

The Fundamental Antagonism: Veritism and Commerce in Medical Practice (1905-1920)

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1. Progress and Certainty?

[Austin Bradford] Hill's work had outlined the basic structure within which clinical trials would subsequently be conducted ... The Laplacian vision of the determination of medical therapy on the basis of the calculus of probabilities had finally found its spokesman.

(Matthews, 1995, p. 130)

In *Quantification and the Quest for Medical Certainty*, Matthews (1995) traces back the intellectual history of Austin Bradford Hill—the head of the United Kingdom's Medical Research Council (MRC) when it conducted the first modern clinical trial. In fact, just prior to the famous clinical trial of streptomycin, Hill had assumed both his position at the MRC and a professorship at the London School of Hygiene from his mentor, Major Greenwood. Greenwood was, in turn, a student of Karl Pearson, who himself was the protégé and intellectual heir of his benefactor Francis Galton. Though the line of direct instruction ends here, Matthews represents Galton and the British biometric school as pursuing, at the turn of the twentieth century, the same project as Radicke had attempted unsuccessfully in Germany during the late nineteenth century, and that Gavarret had failed to introduce in mid-nineteenth century France; namely, the medical application of the probability calculus as propounded by Pierre-Simon de Laplace in the early nineteenth century (and as developed by Quetelet and Poisson).

In fairness to Matthews, his book includes fascinating investigations into disciplinary disputes over which profession has intellectual authority in judgments of therapeutic efficacy and debates about the source of objectivity. Yet as Harry Marks (1997) has pointed out of it and other histories on the same subject, it is a collection of “disparate episodes ... linked in a transhistorical narrative of antecedents deemed to constitute the history of the present day randomized clinical trial” (p. 6). To replace such a view, Marks' *Progress of Experiment* united the work of interdisciplinary efforts into what he called a

history of “therapeutic reformers.” Specifically, Marks identified the defining characteristics of reformers as “the shared belief that better knowledge about the effects and the uses of drugs will lead to better therapeutic practice” (p. 3). While Marks’ contribution is to be lauded for contextualizing the work of statisticians, pharmacologists, chemists and other reformers, it remains conceptually problematic. Like the histories Marks critiqued, the history of the clinical trial is treated as an essentially cumulative and progressive endeavor. Such a history entails that as the clinical trial is refined, successive generations are in increasingly better epistemic positions and have *progressed* closer to the attainment of medical certainty.

What is lurking in the background, but never clearly articulated by Marks, is an explicit role for the entities that reformers reacted against and a realization that therapeutic reform required far more than improving scientific methodology. Rather than a gradual progress of experiment, I suggest that medical reformers are better conceptualized as one party in an asymmetric arms race, a series of moves and countermoves between competing parties who are adjusting to one another's behavior.

Of course, it is possible to focus on changes in medical epistemology; just as one could trace back the technological and engineering developments in mediaeval fortification. Yet, without an equally clear understanding of advancements in siege weapons, such a history would fail to reveal both their strategic importance and the impetus for the creation and refinement of battlements and bulwarks. Likewise, I maintain that the development of medical epistemology cannot be adequately understood apart from the corresponding developments in the pharmaceutical industry.

Accordingly, in what follows I trace back both the developments in medical epistemology and the pharmaceutical industry. I propose that the antagonism stems from a conflict between pharmaceutical companies pursuing economic self-interest and reformers promoting maximally efficacious treatments. While such a dynamic can explain a number of large-scale developments in the history of medicine, this

chapter focuses solely on the first group of reformers examined by Marks: the Council of Pharmacy and Chemistry (CPC).¹

The council plays a significant, though underappreciated, role in the history of evidence-based medicine. They were the first group to be dedicated to regulation of the pharmaceutical industry and, as I will argue below, should be credited, rather than Hill, as the actual originator of the double-blind randomized clinical trial. The council's vision of clinical pharmacology as the gatekeepers of medical practice was the basis of the regulatory model adopted by the United States Food and Drug Administration in the 1960s, and worldwide in the decades that followed. In this regard, previous writers on evidence-based medicine have given the council short shrift. However, even if they were to be recognized for these contributions, the central lessons of their attempts at reform would remain obscured.

Previous histories have focused on one or two innovative studies conducted by the council as part of a larger sweeping narrative tracing the intellectual development of trial methodology in medical research. In contrast, the present work primarily draws from the collection of reports that the council published between the years 1905 and 1920. The result is a dramatically different picture. First, there is significantly less focus on the role clinical testing. More importantly, the essential relation between the scientific standards employed by the council and the advertising strategies of pharmaceutical companies comes to the fore. As I will argue, constructive research (i.e., establishing new knowledge or methodology) is only half the story (probably far less). The movement led by the council was not merely an attempt to establish a scientific means of evaluating treatments; it was a reaction against a marketplace that was overrun with hucksters, quacks, and miracle cures.

¹ I will generally refer to the CPC as they referred to themselves, simply as "the council." Any other AMA council will be further specified (e.g., the council on medical education).

While it is often constructive work that is built upon and elaborated by future generations (e.g., clinical trials), the success of the council's constructive work depended on ephemeral and contextual responses to contemporaneous methods of drug promotion. These contextual responses have been neglected both historically and in contemporary work on medical epistemology, yet were central to changing the standards of knowledge in the medical community. Further, if we see a physician's prescription as a rough proxy for the state of that doctor's knowledge, then it is possible to gauge the collective knowledge of doctors by looking at nationwide sales data.² In cases where conclusive evidence shows a drug to be strictly inferior to other available treatments, it is possible to examine why doctors continued to believe the contrary.

Referred to as "irrational prescription," the continued use of worthless products became a central focus for the council. Though they began with the belief that all the profession lacked was access to reliable information, years of struggle taught them that "the difficulty has been, and always must be, the fundamental antagonism between objectives that are largely commercial on the one hand and purely scientific on the other" (CPC, 1920, p. 1,235). In this paper I will make the case for, and elaborate the consequences of, recognizing this fundamental antagonism in medical research.

² In short, reference to prescription data seems to be a far superior gauge of "medical knowledge" than the results of the most rigorous experiments available at a given time. If an elite group of researchers has established some therapeutic fact, but this is not actioned by the medical community at large, then the therapeutic fact is not known in the most relevant sense (i.e., it does nothing to improve patient outcomes). Surely there are other factors that affect prescription decisions (e.g., cost, availability, etc.), but this seems like a good (and accessible) first approximation. Further, I will charitably assume that doctors prescribe what they believe is in the best interest of their patient, though I also believe this is generally true. It seems that doctors' prescription habits present an excellent example of applied social epistemology; if there are shortcomings with using doctors' prescriptions as an operationalization of their knowledge, hopefully critiques will lead to conceptual progress in the matter.

2. Pecksniffian Virtue (1905-1910): The General Incompatibility Between Good Health and High Profits

The council is bound to conflict with the commercial element where this element conflicts with scientific progress; the manufacturers, on the other hand, must keep an eye to dividends. (Sollmann, 1908)

In the years preceding the council's formation, the use of patent medications had exploded from 28 percent of all drugs produced in 1880 to 72 percent in 1900 (Marks, 1998).³ In principle, the primary difference between the despised patent-medicine makers and ethical pharmaceutical companies was determined by what types of products a company produced and how the company promoted these items.⁴ Ethical manufacturers made known ingredients that were sold in bulk to compounding pharmacists to be used when filling doctors' prescriptions. They did not advertise to the public, but instead garnered sales within the medical community via reputations of integrity and quality. Patent-medicine companies were seen as, and often were, snake-oil salesmen who were duping the public with panaceas (Young, 1961). Their products were not actually patented, but rather contained secret ingredients said to be responsible for their remarkable curative powers.⁵

In the late nineteenth century, a type of manufacturer emerged that was neither decisively a patent nor an ethical manufacturer. These "proprietary medicines" were marketed to doctors, but they

³ Indeed, physicians had steadily begun to transition to writing prescriptions for patent medications, going from less than 1 percent in 1874 to close to 25 percent by 1902 (Jacobi, 1906).

⁴ The term "ethical" is used in a nominal sense to refer to companies who publically avowed the ethical norms of the medical community. It is not an assertion that business practices used were in fact more ethical.

⁵ It is worth noting that patent-medicine companies competed with doctors for medical authority in the eyes of the public. Moreover, given the state of medical practice at the time, it is not clear that people were better off visiting physicians. Likewise, some patent medicines were efficacious treatments. For example, Dr. Sappington's Anti-fever Pills (secretly) contained quinine and were thus often effective against fevers, particularly in the south where malaria was endemic. Whereas medical reformers viewed secrecy with distrust, manufacturers saw it as necessary to avoid being undercut by inferior rivals—a fate Sappington indeed faced when he succumbed to pressure to reveal his ingredients (for this case in particular, and the evolution of these categories and the respective types of companies more generally, see Gabriel, 2014)). Nevertheless, patent medicines that were effective, nearly always worked because they included ingredients known to be effective, and which could be bought much more cheaply from a reputable pharmacist, instead of the exorbitant prices charged for the readymade patent drug (Hopkins, 1907).

were readymade products (rather than ingredients) and they were promoted with all of the garish promises that epitomized patent medicine and medical quackery. It was with the aim of eliminating this penumbra of ethical practice that a small group of men within the American Medical Association (AMA) dedicated themselves to founding The Council of Pharmacy and Chemistry.

Early on, the council generally believed that doctors had been duped and/or merely lacked information to prescribe rationally. Thus, the council's initial actions were targeted at exposing the fraud and deception of manufacturers with the full expectation that sunshine would be a sufficient disinfectant (Simmons, 1906).⁶ The first five years of the council's work can roughly be thought of as the optimistic phase. The council focused their efforts on exposing deceitful advertising practices with the confidence that doctors would cease patronizing companies so exposed. Moreover, they expected reputable manufacturers to welcome the fact that they no longer needed to compete with such dishonesty. Ultimately, the council was wrong on both accounts. Nevertheless, an examination of their early efforts remains an excellent illustration of the driving force of the arms race—namely, that the satisfaction of the veritistic aims of the council typically frustrated the commercial aims of the products' manufacturers (and vice versa).

The first task the council set for themselves was to evaluate an entire class of proprietary medicines (Sollmann, 1908) and set rules for their promotion. To entice compliance, the council had “sticks” such as being able to prevent products from being advertised in *JAMA*, and “carrots” such as deciding which products to include in CPC publications such as *Useful Drugs*. The primary goal of the council was to deprive from the ranks of respectability the supposedly ethical drugs that were nothing but quack remedies wrapped in the cloak of pseudoscience (derogatively referred to as “nostrums”). A secondary function of this evaluation was to elevate the behavior of the truly ethical firm. Though some

⁶ Hatcher (1916) reports that it seemed almost self-evident that exposure of fraud would lead to its disappearance.

proprietary medication, such as aspirin, were valuable drugs produced by reputable companies, the council began with the suspicion that only a small number of the over 600 proprietary drugs were worthy of any real distinction (Sollmann, 1908).

The cause for the disparity between the council's opinion and general consensus lay primarily in the council's commitment to rational therapeutics in place of empirical therapeutics. The latter held that doctors should employ what they found to work in their practice and not rely on a dogmatic therapeutic system. In contrast, the council championed an alternative epistemological foundation: laboratory science. Crucially, rational therapists rejected standard clinical experience as a wholly unreliable source of knowledge.⁷ Rational therapeutics required that doctors prescribed a specific substance in order to obtain a specific effect (Davis, 1902).

More than just extolling the virtues of science, the actions of the council were tailored to the specific practices perceived to threaten ethical medicine. While most of the council's reports were technical analyses of particular drugs, they occasionally made their review of a product into a lesson for the profession in rational therapeutics. The campaign against headache powders, discussed below, is an illustrative example of such a lesson. Further, it captures a number of predominant themes that run through the council's early work: it included concerns about deception, secrecy, and direct appeal to the laity by the manufacturer; advocacy of science; and condemnation of the corrupting influence of commercial imperatives. In short, the campaign demarcated the aims of reformers from the aims of business and exhorted America's doctors to frustrate commercial strategies that were fiscally successful, but that came at the cost of patient well-being.

⁷ For example, in response to a doctor basing his arteriosclerosis treatment on the beneficial results he obtained in his practice, the council rejoined: "So unscientific is the empirical method that it is hardly worth taking the space to demonstrate its imperfections" (CPC, 1914a, p. 1,035). For an earlier discussion of the imprecision of clinical experience, see Sollmann (1908) and Marks (1997).

2.1 The Most important medium of advertising: Headache powders and the struggle for doctors' hearts and minds

One of the most important commercial assets of a patent medicine was the veil of secrecy concerning its contents. By keeping their ingredients secret, manufacturers could make grandiose claims for products with ordinary components. In an attempt to remove such lucrative façades, one of the first reports put out by the council was a laboratory analysis revealing that a number of headache powders were essentially nothing but acetanilid, a well-known substance that could be purchased for pennies on the dollar (CPC, 1905a).⁸ Given the possibility of addiction, poisoning, and death associated with the use of acetanilid, the drugs served as an example of why empirical therapeutics was problematic (Austin & Larrabee, 1906). The acetanilid mixtures illustrated the dire need for doctors to know not only what they were prescribing, but in what amounts. While the council did not attack a doctor's right to prescribe a drug they believed to be helpful, they enjoined that "no physician, however, has any right, either moral or professional, to prescribe a preparation, concerning the ingredients of which he knows absolutely nothing" (CPC, 1907a; cf. CPC, 1905b). This was one of many ways the council framed their alternative epistemic framework as a doctor's ethical duty.⁹

⁸ Acetanilid was one of three (along with antipyrine and phenacetin) coal-tar-derived products discovered in the mid-1880s that helped legitimate the role of pharmaceutical companies introducing products into the market. These raw products should not be confused with products such as Antikamnia, which contained acetanilide, antipyrine, or phenacetin as a (secret) ingredient. The promotion of the former were far more in line with the ethical standards of the day. For an exploration of how headache powders gave birth to the modern pharmaceutical company and shaped professional disputes about the appropriate roles for doctors and pharmacists, see McTavish (2004). Though Antikamnia became one of the first extended battlegrounds for the council, they were not the first to reveal that it contained acetanilid (e.g., Robinson, 1904).

⁹ These concerns were most pressing for potentially poisonous substances such as acetanilid or iodids, yet they were by no means confined to such substances. For example, the council decried the duplicity of Hagee's Cordial of Cod-liver Oil. Hagee's had cleverly addressed the unpalatableness of cod-liver oil by removing it from the cordial, but not from the name (CPC, 1906a). For an example of iodids see Puckner and Clark (1908).

Of the headache cures, Antikamnia became the paradigm of a proprietary nostrum. Shortly after its contents were exposed (a claim the company denied), the federal government classed acetanilid with opium and cocaine among dangerous ingredients that must be disclosed. It seemed the manufacturer would now either have to admit that Antikamnia contained acetanilid or face federal prosecution. Yet rather than do either, the company replaced acetanilid with a more costly, but related and equally dangerous ingredient (phenacetin). Though this ingredient was also required to be listed, Antikamnia manufacturers used an obscure technical term instead of the popular designation (CPC, 1908a). When secrecy became too risky, the company took refuge in subterfuge. In the council's opinion, the only reasons for secrecy were because a product contained an ingredient such as acetanilid that doctors would only use with caution, or that a product used ingredients that had no expected benefit and was thus something doctors would not use at all (Sollmann, 1908).¹⁰

The council chose Phenalgin, a second acetanilid-containing remedy, to illustrate fraudulent advertising and exploitation of the laity. As with Antikamnia, the manufacturers of Phenalgin hid the fact that it contained toxic components and falsely claimed that Phenalgin was a unique chemical substance. Ads run in 1905 maintained that Phenalgin was manufactured "under the immediate personal supervision of the original inventor," a remarkable feat for a man who had been dead for two years (CPC, 1906b). The council felt that such deceitful claims were merely an indication of duplicity that extended beyond the ad copy, pervading every aspect of the company.

¹⁰ Though this critique of secrecy was implicit in criticisms of proprietary medication, it was sometimes plainly stated. For example, the makers of Micajah's Medicated Uterine Wafers claimed that their product could cure serious diseases such as uterine cancer and gonorrhoea. After laboratory analysis showed the wafers were composed of an astringent and a weak antiseptic, the council noted that the mixtures of common and well-known ingredients "are foisted on the medical profession with no hint as to their composition and with claims made that are not only false, but would immediately be recognized as absurd, if their actual composition were known" (CPC, 1910a, p. 1,216).

By taking a common substance (acetanilid) and combining it with starch and a liberal amount of printer's ink, manufacturers of Phenalgin had convinced doctors to prescribe a drug in situations where it would not help, and caused patients to pay exorbitant fees as a result.¹¹ In addition to advertising, manufacturers could prompt wider initial use by distributing free samples or by selling doctors stock in the company in exchange for their agreement to prescribe the drug. The council attempted to harness the animosity that doctors harbored for patent medications, reminding doctors that many had begun as proprietary drugs:

When the history of the "patent medicine" business comes to be written impartially and fairly, it will be realized that we, the medical profession, have been in no small degree responsible for its growth. Not a few widely advertised nostrums owe their commercial success solely to the ill-considered use accorded them by physicians, to whom they were first exploited. (CPC, 1912b, p. 666)

By including a pamphlet with each bottle, manufacturers informed patients that their new remedy could cure everything from alcoholism to worry (CPC, 1908b).¹² So informed, the patient could avoid the doctor's fee the next time they were ill and procure the nostrum directly from the pharmacist. *Printer's Ink*, the nation's first advertising trade magazine, noted that

in this way the name of the remedies advertised only to physicians get abroad to the general public ... the physician himself ... will be the most important medium of advertising at the command of the proprietary manufacturer. In fact, he is that today. (as quoted in Sollmann, 1908, p. 25)

In the end, patients who abided by the pamphlet would use Phenalgin when acetanilid would do just as well and Phenalgin when something else was rationally indicated. As a result, the only thing many patients had been relieved of was their money. By pointing out such abuses, the council expected the

¹¹ In 1912, a dollar's worth of phenalgin contained four cents' worth of acetanilid (CPC, 1912). Even in cases where the drug was appropriate, the council mourned the pecuniary exploitation caused by a reliance on "ready-made" products. A name-brand deterred doctors from knowing the simple and cheap ingredients that were responsible for the product's efficacy and which could be prescribed in their place by a respectable and competent physician. Given the pseudoscientific verbiage used to obscure the true composition, the council found it "hard to conceive of any one thing that operates more disastrously against scientific therapeutics than the vicious practice of marketing under proprietary names standard and valuable drugs" (Puckner & Hilpert, 1908a, p. 773f).

¹² An alphabetical list of 122 ailments was attached to Antikamnia, but such material was in no way unique.

scales to fall from the medical profession's collective eyes and for the profession to adopt the broader aims of the council of pharmacy and chemistry as their own.

2.2 The fine art of equivocation: Measures and countermeasures

Of the 10 rules instituted by the council, even the brief discussion above identifies several violations and provides an indication of the local environment the council was responding to. Given that rational therapeutics requires the prescription of a specific ingredient for a specific purpose it may seem that only the prohibition of unwarranted therapeutic claims (Rule 6) and the prohibition of unscientific mixtures (Rule 10) are so motivated. However, with proper appreciation of the council's context, every other rule can be seen as promoting rational therapeutics because they were countermeasures to commercial practices that were at odds with best practice.

In order to prevent exploitation, advertising to the public was prohibited whether it was direct (e.g., newspaper ads; Rule 3) or indirect (e.g., listing of indications on the bottle; Rule 4). In the council's eyes, the proliferation of quack remedies was a testament to both the power of advertising and the ignorance of the public. The prohibition on advertising to the public was intended to have the doctor intervene on behalf of the patient, where doctors would use their expertise and training to prescribe remedies that had withstood the tests of the laboratory, instead of those that had withstood the tests of the market.

The need to specify ingredients (Rule 1), especially toxic ingredients (Rule 7), on the label was a direct response to the way that manufacturers were circumventing or manipulating doctors' judgment. Sollmann (1908, p. 37) noted, "it is a puzzling psychological problem, but it seems to be a fact, that it is easy to persuade the physician that the same substance acts differently when it is prescribed as 'Antikamnia' and as 'acetanilidum'." The council assumed that disclosure would make inflated claims

untenable. Further, any company claiming efficacy over and above what could be rationally expected from the ingredients had to support their claims with sufficient evidence (Rule 6).

Many drugs adopted the same tactics as Phenalgin and falsely maintained were not mere mixtures of ingredients, but new synthetic compounds with medicinal properties over and above what could be achieved by the ingredients.¹³ Such claims also protected the manufacturers market share even if they disclosed ingredients. While mixtures could be cheaply duplicated by any competent pharmacist, creating synthetic chemicals was beyond their capacity. Consequently, the council required companies making such claims to include with their submission the proper chemical tests for identity, purity, etc. (Rule 2). Even in cases of genuine synthetics, the requirement to provide the council with such tests was a prerequisite for rational prescription of known ingredients.¹⁴

With the rules in place, the possession of a laboratory allowed the council to independently verify manufacturers' formulae. Given the potential for exposure, reputable firms ceased to make such easily falsifiable claims within a few years of council's establishment (CPC, 1911a). While this was no doubt a positive development in and of itself, it also illustrates a second shortcoming of previous historians' focus on methodological sophistication in isolation: such a view fails to capture the dynamic relation between epistemic aims and the commercial imperatives of medicine. Just as the benefits of castle walls are lessened with the development of siege weapons, the epistemic benefits bestowed by improved methodology only endure as long as they cannot be undermined or circumvented.

¹³ This was a common advertising strategy. For examples, see CPC (1906b, 1910b), cf. Simmons (1907).

¹⁴ Not exemplified above are: honesty in the origin of ingredients (Rule 5); a prohibition of drug names that did not indicate their main ingredient, especially if they indicated the disease to be treated (e.g., Diabetin, Gonosan, Migrainin, etc.; Rule 8); a requirement to inform the council if patent rights are claimed (Rule 9); and a ban on unscientific and useless mixtures (Rule 10). With the exception of Rule 10, these were rarely cited as reasons to reject applications.

When the council made disclosing accurate information about drugs a requirement, companies responded with counter-countermeasures. Specifically, manufacturers started finding ways of making technically true, but vague statements that would satisfy the letter, but not the spirit, of the rule (CPC, 1914b; Puckner, 1919). Especially when it came to claims related to efficacy (Rule 6), the council noticed

the skilful indefiniteness that pervades the claims made for [new drugs] which defies scientific refutation. This verbal obscurity is becoming daily more common in the "literature" of firms marketing nostrums ... they have reduced equivocation to a fine art. Wherever it was possible to put forward claims by implication rather than by expression this has been done. (Puckner & Hilpert, 1908b, p. 1,706)¹⁵

Where the council sought to eliminate dishonest advertising, manufacturers used words to conceal rather than express, carefully crafting the same message in naively defensible terms. Where the council closed a door to dishonesty, industry searched for an open window.

The matter was complicated by the fact that, much to the council's surprise, doctors did not stop prescribing drugs exposed as fraudulent. Instead, doctors bristled at being told how to practice medicine (Buck, 1909). Likewise, companies protested that the council was being too harsh, or had unfairly judged them and falsely impugned their fine product: "so vehement were their protestations and so well simulated were their declarations of Pecksniffian virtue that many physicians were deceived thereby" (CPC, 1908a, p. 467). Whether or not doctors were deceived, it was at least clear that many paid no heed to the council. An examination of prescriptions three years after the council's inception showed that roughly half were being written for proprietary concoctions (Motter, 1908, as cited in Flexner, 1910). The next section further examines some of the ways that industry had found to sell products.

¹⁵ In the case under discussion here, a firm had dropped a drug publicly savaged by the council and then introduced a "new drug" that was virtually identical chemically, but which was advertised with a distinct name and indistinct claims (cf. Lapius, 1918).

3 Humbug is the order of the day: Drug promotion in the early twentieth century

The tensions caused by commercial imperatives had been recognized long before the CPC was founded. The vast majority of the efforts by the council were aimed not at *generating* better evidence, but at altering the communication structure of medical knowledge. Before exploring these changes in Section 4, it is imperative to consider possible sources of medical knowledge and how these were impacted by the promotional efforts that such reforms were attempting to mitigate.

While the council adopted the mantle of champion of the good and the true, this was not how they were universally seen by the profession they tried to reform. Unsurprisingly, irregular physicians (e.g., homeopaths, osteopaths, etc.) reacted negatively to “being ‘bossed’ around by ‘Simmons’ gang” (CPC, 1918a, p. 1,158; cf. CPC, 1919a). Manufacturers promoted a view that resonated with many practitioners, that the council was a group of “theorists” obsessed with experiments, whereas the proprietary medicine makers were practical men interested in treating the sick (Sollmann, 1908). Additionally, manufacturers attempted to undercut the image of the council in the mind of the public by promulgating the claim that, in opposing self-medication, the council was promoting the interest of the doctors, not patients (CPC, 1915a).

At the turn of the century, doctors could learn about new products from colleagues, medical journals, and advertising. Especially for doctors who practiced outside of the major cities on the east coast, the latter two were particularly prominent. Yet as we will see below, journals and advertising were not as clearly distinct, nor as independent, as they might seem at first blush.

3.1 Whose bread I eat, his song I sing: Medical journals and detail men

The ubiquity of the print ad in medical journals provides prima facie evidence that such expenditures provided good returns on investment. Indeed, managers in charge of the economic health of medical

products had long advised their clients that: “Humbug is the order of the day ... It is these efforts that make medicines sell, not so much their intrinsic value. Economy here is no economy at all” (Bickell, 1846, as quoted in Gabriel, 2014, p. 57). Even advertising of the more ethically minded houses evolved from subdued, text-based lists of available products, to eye-catching ads laced with illustrations and testimonials from “independent doctors” extolling the product’s merits (McTavish, 2004).

In addition to influencing doctors directly, advertisements in medical journals had indirect effects by altering the content of the journal outside the advertising pages. In 1895 and 1900, the AMA judicial council reprimanded *JAMA* editors for putting financial considerations ahead of scientific and ethical obligations. Recognizing such problems as endemic, the editor of the *Cleveland Medical Journal* fulminated against “the greed for advertising patronage [which] leads the editor only too often to prostitute his pen and his pages to the advertiser so long as he can secure the coveted revenue” (Forshay, 1900, as quoted in Dykstra, 1955, p. 410). It was felt that no periodical could escape the influence of its advertisers. As evidence, the council detailed the practices of journals that ran advertisements disguised as articles (therapeutic notes, commercial news, etc.), noting that it was tacitly acknowledged that it was not just the advertising pages that were under the control of sponsors (Salisbury, 1906).

In addition to advertising, journals earned income from reprints. In 1913, for example, *The Army and Navy Medical Record* ran a laudatory article for a cod-liver oil called Waterbury’s Compound (cod-liver oil was a commonly recommended nutrient for diabetics). The company in turn purchased reprints of “One of America’s Most Valuable Preparations” and sent them to doctors across the country. *JAMA* ran a piece reminding doctors that the council’s laboratories had shown that if Waterbury’s Compound had any merits, containing cod-liver oil was not amongst them (CPC, 1913a).

In numerous ways, the editorial staff of journals that ran copy for such questionable products defended the interests of their advertisers. When the council found a product to be worthless, journals

who profited from the accused defended their patrons in print and cast aspersions on the council (for examples see: *The Medical Brief*, 1910; *Medical Standard*, 1911). Likewise, editors of such journals censored out or refused to print articles that threatened the financial interests of companies that purchased advertising from them. As one particularly blatant example, consider the curious editorial from the October issue of *The Atlanta Journal—Record of Medicine*. The September issue had published a government list of fraudulently marketed products, which included a product advertised in the *Atlanta Journal*. The following edition apologized for including Gray’s Glycerine Tonic in the list. The council wondered,

if ‘Gray’s Glycerine Tonic’ was fraudulently exploited—and the government and the courts have so declared it—why is it necessary for the editor of a medical journal to apologize to his subscribers for having told them so? The only reason that occurs to us is expressed in the caption to this article [Whose bread I eat, his song I sing]. (CPC, 1916a, p. 38)

In addition to print ads, pharmaceutical manufacturers were constantly in search of ways to influence doctors. They sent detail men to visit doctors and inform them of “the details” about the myriad new products being offered by the company. They were not salesmen *per se* because there was never any sale, but detail men did not come empty handed. Manufactures of remedies such as the digestive tablet Bell-ans were “lavish in [their] distributions of free samples, blotters and other paraphernalia direct to the profession” (CPC, 1915b, 1815).¹⁶ In order to “assist the doctor,” drugs often came with pamphlets explaining the theory behind the drug’s action and extolling its fantastical curative effects (CPC, 1907b, 1914c). Prior to the establishment of the council and their reports, doctors were

assailed from all sides by the din of the detail man, by the laudatory ‘literature’ of the advertising pages, the reading-matter, and even the editorial comments of some respectable journals, he was a helpless and easy victim for the skillful proprietor (Sollmann, 1913, p. 6).

¹⁶ It seems that ink blotters were the free pens of the day. It will be interesting to see what happens when doctors no longer literally write prescriptions. For a historic account of detailers see Brody (2008).

3.2 One of the most dangerous forms of quackery: The commodification of medical evidence

One of the clearest reasons that changes in evidence cannot be considered separately from the responses of commercial firms to changing epistemic standards is due to the commodification of medical evidence. As doctors begin to rely on a certain form of evidence, the commercial value of that type of evidence increases and commercial firms begin trying to produce it as a means of increasing sales. For example, in the early twentieth century the coin of the evidential realm was testimonials from other doctors.

The testimonials for Buffalo Lithia Water provide a clear example such promotion (CPC, 1914d). A discredited but popular theory held that uric acid was at the root of a number of diseases and given that uric acid was dissolved by lithium, Buffalo Lithia Water was promoted as a new elixir of life. In advertising their products, manufacturers obtained glowing recommendations from prominent figures such as a former professor of clinical medicine and current vice president of the AMA: “[Buffalo Lithia Water] is strikingly superior to emergency solutions of lithia tablets and pure water, even where the said solution is an exceedingly strong one” (CPC, 1914d, p. 835). It is not clear whether the doctors providing testimonials were guilty of fraud or simply duped, though given the contents of the product and the therapeutic claims made by the manufacturer, the former appears somewhat more likely.

The plausible efficacy of the product can be determined irrespective of whether the uric acid theory of disease was respectable at the time—Buffalo Lithia Water was just bottled water. Lithium was present in such small amounts that chemists estimated a person would have to drink between 150,000 to 225,000 gallons a day to imbibe a therapeutic dose of lithium, and this fact was available to anyone with a modicum of skill in chemistry. Of course, many doctors did not possess any such skills and by soliciting feedback from a fairly large number of doctors, companies were virtually certain to secure a few favorable testimonials and doctors willing to write up their clinical experiences for publication. The manufacturer was also virtually certain to have such articles published in medical journals they purchased advertising in

(CPC, 1914e).¹⁷ One way or the other, Buffalo Lithia Water touted the endorsements of college faculty, the heads of medical societies, and even the Pope's physician.

Buffalo Lithia Water was just one of the worthless products of high reputation that were kept afloat commercially. As the nostrum business grew in size it spawned further economic opportunities:

Whenever a business assumes certain proportions, subsidiary businesses spring up to cater to the needs of the larger enterprise. For some years the nostrum business has grown so large that it has furnished a more or less precarious life for many individuals who have catered to it. There are, for instance, men whose trade it is to obtain testimonials; others, claiming a long string of imposing degrees, will furnish fake reports and bogus analyses; still others issue at irregular intervals publications with high-sounding names which sell editorial endorsement [sic] to the products of concerns such as are willing to pay the price asked. (CPC, 1913a, p. 1,553)

With the rising importance of classic pharmacology in early 1900s, companies began hiring pharmacologists to provide the type of evidence that doctors thought most reliable.¹⁸ These reports were not just used to detail doctors, but found their way into prestigious journals, as when the manufacturer of Santogen (a "blood rejuvenator" that was essentially cottage cheese) was able to publish a fraudulent pharmacological report in *Lancet* (CPC, 1914f).

Industrial pharmacologists were barred from professional societies and their work was treated with mixture of contempt and pity as

nearly all workers in commercial houses deplore the limitations of their work due to the pressure for financially productive results, and to the necessity of avoiding publications that are inimical to financial interests ... [one] need hardly ask for proof that pressure is often put on investigators to supply desirable results. (Hatcher, 1919, as quoted in Parascandola, 1992, p. 118)¹⁹

¹⁷ Incurable diseases that had temporary reprieves (e.g., tuberculosis) were especially susceptible to overly optimistic, but commercially valuable, testimonials. As a result, this kind of evidence drew early and heavy criticism from the CPC: "A year later, the [tuberculosis] patient reposes peacefully under the sod; but the testimonial lives on" (Sollmann, 1908, p. 21). To prevent overenthusiastic and impulsive endorsements, Sollmann advised doctors to put aside for a year any testimonials they planned on submitting.

¹⁸ For a discussion of classical versus clinical pharmacology, see Parascandola (1992, esp. introduction and Chapter 6). For a discussion of the gradual incorporation of pharmacologists into the pharmaceutical industry, see Swann (1988).

¹⁹ The hackish nature of commercial pharmacology even found its way into popular culture in the Sinclair Lewis' (1925) Pulitzer prize winning novel *Arrowsmith* (see especially Chapter 13 and the description of working for the "pill

In general, manufacturers treated evidence in terms of its economic impact, and were often willing to manipulate findings in order to increase the economic value of the underlying product. While the standards of what constitutes evidence change, the general strategy did not. Whether it is slanted research produced by a sham laboratory, the clinical report from one of the “stables” of uncritical physicians, or cherry-picked testimonials from elite physicians, “the exploitation of new products by exaggerating their merits and repressing knowledge of failures is one of the most dangerous forms of quackery” (Stewart, 1901, p. 1,177).

4 Still in the realms of superstition (1910–1920): Accumulating costly countermeasures

While it would be impossible to draw a sharp line, it is clear that, as the years went on, the council became progressively unsatisfied with the profession. The same ploys that had once been exposed with crusading zeal became formulaic and perfunctory. In one case, after detailing a kickback scam for a nonsensical goat-gland goiter cure, the council began a standard condemnation of the *Official Bulletin of the Chicago Medical Society* for advertising the product, but lost the will to editorialize in mid-sentence: “And this sort of pseudo-scientific claptrap is presented to a presumably learned profession through its own official Bulletin—but what’s the use of commenting!” (CPC, 1916b, p. 970).

In another instance, the council was confronted with a “new product” that was nothing more than a mixture of aspirin, lithium, and a trademarked name. The council lamented: “We had hoped that the time had passed for reputable houses to employ such time-worn methods, but probably they will not stop so long as physicians encourage them by continuing to use such preparations” (CPC, 1910d, p. 1,803; cf. CPC,

peddlers” compared to later descriptions of free and unconstrained research at the McGurk Institute (presumably an allusion to The Rockefeller Institute for Medical Research, a non-profit institute, founded in 1901, devoted to biomedical research.

1915c; CPC, 1916c; Edmunds, 1909).²⁰ While the council continued to agitate for rational therapeutics, when they assigned blame for the persistence of irrationality their rhetoric became progressively less disparaging of manufacturers and increasingly opprobrious of doctors:

Unfortunately we have seen that the most stirring appeals fall on deaf ears; that those who hear consider that they are not concerned in the abuses; and that the abuses continue unchecked despite the clearest analyses and the most earnest entreaties that can be urged. The time has come to consider whether other measures should not be adopted. (Hatcher, 1916, p. 1,341)

Whereas therapeutic monstrosities had previously appeared to the council as proprietary humbug being foisted on doctors, the continued existence of nostrums became a “slur” or a “sad commentary” on the intelligence of a supposedly learned profession (CPC, 1917a, 1917b).

Commenting on the “educational material” sent out to doctors by manufacturers, the great advocate for residential training, William Osler, wrote in the last contribution of his illustrious career:

For years the profession has been exploited in this way, until the evil has become unbearable ... We have been altogether too submissive, and have gradually allowed those who should be our willing helpers to dictate terms and to play the role of masters. Far too large a section of the treatment of disease is today controlled by the manufacturing pharmacists, who have enslaved us in a plausible pseudoscience. (Osler, as quoted in CPC, 1919, p. 109)

Osler hoped that better education would extricate doctors from their “state of thralldom,” a commitment shared by the council. In an effort to reform the field, the council precipitated calls for education reform as part of a long-range effort to create doctors who were familiar with laboratory methods and that would share the council’s standard of evidence. In the meantime, the council also attempted to apply direct pressure by raising the standards to earn their approval and by recruiting others into their sphere of influence so that their decisions were of greater consequence.

²⁰ This issue was discussed in some detail in: CPC, 1920. The belief that manufacturers will continue to supply an existing demand was at least in part a result of explicit statements made by manufacturers to the council (CPC, 1918b).

Here we see a crucial insight revealed by the arms race framework: reformers are interested in creating knowledge only to the extent that new knowledge improves treatment choices.²¹ In the early years, the council labored under the illusion that poor treatment stemmed merely from the lack of a prominent source of reliable evidence. If they had been primarily interested in knowledge for its own sake, the council's task would have been largely complete in 1907. But as the primary driver of reformers was better patient outcomes, the council began to shift their attention towards the packaging and distribution of knowledge, though, as will be discussed in Section 4.2, some of their efforts remained focused on improving the constitution of knowledge.

4.1 Nobody who is absolutely worthless gets in: Reforming medical education

Reformers within the AMA, including many on the council, felt that poor education was one of the primary reasons that worthless remedies remained commercially successful after being exposed by the council. This was true in part because of the extremely low entrance standards at many medical schools and because only the elite medical schools trained doctors in laboratory science.²² Many of the council

²¹ By "known," I mean to indicate only the maximal epistemic position that an agent could be in given the available evidence at the time, regardless of how many agents actually occupied such a position. For example, it could be said that it was known that Antikamnia worked no better than acetanilid because that is what the best available data justified one in believing. It could be further argued that the extent to which such knowledge was *widely* known is irrelevant to epistemology. I disagree. Elsewhere I have argued that social epistemology offers a different account of knowledge that is far more applicable to the concerns of medical epistemology (Holman, 2015).

²² As an illustration of what could pass for a medical school, consider the "laboratory facilities" at Georgia College of Eclectic Medicine and Surgery. The school was housed in "a building which, in respect to filthy conditions, has few equals, but no superiors, among medical schools. Its anatomy room, containing a single cadaver, is indescribably foul; its chemical 'laboratory' is composed of old tables and a few bottles, without water, drain, lockers, or reagents; the pathological and histological 'laboratory' contains a few dirty slides and three ordinary microscopes" (Flexner, 1910, p. 205). Even more disturbing is the thought that these schools were in the vast majority. Flexner described, with a mixture of disdain and eloquence, libraries innocent of books, "laboratories" in proud possession of a single microscope, and dissecting rooms that doubled as chicken coops (pp. 80–89). Still, one might note that even having laboratory space, though foul and ill kept, was a tacit acceptance of the emerging importance of laboratory study for medical education.

members reasoned that if doctors were better educated they would be far more likely to appreciate the efforts of the council.

In order to appear as a neutral third party, the AMA requested that the Carnegie Foundation for the Advancement of Teaching assess the state of medical education. Abraham Flexner was appointed to survey and evaluate each of the 155 medical schools in the US and Canada. Yet it is more accurate to think of Flexner as a front for reformers at the AMA. The criteria that Flexner used to evaluate the schools were precisely the same as those advocated by the AMA's Council on Medical Education and the content of the report was substantially similar to an earlier CPC report.²³

Moreover, the document was more than just a progressive-era equivalent of *The US New and World Report* medical school ranking; it was a systematic treatise on medical education. The first part of the report covered the history of medical training, the economic and professional impacts of over-producing doctors, the necessary qualifications for incoming students, the proper organization of medical schools, the role of state medical boards, and even pressing social questions such as the legitimacy of medical sects, and the education of women and "Negros." The report espoused a revolutionary vision of medical education based on newly emerging laboratory science. It combined soaring rhetoric with caustic assessments, exhorting all concerned to adopt "scientific medicine" and a scientific mindset (even in regular practice).²⁴ Chapters were devoted both to excoriating the state of education in most institutions

²³ This council inspected every medical school in the nation and found that approximately half were acceptable as of 1907 (for more on this report, see Rosen (1983)). This report, while available to Flexner, was unpublished due to AMA ethics codes prohibiting doctors from publicly critiquing other doctors (Starr, 1982). This suggests a likely reason that Flexner, an education specialist, was tasked with the job. For an example of the overlap in evaluative criteria, compare the Flexner report with the criteria advocated by the secretary of the Council on Medical Education for the AMA: Colwell (1909). The extent of Colwell's involvement is unclear, though he may have been Flexner's travel companion for many inspections. While the Flexner Report was ostensibly an independent report, it is clear that the AMA was highly involved. The AMA history identified Colwell as a partner of Flexner's and discussed "their results" (Johnson, 1947).

²⁴ For example, "scientific medicine, therefore, has its eyes open; it takes risks continuously; it does not cure defects of knowledge by partisan heat; it is free of dogmatism and open-armed to demonstration from whatever quarter"

and lauding the ideal medical education (e.g., Johns Hopkins, Michigan, and Harvard).²⁵ It was a standard that few schools could hope to achieve; however, given the superfluity of doctors, Flexner explicitly advised the shuttering of most schools, seeing “no need to make poor doctors—still less to make too many of them”(Flexner, 1910, p. 15).²⁶

Though the ideas expressed in Flexner’s report were neither wholly original nor clearly decisive in changing medical education, the report still retains its importance as a historical document. It is a stirring and vivid portrait of the consequences of unregulated medical practice, and serves as a reminder that while the council was extolling the virtues of scientific therapeutics, only a handful of schools were teaching doctors pharmacology.²⁷ In trumpeting the victories of the emerging discipline of pharmacology, Flexner reprised the propaganda for reform.²⁸ Above all, the document is permeated with two themes that loom large: (1) An encomium to science as the proper foundation for medical knowledge; and (2) a repudiation of commercial forces that threatened to sully the doctors’ noble reputation as healers of the

(Flexner, 1910, p. 53). For discussion of the importance of a scientific approach to clinical practice see (pp. 54–57; 92).

²⁵ Flexner’s alma mater Johns Hopkins served from the beginning as the paradigm of medical education. In preparation to conduct the evaluation, Flexner travelled to Baltimore and spoke with faculty about a scientifically based medical education (Flexner, 1960).

²⁶ State-by-state recommendations followed the assessments of each of the states’ medical schools in Part II. A summary can be found in Part I (Flexner, 1910, pp. 143–155), in which Flexner recommended the elimination of roughly 80% of the existing medical schools.

²⁷ At the turn of the century, pharmacology was only taught at Johns Hopkins (John Able), Michigan (Arthur Cushney), and Western Reserve (Torald Sollmann). Another 10 schools had added a professor of pharmacology by the end of the decade. See Parascandola (1992, Chapters 3 and 4 for an in-depth discussion of the establishment of academic pharmacology in the US).

²⁸ Flexner treated pharmacology most thoroughly in his chapter on the ideal course of study during the first and second year (Flexner, 1910, pp. 63–65). After giving a brief history of the accomplishments of pharmacological research, Flexner (p. 64) noted that the modern doctor is threatened both by the tradition of empirics and “the steady bombardment of the unscrupulous manufacturer.” He found that what was needed was training in the ability to properly appreciate evidence so that a doctor could both “reject humbug” and accept “really authoritative suggestion” (p. 65). If there was any doubt what authority he had in mind, he directed his readers to *The Propaganda for Reform in Proprietary Medicine* published by the Council of Pharmacy and Chemistry of the American Medical Association.

sick, which, if left unchecked, would ultimately bring medical practice to rack and ruin. Together, it was hoped that such an education would deprive manufacturers of untrained minds susceptible to commercial exploitation.

4.2 The committee on therapeutic research: Reforming the clinical trial

Even if successful, the fruits of education reform would take a generation. In the meantime, the council also focused on more immediate issues. When the council was formed, the evidence required to support therapeutic claims was liberal, prohibiting only the grossest abuses and giving the benefit of the doubt to respectable firms. Yet as they became established, the council began to require more exacting evidence than testimonials. As a result, manufacturers of drugs that had previously been included in *New and Nonofficial Remedies* were asked to submit experimental evidence or be omitted from ensuing editions (Sollmann, 1913; for an example, see CPC, 1913b)

A second change was the development of a new way to assess efficacy. As noted above, once the council's laboratory testing made it consequential for companies to misrepresent their ingredients, they began making claims about efficacy where there was no definitive scientific standard beyond what doctors were willing to provide testimonials for. In 1912, the council responded by establishing the Committee on Therapeutic Research under the chairmanship of Torald Sollmann. While many projects were dedicated to identifying drug action, the committee also introduced an innovative method of studying drugs in ways that sought to eliminate personal bias.²⁹

²⁹ For a broader context of methodological development in medical research, see Kaptchuk (1998). While the article is generally enlightening, it fails in several regards concerning the council. First, while Kaptchuk suggested, "the term clinical trial itself was probably coined as late as 1931" (p. 423), the council described its work as performing "clinical trials" (e.g., CPC, 1913c). That said, the meaning of the term has clearly evolved. In the early 1900s, the term applied to a wide assortment of evidence gained from administering drugs to humans instead of animals. The significant distinction for the council was between "haphazard clinical trials" in which doctors tried new drugs on a few patients, and trials like those conducted by the Committee on Therapeutic Research, which were "carefully controlled." The

For example, salicylates occurred naturally, but had also been recently synthesized. Companies that had done so, claimed that synthetic salicylates were therapeutically more efficacious than natural salicylates, and charged higher prices for their product. These claims were substantiated by the testimony of numerous doctors. The council designed a comparative trial to assess the validity of such claims (Hewlett, 1913). The trial began with the committee distributing to clinicians an assortment of numbered—but unlabeled—jars containing either natural or synthetic salicylate. Special care was taken to ensure that neither the patient nor the clinician knew exactly what was being prescribed. Finally, doctors sent back their clinical experiences with the substances so the committee could assess whether assessments differed when doctors were unaware of what they were administering. The design was, in modern parlance, the first double-blind randomized controlled trial.³⁰ Though such trials were infrequent,

term “controlled” was used more broadly than today, and implied only that the investigator had somehow taken into account confounding factors (Marks, 1997). Second, according to Kaptchuk, Anglo-Americans were not concerned with the effects of suggestion and used placebos to keep patients in the trial to control for the natural history of disease (Kaptchuk, n. 102). If this is true more broadly, it does not apply to Sollmann or the council more generally. Sollmann explicitly recommended the use of placebos over a no-treatment control (i.e., natural history) because the “blind test” is “the only method that makes the results purely objective, *really independent of the bias of the observer and the patient*” (Sollmann, 1917, p. 199; emphasis added). Similarly, the council frequently discussed “psychic effects” of inert substances, a concern Kaptchuk claimed entered the literature in the mid-1930s (for a few of many examples, see CPC, 1910e, 1914g, 1915d). Third, Kaptchuk identified the work of Harry Gold as the beginning of the modern era in clinical testing, marking a shift in the American and British understanding of the need for placebos; however, Gold’s work merely reflected a continuation of the attitudes of the council. Kaptchuk attributed the first recognition that a sham treatment had an effect to Harry Gold (1931), because he identified an effect of the “encouragement of any new procedure” over and above the effect of spontaneous recovery (p. 426). However, to provide just one example, the council clearly identified this effect in their campaign to end the indiscriminate use of injections: “The patient is usually interested and impressed by this new, and, to him, mysterious method. There is a psychic element in his reaction to the injection which is not a factor in his reaction to the same drug when given by mouth” (CPC, 1916d, p. 1,451). The council clearly identified that injection has an effect over and above that caused by the physical effects of the drug (if any). Despite the added effect, the council argued that the practice did not justify the danger that accompanied injections, especially in the hands of amateurs. The shared ideas are no coincidence; Gold counted himself as the intellectual heir of Hatcher, council member and student of Torald Sollmann (Gold, 1973). Ultimately, I see no argument for starting the modern era with Gold that does not apply with greater force to the work of the council.

³⁰ Marks (1997) claimed that “as late as 1916 Torald Sollmann was still citing this innovative study as the principle example of the council’s work in clinical investigation” (p. 36). However, this study was really one of many Sollmann and the council had organized. The work Marks cited in support of this claim is a summary article of the work of the Committee in the first four years. First, the Hewlett study does not receive special acclaim in the article; moreover, another study discussed in the review article used the same methodology (though its methodology is suppressed in

they served not only to answer an empirical question, but as methodological exemplars of clinical research that the council expected others to adopt.³¹

4.3 Useful drugs: Reforming easily accessible knowledge

Similar to their increasing standards for evidence of efficacy, the council also introduced and strengthened their rules over time. When the council began, many of the most lucrative products were what it called “mixtures.” Due to advances in chemistry, professional pharmacy had split into manufacturing and dispensing pharmacists (druggists). Traditionally, manufacturing pharmacists supplied the raw ingredients to local pharmacies, where druggists would compound the final product. A doctor’s prescription was a formula of botanicals and/or chemicals to be compounded into a pill, tincture, or elixir by the druggist. While there was a small mark-up on raw ingredients (e.g., acetanilid), much larger sums could be garnered by ready-made products (e.g., Antikamnia). A few products required steam machinery or other apparatus not feasibly owned by dispensers; however, manufacturing pharmacists in no way confined themselves to these products alone.

Simply put, eliminating mixtures would have been a terrible business decision for manufacturing pharmacists. By taking a commonly known substance and adding other ingredients, or by reviving a recipe from the therapeutic scrap heap, companies could create “new” products. As Sollmann noted with

the review—for the full article, see Bastedo (1915). In addition, another double-blind trial was carried out in 1913, using a mixture of oil, cumin, sugar, alcohol, and water as an inert comparator (i.e., a placebo) (CPC, 1913c) and others were carried out subsequently (e.g., CPC, 1917c). While their numbers were not overwhelming, the committee had conducted far more than one clinical trial.

³¹ For example, Sollmann (1917, p. 199) advocated “the blind test” as the only form of clinical evidence that “avoids the pitfalls of clinical observation.” To emphasize the novelty of these trials, a canonical history of the emergence of the clinical trial identifies the first collaborative trial as the 1934 serum treatment of pneumonia and the first double-blind trial as the 1931 trial evaluating sanocrysin (Lilienfeld, 1982). Except for formal statistical analysis, the 1913 trial of salicylates had every component of the modern trial. This included random assignment—“the major theoretical innovation traditionally considered to have spawned the modern clinical trial” (Matthews, 1995, p. 128), even though randomization was not formally implemented until 1926 (in the work of R.A. Fisher).

acetanilid and Antikamnia, doctors would believe that a brand-name product could cure a disease the raw product could not.³² Alternatively, manufactures could claim their mixtures mitigated the well-known drawbacks of standard remedies, and capitalizing on such credulity was lucrative.³³ While this may have been good business practice, it was contrary to the principles of rational therapeutics.

The council argued that prescribing name brands instead of their ingredients meant that doctors could not control the dosage of the active ingredient; indeed, it allowed them to be completely ignorant of what the active ingredient was. As a result, doctors could not apply their experience of one drug to others that were essentially the same. When mixtures contained multiple active ingredients, a prescription necessarily required their administration in a fixed ratio instead of allowing doctors to intentionally prescribe each substance for their patients in the desired amount.³⁴ Further, doctors would not know what accounted for any observed effect. Above all, the trademarked name of a proprietary mixture sustained a specious mystique. Even in cases where a product was exactly what the doctor intended, the doctor's inability to write their own prescription invariably increased the cost to the patient.

Though the council railed against the unscientific nature of mixtures and banned them in 1909, they implemented the ban cautiously at first. It was the first time the council had substantially changed their rules. In their initial application of the ban on mixtures, the council gave manufacturers the benefit of the doubt, but after years of leniency failed to yield a single instance in which a stricter policy would have deprived the profession of a useful drug, the council began requiring definitive evidence of

³² For another example, though antipyrin was the active ingredient in the proprietary medicine advertised as Migrainin, the manufacturers claimed "In the treatment of migraine with phenacetin or antipyrin, the attack is delayed, while with Migrainin it is usually permanently stayed" (CPC, 1909a; cf. CPC, 1915e, 1918c).

³³ Examples include, but are by no means limited to, non-nauseating opium (CPC, 1908c, 1911b) and iodine that would not cause iodism in overdose (Puckner & Clark, 1908).

³⁴ For an example of a mixture with multiple active ingredients, see CPC (1915f). Marks (1997) noted that council discussions showed considerable difficulty in formulating a uniform policy on mixtures with multiple active ingredients.

therapeutic value.³⁵ By taking a harder stance on mixtures, the council reduced the number of drugs that intelligent physicians had to consider. While the constructive research (e.g. clinical trials) conducted by the council was valuable,

destructive work is equally as valuable in the drug line. We are still in the realms of superstition ... if one goes through these mixtures with a red pencil he will find that a minute portion of an iodid, for instance, or a small amount of salicylic acid, that is doing the work and the rest is nonsense. I believe the only official way to show this fact is through the American Medical Association. (Sollmann, 1916, p. 1,442)

The elimination of products was consistent with the council's larger belief that much more therapeutic progress could be made via the simplification of available remedies than by making new ones.

The effort to reduce the number of therapeutic options lay behind a number of the reference books published by the council. Two years after the council's establishment, they compiled their reports into *New and Nonofficial Remedies* and made this available "for the trivial price of 25 cents." While *New and Nonofficial Remedies* contained drugs that had passed the council, many such drugs were not therapeutic advances. The council noted that the "change of a side-chain makes a new drug; but it may have no more importance than would a change of flavor" (Sollmann, 1913, p. 6).³⁶ Moreover, while *New and Nonofficial Remedies* supplemented the *Pharmacopia* and *The National Formulary*, the latter two contained hundreds of drugs that were maintained in new editions based on usage, not effectiveness (Sollmann, 1908). With the publication of *Useful Drugs*, the council sought to give a concise list of well-established drugs that could serve as a foundation for doctors' knowledge of therapeutics and an accessible reference for practitioners. Ultimately, the book became a textbook in many medical schools

³⁵ For examples of drugs that were rejected or omitted because of the stricter application of rule 10, see CPC (1918 d, 1918e).

³⁶ The exclusion of unessential modifications was one of the effects of a stricter implementation of useless and unscientific products (Rule 10) in 1918.

and, not incidentally, was adopted by many state licensing boards as definitive of what students were required to know of therapeutics to become doctors.³⁷

4.4 *The editor's salary: Reforming the finances of medical journals*

The enlistment of state boards provides an example of the growing complexity of the council's attack. Another was the council's concerted effort to cut off the lifeblood of nostrum promotion: medical journal advertising. While the council had encouraged medical journals to follow their lead and reject any advertising from a product they rejected, high standards had very real economic costs.³⁸ The prospect of less revenue led a number of smaller journals to resist following *JAMA's* lead. While advertising policy was ultimately an individual editorial decision, retaining disapproved advertising risked the publication's reputation, as the council made no secret of which journals were towing the line and which remained a "gallery of nostrums."³⁹ Journals that were out of step with the AMA fired back, casting aspersions on the integrity of the council and characterizing the "propaganda for reform" as a self-interested scheme to enhance the AMA's power (The Medical Brief, 1910; Medical Standard, 1911).⁴⁰

In 1912, the council did effectively increase their sway when a number of state journals agreed to abide by the same policy as that of *JAMA*. The council gained such support by providing organizational help in securing advertising for state journals in exchange for control over their advertising policy. The following year, the AMA further relieved the burden of individual journals by forming the Bureau of State Journals to vet advertising for state medical societies (Burrow, 1963; Dowling, 1973). This infrastructure

³⁷ For a list of other examples of council produced literature, see Puckner (1919).

³⁸ *JAMA* reported losing \$25,000 in advertising revenue in the first year that the policy was in action (CPC, 1907c).

³⁹ This particular rebuke of the *International Journal of Surgery* appeared in a review of Sulfuryl Monal, but such comments were by no means isolated (cf. Burrow, 1963, esp. pp. 111–4).

⁴⁰ While the original name of the council's weekly column was "Pharmacology," this was changed in 1911 to the apposite "Propaganda for Reform."

was supplemented by liberal amounts of public shaming. Between 1912 and 1915, when the council dealt with a particularly reprehensible violation, they also included a list of journals carrying advertising for the products (e.g., CPC, 1912c, 1914e, 1915d). To the extent that the profession followed the council's advice to neither contribute nor subscribe to such journals, at least some of the lure of added revenue from disreputable products was offset by fewer subscriptions. Though such actions brought every state society (except Illinois) under the domain of the council's verdict by 1917, a number of other leading journals continued to advertise fraudulent products as before (Hatcher, 1916; Sollmann, 1913).⁴¹

This decision to appeal to other organizations (state societies, licensing boards, etc.) reflected a strategic shift for the council. It reflected a hard-learned lesson: information was not enough. If the goal of the rational therapeutics movement was to improve the care of patients, then the council had to pay as much attention to communication structures as to information being communicated. While it may not count as a "methodological innovation," the publication of *Useful Drugs* had a far greater impact on public health than did publication of the first randomized clinical trial. Similarly, while some journals adopted stricter advertising standards of their own accord, most did not make the switch until the council had created the infrastructure to eliminate the financial cost of acting ethically. While it is possible that the simultaneous campaign launched by the council awoke the moral conscience of editors, it seems more likely to be an illustration of Upton Sinclair's (1935/1994) insight: "it's difficult to get a man to understand something when his salary depends on not understanding it" (p. 109).

⁴¹ While many top journals continued to run objectionable advertising, others abided by the dictates of the council, especially publications such as *Journal of Pharmacology and Experimental Therapeutics*, where council members served on the editorial board (of the 13 original associate editors, D. Edsall, R.A. Hatcher, R. Hunt, and T. Sollmann were also council members at the time the journal was founded, and one other (C.W. Edmunds) would later become so; for further information on the journal see Parascandola (1992, esp. pp. 136–146)

5 The propaganda for reform

The council was created in order to provide the intelligent physician with a source of information about new products independent from “interested manufacturers.” Though the widespread use of worthless products prior to the council was regrettable, it was excusable:

At first sight it seems disheartening to find that physicians are so easily humbugged. Yet when it is remembered that it is impracticable for physicians either to analyze such products themselves or to go to the expense of having chemists do it for them, it is evident that the fault lies not so much with the physicians as with the conditions that make the exploitation of such frauds possible. (Puckner & Warren, 1910)

Yet, the CPC did not seek merely to replace ignorance with knowledge; it confronted deceit and shaped their rules accordingly. For the first three years, they systematically evaluated an entire class of products and published the sum total of its investigations so that any doctor may have access to these findings.

Much to the council’s surprise, this effort failed to result in a sea change.

Though the council continued to publish reports, their understanding of the situation changed. They shifted their focus from knowledge production to knowledge distribution. They began to look for ways to amplify their message and to limit the information coming from unreliable sources. In the years between 1910 and 1920, they engaged in activities aimed at promoting a few established drugs of clear merit. They enlisted influential allies inside and outside the profession and created organizational infrastructure to overcome the financial obstacles that held some back from supporting their work.

While they also developed the method of the “blind test,” such research was literally a side-project. The council discovered that what is “known” does not matter if it is not acted upon. Ultimately, the dictates of the council mattered only insofar as they informed doctors’ beliefs. The collective knowledge of the profession manifested itself in the choices each doctor made, for “with each prescription he renders a decision whether truth or falsehood shall prevail” (Sollman, 1908, p. 46).

Towards this end were directed the main efforts of the council: to focus primarily on their role in developing trial methodology would obscure the day-to-day struggle that led to lasting change.

Additionally, the details of the council's struggle serve two larger purposes. First, they illustrate that a progressive picture of medical epistemology is seriously incomplete. In place of Matthews' "quest for certainty" or Marks' "progress of experiment," I have argued that medical epistemology is best understood as a competitive interaction in which the commercial drivers of medicine can lead to worse prescription practices. Furthermore, that veritistically oriented developments, such as the council's rules and actions, occur directly in response to, and cannot be understood apart from, the marketing ploys of pharmaceutical manufactures.

Asymmetric races have the following set of features: (1) the reliability of any strategy (once it is employed) typically decreases over time; this is because both (2) opponent responses often attenuate the efficacy of one's strategy and (3) opponents engage in a search process to identify and exploit weaknesses; however, (4) because measures are costly it is often disadvantageous to adopt new strategies until they are necessitated by an opponent; and (5) the process results in the gradual accumulation of costly measures (Holman, 2015).

All arms races are driven by incompatible aspirations. In the medical context, I propose that the antagonism stems from a conflict between pharmaceutical companies pursuing economic self-interest and reformers promoting maximally efficacious treatments. The council found such conflicts even at the most reputable firms. Moreover, when the council's actions threatened companies' most profitable products, even reputable manufacturers sought out new promotion techniques that would keep maintain their profits while technically abiding by the council's rules. In response to such countermeasures, the council frequently found that old rules needed to be amended or new rules added (Criterion 1), because manufactures had indeed found ways to circumvent the original strictures (Criterion 2). For example, as

chemical formulae were easy to verify, companies generally stopped misrepresenting drug composition in their advertisements. On the other hand, companies found that they could make claims regarding efficacy without encountering such exacting scrutiny. The prime objective of pharmaceutical marketers became promising as much as possible in advertising, without actually saying anything that could be shown to be literally false. This ultimately led the council to begin enforcing stricter requirements for efficacy claims and the development of “the blind test” (see Section 4.2). Indeed, as argued in Section 2.2, once placed in their historical context, every rule of the council can be seen as a countermeasure to a commercial practice that threatened rational prescription. A similar dynamic of measure–countermeasure was also seen on a smaller scale in the regulation of the chemical constitution of the headache powder Antikamnia in Section 2.1.

The actions of the council were not limited to countermeasures. Once the council realized that information was not enough, they ceased to be merely reactive. The attempted reform of medical education was not a response to a strategy being employed by manufacturers; it was an innovative move that the council hoped would make advertising inferior products less lucrative (Criterion 3).

One of the less perspicuous aspects of the epistemic arms race is the fact that getting too far ahead is disincentivized (Criterion 4). In some cases the added costs are clear, as when Antikamnia switched to using the more expensive ingredient (phenacetin) only when the use of the cheaper ingredient (acetanilide) became stigmatized). The case is less apparent with some of the veritistically oriented measures taken by the council. One might object that apart from bad luck, no one could be epistemically worse off by gathering better evidence.

To appreciate the sense in which this is mistaken, consider a city that constructs a second wall prior to the invention of siege warfare. One might say that they are no worse off for having the second wall. But tactics are not cost free. The reason that participants in an arms race are disincentivized from

getting too far ahead is because the costs outweigh the prospective gains. A second wall adds no further protection against a roving band of marauders and these are costs that should not be paid unnecessarily.

In the same way, the council would not have been veritistically better off if they had subjected every product they assessed to “the blind test” for the simple reason that they lacked the fiscal resources and time to run such tests on every product. Given these limitations, conducting blind tests on one drug comes at the expense of some other endeavor. Thus, there were no expected epistemic gains to be had by conducting an randomized clinical trial on a drug that was a mere mixture, but falsely represented as a new synthetic—time and money were better spent on other endeavors. Yet even with far greater resources, running a clinical trial on these drugs, which were the vast majority of products considered by the council, would not have been the best use of funds given the aims of reformers. With regard to the impact on actual prescription practice, whatever minor gains in knowledge would have been made by running such trials (assuming there were any), a far greater impact on patient outcomes would be had if the funds were put toward more pressing issues, such as the need for reform in medical journals or medical education.

Along the way, the endeavor did become far more extensive and expensive (Criterion 5). The council built a laboratory, published numerous references, began to manage an agency to coordinate the advertising policy of other journals, and lobbied for a number reforms to medical practice. Likewise, the costs of getting a drug on the market began rising as companies began to invest in laboratories of their own and to employ pharmacologists to provide the type of evidence demanded by the council.

In closing, it is worth noting that, contrary to Marks’ (1997, p.20) account, the council’s goal was not “to purge professional therapeutics of commercial influence.” The council did not aim to drive medicine from the marketplace, but to create a market that rewarded effective products:

The difficulty has been, and always must be, the fundamental antagonism between objectives that are largely commercial on the one hand and purely scientific on the other. Nevertheless,

the Council has always believed and has acted on the belief that there is a possible middle ground wherein the interests of therapeutics would not be injured but would go hand in hand with a commercial development based on enlightened self-interest. (CPC, 1920, p. 1,235)

The goal of reform was not the elimination of private interest from medicine, but the corralling of such interests into epistemically reliable channels. Nevertheless, the council's hope that the more reputable firms would celebrate their work did not transpire; instead, even "the large and old-established firms were not only unwilling to cooperate with the Council, but in many instances exhibited a definite antagonism to the Council's work" (CPC, 1920, p. 1,235). Instead of the progress of experiment completing the quest for medical certainty, the council found themselves engaged in an epistemic asymmetric arms race.

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