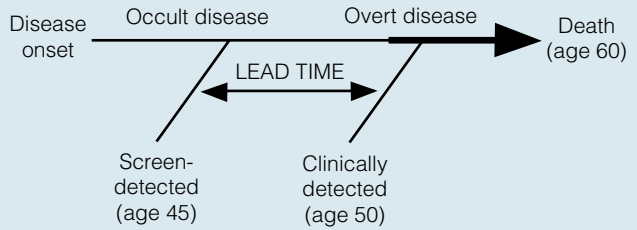
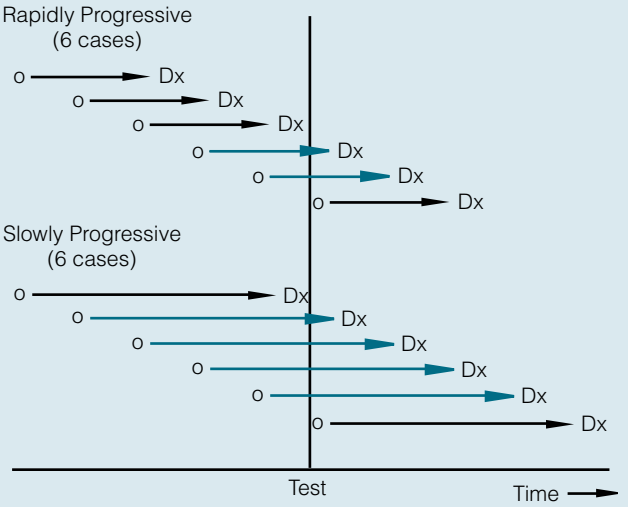
Primer on Lead-Time, Length, and Overdiagnosis Biases

The apparent effects of early diagnosis and intervention (measured in terms of how screening-detected cases compare with cases detected by signs and symptoms) are always more favorable than the real effects (measured in terms of how a population that is screened compares with a population that is not). The comparison between screening-detected cases and others overestimates benefit because the former consists of cases that were diagnosed earlier, progress more slowly, and may never become clinically relevant. This comparison, therefore, is said to be *biased*. In fact, three biases exist that inflate the survival of screen-detected cases.

1. Lead-time bias: Overestimation of survival duration among screen-detected cases (relative to those detected by signs and symptoms) when survival is measured from diagnosis. In the figure below (representing one patient), the patient survives for 10 years after clinical diagnosis and survives for 15 years after the screening-detected diagnosis. However, this simply reflects earlier diagnosis because the overall survival time of the patient is unchanged.



2. Length bias: Overestimation of survival duration among screening-detected cases caused by the relative excess of slowly progressing cases. These cases are disproportionately identified by screening because the probability of detection is directly proportional to the length of time during which they are detectable (and thereby inversely proportional to the rate of progression). In the following figure (representing 12 patients), 2 of 6 rapidly progressive cases are detected, whereas 4 of 6 slowly progressive case are detected.



3. Overdiagnosis bias: Overestimation of survival duration among screen-detected cases caused by inclusion of *pseudodisease*—subclinical disease that would not become overt before the patient dies of other causes. Some researchers further divide pseudodisease into two categories: one in which the disease does not progress (type I) and another in which the disease does progress—but so slowly that it never becomes clinically evident to the patient (type II). Inclusion of either type as being a "case" of disease improves apparent outcomes of screening-detected cases.