Commentary: The Once and Future Psychiatry

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Abstract

Psychiatry's traditional strengths have lain in an appreciation of the philosophy and psychology of treatment rather than in an ability to advance the public health through the mass delivery of treatment programs. Given how insecurely established treatment effects are for current interventions, and the capacity for developments in neuroscience to create markets rather than to advance understanding, it seems important to maintain traditional strengths. To have a clinical evidence base, consistent with a wider public health mission, psychiatry would need to track more rigorously the effects of the treatments it now administers before advocating for even wider distribution of even more interventions with physical treatments than happens at present.

Acad Med. 2009; 84:000–000.

Dr. Reynolds and colleagues wish to strengthen psychiatry's future, enhance its public health relevance, and underscore its importance to the rest of medicine. These were precisely the goals Philippe Pinel2 had 200 years ago when writing the first textbook of psychiatry. It seems opportune, therefore, to compare Pinel's vision with that of Reynolds and colleagues.

Pinel was the first to introduce and practice what is now termed evidence-based medicine, to which Reynolds and his coauthors appeal when they state that psychiatry has a rich evidence base. Pinel's collating of the evidence led him to the famous aphorism, "It is an art of no little importance to administer medicines properly, but it is an art of much greater and more difficult acquisition to know when to suspend or altogether to omit them." Reynolds and colleagues, in contrast, seem to see psychiatry's public health mission as ensuring that as many people get treated as early as possible.

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Editor's Note: This is a commentary on Reynolds CF, Lewis DA, Detre T, Schatzberg AF, Kupfer DJ. The future of psychiatry as clinical neuroscience. Acad Med. 2009;84:XXX–XXX [fill in x-refs at proofs].

This difference in stance between 1809 and 2009 could stem from the fact that psychiatrists have now amassed more evidence as to what they can usefully do. There are two problems with the notion that our current evidence base accounts for the difference in approach between Pinel and Reynolds and his colleagues. The first is the quality of the current evidence base. The second problem is the divergent interpretations as to what actions this evidence base mandates. It is in the examination of these two problems that the future and credibility of psychiatry, and other disciplines in medicine, lies.

Dr. Reynolds and colleagues refer to psychiatry's broad, "systematic evidence base." The clinical trials of antidepressants in minors, however, illustrate at least two problems with this evidence. First, as of the summer of 2004, these clinical trials provided the greatest known chasm in all of medicine between what the published literature said about the efficacy and safety of these drugs and what it is now known the raw data actually show.

Second, every published controlled trial in the treatment of pediatric depression domain as of 2004 seems to have been either ghostwritten or company written. There is little reason to think that the processes that led to the dissemination of these ghostwritten papers do not still apply in the pediatric domain, to the rest of the evidence base in psychiatry, and, perhaps, in most of medicine. There is nothing about this evidence base on which we can properly rely.

Aside from the quality of the published trials, there is the matter of divergent interpretations. In the combined data from all randomized controlled trials of placebos and antidepressants in adults, drawing on approximately 100,000 subjects, recently published by the U.S. Food and Drug Administration (FDA), 5 out of 10 subjects show a response to active treatment and 4 out of 10 respond to placebo. Dr. Reynolds and colleagues seem to take such data to indicate that these drugs work. An alternate view is that these data suggest that 80% of those apparently responding to an antidepressant would have responded to placebo and that only 1 in 10 people have a response specific to active treatment. Following the evidence on the latter interpretation would prescribe putting a brake on prescriptions and a focus on nonpharmacological treatments.

As of 2004, there had been approximately 70 open studies of antidepressants in minors, all endorsing these agents as safe and effective. We would again argue that the data from even the ghostwritten, selectively published controlled trials in minors should have halted prescribing, but, instead, these controlled trials, published in the best journals with the best known names in the field on the bylines, became the fuel for a therapeutic bandwagon and established a template for companies to use clinical trials to market drugs for unlicensed indications rather than submit data to a regulator.

Dr. Reynolds and his colleagues could have held up this 2006 FDA study, as Pinel almost certainly would have done, as a powerful demonstration of the merits of controlled observations to limit the exploitation of distress. They might have questioned how clinical trials of this
sort in company hands have been used to promote prescribing rather than to temper it. Instead, they have cited the study by Robinson et al9 as evidence for promoting pharmacotherapy in a public health—prevention model for psychiatric illness.7 In that study,8 80% of people taking placebo remained well. Further, there was no difference in efficacy between drug treatment and problem solving. Given the hazards of these drugs, particularly in the elderly, we were surprised that Robinson and colleagues give more space to discussing and recommending escitalopram than the nonpharmacological alternatives.

The divergent interpretations of evidence are strikingly demonstrated in the burgeoning prescription of antipsychotics to infants with supposed bipolar disorders. For 50 years, psychiatrists viewed antipsychotics as too dangerous to use outside secondary care. Now, an extraordinary number of preschoolers in North America are given these drugs on the basis of trial data that show minimal benefits for bipolar disorder in adults.6 To make matters worse, most of the rest of the world does not believe children can have bipolar disorder. The clinicians administering these drugs must simply not register the ballooning weight gain, profound demotivation, and neuropsychiatric syndromes such as tardive dyskinesia that result.

This lack of observation might suggest that, far from advancing, clinicians are actually losing the basic observation skills that were once the bedrock of all medicine and research. Given the authors’ call for a rapprochement with medicine and research. Given the hazards of these drugs, particularly in the elderly, we were surprised that Robinson and colleagues give more space to discussing and recommending escitalopram than the nonpharmacological alternatives.

There is a basis in the way we conduct trials across medicine for a systematic divergence between what the evidence base might seem to show and what really happens before a clinician’s eyes: An active agent may show both a benefit on a surrogate outcome compared with placebo but also produce a higher mortality. This divide occurs in data from trials of SSRIs, COX2 inhibitors, phen-fen, rimonabant, troglitazone, and rosiglitazone and should provoke reflection on the nature of evidence in medicine.

Rather than advocate for more reflection on the nature of evidence in medicine, Dr. Reynolds and his coauthors call on us to refine our means of assessment and to adopt the disciplinary approach of public health medicine. They fail to consider the possibility that this increased assessment might simply make us all more ill, seemingly failing to note the warnings from public health: “All screening does harm, some does good as well.”

Epidemiology sheds light on the complex causal pathways to illness, but risk factors do not necessarily perform well as screening tests. Despite strong associations between risk factors and subsequent disease in epidemiological research, these associations are rarely valuable for early diagnosis or prediction in individuals.9

For example, DEXA scans enhanced our abilities to assess the state of bones in healthy women, but they deliver minimal, if any, clinical benefit. Instead, their widespread use has contributed to the majority of postmenopausal women being defined as having osteoporosis or osteopenia, with an indeterminate number injured by treatments for these conditions. Similarly, the ability to measure lipids has resulted in less than discriminatory prescribing. Large sections of the well population are now exposed to these drugs for primary prevention when they have no prospect of benefit. There is no evidence that women or the elderly benefit from statin prevention, yet practice is not based on this evidence.10 Why? Because not treating “abnormal” numbers is difficult. Still, using numbers and scores as intermediate outcome indicators without showing that these actually benefit patients in the long term is not good clinical medicine.

Psychiatry is certainly making advances in brain scanning and genetic technologies, but it is far from clear that these advances will yield clinical benefits, and it is quite conceivable that within the current framework, as with DEXA scanning, the domains of variation they reveal will be colonized by developments that are not in our patients’ best interests. Any useful signals from research are likely to be buried in the background noise of commercially generated “evidence.”

Aside from these philosophical issues, there are psychological ones also. Kahnemann et al 11 ran an experiment on representativeness bias, in which experimental participants given descriptions of a shy, retiring, and bookish personality were asked to judge whether the person was a nurse or a librarian. It seems that, more confident with stereotypes than with a rational analysis of the probabilities of a situation, people plump for the librarian label, even when provided with the information that the personality profile was selected from a group of 10 profiles, 8 of which were of nurses and 2 of which were of librarians. When faced with exactly the same responses in antidepressant trials—eight responses on placebo for every two specific to active treatment—and asked what has led to a treatment response, we plump for the antidepressant.

It may be that the availability of representative examples like penicillin bias clinicians toward believing that drugs “work,” even though, in the cases of antipsychotics and antidepressants, there are more dead bodies in the active treatment arms of trials than in the placebo arms, which is not what would be expected for penicillin. The bias to seeing treatment efficacy is likely reinforced by recency effects stemming both from hearing “experts” claim that just such evidence points to treatment efficacy and from the availability of authoritative, high-impact-factor publications that make such claims—seemingly to the point at which such influence trumps the evidence of a clinician’s own eyes. Added to this is the therapeutic imperative inherent in medicine, the desire to alleviate distress, which leads to treatment use by the therapeutically impoverished.

Medicine has to be evidence based, but it is, at present, collecting exactly the
wrong sort of evidence if it is to be discriminating in the way that Pinel envisaged. We track the fate of the parcels we put in the post 100 times more accurately than we track the extent to which our treatments may be causing injuries. Time is now for those who care about medicine to decide whether the medical brief should be meeting targets for statins prescribed to lower lipid levels or whether the key numbers to collect are data on those injured by statins, whether we should ensure that everyone who is unhappy or nervous or might become so in the future ends up on a psychotropic drug, or whether we should track the injuries these drugs cause.

Psychiatry did a great deal to introduce controlled trials to medicine, and, of course, it was also the field that took it upon itself to analyze the biases to which all clinicians are subject. We arguably need more, rather than less, philosophy and psychology within the discipline. It is difficult to argue with a plea for the integration of disciplines in research and clinical practice, but we suggest that in enhancing traditional domains, psychiatry will strengthen its broader relevance to public health, its relationships to the rest of medicine, and its future as a discipline. The emphasis in the article by Reynolds and colleagues has been on neuroscience and discipline mongering: we would prefer to see an emphasis on critical clinical skills and professionalism.

References
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