

The Problem of Overdiagnosis

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Clinical tests always have to calibrate sensitivity – the ability to avoid false negatives – and specificity – the ability to avoid false positives. This is a well-known problem, and is inherent to pretty much any process of looking for something. The TSA has to calibrate its airport machinery to detect explosives but not to ring the alarm at deodorant. It's been getting a lot of attention in the context of mammography, as screening technology gets more and more sensitive. Getting this right is hard, and of course is an ethical judgment at the end of the day. How much anxiety in false positives is “worth it” for detecting an actual cancer? At what age is the underlying risk great enough to warrant screening?

Today I want to look at a different, perhaps even more difficult problem. It's one that's gotten less attention, but is equally as serious. “Overdiagnosis” happens when one treats as clinically relevant a tumor that is not. More specifically, a current (June, 2018) [paper by Louise Davies *et al.*](#) proposes defining it as “the detection of a (histologically confirmed) cancer through screening that would not otherwise have been diagnosed in a person's lifetime had screening not been done.” Lynette Reid, a bioethicist at Dalhousie University (and Ethics Center speaker last year) frames [her discussion of the problem](#) with a pair of seemingly-contradictory data points. On the one hand, the evidence says we are getting a lot better at breast cancer screening. Detection rates are way up. On the other hand, mortality rates are barely budging. The problem seems to be that we are treating tumors that would never be clinically significant. That the problem is overdiagnosis and not something else is suggested by autopsy studies, which show that by the time someone reaches old age, they almost certainly have a number of indolent tumors in their body. This “disease reservoir” represents a potentially serious overdiagnosis problem; Reid quotes research indicating that if all of the indolent tumors had been detected with screening, then more than 99% of all thyroid cancers would be overdiagnoses. Even now, perhaps nearly a third of breast cancers are overdiagnoses. That said, a number of population-level variables influence whether a cancer is likely an overdiagnosis, making such estimates difficult. For example, Davies *et al.* point out that overdiagnosis is less likely in a population with a lower life expectancy from time of diagnosis, since a patient is more likely to die of other causes before a slowly-growing cancer could become clinically relevant. So too, there is a fundamental conceptual difficulty: whatever can be said at the population

level, it is impossible to know if a given cancer, once treated, represented an overdiagnosis.

These conceptual difficulties turn into clinical ones. Davies *et al.* cite a significant body of research indicating, in essence, that difficulties in understanding and communicating screening risks and benefits of screening generally, and of overdiagnosis specifically, make it hard to reach clinical decisions guided by patients' values and risk tolerances. Even more fundamentally, Reid concludes by pointing out that the statistics put us in a paradoxical situation:

“The more overdiagnosed cancer we detect, the less predictive of clinically significant outcomes it will be; at some point, its detection will confer no elevated risk of mortality. At some point before we get that far ... it will no longer make sense to consider the finding a risk factor” (397).

In other words, detecting a tumor may someday not actually predict disease progression, or at least not well enough to guide clinical decision-making.

Importantly, though, overdiagnosis is real: each overdiagnosis stands for someone who will most likely undergo a physically-demanding and potentially dangerous treatment regimen and (hopefully) emerge on the other side with the socially-difficult label “cancer survivor.” In short, and paradoxically, improvements in cancer screening are making ethical choices about how to treat cancer harder, not easier.