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FEATURE

MEDICALISATION

A new deal on disease definition

How do we replace the old panels of conflicted experts? Ray Moynihan investigates

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As this still-fresh century rolls forth, medicine's imperial project looks on the whole to be in remarkably good health, despite the odd failed campaign. With our new found fondness for preventing disease and premature death we're redefining more and more of the healthy as sick, and then prescribing our new patients lifelong pharmaceutical solutions to reduce their risks. One recent analysis suggests that the definitions of common conditions have broadened so much that virtually the entire older adult population is now classified as having at least one chronic disease.[1]

Yet a growing scrutiny of the seemingly well meaning march of medicalisation suggests we may sometimes be pushing boundaries too wide, and setting treatment thresholds so low, that people with mild problems or modest risks are exposed to the harms and costs of treatment with little or no benefit.[2] It has also become clear that many of the people on the panels that are widening the patient pool have direct financial ties to the companies benefiting from that expansion. Concerns are mounting that doctors are collectively overdiagnosing millions of what were until very recently considered healthy people, and leading voices are asking whether it is time society at large took a more direct role in deciding who really warrants a medical label.[3] Some are now calling for a major renovation of the way in which we define disease.

Conflicted panels widen diseases, lower treatment thresholds

Among the 12 members of the panel that created the controversial diagnostic category "pre-hypertension" in 2003, 11 received money from drug companies, and half of those people declared extensive ties to more than 10 companies each.[4] Critics have rejected "pre-hypertension" as a dangerous pseudo-syndrome that could increase drug company markets,[5] while others point out that it gives a diagnostic label to nearly 60% of the adult population of the United States.[1] Similarly, 11 of the 12 authors of a 2009 statement on type 2 diabetes were heavily conflicted, with authors working as consultants, speakers, or researchers for an average of nine companies each.[6] That panel advocated a contentiously low blood sugar target, and explicitly defended the use of rosiglitazone, a drug since suspended from the European market because of its hazards to human health. Within the field of sexual dysfunction, conflicts of interest have reached new heights of absurdity, with drug company employees joining their paid consultants to design diagnostic tools to identify and then medicate millions of women with a disorder of low desire that may not even exist. [7 8]

One of the best known examples of conflicted panels widening disease definitions comes from the *Diagnostic and Statistical Manual of Mental Disorders.* An examination of those who produced its fourth edition found 56% of panel members had financial ties to drug companies, although for some panels, including that for mood disorders, the figure was 100%.[9] Despite a new American Psychiatric Association policy aimed at reducing conflicts, an analysis of the forthcoming fifth edition found that of those panel members who'd made disclosure statements, exactly 56% had financial relationships with pharmaceutical companies.[10]

"We've got to take this away from the American Psychiatric Association," said Allen Frances, the psychiatrist who chaired the taskforce for the fourth edition, the DSM-IV. He now believes that that edition unwittingly contributed to an explosion of unnecessary diagnoses in the areas of attention deficit, autism, and bipolar disorder. Frances argued that it was not just financial ties that were important, but intellectual conflicts too, where researchers pushed for greater recognition of their own pet conditions. To emphasise this point, he said that he did not believe a drug industry push was behind even those decisions that would most benefit the industry. Today he warns that the forthcoming DSM-V could unleash multiple new "false positive epidemics," where common experiences including binge eating and temper problems are mistaken for the "symptoms" of new disorders.[11] "Experts tend to loathe the idea of missing a potential patient, and they lack the ability to assess the risks and benefits of creating new conditions or widening old ones," he explained to the *BMJ*. "This sort of work should no longer be done by any

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professional association. A new way to define disease is needed."

New panels, free of conflicts of interest

One of the strongest arguments for maintaining conflicted individuals on influential panels is that most leading medical experts do paid work for drug or device companies, and it is almost impossible to find respected individuals who do not. But a recent policy change at the US Food and Drug Administration has made that argument look extremely shaky. Since 2008, tough new guidelines have strongly discouraged doctors with major financial conflicts from taking part in the powerful panels advising on which new drugs should be approved.[12] "It's just laziness, because it's much easier to find a conflicted expert," said Sidney Wolfe, a member of one of the newly constituted panels, and director of the health research group at the Washington, DC based organisation Public Citizen, which has long pushed for such a clean up. Importantly, the Institute of Medicine's landmark report in 2009 also recommended that committees that write clinical practice guidelines should exclude individuals with conflicts of interest.[13] Wolfe argues that the same rules should apply to the panels that define disease, and create the cut-offs for treatment.

"The stakes are very great in terms of public health," Wolfe told the *BMJ*, because the old panels are "constantly broadening the numbers of people defined as ill and recruiting millions of people to drug treatments that may not benefit them." The youthful 73 year old physician cites the example of cholesterol, where people like him in good health have lipid levels defined as "above-optimal," which can lead some doctors to prescribe unneeded cholesterol lowering drugs. Others have observed that treatment thresholds have now become so low that in some cases hundreds of people at low risk of future illness need to take medications for a year, in order for one of them to benefit by having a bad event prevented.[14]

Just a short metro ride from downtown Washington, DC is the sprawling campus of the US National Institutes of Health. The epicentre of the global biomedical project, it also boasts the world's toughest policies on conflicts of interest for panels that draw the lines between health and sickness. "We don't manage conflicts of interest on those panels," says Barry Kramer, until recently a senior manager at the National Institutes of Health, "we simply avoid them." Not only are experts with financial ties prohibited from sitting on the National Institutes of Health state-of-the-science and consensus panels, if a researcher has a declared view on a question being considered, he or she too will be excluded. "Intellectual conflicts of interest can be equally potent," Kramer told the *BMJ*.

A recent example of this model in action was the 2009 state-of-the-science conference on the diagnosis and management of ductal carcinoma in situ of the breast, a condition often treated aggressively.[15] The 14 member panel—which included representatives from nursing, social work, and population health alongside surgeons, radiologists, and oncologists—made the dramatic recommendation to change the very name of the condition. The panel wanted to remove the "anxiety producing term carcinoma" because of the "non-invasive nature" of ductal carcinoma in situ coupled with its "favourable prognosis." The group also highlighted the need to better identify women for whom tissue abnormalities would not progress to breast cancer, in order to prevent them having to risk the side effects of unneeded treatments including tamoxifen and radiotherapy—"both of which are proven to cause cancer," says Kramer, currently a contractor to the National Cancer Institute, and editor of the cancer journal *JNCI*. "I view it as the high court of medicine," he says, referring to the panels that strictly excluded the conflicted, "and the judges are picked for their respect in the field and their ability to assess evidence."

This tough model is endorsed across the other side of the Atlantic by Sir Michael Rawlins, chair of the UK National Institute for Health and Clinical Excellence (NICE). As to the broader question about the risks of over-medicalisation, Rawlins told the *BMJ* that he didn't believe the boundaries of disease were being inappropriately widened, but he agreed that panels writing definitions or setting treatment thresholds should be as free as possible of conflicts, both financial and reputational.

Panels with broad representation, evidence based

The National Institutes of Health model also calls for panels to be more broadly representative than just those within a particular subspecialty. It specifies that as a general rule, along with practising clinicians and researchers, panels should include biostatisticians, epidemiologists, non-health professionals, and people representing the wider public interest.[16] The addition of a health economist is also critically important, to assess the cost effectiveness of changing diagnostic categories.

Given the growing evidence on the social and environmental determinants of health and disease,[17] perhaps the membership of newly renovated panels might be broadened even further. For example, might it be possible that the myriad panels that focus in a fragmented way on treating surrogate end points like blood pressure or lipids be subsumed into a broad new panel addressing multiple measures to fight cardiovascular disease in a more holistic way, which would include representatives from the worlds of transport, building design, and food regulation, along with doctors and others? Fran Baum, public health professor at Flinders University in Australia and a member of the World Health Organization's Commission on the Social Determinants of Health, says that the idea of panels combining a clinical and social approach is feasible. "It would be good to have the conversation," she told the *BMJ* cautiously, "but it would need to happen in the context of government policy less dominated by clinical medicine and more interested in addressing social determinants."

Whatever the make-up of new more independent and broadly representative panels, everyone agrees on the need to inform decisions with the best evidence, such as that currently produced by systematic reviews, including those from the international Cochrane Collaboration. Yet groups like Cochrane have so far focused their reviews far more on interventions, rather than assessing the different forms of evidence used to make decisions about disease definition or diagnosis. As a result the claims about the nature or extent of medical conditions are rarely exposed to the same rigorous systematic scrutiny as the studies of treatments for them.

Jeremy Grimshaw, co-chair of the Cochrane Collaboration Steering Group, says a key problem is the lack of a gold standard "against which to judge different claims around how to define disease." Further complicating matters, the judgments about what constitutes sufficient distress or risk to warrant a definition of "case-ness," and what might best be considered normal life, are "highly subjective decisions." Despite the complexities, Grimshaw sees some merit in the idea of new citizens' panels making these judgments, empowered and informed by the evidence from systematic reviews by groups including the Cochrane Collaboration.

Perhaps one of the most contentious questions is whether the process of disease definition is deemed so important that it warrants more regulatory oversight, rather than the loose self regulating system that currently exists. While the US National Institutes of Health consensus panels may have a strict model, many of the groups around the world deciding who is normal and who is not are simply self interested professional societies, whose panels are riddled with conflicts. "New diagnoses are as dangerous as new drugs," said Allen Frances. "We have remarkably casual procedures for defining the nature of conditions, yet they can lead to tens of millions being treated with drugs they may not need, and that may harm them." Frances wonders whether regulatory agencies should play more of a role in overseeing new panels, and is developing proposals as part of a forthcoming book.

Medicalisation and its discontents

Meanwhile medicalisation and its discontents continue, with one of the latest controversies being gestational diabetes, a condition of raised blood glucose in pregnant women. A 2010 revision of the definition by an international panel of professional societies has just dramatically lowered the threshold for diagnosis, more than doubling the number of women classified as having the condition, to almost 20% of the entire pregnant population.[18] While the new definition is already being adopted in a number of jurisdictions, serious concerns are being expressed in the medical literature that the proposed screening test has poor reproducibility for mild cases, the evidence of benefit for the newly diagnosed pool of pregnant women is weak, and the magnitude of that benefit modest at best.[19] The international panel's report argues that the widened definitions will reduce health problems, including babies being "large for gestational age," but it concedes that some recommendations are based on opinion because good evidence is not yet available, and that the new expanded definition "will substantially increase the frequency of hyperglycaemic disorders in pregnancy."[18] According to the critics, another case study of over-medicalisation is in the making, with the risk that millions of women will receive an unneeded label, and vast resources will be wasted. Perhaps those planning to conceive a new deal in defining disease should find a hotel room, and quick.

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1 Kaplan R, Ong M. Rationale and public health implications of changing CHD risk factor definitions. *Annu Rev Public Health* 2007;28:321-44.
2 Welch G, Schwartz LM, Woloshin S. Over-diagnosed: making people sick in the pursuit of health. Beacon Press, 2011.
3 Godlee F. Are we at risk of being at risk? *BMJ* 2010;341:c4766.
4 Chobanian A, Bakris G, Black H, Cushman W, Green LA, Izzo JL Jr, et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003;42:1206-52.
5 Moynihan R. Who benefits from treating prehypertension? *BMJ* 2010;341:c4442
6 Rodbard H, Jellinger P, Davidson J, Einhorn D, Garber AJ, Grunberger G, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control *Endocr Pract* 2009;15:540-59
7 Clayton, A, Goldfischer E, Goldstein I, Derogatis L, Lewis-D'Agostino DJ, Pyke R. Validation of the Decreased Sexual Desire Screener (DSDS): a brief diagnostic instrument for generalised acquired female hypoactive sexual desire disorder (HSDD). *J Sexual Med* 2009, published online 13 January.
8 Brotto L. The DSM diagnostic criteria for hypoactive sexual desire disorder in women. *Arch Sexual Behav* 2009, published online 24 September.
9 Cosgrove L, Krimsky S, Vijayaraghavan M, Schneider L. Financial ties between DSM-IV panel members and the pharmaceutical industry. *Psychother Psychosom* 2006;75:154-60.
10 Cosgrove L, Bursztajn H, Krimsky S. Developing unbiased diagnostic and treatment guidelines in psychiatry (letter). *N Engl J Med* 2009 360;19:2035-6.
11 Frances A. The first draft of DSM-V. *BMJ* 2010;340:c1168
12 US Department of Health and Human Services Food and Drug Administration. FDA guidance. 2008. www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM125646.pdf.
13 Institute of Medicine. Conflict of interest in medical research, education, and practice. 2009. www.iom.edu/Reports/2009/Conflictof-Interest-in-Medical-Research-Education-and-Practice.aspx.
14 Yudkin JS, Richter B, Gale EA. Intensified glucose lowering in type 2 diabetes: time for a reappraisal. *Diabetologia* 2010;53:2079-85.
15 NIH State of the Science Conference. Diagnosis and management of ductal carcinoma in situ (DCIS). 2009. http://consensus.nih.gov/2009/dcisstatement.htm.
16 NIH. About the consensus development program. http://consensus.nih.gov/aboutcdp.htm.
17 WHO. Reports of the WHO Commission on the Social Determinants of Health www.who.int/social_determinants/en.
18 International Association of Diabetes and Pregnancy Study Groups. Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy. *Diabetes Care* 2010;33:676-82.
19 Ryan E. Diagnosing gestational diabetes *Diabetologia* 2011;54:480-6.

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Summary points

- Many existing panels that define and expand diseases are heavily tied to drug companies
- Some voices are calling for fresh new ways to define disease, with new panels
- New panels could be independent of industry and entirely free of conflicts of interest
- The constitution of new panels could be broadened, more representative, with more citizens' voices
- The best evidence should inform decisions, including evidence on social determinants