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Editorial

The triumph of medicine: how overdiagnosis is turning healthy people into patients

More and more of our medical activity focuses on 'finding things early'. Based on a longitudinal model of disease, we aim to find disease in a pre-clinical stage when a person does not experience any symptoms, hoping that by intervening early we can avoid the clinical stage when symptoms do occur and ultimately prevent that person to die prematurely. Paradoxically, this optimistic scenario has now become an important threat to the health of our patients.

The crucial problem is that not every pre-clinical disease will automatically progress to clinical disease. Detecting pre-clinical disease that will not cause any symptoms or early death is called overdiagnosis. These people would never have experienced any symptoms and their life expectancy would not have been affected, if they had been left undiagnosed. However, because we are unable to differentiate overdiagnosis from true diagnosis, people with overdiagnosis are treated as truly diseased patients, which in their case causes harm without benefit.

Overdiagnosis is the most important negative effect of cancer screening: some cancer lesions never progress or progress so slowly they never cause symptoms in that person's lifetime (1). Every large dangerous cancer was small once, but not every small cancer will become large and dangerous. As many as 36% of thyroids taken at autopsy are found to have at least one papillary carcinoma (2). The chance of finding a pre-clinical cancer through screening is higher for slow growing cancers than for rapidly growing cancers as the latter have a shorter pre-clinical stage and are therefore more likely to become clinically apparent between screening rounds. It is estimated that one in four breast cancers that are detected with mammography screening are the result of overdiagnosis (1). Similar rates are found for prostate cancer (3).

The American Diabetes Association defines pre-diabetes as a risk factor for diabetes, characterized by impaired glucose tolerance, impaired fasting glucose or raised HbA1c levels (4). Using these criteria, one in three of the UK adults and one in two of the Chinese adults would be labelled as pre-diabetic (5). The study by Ureña-Bogarín published in Family Practice (6) shows that 14.6% of healthy young adults (aged 18–30 years) in Mexico are pre-diabetic. Strikingly, at least 65% will not progress to diabetes within 10 years if left untreated (7). Treating people with pre-diabetes delays the development of diabetes by 2 years but provides no long-term benefits (8) and has two important side effects: it increases the number of patients on diabetes drugs (many of whom would never develop diabetes), and it prolongs the duration of treatment in those who do develop diabetes since treatment for pre-diabetes and diabetes are the same (4).

Advances in diagnostic technology are one of the drivers of overdiagnosis. Computed tomography pulmonary angiography is able to pick up pulmonary emboli as small as 2–3 mm in diameter (9), but their clinical relevance is questioned (10). Other causes include broadening disease definitions, as is the case for pre-diabetes and chronic kidney disease (11). Broader disease definitions or the emergence of a new disease (12) may be in the interest of drug companies and there is evidence of widespread conflicts of interests of panel members and/or direct sponsorship of guideline development by pharmaceutical companies (13). Clinicians also report feeling pushed towards overdiagnosis out of fear for litigation or patient dissatisfaction (14). And finally, many people including clinicians simply attach value to a diagnosis or label irrespective of any subsequent benefit.

But even when there is no apparent benefit, there is always harm. The harms of overdiagnosis are 3-fold: unnecessary treatment, unnecessary labelling and opportunity costs. The harms of unnecessary treatment are obviously directly dependent on the type of treatment: anticoagulation after a pulmonary embolism is associated with a 2.4–19.6% absolute increase in major bleedings after 5 years of treatment (15); for every three men treated with prostatectomy, there will be one with erectile dysfunction (16). The harm from labelling includes no longer being able to get health insurance or a mortgage, rising costs of health care and changed self-image or even mental health problems. Early breast cancer is associated with depression and anxiety up until 5 years after the diagnosis in 15% of women (17). Finally, time spent on overdiagnosis can no longer be spent on truly diseased patients: paying doctors to screen patients for dementia (which carries no proven long-term benefit) takes time away from sick people (18).

One could argue that it is better to be safe than sorry, and that the harm in the overdiagnosed is easily offset by the benefit of the truly diseased. But this may not necessarily be true, or it may not be true for everyone. In cancer screening, a very small number of people will experience very large benefit, i.e. not dying from breast cancer, compared with a much larger group of people who will experience some form of harm, i.e. mastectomy, myocardial infarction and secondary cancers (19). But the benefit may also be negligible, such as in the example of pre-diabetes where the only benefit is to postpone the label of diabetes at the expense of more and longer treatment with diabetic drugs. Whether the benefit outweighs the harms depends on their relative importance including long-term consequences, distribution in the population and a person's individual values and preferences. However, to be able to make that judgement, both have to be acknowledged and measured. So far, we are better at quantifying benefits than harms (20).

Is there a way out? The ultimate solution would be to find better ways to identify those people who will benefit from treatment and

those who will not. This means we need to evaluate innovative diagnostic technology and new disease definitions differently and more rigorously by evaluating the effects of test-treatment strategies rather than diagnosis alone, primarily focusing on the positive and negative effects on patient-related outcomes (21). New machines with higher accuracy or the identification of a risk factor for disease do not necessarily translate into a better life for patients. In the meantime, some terms may be better avoided: the World Health Organization advises to avoid the term pre-diabetes altogether (22); the National Cancer Institute in the USA has advocated to rename cancers that are indolent or low risk to 'indolent lesions of epithelial origin' (23). These initiatives may take time and a lot of persuasion. But there is one thing we could do immediately, and that is informing both the public and clinicians about what overdiagnosis is and what its consequences may be.

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*Ann Van den Bruel**
Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, OX2 6GG, UK.
**Correspondence to Ann Van den Bruel, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, OX2 6GG, UK; E-mail: ann.vandenbruel@phc.ox.ac.uk*

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