

B

Methods Used To Estimate Likelihoods of Cancer for Particular DRE And PSA Results

This appendix describes the derivation of likelihood ratios of different types of cancer for various digital rectal examination (DRE) and prostate-specific antigen (PSA) measurement results presented in tables 3-1 and 3-3 and discussed in the accompanying text. The likelihood ratios are estimates of how many times more likely a patient with a particular test result is to have a given type of cancer than if the patient did not have the test. The probabilities of cancer with no test are the prevalence estimates found in table 2-5. For each test, the likelihood ratios were estimated using the following method:

- Studies of screening tests that provided predictive values for a population of men with a *specified* age distribution were selected; these predictive values were converted into post-test odds of disease.
- Next, the true underlying prevalence of prostate cancer in the general population derived from autopsy studies, displayed in table 2-5, was assumed to be applicable to the populations in these studies of positive predictive values.
- Finally, the post-test odds were divided by the pretest odds of disease (and nondisease) to estimate likelihood ratios.

LIKELIHOOD RATIOS FOR DRE RESULTS

The calculations for DRE results (table 3-1) use data from two studies (79, 279) that provided detailed age distributions of study patients and to which we could apply the estimates of prostate cancer prevalence by tumor volume as presented in table 2-5. Calculations are performed using data for all men ages 50 years and up. “Suspicious” DRE results are defined as palpable asymmetries, nodules, or induration (hardness).

In the Chodak study, although 125 of the 2,131 men ages 45 to 80 in the initial screen group had an abnormal DRE and received a DRE-directed biopsy, the number of men ages 45 to 50 with abnormal DRE is not provided since no cancers were found in this subgroup. Calculations were done using the 1,894 men over 50 years (31 cancers detected in the first year of screening). Systematic biopsies were not performed and volume data for detected cancers were not provided. All were clinically Stage B or higher by the Whitmore staging system (see table 2-3), and it appears safe to assume none were below 0.5 mL.

Subjects in the Richie study (279) with abnormal DRE received systematic and TRUS-guided biopsies in addition to DRE-directed biopsies. Specific volume dis-

tributions are not provided. The 8 percent of detected cancers that were “organ-confined, well-differentiated, and involved only one quadrant” is not necessarily tantamount to a volume below 0.5 mL. We assume 11 percent of detected cancers are below 0.5 mL using data from 208 Stage T1c cancers reported by Oesterling (263). The proportion of cancers in this volume category for T1c tumors (using the TNM staging system described in table 2-3) has been as high as 26 percent (119). Although only 70 percent of patients with abnormal DRE in the Richie study (279) consented to biopsy, and only 63 percent of cancers were surgically staged, our derivations of the post-test odds and likelihood ratios assume perfect biopsy compliance and a comparable proportion of organ-confined cancers in those not receiving radical prostatectomy.

LIKELIHOOD RATIOS FOR PSA RESULTS

Likelihood ratios for PSA results are based on data from four studies: pooled results from studies by Catalona (66) and Brawer (44), results from a study by Richie (279), and results from another study by Catalona (70).

The values derived from pooling data from Catalona (66) and Brawer (44) are probably overestimates for the likelihood ratios for PSA testing alone since only patients who had either abnormal DRE or TRUS in the presence of PSA >4 ng/mL received biopsy. In addition to DRE- and TRUS-guided biopsies, when appropriate, systematic biopsies were performed in willing patients who met these criteria.

Specific volume distributions are not provided by any of the four studies. We again assume 11 percent of the detected cancers are below 0.5 mL based on the study by Oesterling (263). Eleven percent of all PSA 4 to 10 ng/mL detected cancers (presumed to be <0.5 mL) are subtracted from organ-confined cancers to derive the post-test odds for intracapsular cancers >0.5 mL. These likelihood ratios reflect “best case” values because we assume perfect compliance with biopsy (compared with the actual compliance rate of 70 percent in the Oesterling study (263) and a comparable proportion of intracapsular cancers above 0.5 mL in patients not receiving surgery. These “adjustments” were made for data from all four studies in table 3-3.

Patients in the Richie study (279) received both DRE and PSA independently, and the data are presented in a way that allows derivation of the likelihood ratio for PSA alone. However, separate pre- and post-test odds for PSA results of 4.1 to 9.9 ng/mL or PSA > 10 ng/mL cannot be derived from data reported in this study.

The later (and larger) study by Catalona (70) used a protocol similar to his earlier study (66). The derivations of the likelihood ratios used only the data reported for the initial screening of 9,629 volunteers. There is a major discrepancy between the likelihood of intracapsular cancer given a PSA result of greater than 10 ng/mL (3.0) in this study and the corresponding value (0.4) from the earlier pooled studies. This is explained by the observed difference in probability of pathological localization for cancers (>0.5 mL) detected by PSA >10 ng/mL (32 percent vs. 5 percent).