Viewpoint

Overdiagnosis

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"Cured yesterday of my disease, I died last night of my physician."
--Matthew Prior, 1714

Veterinarians are generally well aware of the risks of misdiagnosis (incorrectly identifying a patient's disease or diagnosing a disease the patient does not have) and missed diagnosis (failing to detect a disease present in a patient). Misdiagnoses and missed diagnoses can lead to direct patient harm from inappropriate treatment, harm due to a delay in obtaining a correct diagnosis and rendering appropriate treatment, and increased costs. However, there seems to be little discussion in the veterinary literature or veterinary curriculum of the problem of overdiagnosis and the risks it poses to veterinary patients.

The term overdiagnosis is used in a variety of ways, and there is some debate about how it should be defined.[1–3] In the narrowest sense, however, overdiagnosis refers to the correct identification of a disease that is actually present but that will never cause clinical signs or clinical harm (eg, death).[1] More broadly, the term refers to a constellation of factors that lead to the correct identification of disease for which subsequent testing and treatment, on balance, causes patients more harm than good. These factors include detection of clinically irrelevant disease through diagnostic testing of individuals without clinical abnormalities, the expansion of disease definitions or disease detection thresholds to reclassify individuals without clinical signs as ill, the incidental identification of clinically irrelevant lesions during diagnostic imaging, the process of creating new diseases by reclassifying as abnormal physiological or behavioral phenomena previously considered normal (ie, medicalization), and other practices that lead to diagnoses that are technically correct but do not benefit patients.[1–3]

Importantly, it can be difficult to distinguish overdiagnosis from certain types of misdiagnosis with similar consequences. As an example, false-positive diagnoses provide no benefit to patients and often lead to harm from subsequent diagnostic testing or treatment. However, the key distinguishing feature of overdiagnosis is that the diagnosis is technically correct but such diagnosis leads to no benefit for patients.[1,2]

The problem of overtreatment is often connected to the issue of overdiagnosis. Overtreatment is the application of therapeutic interventions that provide no net benefit or do more harm than good for patients.[1] Because most medical interventions have some potential for harm, and both the benefits and harms of any treatment vary from patient to patient, overtreatment can occur even in the absence of misdiagnosis or overdiagnosis. However, because overdiagnosis is, by definition, the identification of a disease that will not cause clinical symptoms, any treatment implemented as a result of overdiagnosis can have no benefits. Treatment given as a result of overdiagnosis is always overtreatment and can only be neutral or harmful, not beneficial for the patient. Overtreatment is often discussed along with overdiagnosis because reducing overdiagnosis automatically reduces overtreatment and its associated harm to patients.[4–5]

How Much of a Problem is Overdiagnosis?

Overdiagnosis is now recognized as a common and serious problem in human medicine that causes substantial harm in terms of unnecessary costs, wasted resources, and patient and caregiving suffering.[3,6] International conferences and special features in major medical journals have been dedicated to discussions of overdiagnosis and overtreatment[7–9]; in 2012, a consortium of 70 specialty groups created the online resource Choosing Wisely to help physicians and patients make evidence-based decisions that reduce overdiagnosis and overtreatment.[10] Changes in clinical practice guidelines and public education strategies have resulted from the growing recognition of the risk of overdiagnosis in human medicine, including highly publicized changes in recommendations for prostate cancer screening in men and breast cancer screening in women.[11,12]

In human medicine, screening programs intended to detect cancer in asymptomatic individuals

provide a useful illustration of the problem of overdiagnosis. For example, using blood prostate-specific antigen (PSA) concentration as a screening test for prostate cancer in asymptomatic men has been associated with overdiagnosis rates of 5% to 75%, depending on the population evaluated,[4,13–16] with the best estimate suggesting that, among men in whom prostate cancer is diagnosed on the basis of this screening, 25% would be expected to never experience clinical illness or die because of prostate cancer.[3] In the case of mammography to screen women for breast cancer, the risk of overdiagnosis varies with the age of women screened and other factors.[16,17] The best estimates suggest that about 30% of breast cancers detected through mammography screening are overdiagnoses, but estimates range from < 10% to 90%, depending on the population tested.[3,13,18,19,a]

Perhaps the most dramatic example of overdiagnosis in human medicine involves CT of clinically healthy people. This type of screening frequently leads to detection of lesions and, ultimately, diagnoses of cancer. On the basis of mortality figures, however, it is likely that a high percentage of neoplasms found through such imaging would never have led to death and that the detection of these cancers provided no benefit to the patients.[3]

Of course, lesions detected during imaging of normal individuals, or incidental lesions detected during imaging of patients who have other, unrelated, clinical problems, can be clinically important, and the detection and treatment of such lesions can benefit some individual patients. Incidental findings are not automatically overdiagnoses. However, such findings are also not always clinically important, and further diagnostic and treatment interventions may not benefit patients or may even result in net harm. Determining how common overdiagnosis is requires identifying which findings are likely to be clinically important and which probably represent overdiagnosis.

How is Overdiagnosis Identified?

One challenge in identifying overdiagnosis is that it can be identified in individual patients only in retrospect, after any opportunity for making diagnostic or treatment decisions has passed. If, for example, prostate cancer is diagnosed in an asymptomatic man, this diagnosis can only be clearly classified as an overdiagnosis if the condition is left untreated and never results in clinical signs or death. Individual patients, and veterinary clients, sometimes elect not to pursue treatment, and when the identified conditions they choose not to treat regress spontaneously or fail to produce clinical signs, we can classify these diagnoses as examples of overdiagnosis. However, although such outcomes provides evidence for the existence of overdiagnosis, they are not very useful in guiding diagnostic and treatment recommendations for individual patients at the time of initial diagnosis.

Fortunately, it is possible to estimate the frequency of overdiagnosis in specific patient populations by collecting and analyzing epidemiological data about specific diagnoses and relevant outcomes. This information can then help clinicians and policymakers in making decisions that affect the treatment of individual patients by providing a general sense of the potential for overdiagnosis. Such population-level data cannot perfectly predict outcomes or determine the optimal course of action for individual patients. But the use of such data allows clinicians to recognize the potential for overdiagnosis and better assess the risks and benefits of proceeding with diagnostic and treatment interventions.

Overdiagnosis is frequently detected through evaluation of epidemiological data on disease occurrence and outcome.[3,4,13] As an example, consider a usually fatal disease. If an increase in the number of cases of that disease is accompanied by an increase in the number of deaths caused by it, then there likely has been a true increase in disease incidence. However, if the number of cases of the disease increases but the number of deaths caused by the disease remains unchanged, then it is likely that there has been an increase in overdiagnosis, because newly identified cases are not leading to death. Of course, there can be other reasons for this type of pattern, such as discovery of more effective treatments that reduce the mortality rate even as the number of cases increases. But, absent these situations, this pattern can be a useful indicator of overdiagnosis.

Although death is a clear, objective outcome measure, other clinical outcomes can be assessed to evaluate the potential for overdiagnosis. For example, when incidental adnexal masses are detected during imaging of postmenopausal women, diagnostic and treatment choices can be informed by population data concerning the rate of spontaneous resolution or progression and the ultimate histopathologic diagnoses of lesions with different imaging characteristics.[20] Follow-up data for untreated lesions can be a useful source of information to identify overdiagnosis. Such data can reduce overdiagnosis and overtreatment even when the exact outcomes for individual patients cannot be perfectly predicted.

What is the Harm of Overdiagnosis?

Overdiagnosis can cause waste and misallocation of medical resources and can also increase morbidity and mortality rates and have a deleterious psychological impact on individual patients and their caregivers. The testing leading to overdiagnosis and the subsequent follow-up testing and treatment have obvious financial costs. It is estimated, for example, that overdiagnosis and overtreatment of clinically irrelevant lesions detected through mammography cost $4 billion annually in the United States alone.[21] Another study[22] suggested that treatment of people in the United States with mild hypertension that does not result in any benefit in terms of reducing symptoms or early death may cost $32 billion annu-

ally. By increasing overall health care costs, overdiagnosis and overtreatment reduce the affordability of care and consume financial resources that could otherwise be used for treatments that actually reduce clinical illness.

The most direct consequence of overdiagnosis is the physical harm done to patients. All tests and treatments have some associated risks. Even if those risks are small, a substantial number of patients may be unnecessarily harmed if the rate of overdiagnosis is particularly high. For example, even though there is now widespread awareness that a high proportion of prostate cancer diagnoses are overdiagnoses, most men with positive PSA screening test results are still subjected to additional testing.[4] In one review,[16] 85.9% of men with positive PSA screening test results underwent at least one biopsy procedure. And, treatment of prostate cancer can have substantial adverse effects. Approximately 50% of men who undergo surgery because of prostate cancer experience sexual dysfunction, 30% experience difficulty urinating, and 0.1% to 0.2% die.[16]

These risks may be acceptable in men likely to experience clinically important symptoms or to die of their prostate cancer without treatment. However, for men whose cancer would not become clinically relevant in the absence of treatment, such adverse effects are a harm with no offsetting benefit. Given that many asymptomatic men in whom prostate cancer is diagnosed on the basis of PSA screening (likely about 25% and perhaps as much as 75%)[3,4,13–16] will never develop clinical signs or die of this disease if left untreated, the risks of treatment may well exceed the benefits in this population. It is this concern that has led to recent changes in prostate cancer screening guidelines.

There is also potential psychological harm associated with being told one has a serious illness, although the impact of this is less easily measured than the other harms of overdiagnosis. Research has shown, for example, that quality of life diminishes after a diagnosis of prostate cancer is made and that the risk of suicide and cardiovascular death increases immediately following such a diagnosis, even before treatment is started.[23,24] These risks apply equally to men in whom prostate cancer would never have caused clinical consequences.

What Causes Overdiagnosis?

Many factors can increase the risk of overdiagnosis. The expanded use of screening tests, increased sensitivity of diagnostic tests, and use of screening tests in inappropriate populations are leading factors that contribute to the risk of overdiagnosis in human medicine.[3,6,25–30,b] In addition, psychological factors that affect clinicians (physicians and veterinarians), human patients, and veterinary clients can predispose to overdiagnosis.[3,6,25–31,b] The training of physicians and veterinarians, for instance, includes an emphasis on systematic methods to prevent misdiagnosis and, especially, to reduce the risk of failing to diagnose uncommon diseases and diseases that might present in an atypical manner. Medical students are rewarded by instructors for successfully making diagnoses, even when the diseases are rare or of questionable clinical relevance.[32–35] Doctors may also be prone to overdiagnosis because they are likely to be punished, in the form of blame or even litigation, for failing to diagnose medical conditions, whereas there are almost never any negative consequence for unnecessarily diagnosing or treating conditions that would never have caused any harm if undiagnosed. Often, the fact that overdiagnosis and overtreatment have occurred is not even recognized.[3,29,32–35,b]

As patients, human beings are typically inclined to seek a diagnosis and to take action on it even if the statistical evidence suggests it is in their best interests not to do so. One survey,[36] for example, found that 98% of people given an incorrect diagnosis of cancer on the basis of screening test results were still glad they had undergone testing once follow-up evaluations showed they actually did not have cancer. Like doctors, many patients are inclined to believe more care is better care, even if the evidence suggests otherwise.[37,38] It is likely that similar factors influence the decision-making of veterinarians and veterinary clients.

Finally, financial incentives that encourage testing and treatment along with commercial marketing efforts designed to create a demand for testing, diagnosis, and treatment influence the behavior of clinicians and patients, potentially increasing the risk of overdiagnosis.[39–44] Doctors are unlikely to intentionally pursue unnecessary testing and treatment purely for financial gain; however, there is evidence that revenue has some impact on doctors' decision-making. For example, federal law specifically prohibits physicians from referring patients to diagnostic facilities in which they have a financial interest because research has shown these types of financial interests increase the number of tests done and the costs to patients.[44–46]

Overdiagnosis in the Veterinary Context

In contrast to the growing emphasis on recognizing and preventing overdiagnosis in human medicine, little or no attention has been paid to the subject in veterinary medicine. The epidemiological data needed to identify overdiagnosis are rarely collected in the veterinary field, and there appear to be no published reports evaluating the risks of overdiagnosis associated with common diagnostic practices. The frequency and costs of overdiagnosis and the harm done to veterinary patients are unknown. In the absence of relevant data, it is difficult to know how similar the problem of overdiagnosis—especially causes and solutions—is between human and veterinary medicine.

The economic model of veterinary medicine is quite different from that for human medicine, and this

may reduce the risk of overdiagnosis. For example, clients must usually pay directly for testing and treatment, and this may restrain the indiscriminate use of diagnostic testing and treatment. By comparison, in human medicine, the costs to patients of testing and treatment are often indirect and difficult to assess.

Nevertheless, overdiagnosis would still be a waste of veterinary client resources and could reduce the ability of some clients to pay for necessary or beneficial care. Unlike physicians, veterinarians must face the problem of economic euthanasia, which can lead to the death of patients with treatable conditions when resources for care are limited.[47] Overdiagnosis might also lead owners to elect euthanasia if they are emotionally or financially unable to cope with a diagnosis, even if the condition ultimately might not have caused any important clinical consequences.

Psychological factors that drive overdiagnosis in the human medical field, such as financial interests and the expectation that screening and early disease detection always benefit patients, are likely also present in the veterinary field. In the absence of relevant data, it is unknown whether overdiagnosis is more or less of a problem in veterinary medicine, compared with human medicine, but it likely occurs to some extent, given the presence of these and other potential risk factors.

An example of a practice that might lead to overdiagnosis is preanesthetic blood testing of overtly healthy elective surgery patients. Preanesthetic testing of overtly healthy individuals undergoing elective surgery is considered of little value and is not routinely recommended in human medicine because the evidence suggests it does not reliably reduce complications or mortality rates, and it raises the risk of overdiagnosis and subsequent unnecessary or even harmful interventions.[48,49] Although some individuals may benefit, the consensus is that on a population level, the practice does not benefit enough patients to justify the costs or risk of overdiagnosis.

In contrast, preanesthetic screening of overtly healthy patients is often recommended in small animal medicine and is sometimes presented as a necessary part of good patient care.[50–53] The intent is to detect subclinical conditions that might influence the risks of anesthesia and surgery, and there is evidence that such testing frequently uncovers abnormalities.[54–56] However, these abnormalities often do not alter the anesthetic plan or affect the complication rate. This raises the question of whether this practice generates a net benefit or harm or has no overall effect on morbidity and mortality rates in these surgical patients. The evidence does not currently exist to definitively answer this question.

It is worth considering, though, that the potential for net harm does exist, and the practice cannot be assumed to be benign or beneficial overall in the absence of data demonstrating this. Perhaps such testing reduces overall perioperative morbidity and mortality rates by detecting occult disease that would raise anesthetic or surgical risk. Or perhaps it leads to detection and beneficial treatment of disease unrelated to the immediate surgical issue. However, preanesthetic testing of overtly healthy veterinary patients might also lead to the detection and subsequent investigation or treatment of diseases that would never have caused harm to these patients. And such testing might cause harm by discouraging beneficial surgical interventions if owners or veterinarians elect not to proceed with these interventions owing to clinical laboratory abnormalities that might not actually impact the risk of the procedure or well-being of the patients. In the worst case, clients might elect euthanasia sooner on the basis of a perception that their pet has a disease diagnosed by such screening even if that disease is not yet causing clinically important abnormalities. Without relevant data, it is difficult to evaluate the overall benefit or harm of such a practice.

How Can Overdiagnosis Be Prevented?

The first steps in reducing overdiagnosis are understanding the phenomenon and appreciating its causes. Appropriate epidemiological data must be collected and analyzed to determine the risk of overdiagnosis associated with particular diagnostic practices in specific patient populations. Knowing the extent of the problem, the costs and harm to patients resulting from overdiagnosis, and the specific risk factors in veterinary medicine is crucial to developing effective strategies to reduce overdiagnosis and mitigate the harm it causes.

Clearly, research to identify the extent of overdiagnosis in the veterinary context is needed. It may be possible to compare the incidence and mortality rate for typically fatal diseases when screening tests are introduced to determine whether screening reduces the mortality rate or only increases the number of cases diagnosed, as is done in human medicine. Follow-up studies of patients whose owners decline treatment could be done to compare outcomes between treated and untreated patients, which would help clarify the risks and benefits of treatment and the extent of overdiagnosis. Reports of follow-up data for incidental lesions detected on imaging that are left untreated could help determine the rate of progression or spontaneous resolution, which would better inform decisions about when to intervene when such lesions are detected. And postmortem studies can help identify the prevalence of lesions that do not lead to clinical disease or death, which could better inform decisions about treatment when such lesions are detected antemortem (this is one of the key sources of information that has led to a recognition of the extent of overdiagnosis of prostate cancer in men). There are many ways to develop the evidence base necessary to identify and reduce overdiagnosis in veterinary medicine.

However, even in the absence of such data, it may be possible to reduce the risk by applying strategies

found to be helpful in human medicine. The growing awareness of overdiagnosis and overtreatment in human medicine has led to varied efforts to reduce the risk and protect patients. Such efforts have included education of clinicians and patients concerning behavioral risk factors, amendment of clinical practice guidelines to reduce the use of some diagnostic procedures associated with overdiagnosis, and expansion of research efforts to identify and quantify overdiagnosis.[3–12] Similar efforts could be undertaken in veterinary medicine.

For example, greater awareness of the possibility of overdiagnosis and its causes could stimulate veterinarians to reevaluate their diagnostic practices. The authors[46] of one review of overdiagnosis in human medicine suggest that "Investigation and screening should be selective and targeted. …Unexpected abnormal findings should be considered within the context of the full clinical picture, and in most cases repeated or otherwise verified before a diagnosis is made or treatment considered." Applying such a strategy in veterinary medicine might be prudent even without a quantitative understanding of the extent of overdiagnosis in this field.

It is common for developments in human medicine to be borrowed for and adapted to the veterinary context. From specific diagnostic and therapeutic interventions to broad-based concepts and approaches such as evidence-based medicine, veterinary medicine frequently makes use of advances first made in the human medical field. Detecting and reducing overdiagnosis has become an area of intensive research and active changes in policy and practice in human medicine because overdiagnosis has been recognized as a common and important cause of harm to patients. It is incumbent on veterinarians to take note of these developments and make efforts to identify and mitigate overdiagnosis and overtreatment in our own profession for the sake of our patients and clients.

Footnotes

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b. Kaliebe K. How heuristics and mental biases contribute to overdiagnosis (poster presentation). Preventing Overdiagnosis Conference, Oxford, England, September 2014.

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