they were intended to adapt the activities conducted under the agency's aegis to concomitant redefinitions of "the ways that medical research is conducted and, ultimately, how research leads to improvements in health" (ibid). Zerhouni – himself a clinician-sci-

entist from Johns Hopkins' department of radiological science – argued for the necessity of major organizational and infrastructural changes in order to facilitate that discoveries in the laboratory made it into clinical innovations, whereby TR was to constitute itself as "the new paradigm in biomedical research" (Kraft 2013: 43).

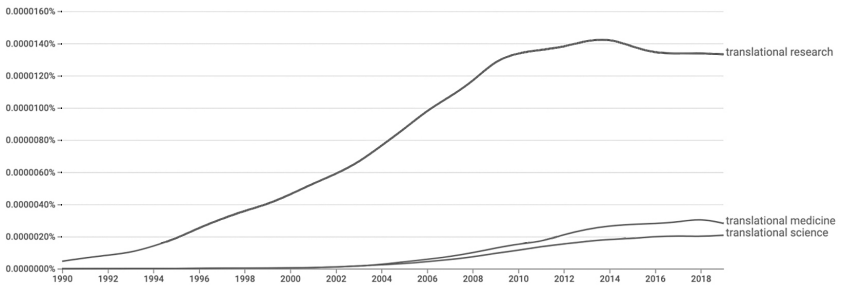

Figure 7.3: Word frequencies of "translational research", "translational medicine" and "translational science", 1990–2019. (Source: Google Books Ngram Viewer, https://books.google.com/ngrams/graph?year=_end=2019&year_start=1990&content=translational+research%2Ctranslational+science%2Ctranslational+medicine&smoothing=3&corpus=26 [accessed September 1, 2020]).

Zerhouni's Roadmap can be regarded as the political strategy that connects the interests of a R&D innovation system understanding itself in linear terms with those of the clinician-scientists, who see themselves straddling at the interface of the laboratory and the clinic. It inspired an era in which more and more policies for TR were implemented in different countries that began to justify the role of the clinician-scientist as an important element in health care innovation (Hendriks/Simon/Reinhart 2019: 227, Kraft 2013: 45f., Mittra 2016: 71ff.). Empirical studies point to how the actual work of clinician scientists "is overburdened with vague or completely unspecified expectations" regarding the task of translating research (ibid: 233). This has to do mostly with the fact that these actors need to operate simultaneously as caregivers in the clinic and as bench researchers. Not only are both activities inherently time consuming, the increasing specialization in biomedical science also makes it nearly impossible to keep up for someone who is not devoted to the field full-time.

I want to nevertheless try and identify professional markers of the clinician-scientist circulating in the discourses of TR, so that it becomes clear how their scientific culture was distinguished from that of the biomedical discipline and from earlier understandings of clinical research. In this

regard, Kraft succinctly notes that the meaning of the term TR is at the same time vague, comprising a range of activities, actors and sectors part of the biomedical enterprise, and also "highly specific, in that in practice it is defined differently by different actors […] in ways that reflect their position within the innovation process" (2013: 46). The long-standing ambiguities in the meaning of clinical science, which I discussed above, made it necessary for its principal actors to redefine their work in a way that would distinguish it from that of the basic researcher. Describing their activities in terms of the vague concept of TR allowed them to be characterized in the new guise of the clinician-scientist and put them at the forefront of the biomedical system in the twenty-first century.

Forming the basis of the Roadmap programs was "an ethos supportive of the view that clinical insight had a role to play in shaping 'basic' research" (ibid: 43). This was a reaction to the overgrown role that basic research, especially in molecular biology, was playing in the fight against disease. Accordingly, a central requirement for any clinician-scientist is "to be able to speak the two languages of research and clinic" (Hendriks/Simon/Reinhart 2019: 233). As a result, in the case of stem cell research, for example, they describe their role as treating patients and contributing to the biological understanding of disease (Wilson-Kovacz/Hauskeller 2015: 501). These are not equal concerns, however. Understanding mechanisms is presented as only secondary to the actual aim of improving patient health (ibid: 503).

In this respect, the clinician-scientist of the translational era differs little from the clinical scientist that emerged as an actor at the start of the twentieth century and who was proficient enough in lab work to aid his/her investigations in the clinic with the aid of the natural sciences (see Harvey 1981). But with the increasing specialization in science and medicine, the clinical researcher taking an integrated pathophysiological approach to the study of disease appeared outdated in a world in which the way that medical research was conducted had become redefined into constituting specialties targeting very specific areas of the human metabolism (Hendriks/Simon/Reinhart 2019: 230). A crucial innovation, therefore, was to make the culture of clinical trials in different configurations a distinguishing feature of the clinician-scientist in the TR discourses.[83] However, trials were no longer aimed mainly at assessing the efficacy and safety of new therapeutics, as they conventionally did, but to answer

83 The Roadmap included a significant push for, in the long run, associating clinical research with the trial (Kraft 2013: 42).

specific research questions pertaining to the functioning of the human body and its responses to deliberate interventions. Moreover, the practice of clinical trials for research purposes endowed the clinician-scientist with an aura of clinical medicine. Thus, it confirmed the relationship between biomedicine and the clinic.

In their study of clinician-scientists in stem cell research, sociologists Dana Wilson-Kovacz and Christine Hauskeller argue that the RCT plays a central role for the scientific culture of TR in stem cell science. They show that such trials "are orchestrated by a distinct type of medical professional who devotes time to biological research and clinical practice", who accordingly incorporates proficiencies of basic and applied science, and therefore presents himself/herself as in possession of "the right skills to translate this knowledge into potential therapies" (2012: 507). The adoption of this form of practice as a professional mark of the clinician-scientist can be traced to the practice of oncology, where the concept of TR first emerged.

In their second major contribution to the social and historical study of science and medicine in the post-war world, *Cancer on Trial*, Keating and Cambrosio, based on a rich historiography of central political, organizational and epistemic moments of clinical oncology in Europe and the United States, demonstrate how since the 1950s clinical trials were developing into their own style of doing biomedical research. Although the authors dismiss the category of TR as a "catchphrase" and as "but the most recent organizational expression of the ongoing molecular biology turn" (Keating/Cambrosio 2012: 348f.), their book nonetheless provides a valuable analytical angle to understand clinical trials as a distinct professional culture defining the jurisdiction of the clinician-scientist in the era of TR. While clinical trials traditionally function to assess the performance of treatments, Keating and Cambrosio argue that in oncology "clinical trials have become full-fledged experiments" (ibid: 21). They have contributed to the generation of "a whole new class of sui generis objects that, in turn, have redefined the practices of clinicians, statisticians, and biologists" and thus constitute a system, which "contains its own reflexive machinery for establishing facts as well as how those facts should be integrated into evolving networks of concepts" (ibid: 21f.).

For Wilson-Kovacs and Hauskeller, moreover, the clinical trial not only represents "an essential step in producing an independent, autonomous and self-contained area of knowledge", it also is a resource for clinician-scientists to "reinforce their key position at the intersection between traditional medical care, scientific research and academic medicine" (2012: 507f.). What distinguishes the research culture of clinical trials in oncol-

ogy, according to Keating and Cambrosio, is its reorientation towards molecular biology (2012: 350ff.). Initially, oncological research was devoted to the classification of cancerous disease in living human subjects. In the context of conducting molecular cancer clinical trials, the adjacent studies "differed from previous laboratory studies by shifting the emphasis from natural history to mechanisms" (ibid: 352). One way to orient the practice of clinical trials within this new regime is, for instance, by integrating biomarkers into the study protocol.

Biomarkers are indicators, which allow the measurement of biological processes or conditions. They hold somewhat of a prominent position within the discourses of TR, since they can link clinical values such as symptoms to detectible bodily processes (Mittra 2016: 80f.). In the context of clinical trials, therefore, biomarkers often function as "surrogate endpoints" as opposed to the traditional clinical endpoints (van der Laan/Boenink 2015: 43, see also Keating/Cambrosio 2012: 367). This means that the outcome of an investigation is no longer if a certain intervention has an effect on a specific condition, but on how it alters and changes bodily processes. The innovation of conducting trials with biomarker endpoints thus lies in the targeted approach, which they enable. It now becomes possible to investigate the correlation of an administered compound to a specific biological process or condition, instead of asking – as in the case of traditional RCTs – how a treatment behaves overall in a certain population (Keating/Cambrosio 2012: 361). The clinical trial of TR thus requires of its practitioners no longer simply clinical and epidemiological skills, but also knowledge of molecular mechanisms – a combination embodied only in the new figure of the clinician-scientist. The University of Bonn accordingly offers physicians inclined to do research in translational medicine the possibility of a three-year scholarship program to become "clinician-scientists" after they have completed their residency. The aim of the course is to, in "cooperation between the clinics and the basic-oriented research groups as well as the theoretical institutes", provide fellows with enough flexibility to pursue their own projects, next to their clinical duties.[84] In a sense, therefore, TR constitutes a program to structurally reinforce the institution of clinical science in a time when academic medicine is dominated by research in molecular biology.

84 See the description on the medical faculty's homepage: https://www.medfak.uni-bonn.de/de/qualifikation-karriere/karriere/karrierewege-und-ausbildung-201eclinician-scientist201c (accessed November 15, 2020).

For Keating and Cambrosio clinical trials in oncology simply constitute a new style of biomedical practice. With Becher and Trowler we could better say that trials in TR show how the academic tribe of clinical science settled on a new territory of biological research. It transformed a method originally designed for the assessment of best evidence for clinical practice into a new scientific tool for drug research. Taken together, we can thus see how the categories of EBM and TR in the current discourse on biomedicine function to confirm the autonomy of the biomedical discipline while at the same time reinforcing the linear legacy it transports, especially regarding the supercategory. This becomes possible because both categories insert ideas of clinical medicine and clinical science into the academic and research policy discourse that have somewhat conflicting meanings and functions. EBM constitutes an emancipation of both biomedicine and clinical medicine from each other by shifting the cultural foundation of clinical practice from biomedical to epidemiological reasoning. This enables biomedicine *qua* biomedical science to continue as an independent academic discipline next to disciplines like physics, chemistry or biology.

TR, in a sense, appropriates the new clinical science culture for biomedicine to, beyond the structural independence of the biomedical discipline, affirm a connection of the vast and heterogenous research field to public health matters. Any basic lab research can now be seen in this light if it adheres to categories like biomarkers. Thus, institutionalization of TR in clinical science and medicine also reinforces the linear legacy in the biomedical supercategory that integrates the various scientific and clinical practices, which make up academic medicine and a large part of research in the biosciences today. While clinician-scientists describe their work in different terms, by framing it as part of TR, the idea of translation itself, "coupled with the rhetoric of a broken R&D system," suggests the existence of a "linear health innovation pathway" and the continuity of a distinction between basic and applied research (Mittra 2016: 59). What is interesting about this constellation, is that TR also affirms the relative distance that biomedicine as a discipline has to improvements in clinical medicine. By introducing a new culture of clinical science, it works similar to the introduction of clinical medicine as a pure science at the start of the twentieth century – wedging a new discipline into the relationship between sciences of the laboratory and the clinic, thereby removing the former from responsibility for the latter.