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FEATURE

MEDICALISATION

Preventing overdiagnosis: how to stop harming the healthy

Evidence is mounting that medicine is harming healthy people through ever earlier detection and ever wider definition of disease. With the announcement of an international conference to improve understanding of the problem of overdiagnosis, **Ray Moynihan**, **Jenny Doust**, and **David Henry** examine its causes and explore solutions

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Medicine's much hailed ability to help the sick is fast being challenged by its propensity to harm the healthy. A burgeoning scientific literature is fuelling public concerns that too many people are being overdosed,[1] overtreated,[2] and overdiagnosed.[3] Screening programmes are detecting early cancers that will never cause symptoms or death,[4] sensitive diagnostic technologies identify "abnormalities" so tiny they will remain benign,[5] while widening disease definitions mean people at ever lower risks receive permanent medical labels and lifelong treatments that will fail to benefit many of them.[3 6] With estimates that more than $200bn (£128bn; €160bn) may be wasted on unnecessary treatment every year in the United States,[7] the cumulative burden from overdiagnosis poses a significant threat to human health.

Narrowly defined, overdiagnosis occurs when people without symptoms are diagnosed with a disease that ultimately will not cause them to experience symptoms or early death.[3] More broadly defined, overdiagnosis refers to the related problems of overmedicalisation and subsequent overtreatment, diagnosis creep, shifting thresholds, and disease mongering, all processes helping to reclassify healthy people with mild problems or at low risk as sick.[8]

The downsides of overdiagnosis include the negative effects of unnecessary labelling, the harms of unneeded tests and therapies, and the opportunity cost of wasted resources that could be better used to treat or prevent genuine illness. The challenge is to articulate the nature and extent of the problem more widely, identify the patterns and drivers, and develop a suite of responses from the clinical to the cultural.

At the clinical level, a key aim is to better discriminate between benign "abnormalities" and those that will go on to cause harm. In terms of education and raising awareness among both the public and professionals, more honest information is needed about the risk of overdiagnosis, particularly related to screening. More deeply, mounting evidence that we're harming healthy people may force a questioning of our faith in ever-earlier detection, a renewal of the process of disease definition, and a fundamental shift in the systemic incentives driving dangerous excess.

Next year, an international scientific conference called Preventing Overdiagnosis aims to deepen understanding and awareness of the problem and its prevention. The conference will take place on 10-12 September 2013 in the United States, hosted by the Dartmouth Institute for Health Policy and Clinical Practice in partnership with the *BMJ*, the leading US consumer organisation Consumer Reports, and Bond University. The conference is timely, as growing concern about overdiagnosis is giving way to concerted action. The *Archives of Internal Medicine*'s feature "Less is More" now regularly augments the evidence base,[9] high level health policy groups in Europe are debating ways to tackle excess,[10] and the recently launched Choosing Wisely campaign warns about dozens of potentially unnecessary tests and treatments across nine specialties.[11]

Many factors—including the best of intentions—are driving overdiagnosis, but a key contributor is advances in technology. The literature suggests several broad and related pathways to overdiagnosis: screening detected overdiagnosis in people without symptoms; overdiagnosis resulting from use of increasingly sensitive tests in those with symptoms;

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overdiagnosis made incidentally—"incidentalomas"; and overdiagnosis resulting from excessively widened disease definitions. These different pathways are not mutually exclusive, and a more rigorous classification of the different forms of overdiagnosis will be a focus of discussion at the 2013 scientific conference.

Screening detected overdiagnosis

This pathway to overdiagnosis occurs when a screening programme detects disease in a person without symptoms but the disease is in a form that will never cause that person symptoms or early death. Sometimes this form of disease is called pseudodisease. Contrary to popular notions that cancers are universally harmful and ultimately fatal, some cancers can regress, fail to progress, or grow so slowly that they will not cause harm before the individual dies from other causes.[5] As we will discuss below, there is now strong evidence from randomised trials and other studies comparing screened and unscreened populations that an important proportion of the cancer detected through some popular screening programmes may be pseudodisease.[4 12] Evidence from autopsy studies suggests a large reservoir of subclinical disease in the general population, including prostate, breast, and thyroid cancer, the bulk of which will never harm.[12] Similarly, screening the hearts of people without symptoms or at low risk may also lead to overdiagnosis of coronary atherosclerosis and subsequent unnecessary interventions.[13] Our understanding of the nature and extent of overdiagnosis and the amount of pseudodisease detected by screening remains limited but is evolving, and as Woolfe and Harris observed recently in *JAMA*, "concern about overdiagnosis is justified."[14]

Increasingly sensitive tests

People presenting to doctors with symptoms can also be overdiagnosed because changes in diagnostic technologies or methods have enabled the identification of less severe forms of diseases or disorders. It is becoming clearer that a substantial proportion of these earlier "abnormalities" will never progress, raising awkward questions about exactly when to use diagnostic labels and therapeutic approaches traditionally deployed against much more serious forms of disease.

Incidentalomas

Diagnostic scanning of the abdomen, pelvis, chest, head, and neck can reveal "incidental findings" in up to 40% of individuals being tested for other reasons.[15] Some of these are tumours, and most of these "incidentalomas" are benign. A very small number of people will benefit from early detection of an incidental malignant tumour, while others will suffer the anxiety and adverse effects of further investigation and treatment of an "abnormality" that would never have harmed them. As others have shown, the rapidly rising incidence for some cancers, set against relatively stable death rates, is a phenomenon suggestive of widespread overdiagnosis, whether from screening or the detection of incidentalomas (figure⇓).[12]

Excessively widened definitions

Another pathway to overdiagnosis is through disease boundaries being widened and treatment thresholds lowered to a point where a medical label and subsequent therapy may cause people more harm than good. Changing diagnostic criteria for many conditions are routinely increasing the numbers of people defined as sick,[16] causing virtually the entire older adult population to be classified as having at least one chronic condition.[17] This widening has happened both with asymptomatic conditions that carry a risk of an adverse event, such as osteoporosis, where treatments may do more harm than good for those at very low risk of fracture,[18] and for behavioural conditions such as female sexual dysfunction, where common difficulties have been reclassified as dysfunctions.[19]

Such changes in diagnostic criteria are commonly made by panels of health professionals with financial ties to companies that benefit directly from any expansion of the patient pool.[20] As definitions broaden and thresholds fall, people with smaller risks or milder problems are labelled, which means the potential benefits of treatment decline, raising the possibility that harms will outweigh benefits. As Welch and colleagues estimated in their 2011 book *Overdiagnosed*,[3] many people diagnosed and treated long term for near-normal cholesterol concentration or near-normal osteoporosis may be "overdiagnosed," in the sense that they would never have experienced the events their treatments are designed to prevent.

A related form of overdiagnosis occurs when people are diagnosed outside of already widened diagnostic criteria, as can occur when inappropriate manufacturers' norms exaggerate the incidence of abnormality,[21] when diagnostic methods wrongly label random or normal fluctuations in biomarkers as true abnormalities,[22] or when important qualifiers are left out of the process of diagnosis.[23]

Examples of overdiagnosis

The growing evidence on overdiagnosis suggests the problem may exist to varying extents across many conditions (box 1), including those for which underdiagnosis may simultaneously be a feature. For some conditions, the evidence remains tentative and speculative, for others it has become much more robust.

Breast cancer

Arguably the strongest evidence of overdiagnosis comes from studies of screening detected breast cancers, though estimates of its extent are wide ranging. A 2007 systematic review in *Lancet Oncology* found the proportion of overdiagnosis of invasive breast cancer among women in their 50s ranged from 1.7% to 54%.[24] An Australian study estimated the rate was at least 30%,[25] while a Norwegian study calculated 15-25%.[26] A 2009 systematic review in the *BMJ* concluded up to one third of all screening detected cancers may be overdiagnosed.[4] However, even with strong evidence from population based studies, it is currently impossible to discriminate between cancers that will harm and those that will not.

Thyroid cancer

While the chances of tests detecting a thyroid "abnormality" are high, the risk it will ever cause harm is low.[3 27] Analysis of rising incidence shows many of the newly diagnosed thyroid cancers are the smaller and less aggressive forms not requiring treatment,[28] which itself carries the risk of damaged nerves and long term medication.[3]

Gestational diabetes

A 2010 revision of the criteria defining gestational diabetes recommended a dramatic lowering of the diagnostic threshold, more than doubling the number of pregnant woman classified to almost 18%.[29] Proponents argue universal screening with the new definition will reduce health problems, including babies being "large for gestational age."[29] Critics, however, are calling

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Box 1: Problems of overdiagnosis

Asthma—Canadian study suggests 30% of people with diagnosis may not have asthma, and 66% of those may not require medications[37]

Attention deficit hyperactivity disorder—Widened definitions have led to concerns about overdiagnosis; boys born at the end of the school year have 30% higher chance of diagnosis and 40% higher chance of medication than those born at the beginning of the year[46]

Breast cancer—Systematic review suggests up to a third of screening detected cancers may be overdiagnosed[4]

Chronic kidney disease—Controversial definition classifies 1 in 10 as having disease; concerns about overdiagnosis of many elderly people [23]

Gestational diabetes—Expanded definition classifies almost 1 in 5 pregnant women [31]

High blood pressure—Systematic review suggests possibility of substantial overdiagnosis[22]

High cholesterol—Estimates that up to 80% of people with near normal cholesterol treated for life may be overdiagnosed[3]

Lung cancer—25% or more of screening detected lung cancers may be overdiagnosed[56]

Osteoporosis—Expanded definitions may mean many treated low risk women experience net harm[18]

Prostate cancer—Risk that a cancer detected by prostate specific antigen testing is overdiagnosed may be over 60%[12]

Pulmonary embolism—Increased diagnostic sensitivity leads to detection of small emboli. Many may not require anticoagulant treatment [39]

Thyroid cancer—Much of the observed increase in incidence may be overdiagnosis[28]

for an urgent debate before the new expanded definition is more widely adopted, because they fear many women may be overmedicalised and overdiagnosed, that the screening test has poor reproducibility for mild cases, the evidence of benefit for the newly diagnosed pregnant women is weak, and the benefit modest at best.[30 31]

Chronic kidney disease

More than 10% of adults in the United States are now classified as having some form of chronic kidney disease.[32] A working definition launched as part of new clinical guidelines[33] asserts that an estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73m^2 and sustained for three months or longer is deemed abnormal, a decision critics argue automatically creates the potential for overdiagnosis, particularly among elderly people.[34]

According to Winearls and Glassock in an article last year the new classification system is "like a fishing trawler" and "captures many more innocent subjects than it should."[23] They estimate that up to one third of people over 65 may meet the new criteria, yet of these, fewer than 1 in 1000 will develop end stage renal disease each year. They also point to major problems with the reliability and consistency of the eGFR test and express concern many older people are being labelled on the basis of a single and potentially inaccurate laboratory measure. Elsewhere they have argued that "the majority of those held to have CKD [chronic kidney disease] have no identifiable kidney disease" and they've highlighted attempts by some organisations to move away from the controversial new definition, raise the threshold for diagnosis, and dramatically reduce prevalence.[35] Responding to criticisms, proponents have defended the new definition as being "clear, simple, and useful."[36]

Asthma

Although asthma can be severe and may be underdiagnosed and undertreated, some studies suggest that there may also be substantial overdiagnosis. One large study in 2008 found that almost 30% of people diagnosed as having asthma did not have the condition, and almost 66% of those did not need drugs or asthma care during six months of follow-up.[37] The authors concluded, "A substantial proportion of people . . . may be overdiagnosed with asthma and may be prescribed asthma medications unnecessarily." In the same year a Dutch study found that of 1100 patients using inhaled corticosteroids, 30% may have been using the drugs without any clear indications.[38]

Pulmonary embolism

Doctors think of pulmonary embolism as a "not to be missed" diagnosis, because failure to detect it can have catastrophic consequences. Historically it was diagnosed only when the blockage was large enough to cause infarction of part of the lung or haemodynamic instability. In such patients, treatment with an anticoagulant or a thrombolytic agent was considered mandatory. Now, however, computed tomography (CT) pulmonary angiography can detect smaller clots, and there is uncertainty about whether treatment is always necessary.[39] Analysing trends before and after the widespread introduction of CT pulmonary angiography, Weiner and colleagues suggested that the almost doubling in incidence "reflects an epidemic of diagnostic testing that has created overdiagnosis," with much of the increase consisting of "clinically unimportant" cases that "would not have been fatal even if left undiagnosed and untreated."[40] An observational study is investigating the safety of not treating people with very small blood clots.[41]

Attention deficit hyperactivity disorder

Much has been written about expanding diagnostic definitions within mental illness and concerns about the dangers of overtreatment.[42] Debate has intensified with suggestions that current processes for defining disease may be contributing to the widespread overdiagnosis of conditions such as bipolar, autistic disorder, and attention deficit hyperactivity disorders.[43 44] One focus of concern is the possible overdiagnosis of children, who have no say in the appropriateness of a label that can permanently change their lives. This is particularly salient with attention deficit hyperactivity disorder.[45] A recent study of almost a million Canadian children found boys born in December (typically the youngest in their year) had a 30% higher chance of diagnosis and 40% higher chance of receiving medication than those born in January, with the authors concluding their findings "raise concerns about the potential harms of overdiagnosis and overprescribing."[46]

Drivers of overdiagnosis

The forces driving overdiagnosis are embedded deep within the culture of medicine and wider society, underscoring the challenges facing any attempt to combat them (box 2). A key driver is technological change itself. As Black described in 1998, the ability to detect smaller abnormalities axiomatically tends to increase the prevalence of any given disease.[5] In turn this leads to overestimation of the benefits of therapies, as milder forms of the disease are treated and improvements in health are

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wrongly ascribed to treatment success, creating a "false feedback" loop fuelling a "cycle of increasing testing and treatment, which may eventually cause more harm than benefit."[5]

The industries that benefit from expanded markets for tests and treatments hold widereaching influence within the medical profession and wider society, through financial ties with professional and patient groups and funding of direct-to-consumer advertising, research foundations, disease awareness campaigns, and medical education.[8] Most importantly, the members of panels that write disease definitions or treatment thresholds often have financial ties to companies that stand to gain from expanded markets.[20] Similarly, health professionals and their associations may have an interest in maximising the patient pool within their specialty, and self-referrals by clinicians to diagnostic or therapeutic technologies in which they have a commercial interest may also drive unnecessary diagnosis.

Avoidance of litigation and the psychology of regret is another obvious driver as professionals can be punished for missing the early signs of disease yet don't generally face sanctions for overdiagnosing. Quality measures focused on doing more may also encourage overdiagnosis in order to meet targets for remuneration incentives.[47]

An intuitive belief in early detection, fed by deep faith in medical technology is arguably at the heart of the problem of overdiagnosis. Increasingly we've come to regard simply being "at risk" of future disease as being a disease in its own right. Starting with treatment of high blood pressure in the middle of the 20th century,[48] increasing proportions of the healthy population have been medicalised and medicated for growing numbers of symptomless conditions, based solely on their estimated risk of future events. Although the approach has reduced suffering and extended life for many, for those overdiagnosed it has needlessly turned the experience of life into a tangled web of chronic conditions. The cultural norm that "more is better" is confirmed by recent evidence suggesting patient satisfaction flows from increased access to tests and treatments, even though more care may be associated with greater harm.[49 50]

What can we do about overdiagnosis?

Building on existing knowledge and activity, the 2013 conference on overdiagnosis will provide a forum for learning more, increasing awareness, and developing ways to prevent the problem (www.preventingoverdiagnosis.net). Research on overdiagnosis is now recognised as part of the future scientific direction of the National Cancer Institute's division of cancer prevention in the United States.[51] The 2013 conference hopes to provide researchers working in this field with the chance to share and debate methods and further advance research agendas. As to education, the development of a range of curriculums and information packages could help raise awareness about the risks of overdiagnosis, particularly associated with screening.[52] In association with the *BMJ,* a series of articles about the potential for overdiagnosis within specific conditions is being planned. And at the level of clinical practice new protocols are being developed to bring more caution in treating incidentalomas.[3] Similarly, some are urging that we consider raising the thresholds that define "abnormal"—in breast cancer screening, for example—and evaluate methods of observing changes to some suspected pathologies over time, rather than intervening immediately.[53] As we've seen, early studies of how to safely undiagnose or de-prescribe are starting to emerge.

At a policy level, reform of the process of defining disease is urgently required, with one model coming from the National Institutes of Health in the United States, where people with financial or reputational conflicts of interest are disqualified from panel membership.[20] Dispassionate assessment of evidence may result in disease definitions being narrowed, as has been seen with the recent tentative proposals to raise thresholds for high blood pressure that could demedicalise up to 100 million people.[54] Processes for defining disease may also benefit from an attempt to synthesise the evidence from clinical medicine with literature on the wider social and environmental determinants of health. Other policy reforms could review the permanency of some diagnostic labels, address calls for increased independence in the design and running of scientific studies,[55] and adjust the structural and legal incentives driving overdiagnosis.

Concern about overdiagnosis does not preclude awareness that many people miss out on much needed healthcare. On the contrary, resources wasted on unnecessary care can be much better spent treating and preventing genuine illness. The challenge is to work out which is which, and to produce and disseminate evidence to help us all make more informed decisions about when a diagnosis might do us more good than harm.

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Drivers of overdiagnosis

- Technological changes detecting ever smaller "abnormalities"
- Commercial and professional vested interests
- Conflicted panels producing expanded disease definitions and writing guidelines
- Legal incentives that punish underdiagnosis but not overdiagnosis
- Health system incentives favouring more tests and treatments
- Cultural beliefs that more is better; faith in early detection unmodified by its risks

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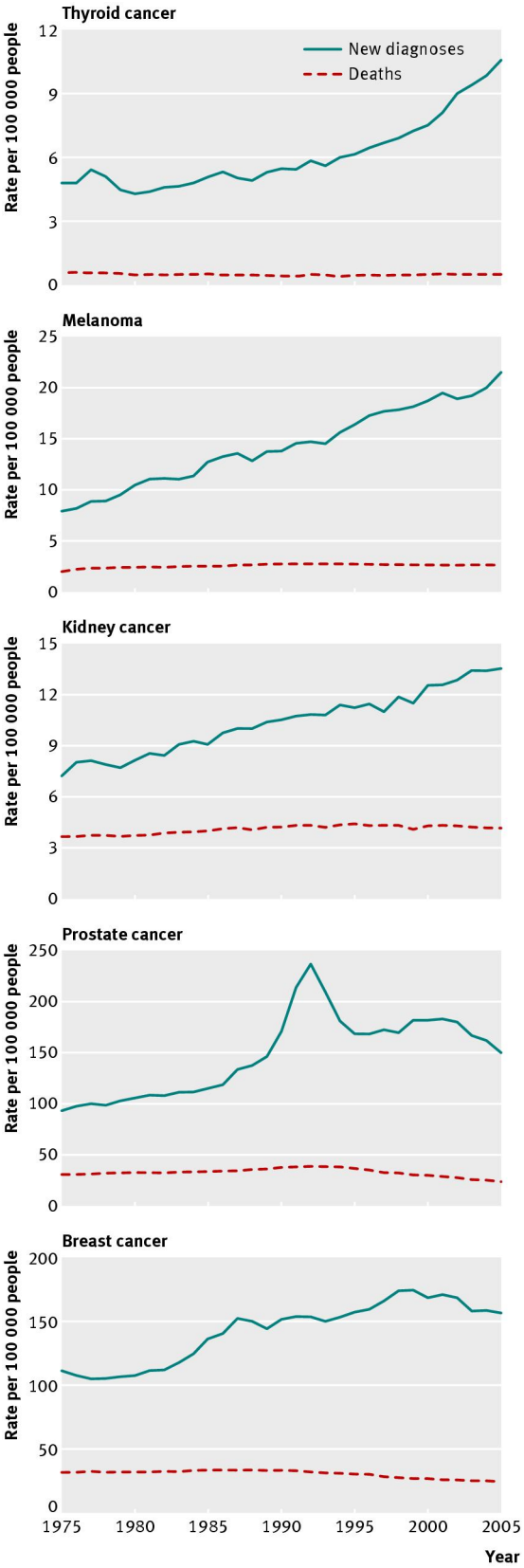
Figure



Rates of new diagnosis and death for five types of cancer in the US, 1975-2005. Adapted from Welch and Black[12]

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