

Overdiagnosis and overtreatment; how to deal with too much medicine

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ABSTRACT

The past few decades have seen medical science making rapid strides in the field of diagnostic technologies, thus making it possible to detect some conditions at a very early stage. An unwanted effect of these developments is overdiagnosis which occurs when a true abnormality is discovered, but detection of that abnormality and its treatment does not benefit the patient. Overdiagnosis is encountered as a result cancer screening, in genetic diseases and in some chronic conditions when disease definition is broadened. There is urgent need of development of evidence based decision-making tools for clinicians which will help patients understand the benefits and harms of different screening and treatment methods. And the treating physician has to play a important role to convince the patient that watchful waiting, for some of the lesions may be the best option available in some circumstances.

Keywords: Overdiagnosis, overtreatment, too much healthcare

Introduction

What is overdiagnosis

Traditionally, a diagnosis is based on a patient's clinical symptoms and signs, and a past medical history. The past few decades have seen medical science making rapid strides in the field of diagnostic technologies, thus making it possible to detect some conditions at a very early stage.^[1,2] An unwanted effect of these developments is overdiagnosis which occurs when a true abnormality is discovered, but detection of that abnormality and its treatment does not benefit the patient. Another word for this could be "too much medicine,"^[1,2] but as this can be confused with "too much medication," a better term might be "too much healthcare," which rather than benefitting the recipient, can have harmful effects.

However, one must be careful to distinguish overdiagnosis from misdiagnosis, in which the diagnosis is inaccurate, and it is not synonymous with overtreatment also, in which patients may be offered treatment which may be either unnecessary or inappropriate, for example, outpatient or inpatient antimicrobial therapy which in many cases is empirical, advanced imaging and acute percutaneous coronary interventions in case of chest pain.

So in other words, overdiagnosis happens when a diagnosis is given to people with either very mild or doubtful symptoms (which usually don't progress further), and then are offered treatment for the same, which may not be required or sometimes even prove harmful for the patient.^[1-3]

Many experts in the field of health care feel that ever increasing advances in screening and the quest for new information have resulted in certain circumstances in harm—not only in the form of overdiagnosis but also in overtreatment. So modern medicine which is often hailed for such wonders as eradications of many infectious diseases and significant increase in life expectancy of humans now faces a burden that too much dependence on

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technology may also cause harm especially to those who are healthy.^[1-3] Overdiagnosis is generally the result of screening that detects early changes or sometimes aberrations from the normal or tiny abnormalities that are very unlikely to never cause symptoms, disability, or death,^[4,5]

Another way in which overdiagnosis can happen is when the definitions of diseases are broadened (e.g., creating the term pre-hypertension, so that more no of people are leveled as hypertensives), meaning that people even at minimal risks receive permanent medical labels and lifelong treatments that will fail to benefit many of them.^[6,7]

According to some estimates, for example, in the United States, more than \$200 bn may be wasted on unnecessary treatment every year,^[8] resulting also in, what is known as overmedicalization, thus diverting funds from more pressing health needs or genuine illnesses of the larger population.

So end result of these diagnostic and therapeutic intervention is that healthy people with either mild problems or with risk factors for the disease are classified as sick.^[9,10] Reflecting the increasing concern over the issue, some experts even advocated stopping the screening programs altogether; as reflected in the title of the article on the issue- “The best method we have to reduce the risk of breast cancer is to stop the screening program.”^[11]

Medical Conditions Commonly Affected by Overdiagnosis

There has been growing interest in problem of overdiagnosis in last few years suggesting that problem exists to varying extents across many conditions, including some of the common conditions for which underdiagnosis may simultaneously be a feature, for example, in underserved communities.^[12,13]

The overdiagnosis in many common chronic conditions (non-neoplastic)

The widening of disease definitions can be categorized into two types:

- When in some very common chronic conditions, a “pre-disease” (such as pre-hypertension and pre-clinical Alzheimer’s) state is added in classification
- When the thresholds for diagnosis is lowered (such as diabetes and depression);

So lowering the thresholds of blood pressure to define hypertension or pre-hypertension dramatically increases the number of patients diagnosed with a condition requiring follow-up and treatment. Studies suggest that over half of people with mild hypertension are treated with drugs even though this approach has not been proved to decrease mortality or morbidity.^[14] Following the same logic, diabetes, pre-diabetes,

and or gestational diabetes as well as osteoporosis can also be overdiagnosed. In case of osteoporosis, where the new expanded definitions means that many more women with very low risk will be advised treatment.^[15]

The method which is used to see for the effectiveness of various interventions in chronic diseases uses relative rather than the absolute risk reduction resulting in exaggerating the risk of these conditions and one gets the false impression of degree of risk reduction which is more that could be expected from screening and treating these conditions.^[12,16] Hence, for an identical reduction in blood pressure, the resulting absolute risk of disease reduction will be much smaller for individuals with blood pressure slightly above the normal level compared with individuals with persistent high readings, resulting in unnecessary treatment and harmful side effects. The other conditions in which overdiagnosis has been reported are asthma in which it has been suggested by an interesting Canadian study that 30% of people with the diagnosis of asthma may not have the disease and 60% of those being treated may not require medications;^[17] and in gestational diabetes where expanded definition classifies almost 1 in 5 pregnant women having the condition.^[18] Another very common condition which is overdiagnosed is COPD, referred to as false-positive COPD by some experts. This diagnosis is usually given to those who are smokers or simultaneously having other medical conditions like asthma or heart disease. However, post-bronchodilator spirometry was found to be unobstructed in 61.9% of these subjects in one study and almost half of those studied were using respiratory medication.^[19] Also a controversial revised definition of chronic kidney disease—classifies 1 in 10 as having the disease which is likely to overdiagnose the condition in many elderly.^[20]

Many studies have found that diagnosis of depression and use of antidepressants has increased substantially in past few years especially in western nations, whereas it has been argued that that depressive symptoms in older adults can be improved with non-invasive behavioral activation techniques.^[21] Similarly there is concern among many that application of new cholesterol treatment guidelines will result in overtreatment of many adults particularly the elderly.^[22] Another interesting observations reported by many investigators is regarding the incidence of pulmonary embolism, after it was observed that 8 years following the introduction of the multi-detector computed tomographic scanners in 1998, the incidence of pulmonary embolism increased from 62.1 to 112.3 per 100,000 adults; however mortality from pulmonary embolism stayed virtually the same during that period. So it follows from this study that increased incidence involved detection and treatment of small sub-segmental emboli that are unlikely to be lethal but at the same time exposing these patients to the risks, costs, and inconvenience of anticoagulation.^[23]

The overdiagnosis is an emerging challenge in genetic screening as discovery of new associations between genes and common conditions are increasingly being used to calculate risks for individuals who have the genes for the conditions, but are

not suffering from the symptoms. The indiscriminate and inappropriate use of genetic testing will unnecessarily lead to fear and anxiety, apart from the wasteful expenditure involved.^[24]

Overdiagnosis in cancer

As availability of modern diagnostic tools have become widespread, there is greater application of these methods to detect malignant lesions at earlier state in those who are thought to be having increased risk of developing the disease with the hope that early detection will result in better outcome and improve overall prognosis resulting in extension of life. It is very appealing to both the treating physician and the general public that outcomes could be improved for most cancer types if detection occurs early enough. Many healthy individuals who participate in screening programs are willing to accept the fact that false-positive results on screening examination can occur, if they believe that an occult cancer might be detected and death averted.^[25] However, negative consequence of overdiagnosis which may be the result of cancer screening is typically not given much importance at the time of screening. Patients and their clinicians are not willing to accept the fact that majority of these “cancerous lesions” may not cause any symptoms in patient’s lifetime. Overdiagnosis is a undesirable consequence of screening because detection and subsequent treatment are unnecessary and many a times results in unpleasant and debilitating sequelae and at worst can even cause premature death.^[25]

Over the past 30 years, awareness and screening have led to an emphasis on early diagnosis of many forms of cancers; the data demonstrate significant increases in early-stage disease, but without a proportional decline in later-stage disease. This suggests that there is a reservoir of slow-growing cancers with limited malignant potential that are being detected because of increasing scrutiny and increasing numbers of biopsies. Autopsy data confirm that subclinical lesions occur at high frequency in thyroid, breast, and prostate cancers. So the stated aim of these efforts to reduce the rate of late-stage disease and decrease cancer mortality, various reviews and pooled data suggest that these goals have not been met.

Overdiagnosis creates at best a false impression of improved survival that encourages more screening and overdiagnosis. Again the use of 5-year survival as a measure of screening effectiveness is particularly misleading, if we include a lot of patients with overdiagnosed cancers that would never be harmful.

At present it is safe to suggest that we need more research to understand the complexity of the process of carcinogenesis. The word “cancer or neoplasm” has become synonym with suffering and death; however, it is also true that cancers are heterogeneous and can follow multiple paths, not all of which progress to metastases and death, and many neoplasms behaves like a indolent disease that causes no harm during the patient’s lifetime.^[25] About 20% of five common cancers are the result of “overdiagnosis,” concludes a recent study^[26] from Australia that

analyzed over 30 years of national healthcare data. The figures were 18% for women and 24% for men, thus roughly about 11 000 cancers in women and 18,000 in men may be overdiagnosed each year in Australia alone. The authors looked at five of the seven cancers for which overdiagnosis has been documented: breast, thyroid, renal, and prostate cancers, and melanoma overall resulting in overdiagnosis in for 22% of breast cancer and 73% of thyroid cancers in females and 42% of prostate cancers, 58% of melanomas, and 73% of thyroid cancers in males.^[26]

When screening was started for breast cancer, it was observed that the incidence of localized breast cancer and ductal carcinoma *in situ* increased from 112 to 234 cases per 100,000 women between 1976 and 2008.^[27] However, the anticipated reduction in late-stage breast cancer during the same period was much smaller, from 102 to 94 cases per 100,000 women, suggesting that 31% of all breast cancers represented overdiagnosis.^[27-29] Thus, it follows that for many women, screening mammography may lead to a diagnosis of breast cancer based on tumors that would never have been noticed or become harmful during their lifetime.^[29] These women are unnecessarily treated with therapies, including surgery, radiation, and chemotherapy, that have adverse effects.^[29-32]

Similarly, the lifetime prevalence of clinically diagnosed prostate cancer has increased to more than 15%, with the introduction of the screening with prostate-specific antigen test, but the risk of dying from prostate cancer has remained at just under 3%. In an interesting study which took into account the routine autopsy findings of trauma patients in an American city of Detroit, it was revealed that histological evidence of prostate cancer was seen in 45% of men in their 50s and nearly 70% in their 60s. However, the lifetime prevalence at the time was only 10% for clinically diagnosed prostate cancer and only 3% for fatal prostate cancer. Thus, most men with screening-detected prostate cancer were overdiagnosed meaning that their prostate cancer was never going to cause symptoms let alone the death. So we need to screen approximately 1,000 men to avert one death from prostatic cancer but at the same time will be psychologically traumatizing many who never would have known about their disease in absence of screening.^[33,34]

Overdiagnosis also occurs with lung, kidney, melanoma, and thyroid cancers, diseases that have had a sharp increase in incidence without any accompanying decrease in mortality.^[35,36]

Thus causes of overdiagnosis can be summarized as follows:

- Screening and increasing sensitivity of diagnostic tests
- Incidental findings following screening and diagnostic tests
- Widening of diagnosis criteria of many common diseases
- Confusion between risk and disease
- Physician’s fear of missing the disease and patient’s expectations
- Insufficient knowledge of natural history of the disease
- Financial incentives involved in increased use of diagnostic and treatment modalities.

Role of primary care physician

The primary care perspective plays an important role in tackling the challenge of unnecessary medicine as various drivers of medical overuse being associated either directly or indirectly with their areas of influence. The primary care physician faces an unselected patient population with a low prevalence of manifest disease. They are confronted with a higher level of uncertainty regarding the correct and final diagnosis. The explosion of medical knowledge and treatment alternatives makes it important to have a generalist (primary care physician) to interpret and advise on the best course of action as patients are more comfortable in discussing their fear and apprehensions with their trusted doctor rather than with specialists, who are usually expert in a specific condition or organ system and may not be able to satisfy patients because of their many other preoccupations.

The special qualities which are possessed by primary care physician to discuss the many problems faced by the patient while dealing with difficult health related issues are:

- an excellent doctor–patient relationship developed through years of shared-decision-making,
- a well-founded wait-and-see approach and stepwise diagnostics with a more focus on history taking and physical examination and less on investigations
- open communication
- a holistic patient assessment,
- understanding the importance of patient education, for example, discussing the possibility of overdiagnosis and overtreatment as harmful side effects of screening as specialists and tertiary care centres are unlikely to address his or her concerns in a manner a primary care physician would.

Measures to prevent overdiagnosis

The most important measure is to create awareness of health professionals and the population about its occurrence and to decide at which risk level to intervene based on the absolute risk of health events and the absolute risk reduction expected from an intervention. Communicating that prolonging survival from the time of diagnosis is not the same as delaying death from that disease should be discussed with the patients. Addressing the increasing concern over the issue, the first international Conference on the topic, “Preventing Overdiagnosis” was held in 2013, and the British Medical Journal produced an overdiagnosis-themed journal issue. Recent activities to create awareness about the overdiagnosis, include the ABIM’s Choosing Wisely campaign (www.choosingwisely.org/), JAMA Internal Medicine’s “Less is More” series, the BMJ’s Too Much Medicine series (www.bmj.com/too-much-medicine) and the discussion over the expanded definitions of psychiatric illness in the recent DSM-5 release which can tremendously increase the number of patients being given the level of the psychiatric illness (www.psychologytoday.com/blog/dsm5-in-distress).

Right now, medical profession is facing challenges at many front—an explosion of new information, the public that is

increasingly aware about its health, doctors who don’t want to miss a diagnosis either for fear of litigation (or thrill associated with early diagnosis) and a pharmaceutical industry that wants to expand its business opportunities by investing in diagnostics and therapeutics; all resulting in too much investigations for the patients. Because of lack of clear evidence in favor of many screening modalities in case of neoplastic lesions and excessive medication in case of other common chronic conditions, the message to the patients and medical fraternity alike should be that in certain situations, less may be more and there should be an open discussion between the patient and healthcare provider before he or she is ready to make an informed decision.

Summary and Conclusion

Overtreatment: The main and worst consequence of overdiagnosis is overtreatment of an indolent lesion or disease which is unlikely to have any benefit for the patient. At the same time the likely interventions like surgery, radiation, and chemotherapy can have side effects resulting in significant morbidity and rarely even fatalities can occur.^[33] As overdiagnosis in some non-neoplastic conditions leads to over-prescription and over-medicalization, resulting in many undesirable and sometimes dangerous side effects; it can also contribute to the release of pharmaceuticals into the environment as, for example, in case of over- and misuse of antibiotics, thus contributing to the proliferation of antimicrobial resistance.

Psychological effects: As screening, unlike other medical interventions, is undertaken in healthy subjects, so the individual in question is labeled as “diseased” or a “patient” based not on presence of symptoms but on some investigations and tests causing unnecessary fear and resulting in increased sense of vulnerability and psychological suffering.^[33] And in non-neoplastic diseases it leads to overemphasis on drug treatment, for example, as in mild hypertension, instead of trying to modify individual lifestyle choices, person becomes dependent on medication.

Economic burden: The cost involved in overdiagnosis and overtreatment of many diseases will make it difficult to keep healthcare systems financially viable. There is also direct relation between overtreatment and under-treatment, as there is risk of limited resources being redirected and shifted away from those who need them most.^[36] And as healthcare is becoming insurance dependent, one more downside of this increased spending will be potential increase in the cost of health insurance or even an inability to procure it for many needy individuals resulting in more suffering and resentment.

Keeping in mind all these points, a working group from the National Cancer Institute recommended more research to develop molecular diagnostic tests and biomarkers that will help us distinguish overdiagnosed disease (i.e., the lesions which are unlikely to progress) from the disease requiring treatment.^[35,36] These biomarkers should be able to distinguish lesions which are unlikely to progress from the more aggressive ones. One

more suggestion was to rename or reclassify the lesions which are classified presently as low-grade and pre-malignant neoplasms (removing the word cancer from these lesions).^[36] Finally, there is urgent need of development of evidence-based decision-making tools for clinicians which will help patients understand the benefits and harms of different screening and treatment methods. Eventually the treating physician should be able to convince the patient that watchful waiting, for some of the lesions may be the best option available in some circumstances.^[36]

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Conflicts of interest

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