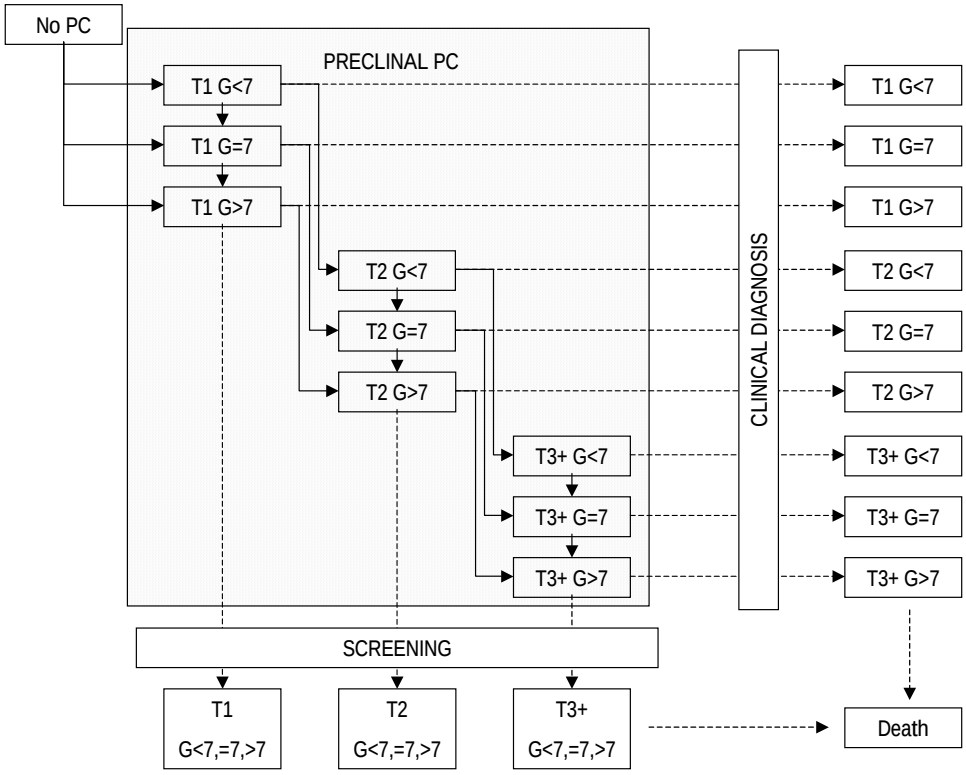
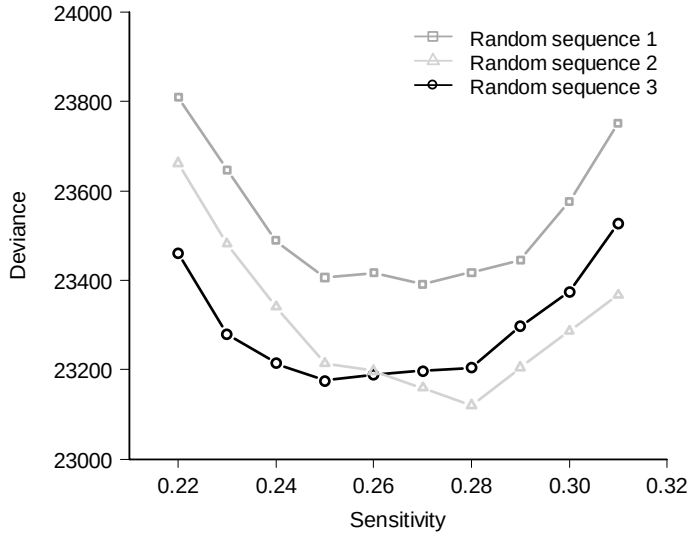


Supplementary Figure 1. The MISCAN prostate cancer model. Prostate cancer develops from no prostate cancer via one or more screen-detectable preclinical stages to a clinically diagnosed cancer. In each preclinical state, a tumor may grow to the next clinical T stage (T1, T2, or T3), dedifferentiate to a higher Gleason score (G < 7, G = 7, or G > 7), or give rise to symptoms and become clinically diagnosed. For these transitions, the time spent in the current state is generated from a Weibull distribution and the choice of the next state is determined by transition probabilities. There is also a risk that a tumor in the local-regional stage (M0) will develop into distant disease (M1). (For simplicity, this possibility is not illustrated).
In the MISCAN model, screening is superimposed on life histories in the absence of screening. Screening may detect cancers earlier in one of the preclinical screen-detectable states. Screen detection depends on the frequency and the sensitivity of the screening test for the specific preclinical state.



Supplementary Figure 2. Calculating plausible values for the estimate of the parameter for sensitivity for a tumor in clinical T stage T3 and in the local or regional stage (M0). Because of the random noise in the simulated predictions and restrictions on the sensitivities (sensitivity increases with clinical T stage and metastatic state), formal 95% confidence intervals are difficult to obtain. However, for fixed values of other model parameters, the range of plausible values for test sensitivities is narrow (0.24–0.29). The range of plausible values contains with near certainty a standard computed 95% confidence interval. The range of plausible values was calculated as follows. First, we computed deviances for the model for different test sensitivities around the maximum likelihood estimate. In this figure we present the different deviances for the model if we vary the sensitivity for three different random sequences. The deviance was computed as usual as 2 × (the log likelihood of a saturated model minus the log likelihood of the model). In standard maximum likelihood estimation, 95% confidence intervals would be calculated, based on the likelihood ratio test, as the interval between the points where the deviance is 3.84 higher (the 95% quantile of 1 df for a chi-square distribution) than the minimum at the maximum likelihood estimate. As this figure shows, the deviances are approximate quadratic functions that have a minimum between 0.25 and 0.28, but random noise prevents the application of the standard 3.84 rule. However, the graphs also show that the likelihood of values outside the range of 0.24–0.29 must be small, which is the range of plausible values.