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Stephen A. Martin

University of Massachusetts Medical School

Et al.

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Opinion Paper

Open Access

Stephen A. Martin*, Scott H. Podolsky and Jeremy A. Greene

Overdiagnosis and overtreatment over time

Abstract: Overdiagnosis and overtreatment are often thought of as relatively recent phenomena, influenced by a contemporary combination of technology, specialization, payment models, marketing, and supply-related demand. Yet a quick glance at the historical record reveals that physicians and medical manufacturers have been accused of iatrogenic excess for centuries, if not millennia. Medicine has long had therapeutic solutions that search for ever-increasing diagnostic problems. Whether the intervention at hand has been leeches and lancets, calomel and cathartics, aspirins and amphetamines, or statins and SSRIs, medical history is replete with skeptical critiques of diagnostic and therapeutic enthusiasm. The opportunity cost of this profusion shapes the other side of the coin: chronic persistence of underdiagnosis and undertreatment. Drawing from key controversies of the 19th and 20th centuries, we chart the enduring challenges of inter-related diagnostic and therapeutic excess. As the present critique of overdiagnosis and overtreatment seeks to mobilize resources from inside and outside of medicine to rein in these impulses, we provide an instructive historical context from which to act.

Keywords: history of diagnosis; overdiagnosis.

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***Corresponding author: Stephen A. Martin, MD, EdM, Assistant Professor of Family Medicine and Community Health, University of Massachusetts Medical School, Barre Family Health Center, 151 Worcester Road, Barre, MA 01005, USA, Phone: 774-443-2246, Fax: 978-355-6549, E-mail: stmartin@gmail.com. <http://orcid.org/0000-0002-0356-5440>**

Scott H. Podolsky: Associate Professor of Global Health and Social Medicine, Harvard Medical School; and Director, Center for the History of Medicine, Countway Medical Library, Boston, MA, USA
Jeremy A. Greene: Associate Professor and Elizabeth Treide and A. McGehee Harvey Chair in the History of Medicine; Departments of Medicine and the History of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

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Introduction

In recent years, an increasing number of clinicians, journalists, health service researchers, and policy-makers have drawn attention to the problems of overdiagnosis and the overtreatment that it so often engenders [1, 2]. Proliferating screening modalities, diagnostic tests, and imaging platforms, often accompanied by strong marketing and weak oversight, present otherwise healthy people with diagnoses that may well lead to more harm than good. Using a variety of descriptions – disease-mongering [3], diagnostic creep [4], or medicalization [5] – critics have pointed to the need to address the issue of overdiagnosis before we enact irreparable cost and harm to our bodies, pocketbooks, and health care systems.

Even though this problem has become particularly acute in the early 21st century, the critique of overdiagnosis is as old as biomedicine itself. Under different terms, overdiagnosis has been iteratively rediscovered since the introduction of laboratory sciences and extensive diagnostic technologies into the field of medicine in the late 19th century. This paper, a brief historical survey of concerns about overdiagnosis, suggests these concerns are grounded in several areas: broader anxieties about the rapidly changing practice of medicine, especially as regards the link between medicine and technology; the interface between medicine and the marketplace; and the prioritization of limited resources within the arena of health intervention.

Medicine and the reign of technology

Many critiques of overdiagnosis are tales of technology run amok. As powerful as our diagnostic technologies have become, the use of imaging techniques and screening modalities now leads to countless invasive interventions on people who may well have lived otherwise perfectly healthy lives [6]. How does one interpret a 3 mm lung nodule? An “elevated” PSA test? What kinds of findings necessitate action, and how do we know such action helps?

The seeds of these dilemmas can be already seen in the first decade of the 20th century, as the concept of a specific diagnostic blood test was first being developed in the research laboratory of the syphilologist August Wassermann. After its introduction in 1906, the Wassermann test for syphilis was applied in many domains outside the syphilis clinic, from military screening to marriage licenses. Clinicians and laboratory researchers at the time knew that the test needed to be calibrated and interpreted (Figure 1) [7]; as the Polish microbiologist and sociologist

Lukwik Fleck later described, the final steps in producing the Wassermann test were like “tuning a [radio] set” [8]. The stakes were high: the medical literature soon became filled with accounts of “false positive” Wassermann results that led to toxicity from unnecessary treatment with arsenicals and mercurials, the rejection of healthy men from military service, and the calamitous prohibition of marriage and accumulation of social stigma among individuals who were free from disease (Figure 2) [9, 10].

The deeper fear that physicians may lose agency to diagnostic technology preceded even the Wassermann test. Oliver Wendell Holmes, in his 1848 *Stethoscope Song*, described to comic effect the misdiagnosis of empyema based on the presence within a hapless physician’s stethoscope of unwanted flies, who buzz upon being pressed against a sick man’s chest:

Then out his stethoscope he took,
And on it placed his curious ear;
Mon Dieu! said he, with a knowing look,
Why, here is a sound that’s mighty queer!

The *bourdonnement* is very clear, –
Amphoric buzzing, as I’m alive!

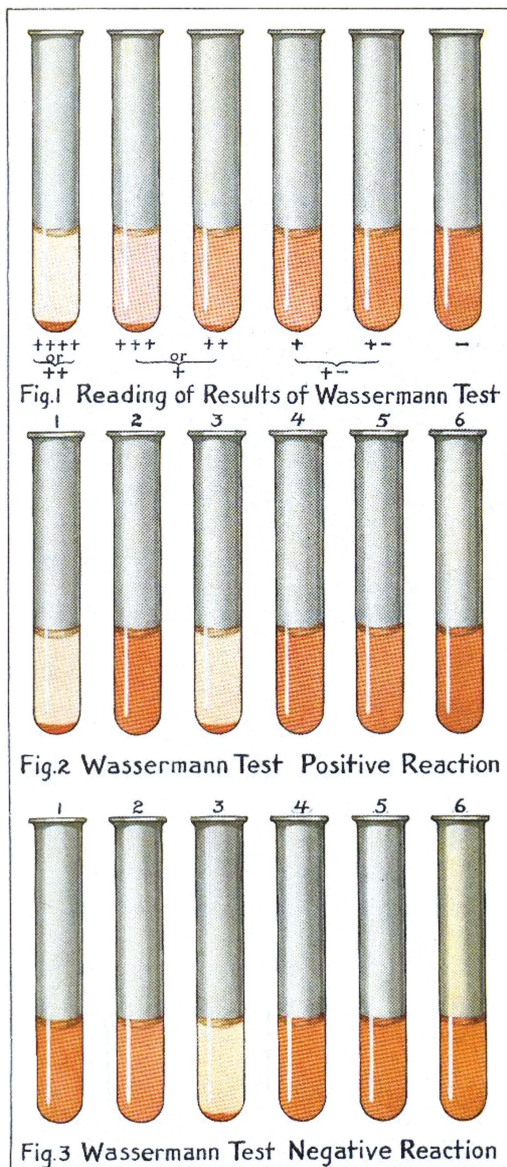


Plate II.

Figure 1: Reading of results of the Wasserman test. Craig, Charles Franklin. *The Wassermann test*. Published with authority of the Surgeon General, United States Army. St. Louis: Mosby, 1918, p. 98.



Figure 2: The sad irony is that false positive rates themselves lead to “false shame and fear.”

Krause EH. *Syphilis False shame and fear may destroy your future: Have your blood tested*. 1938. Available at: <http://www.loc.gov/pictures/item/98514501/>.

Five doctors took their turn to hear;
Amphoric buzzing, said all the five.

There's *empyema* beyond a doubt
 We'll plunge a *trocar* in his side.
 The diagnosis was made out, –
 They tapped the patient; so he died [11].

This was literal “noise,” but since Holmes’ time, critiques of diagnostic technology have been closely bound up in fears of more metaphorical noise (as opposed to signal) and of the runaway power of technology in medicine. From the vantage point of the present, some of these past fears may appear overstated (in the 21st century, the stethoscope is no longer seen as a barrier between doctor and patient), others understated (clinicians all understand the problem of the false positive yet we act as if our test results are absolute).

Either way, false positives of all sorts can lead to both misdiagnosis and overdiagnosis, with potential downstream consequences. And the image of the diagnostic technological Sorcerer’s Apprentice – inherently difficult to control – has persisted. In 1937, cardiologist Paul Dudley White wished aloud for a more specific test to limit the “overdiagnosis” of coronary thrombosis then taking place in hospitals around the country, lamenting: “I now spend more time in excluding the diagnosis of coronary thrombosis than in correcting some other diagnosis.” [12]. Decades after his death, White’s dreams would seemingly be realized in the widespread application of cardiac troponin testing as a specific blood test for myocardial infarction. Yet as with the Wassermann, the troponin test contains its fair share of false positives and “gray area” interpretative challenges [13]. In other words, even technologies developed to limit overdiagnosis can paradoxically reproduce the problem they were intended to resolve.

Medicine and the marketplace

Critics of overdiagnosis have also extended their suspicions beyond the uncaring, disinterested realm of medical technology to actors who are far *too* interested: those who profit directly from the increased diagnosis (and typically treatment) of populations of patients who would have likewise fared just as well, if not better, had they been left undiagnosed and untreated. Over the past decade, Ray Moynihan and Alan Cassels’ influential *Selling Sickness* [14] has been joined by other voices in a movement to identify and expose examples of ‘disease-mongering.’ In a few egregious cases, such as the direct manipulation of

the category of ‘social anxiety disorder’ into a marketable condition to expand sales of Paxil, the benefits to pharmaceutical corporations in selling sickness appear to grossly outweigh the likely public health or clinical benefits to those diagnosed [15]. In many other cases, however, the collision of financial interests and public health benefit is much harder to untangle.

Concerns regarding the effects of Mammon on the purity of diagnostic categories are not unique to the 21st century. Consider, for example, the status of diabetes before and after the marketing of the first oral antidiabetic agent, Upjohn’s Orinase (tolbutamide), in 1957. The development of insulin in the 1920s had changed diabetes from a death sentence into a chronic condition. But the practice of insulin administration entailed a heavy burden and was only accepted by patients who had frankly clinical diabetes, that is, at least evidence of sugar in the urine if not frank symptoms of polydipsia, polyuria, and autophagia on diagnosis.

The development of Orinase created new horizons for Upjohn’s marketers and diabetologists alike, in the emerging field of “prediabetes” or “chemical diabetes.” [16]. Why wait for evidence of sugar in the urine when a far larger population of people could be diagnosed and treated on the basis of high fasting blood sugar alone? In the early 1950s, such individuals would not have been considered diabetics. By the middle of the 1960s, millions of people with this “chemical diabetes” had been diagnosed and placed on regimens of Orinase indefinitely. Upjohn funded several academic diabetologists to research the logic of early treatment. From the perspective of public health officials, this was a progressive venture to intervene on the dread disease of diabetes long before loss of life or limb. From the perspective of Upjohn’s marketers, expanded screening, diagnosis, and treatment helped Orinase sales expand to ever-larger populations of newly defined patients.

Several critics within academic medicine and consumer advocacy groups, however, asked whether the widespread treatment of “asymptomatic diabetes” was justified on any grounds beyond theory and marketing, or whether it constituted a widespread and uncontrolled experiment in medical intervention on large populations. Mass screening for chemical diabetes, from this perspective, became a key example of overdiagnosis and overtreatment, led by the improper collusion of a small group of diabetes specialists and a powerful market incentive. As the controversy rankled and deepened, the NIH agreed to fund a multi-arm study of unprecedented scale, the University Group Diabetes Project (UGDP), to settle whether intervention with tolbutamide could be found to produce

any benefit in patients with asymptomatic diabetes. All parties were surprised, however, when the trial was aborted early not due to lack of evidence but due to evidence of harm: the tolbutamide arm showed increased cardiovascular mortality compared to placebo [17].

In the years since the UGDP study, the initial consensus on the prevention of neuropathy, nephropathy, and retinopathy via glucose reductions has been questioned [18]. Debate over the proper public health calibration of the ideal HbA1c also persists, as does the cost-benefit of enrolling populations with borderline glucose metabolism into regimens of long-term pharmacotherapy [19]. The story of Orinase illustrates the hidden risks to “win-win” collusions between public health and private markets.

Overdiagnosis and underdiagnosis

Finally, throughout history critiques of overdiagnosis have been fueled by a third concern: that attention given to diagnosing and treating conditions of negligible clinical or public health value comes at the cost of neglecting conditions of real significance.

These opportunity costs are perhaps most tragically evident in the case of mental health. Since the labeling and antipsychiatry critiques of the 1960s and 1970s – and through the subsequent debates in the 1980s and 1990s over the expanding role of anxiolytics, antidepressants, and psychostimulants in everyday life – the field of psychiatry has long been the subject of critiques of overdiagnosis [20]. And yet at the same time that the “worried well” of the middle class are supposedly consuming record amounts of psychopharmaceuticals in conjunction with an expansive lexicon of mental disorders (15 new diagnoses were added between DSM-IV and DSM V), a core subset of individuals who are unquestionably suffering from major psychotic or affective disorders remain untreated or undertreated [21]. Over the past half-century, the US has exchanged a flawed system of institutionalized care for a system of non-care and subsequent mass incarceration; the percentage of inmates with serious mental illness now approaches that of the 1840s [22]. Recent data suggest that fewer than half of those in the general population with a mental health disorder received treatment, while only 10% of those with substance addictions other than nicotine are able to find treatment in the health care system [23].

This critique only builds in valence when one links the markets for overtreatment in the global North with the structures of market failure that lead to undertreatment in the global South – not only in terms of mental health, but also in terms of cancer care, cardiovascular health, and

other noncommunicable diseases [24]. This, too, can be traced back almost a half century: One of the World Health Organization’s first symposia on the *Consumption of Drugs*, held in Oslo in 1969, explicitly compared the overconsumption of pharmaceuticals in rich European countries with their relative underconsumption in other parts of the world [25]. In 1971, Julian Tudor Hart codified this effect as the Inverse Care Law: “The availability of good medical care tends to vary inversely with the need for it in the population served” [26, 27]. Part of the longstanding moral critique against overdiagnosis and overtreatment of trivial conditions, then, is that it is linked to underdiagnosis and undertreatment of substantial ones.

Conclusions

As this brief review has demonstrated, while the critique of overdiagnosis has become uniquely resonant in the early 21st century, it is not at all new. Concerns about overdiagnosis – by one name or another – have been present in some form since before the 20th century. These concerns are not sporadic or random but are clearly related to broader concerns about the intersection of medical science, medical industry, medical policy, and medical practice. Tracing the fate of overdiagnosis over time alerts us to larger relationships between medicine and technology, medicine and industry, and medicine and the focus of its analysis and interventions. As medicine continues to evolve in the 21st century, we suspect that such enduring concerns will persist. The history of overdiagnosis teaches us that the problem we are facing is not something extrinsic to medicine, or something that has been recently acquired, but a demon at the heart of the biomedical enterprise that we must continue to work to tame so that our collective efforts might help more than harm those whom we serve.

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