Probability Modeling of the Number of Positive Cores in a Prostate Cancer Biopsy Session, with Applications

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August 2, 2015

Abstract

Among men, prostate cancer (CaP) is the most common newly diagnosed cancer and the second leading cause of death from cancer. A major issue of very large scale is avoiding both over- and under-treatment of CaP cases. The central challenge is deciding clinical significance or insignificance when the CaP biopsy results are positive but only marginally so. A related concern is deciding how to increase the number of biopsy cores for larger prostates. As a foundation for improved choice of number of cores and improved interpretation of biopsy results, we develop a probability model for the number of positive cores found in a biopsy, given the total number of cores, the volumes of the tumor nodules, and – very importantly – the prostate volume. Also, three applications are carried out: guidelines for the number of cores as a function of prostate volume, decision rules for insignificant versus significant CaP using number of positive cores, and, using prior distributions on total tumor size, Bayesian posterior probabilities for insignificant CaP and posterior median CaP. The model-based results have generality of application, take prostate volume into account, and provide attractive tradeoffs of specificity versus sensitivity.

1 Introduction

Among men, prostate cancer (CaP) is the most common newly diagnosed cancer and the second leading cause of death from cancer, with over 200,000 new cases and about

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30,000 deaths annually in the U.S. alone [1]. Noninvasive screening for CaP is carried out by digital rectal examinations and PSA blood tests, often conducted annually on men age 40 years and over. Abnormal findings are followed by invasive needle biopsy procedures typically acquiring 6 to 12 or more cores of prostate tissue. If the biopsy result is positive, should one undergo aggressive treatment or opt for "watchful waiting" or "active surveillance"? Strongly positive results trigger aggressive action selected from a variety of possible treatments each carrying serious and permanent side-effects impacting quality of life for both patient and family. Completely negative results, on the other hand, unequivocally support deferral of treatment in favor of either "watchful waiting" or "active surveillance", taking advantage of the fact that prostate cancer tends to progress slowly.

However, the answer is not so immediate in the many cases that are positive but only marginally so, involving relatively few positive cores and thus challenging interpretation. In a high proportion (up to 50%) of treated CaP cases, it ultimately is found that the total tumor volume is not clinically significant, so that "overtreatment" has occurred with unwarranted consequences [2, p. 2789]. The millions of biopsies for possible CaP performed annually pose a large-scale worldwide dilemma of avoiding "overdiagnosis" and "overtreatment" of CaP. Likewise, "underdiagnosis" of clinically significant cases presents a problem, especially for men with larger prostate volumes in which the presence of CaP can be more easily missed [3]. Here the challenging question is how exactly to increase the number of biopsy cores in the case of a larger prostate, realizing that the side effects also increase. In sum, key issues are that (a) current diagnostic methods inadequately judge which marginal cases to treat and which not, and (b) often too few cores are taken in larger prostates.

An issue related to (a) is that PSA screening triggers biopsies which all too often detect cases of clinically insignificant CaP that nevertheless become treated. Thus the efficacy of PSA screening has become a center of controversy, especially since there lacks definitive evidence that it improves the CaP mortality rate [4], [5]. Strikingly, the U.S. Preventive Services Task Force recently recommended dropping PSA screening completely for men with no symptoms of CaP [6], and this is supported by the CDC. More moderate guidelines issued by the American Urological Association and the National Comprehensive Cancer Network, for example, reflect a hopeful perspective of continuing PSA screening while increasing effort to direct it toward just those men who will more likely benefit [7]. However, *if the interpretation of marginally positive biopsy results can be improved, then the continued use of PSA screening can become more warranted and more beneficial.*

Addressing these problems and issues, this paper develops *improved guidelines for selection of the number of cores for a biopsy session*, *improved decision rules for distinguishing between clinically significant and insignificant biopsy results*, and *Bayesian posterior information adding perspective in using the decision rules.* More precisely, the contributions of the paper are as follows:

(1) A probability model is developed for *the number D of positive cores* found in a biopsy, given specification of: the prostate gland volume V, the number n of biopsy cores, and the volumes $v_1, \ldots, v_k$ of a specified number k of tumor

nodules randomly distributed into the prostate.

(2) For any given (V, n) and potential threshold x_0 of D for deciding insignificant versus significant CaP, the *model-based specificity (SP) and sensitivity (SE) values* are derived using the model in (1). This enables *pre-biopsy* choice of n and x_0 to achieve a preferred combination of SP and SE among the available possibilities, and then *post-biopsy* use of D and the chosen x_0 as a decision rule achieving the selected (SP, SE).

(3) For any given (V, n) and selected prior distributions on the (unknown) total tumor volume T for specified age and PSA score, the corresponding *Bayesian posterior distributions* for T are derived using the model in (1) for the data D. These yield Bayesian *posterior probability of insignificant* T (PPI) and *posterior median* T (PM), which in turn, in conjunction with use of a decision rule as in (2), support enhanced interpretation of positive biopsy results, by taking into account age and PSA score.

(4) A *fully structured decision rule* is designed which includes (2) and (3) but also incorporates *tumor length* and *Gleason score* as inputs that are to be examined prior to using (2) and (3) in interpreting biopsy results. In this way, clear-cut cases of significant CaP can be identified and eliminated without the need of (2) and (3), whose chief importance is for interpretation of *marginally positive* biopsy results.

Reflecting the above considerations, our fully structured decision rule is formulated as follows.

STRUCTURED DECISION RULE FOR INSIGNIFICANT OR SIGNIFICANT CAP

1. *Check the Gleason sum.* If **7** or higher, conclude **Significant CaP**. Otherwise proceed to the next step.
2. *Check tumor lengths in the positive biopsy cores.* If
   - At least 1 core contains ≥ 1.0 cm tumor (67% of core length),
   - Or at least 2 cores *each* contain ≥ 0.8 cm tumor (53%),
   - Or at least 3 cores *each* contain ≥ 0.7 cm tumor (47%),
   - Or at least 4 cores *each* contain ≥ 0.65 cm tumor (43%),

   conclude **Significant CaP**. Otherwise proceed to the next step.
3. *Apply model-based decision rules based on number of positive cores D, for given V and n.* Conclude *either* **Significant CaP** *or* **Insignificant CaP**. For enhanced interpretation, also examine Bayesian PPI and PM.

If one reaches Step 3, then the contributions of this paper come directly into play.

We now discuss the organization of the remainder of the paper and summarize the key results. Our probability modeling is developed in Section 2. **Theorem 1** gives the probability distribution of D for a biopsy session involving n cores and k tumors

with volumes $v_1, \ldots, v_k$ distributed at random into a prostate of volume V. For $k =$ 6 nodules, $n =$ 6, 12, 18, and 24 cores, and V from 10 to 200 cc, this distribution is shown in **Tables 1 and 2** for total tumor volumes 0.25 and 2.0 cc, respectively, which are the two cases we use in defining SP and SE for particular decision rules. The proof of Theorem 1 in the Appendix establishes a more general result modeling separate allocations of cores into the transition and peripheral zones of the prostate.

Section 3 treats key applications of our probability modeling. Section 3.1 identifies favorable decision rules for "$T \leq 0.5$ cc" versus "$T > 0.5$ cc", i.e., insignificant CaP versus significant CaP, using a threshold x_0 for D. First, using Tables 1 and 2, the SP and SE for any prospective x_0 may be derived, separately by (V, n). High SP is needed to avoid overtreatment and high SE to avoid undertreatment, and in practice high SP is favored over high SE, since prostate cancer proceeds relatively slowly and might be found later if not early [22]. For each of our combinations of (V, n), **Table 3** displays favorable (x_0, SP, SE) combinations of practical interest. For example, for a patient with prostate volume $V = 30$ cc, a favorable decision rule according to Table 3 is to use a 6-core biopsy and decide "insignificant CaP" ($T \leq 0.5$ cc) if either 1 or 0 cores are positive, in which case (SP, SE) = (0.95, 0.45). On the other hand, with volume $V = 80$ cc, favorable choices are either a 12-core biopsy with (SP, SE) = (0.97, 0.34) or an 18-core biopsy with (SP, SE) = (0.92, 0.62), each associating 1 or 0 positive cores with insignificant CaP.

Section 3.2 derives Bayesian posterior information for enhanced interpretation of positive biopsy results when used in conjunction with model-based decision rules as per Table 3. In particular, using the modeling (1) with selected SEER-based [21] prior distributions on T, corresponding Bayesian PPI and PM are derived for selected possible values of D, separately for each of our combinations of (V, n) and for three PSA ranges. These are displayed in **Tables 4A-B, 5A-B, and 6A-B**, which for convenience also include the relevant thresholds x_0 and (SP, SE) from Table 3. Section 3.2.1 discusses the technique of application of the Bayesian posterior information in conjunction with such decision rules. For example, it is seen that for a patient with prostate volume $V = 30$ cc, decision-making on the basis of a marginally positive biopsy result of $D = 1$ and using the auxiliary posterior information for enhanced interpretation will be much more effective with a 12-core biopsy than a 6-core biopsy, even though (SP, SE) are about the same for the two cases.

Section 3.3 derives the above fully structured decision rule that also takes into account the tumor lengths in the cores and the Gleason scores of the tumor. Finally, Section 4 provides discussion and concluding remarks.

2 Distribution of number of positive biopsy cores

The probability distribution of the number of positive cores in a biopsy session is given as a function of prostate volume, number of cores, number of tumor nodules, and the tumor nodule volumes. Following preliminaries in Sections 2.1 and 2.2, the key result is provided in Section 2.3. Also, the conditional distribution of the number of positive cores, given that the number is positive, is provided in Section 2.5.

2.1 Basic assumptions and notation

1. Following previous modeling [13], [14], we make the technical assumption: *A number k of spherical tumor nodules are distributed into the prostate independently and "at random"*. More precisely, each *nodule center* is distributed at random within the prostate volume. This allows the possibility that a portion of a tumor nodule (but not its center) lies outside the prostate, consistent with the fact that prostate cancer tumors often do indeed extend outside the prostate. Although our formulas allow any $k \geq 2$, a representative choice that we use in our numerical applications is $k = \mathbf{6}$. The modeling results change little for, alternatively, $k = 4$ or $k = 8$.

2. We assume: *A number n of cylindrical biopsy cores of length L and radius s are placed into the prostate according to some protocol*. Biopsy needles vary in length and diameter. Here L is the typical length of prostate tissue effectively captured by a somewhat longer needle. Although our formulas allow general L and s, the choices used in our numerical applications are representative of practice [23], [24], [25] and correspond to an 18-gauge biopsy needle: $L = \mathbf{1.5\ cm}$, $s = \mathbf{0.06\ cm}$. The modeling results change little with variations in L, such as $L = 1.4$, 1.6, or 1.7 cm.

3. We make the technical assumption: *A tumor nodule may hit at most one core*. A tumor nodule "*hits*" a biopsy core if it intersects that core. Even the smallest of prostate volumes is hundreds-fold greater than a core volume. Although the above assumption can be violated if a sufficiently large tumor nodule is distributed into a sufficiently small prostate containing more than a minimal number of cores, in practice fewer cores are used in smaller prostates. The above assumption is tenable for our primary purposes. Sections 2.2.1 and 2.2.3 provide more precise discussion.

4. Key notation: V = prostate volume; n = number of biopsy cores; $R = n/V$ = number of cores per unit prostate volume; k = number of tumor nodules; $v_1 \geq v_2 \geq \ldots \geq v_k$ denote nodule volumes in decreasing order; $T = v_1 + \cdots + v_k$ denotes total tumor volume; H = number of hits of the n cores by the k nodules ($H \leq k$); D = number of positive cores ($D \leq \min\{H, n\} \leq \min\{k, n\}$).

5. A key quantity is the *probability that a tumor nodule of volume v hits one of n cores when distributed at random into a prostate of volume V*. It *depends on V and n only through the ratio R*, justifying convenient dual notation $\theta(v, V, n) = \theta(v, R)$.

6. For integers $1 \leq g \leq G$, we denote by $\sum_{C_{g,G}}$ summation over the $\binom{G}{g}$ combinations $\{\gamma_1, \gamma_2, \ldots, \gamma_g\}$ of g distinct indices from $\{1, 2, \ldots, G\}$, and we put $\overline{\{\gamma_1, \ldots, \gamma_g\}}_G$ for the complement of $\{\gamma_1, \cdots, \gamma_g\}$ in the set $\{1, 2, \ldots, G\}$.

7. We write $x^+ = \max\{x, 0\}$ for "positive part".

2.2 Key formula for $\theta(v, V, n) = \theta(v, R)$

2.2.1 Effective core volume

Following previous modeling [13] and [14], a single spherical tumor nodule intersects a cylindrical biopsy core if the *center* of the nodule falls within an *effective biopsy core region* defined by extending the core cylinder in all directions by a distance equal

to the radius of the tumor. The volume of this region is called the "*effective core volume*", $V_{\text{eff}}(v)$. For a sphere of volume v (cc), the radius is $r(v) = (3v/4\pi)^{1/3}$ (cm). Hence, by elementary geometry and calculus, $V_{\text{eff}}(v) = V_{\text{cyl}}(v) + 2\,V_{\text{cap}}(v)$, with $V_{\text{cyl}}(v) = L\,\pi\,(r(v)+s)^2$, the volume of a cylinder of length L and radius $r(v)+s$, and $V_{\text{cap}}(v) = (2/3)\,\pi\,r(v)^3 + (1/2)\,\pi^2\,r(v)^2\,s + \pi\,r(v)\,s^2$, the volume of the rounded cap extending the end of such a cylinder. Thus

$$V_{\text{eff}}(v) = \pi L s^2 + 2(3/4\pi)^{1/3}\pi s(L+s)\,v^{1/3} + (3/4\pi)^{2/3}\pi(L+\pi s)\,v^{2/3} + v, \quad (1)$$

an increasing polynomial function of v that becomes roughly linear. Its minimal value is $V_{\text{eff}}(0) = \pi L s^2$, the volume of the core itself. (For $L = 1.5$ cm and $s = 0.06$ cm, we have $V_{\text{eff}}(v) = 0.017 + 0.365\,v^{1/3} + 2.041\,v^{2/3} + v$.)

2.2.2 Considerations on application of the effective core volume

1. The total volume $\pi L s^2$ occupied by a biopsy cores is miniscule relative to the prostate volume V. Indeed, for $V \geq 10$ cc, $L = 1.5$ cm, and $s = 0.06$ cm, we have $V/(\pi L s^2) \geq 588$, whereas typically n ranges merely from 6 to 24.

2. We make the technical assumption: *The effective core regions for a tumor nodule are disjoint.* Thus a tumor nodule center falls within at most one effective core region, consistent with our previous assumption that a nodule hits at most one core. In this case, for a given tumor nodule of volume v, the total volume of the associated effective core regions is $n \times V_{\text{eff}}(v)$. For a *very small* tumor volume $v \approx 0$, this total approximates $n \times \pi L s^2$ and lies far below V. As v increases, however, so does $n \times V_{\text{eff}}(v)$, eventually reaching or exceeding V, in which case with certainty some core is "hit" and $\theta(v, V, n) = 1$ for that tumor nodule. The following table illustrates the possibilities for 6- and 12-core biopsies with the above needle dimensions and for a range of small to moderate size tumors ($v = 0.25$, 0.50, and 1.0 cc).

v	.25 cc	.50 cc	1.0 cc
$V_{\text{eff}}(v)$	1.3 cc	2.1 cc	3.4 cc
$6\,V_{\text{eff}}(v)$	7.8 cc	12.6 cc	20.5 cc
$12\,V_{\text{eff}}(v)$	15.7 cc	25.1 cc	41.1 cc

Thus, for the worst case of a 0.50 cc tumor nodule, the above assumption is violated with a 6-core biopsy for small 10 cc or 20 cc prostates and with a 12-core biopsy for prostates of volume 40 cc or lower. In such cases, the number of positive cores associated with that single nodule is more than one. However, given that there are additional nodules also potentially providing hits, the overall number of positive cores is not dramatically larger than as modeled. And when it is, this corresponds to a more strongly positive biopsy result, so that our modeling is conservative in the appropriate sense. A small simulation investigation has shown that this technical modeling assumption introduces little error in the resulting probability distribution, as regards its role in formulating decision rules. In practical application of our model, we focus primarily on the case that the number of nodules is $k = 6$ with volumes decreasing by halves with the largest ≤ 1.0 cc, and that $R = n/V$ is not large.

2.2.3 Formula for $\theta(v, V, n) = \theta(v, R)$

Applying our assumptions and notation, the probability that a tumor nodule of volume v is *not detected* is given by the fraction of prostate volume outside the disjoint effective core regions, $(1 - n\,V_{\text{eff}}(v)/V)^+ = (1 - R\,V_{\text{eff}}(v))^+$. Hence the probability of a "hit" by that nodule is

$$\theta(v, R) = 1 - \left(1 - R\,V_{\text{eff}}(v)\right)^+ = \begin{cases} 1, & \text{if } R\,V_{\text{eff}}(v) \geq 1, \\ R\,V_{\text{eff}}(v), & \text{otherwise} \end{cases}, \tag{2}$$

taking the same value for all combinations (n, V) having the same ratio $R = n/V$.

2.3 Probability distribution of D

In stating the distribution of the number of positive cores D, the distribution of the number of hits H is used. Immediately, $P(H = 0) = \prod_{j=1}^{k} [1 - \theta(v_j, R)]$ and, for $1 \leq x \leq k$, $P(H = x) = \sum_{C_{x,k}} P(\text{exactly } x \text{ hits, precisely by nodules } i_1, \ldots, i_x)$. Thus the probability distribution of H is given by

$$P(H = x) = \begin{cases} \displaystyle\prod_{j=1}^{k} [1 - \theta(v_j, R)], & x = 0, \\ \displaystyle\sum_{C_{x,k}} \prod_{i \in \{i_1, \ldots, i_x\}} \theta(v_i, R) \prod_{j \in \overline{\{i_1, \ldots, i_x\}}_k} [1 - \theta(v_j, R)], & 1 \leq x \leq k, \end{cases} \tag{3}$$

and depends on n and V only through $R = n/V$. We now state our key result.

Theorem 1 *The probability distribution of D is given by*

$$P(D = y) = \binom{n}{y} \sum_{x=y}^{k} \frac{\binom{x-1}{y-1}}{\binom{n+x-1}{x}} P(H = x), \;\; y = 0, \ldots, \min\{k, n\}. \tag{4}$$

Here (3) is used for the quantities $P(H = x)$ in (4). The quantities $P(D = y)$ depend on both n and R. The above result is proved in the Appendix, in a more general version of which allowing possible stratified distribution of tumor nodules into the separate peripheral and transition zones within the prostate.

2.4 Parameterization by total tumor volume T

A very productive simplification acceptable in practical applications (see [13]) is to let each tumor nodule have volume one-half that of the next larger nodule. That is, with v_1 the largest volume, let $v_i = v_1(1/2)^{i-1}$ for $i = 2, \ldots, k$. Then the *total tumor volume* T is given by

$$T = v_1 \left(1 + (1/2) + \cdots + (1/2)^{k-1}\right) = v_1 \left(2 - (1/2)^{k-1}\right). \tag{5}$$

Thus $v_i = T/(2^i - 2^{i-k})$, $i = 1, \ldots, k$. (For $k = 6$, the volumes $v_1, \ldots, v_6$ are $0.508T$, $0.254T$, $0.127T$, $0.064T$, $0.032T$, and $0.016T$, respectively.) With these volumes, the quantities in (3) that are used in (4) become expressed as

$$P(H = x) = \tag{6}$$

$$\begin{cases} \displaystyle\prod_{j=1}^{k} \max\left\{0, 1 - R\,V_{\text{eff}}\left(\frac{\left(\frac{1}{2}\right)^{j-1} T}{2 - \left(\frac{1}{2}\right)^{k-1}}\right)\right\}, & x = 0, \\ \displaystyle\sum_{C_{x,k}} \prod_{i \in \{i_1, \ldots, i_y\}} \min\left\{1, R\,V_{\text{eff}}\left(\frac{\left(\frac{1}{2}\right)^{i-1} T}{2 - \left(\frac{1}{2}\right)^{k-1}}\right)\right\} & \\ \qquad \times \displaystyle\prod_{j \in \overline{\{i_1, \ldots, i_y\}}_k} \max\left\{0, 1 - R\,V_{\text{eff}}\left(\frac{\left(\frac{1}{2}\right)^{j-1} T}{2 - \left(\frac{1}{2}\right)^{k-1}}\right)\right\}, & 1 \le x \le k-1, \\ \displaystyle\prod_{i=1}^{k} \min\left\{1, R\,V_{\text{eff}}\left(\frac{\left(\frac{1}{2}\right)^{i-1} T}{2 - \left(\frac{1}{2}\right)^{k-1}}\right)\right\}, & x = k. \end{cases}$$

Using (4) with $P(H = x)$ given by (6), we can readily compute the probability distributions $P(D = y)$, $y = 1, \ldots, \min\{k, n\}$, for any choice of L, s, k, n, V, and T. In particular, for $L = 1.5$, $s = 0.06$, $k = 6$, $n = 6$, 12, 18, and 24, $V = 10$, 20, 30, ..., 60, 80, 100, ..., 200, we provide these probabilities for $T = \mathbf{0.25}$ and $T = \mathbf{2.0}$ in **Tables 1 and 2**, respectively. In Section 3.1.1 these tables are used to derive the specificities and sensitivities of threshold-type decision rules based on D.

2.5 Conditional probability distribution of D, given $D > 0$

An important role is played by *the conditional distribution of the number of distinct cores hit, given that at least one hit occurs (i.e., given that cancer is detected)*:

$$P(D = y \,|\, D > 0) = \frac{P(D = y)}{1 - P(D = 0)},\ y = 1, \ldots, \min\{k, n\}. \tag{7}$$

Using (4) with $P(H = x)$ given by (6), we can readily compute this conditional distribution for any choice of L, s, k, n, V, and T. In Section 3.1.2 this is used to derive *Bayesian posterior probability distributions on* T, given $D > 0$, based on prior distributions on T obtained using the SEER database [21] of tumor volumes for actual prostate cancer cases.

3 Techniques of application

We indicate several lines of application of the distribution of D. Section 3.1 discusses threshold rules to decide "insignificant CaP" versus "significant CaP", based on D as data, and treats the specificity and sensitivity of these rules. Guidelines are derived for selecting the number of cores for the most favorable tradeoffs between specificity

and sensitivity. Section 3.2 introduces Bayesian posterior distributions on T. Section 3.3 exhibits a fully structured decision rule based not only on D as data but also on *the tumor lengths in the cores* and *the tumor Gleason score* as additional data.

3.1 Model-based threshold-type decision rules using D

In evaluating prostate cancer biopsy results, a key question is whether the total tumor volume represents "insignificant CaP", which is generally defined clinically [18], [19], [26] as *organ-confined disease with histologic Gleason sum* < 7 *(with overwhelming probability, this is equivalent to both Gleason grades* < 4*) and total tumor volume* $T \leq 0.5$ *cc*. As seen in Section 3.3, if the percentage tumor length in one or more cores is sufficiently high, one may immediately conclude that $T > 0.5$ cc. However, if this is not the case and also the Gleason sum is < 7, then one may proceed to use a threshold-type decision rule based on the number of positive cores D, i.e., a rule of form

$$\text{Decide } T \leq 0.5 \text{ cc} \iff D \leq x_0, \tag{8}$$

for a specified threshold x_0. Associated with any such threshold is a particular tradeoff between *specificity (SP) and sensitivity (SE)* (as discussed in Section 3.1.1 below), so that selection of the threshold x_0 represents selection of an SP-SE tradeoff. Since SP and SE are based on the distribution of D and thus on a given prostate volume, the resulting model-based threshold rules of form (8) specifically take account of the patient's prostate volume. This is an important advance over the decision rules used in current practice, which are each crafted from exploring a particular data set of prostatectomies and have associated SP and SE determined empirically using that particular data set. Such study-based (SP, SE) do not necessarily apply in general, whereas our *model-based* (SP, SE) is not tied to any particular data set and thus has generality of application, as well as being sensitive to prostate volume. Also, besides having a role in the interpretation of biopsy results, the (SP, SE) information can be exploited in choosing the number of cores to be used in a biopsy session.

3.1.1 Model-based specificity and sensitivity of threshold-type rules

The *specificity* of a decision rule as above is the conditional probability that it decides "insignificant CaP", given that the CaP truly is insignificant. For this we choose a particular value of T below the clinically significant threshold 0.5 cc. In particular, we use $T =$ **0.25 cc** and define our *model-based specificity* by

$$\text{SP}(x_0 \,|\, n, V) = \sum_{y=0}^{x_0} P(D = y \,|\, n, V; T = 0.25 \text{ cc}), \tag{9}$$

i.e., $P(D \leq x_0 \,|\, n, V; T = 0.25 \text{ cc})$, which can be evaluated using **Table 1**. On the other hand, the *sensitivity* of such a decision rule is the conditional probability that it decides "significant CaP", given that the CaP truly is significant. For this we choose a value of T above the clinically significant threshold 0.5 cc. In particular, using $T =$

2.0 cc, we define our *model-based sensitivity* by

$$\mathrm{SE}(x_0 \,|\, n, V) = \sum_{x=x_0+1}^{\min\{k,n\}} P(D = x \,|\, n, V; T = 2.0 \text{ cc}), \tag{10}$$

i.e., $P(D > x_0 \,|\, n, V; T = 2.0 \text{ cc})$, which can be evaluated using **Table 2**. High values of both $\mathrm{SP}(x_0)$ and $\mathrm{SE}(x_0)$ are desired, but as x_0 is altered to increase one of these, the other decreases.

3.1.2 Favorable specificity-sensitivity tradeoffs

The threshold x_0 in (9) and (10) is selected prioritizing $\mathrm{SP}(x_0)$ over $\mathrm{SE}(x_0)$. False negative results typically are followed eventually by further biopsies and thus further opportunities for reasonably early detection of significant CaP when present, so they can be tolerated more than false positive results, which typically generate agressive but unwarranted treatment with serious adverse impacts on quality of life. [22, p. 235]. Still, in favoring SP, we do not completely sacrifice SE.

The choice of x_0 is carried out separately for each case of (V, n). As an example, consider $(V, n) =$ **(30, 12)**. For each of $x_0 = 0, 1, 2, 3$, we find $(\mathrm{SP}(x_0), \mathrm{SE}(x_0))$ and then choose a preferred tradeoff, as follows.

1. From Table 1 obtain SP(0) = 0.35, SP(1)= 0.80, SP(2) = 0.97, and SP(3) = 1, and from Table 2 SE(0) = 1, SE(1) = 0.91, SE(2) = 0.52, and SE(3) =0.13. These yield the pairs (SP(0), SE(0)) = (0.35, 1), (SP(1), SE(1)) = (0.80, 0.91), (SP(2), SE(2)) = (0.97, 0.52), and (SP(3), SE(3)) = (1, 0.13).

2. Giving priority to SP without unduly sacrificing SE, we immediately reject both $x_0 = 0$ and $x_0 = 3$. We prefer $x_0 =$ **2** because it provides very high SP and moderately high SE. Although $x_0 = 1$ is competitive, its SP of 0.80 is too low when SP = 0.97 is available and accompanied by moderately high SE of 0.52.

Thus, for $(V, n) = (\mathbf{30}, \mathbf{12})$, our recommended model-based decision rule is: *Conclude "insignificant CaP" if the number of positive cores D is* ≤ 2. This rule has (SP, SE) = (**.97**, **.52**). However, for a given prostate volume V, one can choose the number of biopsy cores n by comparing the associated (SP, SE) tradeoffs for each choice of n. Thus, continuing the above illustration by determining in similar fashion the most favorable rules for $(V, n) =$ (**30**, **6**), (**30**, **18**), and (**30**, **24**), we obtain the favored thresholds x_0 and associated (SP, SE) for $V =$ **30** cc and $n = 6, 12, 18, 24$ are:

n	6	12	18	24
x_0 (SP, SE)	1 (.95, .45)	2 (.97, .52)	2 (.91, .82)	3 (.96, .65)

Among these, the choice $n =$ **6** offers the most appealing tradeoff. Although $n =$ 12 offers modest improvement in both SP and SE, it doubles the number of cores, burdening the patient. The choice $n = 18$ offers better SE but considerably reduces SP and triples the number of cores, and $n = 24$ offers better SE but about the same SP while quadrupling the number of cores.

Following the above approach, one obtains recommended decision rules (choice of threshold x_0) for all combinations of (V, n), for V = 10, 20, 30, ..., 60, 80, 100, ..., 200 and n = 6, 12, 18, and 24. These are presented in **Table 3** and show how the preferred number of cores and associated decision rule varies with the prostate volume V. In particular, this quantifies the principle that the finding of any particular number of positive cores is more significant, the larger the gland volume.

Remarks. (a) Table 3 suggests the threshold $x_0 = \mathbf{1}$ for insignificant CaP for all combinations of (V, n) except the cases $V = 10$ cc with 6 cores and $V = 40$, 50, or 60 cc with 18 cores, in which case $x_0 = \mathbf{2}$ is recommended. Note also, however, that to maintain attractive (SP, SE) it is essential to increase n as V increases, as follows:

V (cc)	10-30	4-50	60-100	110-200
n	6	6-18	12-18	18-24

For very large V, even 32 cores may be considered [27], [28].

(b) The $x_0 = \mathbf{1}$ threshold is actually quite common in current practice, but it is not always used optimally, since the higher n needed for larger V as indicated above is not typically adopted. For example, a review of leading methods [19] indicates (SP, SE) such as (100, 14), **(99, 70)**, (99, 34), (98, 53), (98, 52), (98, 23), **(97, 67)**, (96, 50), (96, 27), (95, 56), (89, 33), (78, 71), and (75, 77), the two in bold including prostate volume as an input. These typically are derived for rules determined by logistic regression using selected predictors and decision criteria, but across different data sets of patients, thus obtaining different "optimal" fitted models, making it problematic to decide which to use with a given patient. Also, these concern a range of only 6 to 12 biopsy cores. In contrast, our recommendations in Table 3 not only compare well in (SP, SE) but also have generality of application and, very importantly, properly adjust n for increasing prostate volume V.

(c) A small simulation experiment with assumptions somewhat different from our model yields similar SP but higher SE, *yet exactly the same recommended thresholds x_0 for given n and V as in Table 3.*

(d) Further, in a validation study to be reported, our fully structured rule with the same SP as in Table 3 but even higher SE exhibits superior (SP, SE) performance over the current data-based rules.

3.2 Bayesian posterior distributions for T, given $D > 0$

A standard Bayesian approach using the distribution of D (given T) in conjunction with a prior probability distribution on T yields a *posterior probability distribution on T* and thus a *Bayes estimator of T* (the mean or median of the posterior) and a *posterior probability of "insignificant CaP"*. Prior distributions are constructed in [20] using the SEER database [21] providing age, dominant tumor nodule volume, PSA score, and Gleason score for patients undergoing prostatectomies over the period 1973-2010. The dominant nodule volume is converted to a corresponding total tumor volume using formula (5) with $k = 6$, assuming that each nodule has volume one-half that of the next larger nodule. Here the *conditional distribution of D, given $D > 0$*, is

used, since the SEER database consists of patients for whom the biopsy was positive. For each relevant value of T, the needed conditional distributions are derived from the corresponding unconditional distributions of D, which can be computed for any T (as illustrated in Tables 1 and 2 for $T =$ **0.25** and **2.0**, respectively).

Separate SEER-based prior distributions on T for each combination of age range, PSA score range, and Gleason score range are developed in [20] and shown to be compatible with a range of study-based priors in the literature. Combined with the distribution of D given T, which depends on the gland volume V and the number of biopsy cores n, the priors yield separate posterior distributions on T for each combination of V, n, age range, PSA score range, and Gleason score range. Such posterior distributions may be used as *auxiliary information* in conjunction with the model-based decision rules treated above.

More specifically, SEER-based prior probabilities are developed for T (cc) in the intervals 0-0.5, 0.5-1.0, 1.0-1.5, 1.5-2.0, 2.0-4.0, and 4.0-∞, and these are used as a prior probability distribution over nominal values of T (cc), **0.25**, **0.75**, **1.25**, **1.75**, **3.0**, and **4.0**, associated with these intervals, respectively. Accordingly, using the conditional distributions of D given T, for $T = 0.25$, 0.75, 1.25, 1.75, 3.0, and 4.0, for each prior we obtain an associated *Bayesian posterior distribution over these values of* T. In turn, these yield *posterior probabilities for "insignificant CaP"* (PPI) and *posterior medians* (PM). **Tables 4A-B, 5A-B, and 6A-B** provide PPI and PM for age range **40-75** years and PSA score ranges **0-2**, **2-4**, and **4-10** ng/dl, respectively, for all combinations of (V, n), for V (cc) = 10, 20, 30, ..., 60, 80, 100, ..., 200 and $n = 6$, 12, 18, and 24.

3.2.1 Technique of application of the Bayesian posterior information

A key application of the PPI and PM information is to provide added perspective on a decision rule selected via Table 3. Let us briefly illustrate. For example, for a patient with $V =$ **30** cc, that a 12-core ($n =$ **12**) biopsy is to be carried out. From Table 3, for $(V, n) = (30,12)$ our recommended model-based threshold for *insignificant CaP* would be $x_0 =$ **2**, with favorable (SP, SE) = (**0.97**, **0.52**). For perspective on the choice $x_0 =$ **2**, we compare it with the next lower threshold, $x_0 =$ **1** with (SP, SE) = (0.80, 0.91), which provides higher SE but much lower SP. For further perspective, if for example we have a patient with age range = **40-75** years and PSA score range = **4-10** ng/dl, we can also examine the PM and PPI from the relevant posterior probability distributions on T, given D, for selected choices of D. From **Table 6A** we have the following information:

$x_0 = 1$: (SP, SE) = (0.80, 0.91)
$x_0 =$ **2**: (SP, SE) = (**0.97**, **0.52**)
$D =$ **1**: PPI = **0.68**; PM = **0.36**
$D = 2$: PPI = 0.17; PM = 1.88
$D = 3$: PPI = 0.02; PM = 4.0+

The clinician may examine all of this together as follows. From the standpoint of favorable SP versus SE tradeoff, the threshold $x_0 =$ **2** is preferred over $x_0 = 1$. On

the other hand, from the standpoint of both PPI (desirably high) and PM (desirably low), the threshold $x_0 = 2$ has very low PPI and very high PM, suggesting *significant CaP*, whereas the threshold $x_0 = \mathbf{1}$ has high PPI and low PM. However, the latter choice has (SP, SE) = (0.80, 0.91), reflecting a reversal of the desired priorities on SP versus SE and exhibiting an SP which is only marginally acceptable. Consequently, the overriding choice remains the threshold $x_0 = \mathbf{2}$, *but the accompanying Bayesian analysis provides useful perspective*, as follows. Namely, if $D = 1$ is observed (lower than the threshold $x_0 = 2$), then "insignificant CaP" is readily concluded, and this is strongly supported with fairly high PPI = 0.68 and low PM = 0.36. Likewise, if $D = 3$ is observed (exceeding the threshold), then *significant CaP* is readily concluded, and this is supported with fairly low PPI = 0.02 and PM = 4+. However, if the *boundary threshold* $D = \mathbf{2}$ is observed, then again "insignificant CaP" is concluded, but now with unsupportive PPI = 0.17 and PM = 1.88. Thus when D equals the threshold x_0, this represents ambiguous evidence, and in opting to let it be associated with *insignificant CaP*, one is prioritizing very strongly in favor of high SP.

Note, however, that in fact Table 3 used by itself would support using a 6-core biopsy with nearly as good (SP, SE), thus reducing the biopsy burden with but little loss in terms of (SP, SE). In this case, for added perspective, we would examine the following information from Table 6A:

$x_0 = 0$: (SP, SE) = (0.61, 0.91)
$x_0 = \mathbf{1}$: (SP, SE) = (**0.95**, **0.45**)
$D = \mathbf{1}$: PPI = **0.35**; PM = **1.29**
$D = 2$: PPI = 0.06; PM = 4.0+

In this case the clinician might reason as follows. From the standpoint of favorable SP versus SE tradeoff, the threshold $x_0 = \mathbf{1}$ for insignificant CaP is preferred over $x_0 = 0$, which reverses the priority of SP over SE. On the other hand, the threshold $x_0 = 1$ has quite low PPI and fairly high PM, suggesting *significant CaP*. Now, if $D = 0$ is observed (lower than the threshold $x_0 = 1$), then "insignificant CaP" is readily concluded, of course. Likewise, if $D = 2$ is observed (exceeding the threshold), then *significant CaP* is readily concluded, and this is supported with very low PPI = 0.06 and PM = 4+. However, if the *boundary threshold* $D = \mathbf{1}$ is observed, then again "insignificant CaP" is concluded, but now with rather unsupportive PPI = 0.35 and PM = 1.29. Thus when D equals the threshold x_0, again we have ambiguous evidence.

This clarifies the choice of 6-core biopsy versus 12-core biopsy. For the 6-core case, a marginally positive biopsy result ($D = 1$) is inevitably rather ambiguous. On the other hand, for the 12-core case, the marginally positive case ($D = 1$) is rather clear-cut evidence favoring *insignificant CaP*.

3.3 Construction of a fully structured decision rule

In practice, the pathology results of a biopsy session yield not only the number of positive cores but often also the *tumor lengths in the cores* and the *Gleason scores*. Many decision rules in the literature utilize some or all of these variables, which are

routinely available. In this vein, for practical use, we embed our decision rule based on D into a more structured decision rule also utilizing these further variables.

Regarding *Gleason score*, we consider a Gleason sum of **7** or higher **Significant CaP**, regardless of the amount of tumor [19], [26]. For treating *tumor length*, we adopt the (conservative) simplifying assumption that if a biopsy core intersects a tumor nodule, it passes through the middle of the nodule, so that the observed tumor length in the core corresponds to the diameter of the nodule. The following table shows the resulting correspondence between tumor length in a core and volume of the associated tumor nodule. Due to our simplifying assumption, the given tumor volume is a lower bound to the actual tumor volume. As previously, we assume that the core has length $L = \mathbf{1.5}$ cm.

tumor length (cm)	0.60	**0.65**	**0.70**	0.75	**0.80**	0.85	0.90	0.95	**1.00**
tumor volume (cc)	0.11	0.14	0.18	0.22	0.27	0.32	0.38	0.45	0.52
% of core CaP	40.0	**43.3**	**46.7**	50.0	**53.3**	56.7	60.0	63.3	**66.7**

For example, if at least one core has tumor length ≥ 1.0 cm, then the corresponding tumor volume is at least 0.52 cc, which is "significant". Likewise, if two or more cores each contain at least 0.8 cm tumor length, then the associated total tumor volume is at least $0.27 + 0.27 = 0.54$, again "significant". Continuing in this fashion, we arrive at the fully structured decision rule exhibited in Section 1.

4 Discussion and Concluding Remarks

We have developed a foundational probability model for the number of positive cores in a biopsy session and applied it to generate new guidelines and decision rules for interpretation of biopsy results as well as to derive Bayesian posterior probabilities of insignificant CaP and posterior median CaP. The guidelines reflect favorable model-based tradeoffs between specificity, sensitivity, and the chosen number of cores, and the posterior information takes into account prior knowledge of age and PSA score. Regarding the practical use of these contributions, several perspectives are relevant, as follows.

Remarks on the probability model. (a) A patient's prostate volume V as an "input" in (1) is readily available by noninvasive methods such as transrectal or transabdominal sonogram, or MRI, or CT, as well as early in the course of conducting a biopsy session.

(b) The crucial relevance of V to the efficiency of CaP detection is well understood [8], [9], [10], [3], [11], a given amount of tumor being harder to detect in a larger prostate. Indeed, the variable V is now being incorporated as an input into data-based "risk calculators" which play a role in deciding whether or not to conduct a biopsy by giving an estimate of the chance of detecting CaP should a biopsy be conducted [12], [11]. Now, *model-based* "risk calculators" can be derived.

(c) The probability modeling involves the geometry of spherical tumor nodules of given volumes distributed randomly into a prostate of given volume containing a specified number of cylindrical biopsy cores. Classical probability results involving

distributions of balls into urns have been exploited. The present model extends previous modeling [13], [14] that incorporates V as an input but only treats whether CaP is detected or not, that is, only treats whether the number D of positive cores is zero or nonzero without using its actual value when positive. That modeling is useful for planning the number of cores and also has been applied to explain certain unexpected findings in the Prostate Cancer Prevention Trial (see [15], [16], and [17]). However, by incorporating the actual value of D, the present more extensive modeling yields not only *improved criteria for selection of number of cores* n, but also, most importantly, *guidelines for interpretating marginally positive biopsy results on the basis of the value of* D *relative to* n, specialized to prostate volume V.

(e) The general model treated in the Appendix actually treats jointly the numbers of positive cores found, respectively, in the *transition and peripheral zones* of the prostate, under *stratified* distribution of the tumor nodules separately into these zones. This supports more elaborate schemes for choosing the number of biopsy cores, for allocation of cores into zones, and for interpretation of consequent biopsy results. However, in the specific application of that model developed here, the prostate is treated as a whole and the representative special case of $k = 6$ tumor nodules with volumes v_i decreasing by halves, enabling parameterization by the total tumor volume T, is emphasized. We have explored the alternative choices of $k = 4$ and $k = 8$ and found that the results change little and yield essentially the same practical implications. Also, this range of k values corresponds well to values found in typical studies of prostatectomy data sets, and in any case this quantity of separate tumor nodules accounts for the bulk of the total tumor. One wants not to give weight to detection of overly minute tumor nodules of no clinical significance. One might let k be random, following some distribution, but there is little basis in the literature for choosing an appropriate distribution. Likewise, we might let the volumes v_i be random or the total tumor volume T be random, but again there lacks a suitable guideline to adopt. Also, although introducing such randomization might add generality, it would also add technical complexity.

Remarks on the model-based guidelines. (a) The threshold we have adopted for insignificant versus significant CaP follows a widely used criterion, total tumor volume $T = 0.5$ cc [18], [19]. For defining SP, we have adopted total tumor volume $T = 0.25$ cc, a value midway between 0 and the threshold 0.50 for insignificant CaP. This seems reasonable and rather natural. For defining SE, we have adopted $T = 2.0$ cc, a convenient and seemingly representative value, in view of the posterior median total tumor volumes of 1.4, 1.9, and 3.0 cc for PSA ranges 0-2, 2-4, and 4-10 ng/dl, respectively, from Tables 4A-6B. The choice $T = 3.0$ cc, for example, would be less conservative and give perhaps unrealistically high SE values.

(b) For interpreting biopsy results once they are obtained, the empirically derived decision rules in current practice either omit the patient's V as an input or use it as a factor in logistic regressions, each idiosyncratic to a particular data set of prostatectomies, and based on particular error distribution assumptions [18], [19] of uncertain validity. On the other hand, our model-based decision rules are not tied to particular data sets and so may apply in a general way across different populations

of patients, and, most importantly, *they provide a guide for properly adjusting n for increasing prostate volume V*. Elaboration of this has been provided in Section 3.1.2.

(c) In contrast to threshold approaches, another approach toward deciding whether a patient has "insignificant CaP" ($T \leq 0.5$ cc) versus "significant CaP" ($T > 0.5$ cc) is to base the decision on a statistical estimate of T. Using the distribution of D, which depends on T, one can develop *maximum likelihood* and *methods of moments* estimators of T, each based on D as data. See [20] for detailed treatment. It turns out that there is strong consistency between these estimators. However, although these estimators offer clues about T, in each case the data D corresponds to a single biopsy for a single patient (i.e., a sample of size 1), and the resulting variability in any of these single-biopsy estimators is too great to be able to rely on them with high confidence in a clinical setting.

Remarks on the Bayesian posterior distributions. The prior distributions on total tumor volume T that we use here are based on the Surveillance Epidemiology and End Results (SEER) data [21] and confined to age range 40-75 years, separately for PSA ranges 0-2 ng/dl, 2-4 ng/dl, and 4-10 ng/dl. Although such priors are not available separately by prostate volume V, the resulting posterior distributions via our model indeed are specific to V, since the model itself is. Further such SEER-based priors separately by both PSA and Gleason score ranges, and including other age ranges, are developed and used in [20]. Techniques of application of auxiliary Bayesian posterior information in conjunction with decision rules have been discussed in Section 3.2.1.

Remarks on the fully structured decision rule. Tumor length and Gleason score as inputs for this rule are routinely available from the pathology report on a biopsy result. Examination of tumor length and Gleason score as a step before proceeding to apply a model-based rule increases the associated SE without decreasing the SP. The model-based (SP, SE) of the fully structured decision rule is found to be superior to the empirical (SP, SE) values associated with existing study-based rules [20], and this finding also has been validated empirically with actual data (report in preparation).

Concluding remarks. The results establish and demonstrate in a quantitative way how, by taking suitably many biopsy cores for larger prostates, the use of prostate-volume-specific decision rules based on the number of positive biopsy cores achieves favorably high SP and SE. Our prostate-volume specific decision rules using D along with Bayesian PPI and PM provide tools for enhanced interpretation of marginally positive biopsy results, facilitating better classification into "watchful waiting" versus "treatment", thus ameliorating both over-treatment and under-treatment and helping make continued use of PSA screening more beneficial and less controversial. Of course, further study is warranted, including more elaborate modeling along with simulation studies and validation studies.

Acknowledgements

The first author thanks Dr. Roger Rittmaster, M.D., for emphasizing the importance and role of a probability distribution for the number of positive cores in a prostate cancer biopsy session, G. L. Thompson for many insights and encouragement, and GlaxoSmithKline for grant support. The work of the second author was conducted under supervision of the first author in partial fulfillment of requirements for the doctoral degree. The authors also thank Michael Yuan for carrying out simulation work verifying the tenability of our modeling assumptions and two anonymous reviewers and the editor for very helpful and constructive comments and suggestions that have been utilized to improve the paper.

APPENDIX

We derive the *joint probability distribution of the number of cores hit and the number of positive cores*, as a function of: prostate volume, possibly separated into peripheral and transition zone volumes; number of biopsy cores; number of tumor nodules; tumor nodule volumes.

Assumptions and notation

1. Denote the peripheral and transition zones by PZ and TZ, respectively. Let $V_1 =$ volume of PZ, $V_2 =$ volume of TZ, $n_1 =$ number of biopsy cores assigned to PZ, and $n_2 =$ number of biopsy cores assigned to TZ. Let $V = V_1 + V_2 =$ total volume of the prostate and $n = n_1 + n_2 =$ total number of biopsy cores. (If desired, the approach used here can be extended to handle a partition of the prostate into more than two designated zones.)

2. Suppose that k spherical tumor nodules with volumes $v_1 \geq v_2 \geq \ldots \geq v_k$ are distributed independently into the prostate, with nodule i distributed into the PZ or TZ with respective probabilities p_i and $1 - p_i$, $1 \leq i \leq k$. Let $\alpha(\emptyset)$ denote the probability of *no nodules to the PZ and all to the TZ*, let $\alpha(\{1, \ldots, k\})$ denote the probability of *all nodules to the PZ and none to the TZ*, and, for $1 \leq \ell \leq k-1$ and each set $\{i_1, \ldots, i_\ell\}$ of ℓ distinct indices from $\{1, \ldots, k\}$, let $\alpha(\{i_1, \ldots, i_\ell\})$ denote the probability of *nodules* $i_1, \ldots, i_\ell$ *to the PZ and the others to the TZ.*

3. Let L and $M = k - L$ denote the random numbers of nodules sent to the PZ and TZ, respectively, through the k independent random assignments, and let $\{i_1, \ldots, i_L\}$ and $\{j_1, \ldots, j_M\}$ be the respective sets of nodule indices (which combined are the set $\{1, 2, \ldots, k\}$).

4. Let $L_1 =$ number of hits of biopsy cores (allowing repeats) by the L nodules sent to the PZ, $M_1 =$ number of hits of biopsy cores (allowing repeats) by the M nodules sent to the TZ, $L_0 =$ number of distinct cores among those hit by the L nodules sent to the PZ, and $M_0 =$ number of distinct cores among those hit by the M nodules sent to the TZ. Thus $L_0 \leq L_1 \leq L$ and $M_0 \leq M_1 \leq M$.

5. Let $p(x \,|\, v_{01}, \ldots, v_{0d}, V_0, n_0)$ denote the probability that the number of hits is x,

when d nodules of volumes $v_{01}, \ldots, v_{0d}$ are distributed independently into a prostate zone with volume V_0 and n_0 biopsy cores, for $x = 0, 1, \ldots, d$. For the case $d = 1$ we use a convenient alternate notation for $p(1 \,|\, v_{01}, V_0, n_0)$: $\theta(v_{01}, V_0, n_0)$.

6. We retain the notation $\sum_{C_{g,G}}$ and $\overline{\{\gamma_1, \ldots, \gamma_g\}}_G$ given previously.

Evaluation of $\theta(v_0, V_0, n_0)$ and $p(x \,|\, v_{01}, \ldots, v_{0d}, V_0, n_0)$

As in Section 2.2.3, with now $R = n_0/V_0$, we have

$$\theta(v_0, R) = 1 - (1 - R\, V_{\text{eff}}(v_0))^+. \tag{A.1}$$

We now derive a general expression for $p(x \,|\, v_{01}, \ldots, v_{0d}, V_0, n_0)$. Let X be the number of hits when d tumor nodules labeled 1 to d with respective volumes $v_{01}, \ldots, v_{0d}$ are distributed randomly and independently into a prostate zone with volume V_0 and n_0 biopsy cores. Then, by the same steps as for (3) in Section 2.4, we obtain

$$p(x \,|\, v_{01}, \ldots, v_{0d}, R) = \tag{A.2}$$

$$= \begin{cases} \displaystyle\prod_{j=1}^{d} [1 - \theta(v_{0j}, R)], & x = 0, \\ \displaystyle\sum_{C_{x,d}} \prod_{i \in \{i_1, \ldots, i_x\}} \theta(v_{0i}, R) \prod_{j \in \overline{\{i_1, \ldots, i_x\}}_d} [1 - \theta(v_{0j}, R)], & 1 \le x \le d. \end{cases}$$

Joint probability distribution of (L_1, M_1)

Recall that $L_1 \le L$ and $M_1 \le M = k - L$. Hence $L_1 = y$ is possible if and only if $L \ge y$. Likewise, $M_1 = z$ is possible if and only if $M \ge z$, equivalently $L \le k - z$. Thus, for $y, z = 0, \ldots, k$ with $y + z \le k$, we have

$$\begin{aligned} P(L_1 = y, M_1 = z) &= \sum_{\ell=0}^{k} P(L_1 = y, M_1 = z, L = \ell) \\ &= \sum_{\ell=y}^{k-z} P(L_1 = y, M_1 = z, L = \ell). \end{aligned} \tag{A.3}$$

Now, for a term in (A.3) with $0 < \ell < k$, we have

$$\begin{aligned} &P(L_1 = y, M_1 = z, L = \ell) \\ &\quad = \sum_{C_{\ell,k}} P(L_1 = y, M_1 = z \,|\, L = \ell \text{ with nodules } i_1, \ldots, i_\ell \text{ to the PZ})\, \alpha(\{i_1, \ldots, i_\ell\}) \\ &\quad = \sum_{C_{\ell,k}} p(y \,|\, v_{i_1}, \ldots, v_{i_\ell}, n_1/V_1)\, p(z \,|\, v_{j_1}, \ldots, v_{j_{k-\ell}}, n_2/V_2)\, \alpha(\{i_1, \ldots, i_\ell\}), \end{aligned} \tag{A.4}$$

where $\{j_1, \ldots, j_{k-\ell}\} = \overline{\{i_1, \ldots, i_\ell\}}_k$. In the above, we have used the fact that the variables L_1 and M_1 are conditionally independent, given the information of which

tumor nodules are sent to the PZ and which to the TZ. For the case of a term in (A.3) with $\ell = 0$ (whence $y = 0$), we have

$$P(L_1 = 0, M_1 = z, L = 0) = p(z \,|\, v_1, \ldots, v_k, n_2/V_2)\, \alpha(\emptyset). \tag{A.5}$$

Similarly, for the case of a term in (A.3) with $\ell = k$ (whence $z = 0$), we have

$$P(L_1 = y, M_1 = 0, L = k) = p(y \,|\, v_1, \ldots, v_k, n_1/V_1)\, \alpha(\{1, \ldots, k\}). \tag{A.6}$$

We next give expressions for the quantities $\alpha(\cdot)$, $p(y \,|\, v_{i_1}, \ldots, v_{i_\ell}, n_1/V_1)$, and $p(z \,|\, v_{j_1}, \ldots, v_{j_{k-\ell}}, n_2/V_2)$ appearing in (A.4), (A.5), and (A.6). For $0 < \ell < k$,

$$\alpha(\{i_1, \ldots, i_\ell\}) = \prod_{i \in \{i_1, \ldots, i_\ell\}} p_i \prod_{j \in \overline{\{i_1, \ldots, i_\ell\}}_k} (1 - p_j). \tag{A.7}$$

Also,

$$\alpha(\emptyset) = \prod_{j=1}^{k} (1 - p_j), \quad \alpha(\{1, \ldots, k\}) = \prod_{i=1}^{k} p_i. \tag{A.8}$$

For $p(y \,|\, v_{i_1}, \ldots, v_{i_\ell}, n_1/V_1)$, we use (A.2) with $x = y$, $d = \ell$, $\{v_{01}, \ldots, v_{0d}\} = \{v_{i_1}, \ldots, v_{i_\ell}\}$, and $R = n_1/V_1$, obtaining

$$p(y \,|\, v_{i_1}, \ldots, v_{i_\ell}, n_1/V_1) = \tag{A.9}$$

$$= \begin{cases} \displaystyle\prod_{b=1}^{\ell} [1 - \theta(v_{i_b}, n_1/V_1)], & y = 0, \\ \displaystyle\sum_{C_{y,\ell}} \prod_{a \in \{a_1, \ldots, a_y\}} \theta(v_{i_a}, n_1/V_1) \prod_{b \in \overline{\{a_1, \ldots, a_y\}}_\ell} [1 - \theta(v_{i_b}, n_1/V_1)], & 1 \le y \le \ell. \end{cases}$$

Similarly, for $p(z \,|\, v_{j_1}, \ldots, v_{j_{k-\ell}}, n_2/V_2)$, we use (A.2) with $x = z$, $d = k - \ell$, $\{v_{01}, \ldots, v_{0d}\} = \{v_{j_1}, \ldots, v_{j_{k-\ell}}\}$, and $R = n_2/V_2$, obtaining

$$p(z \,|\, v_{j_1}, \ldots, v_{j_{k-\ell}}, n_2/V_2) = \tag{A.10}$$

$$\begin{cases} \displaystyle\prod_{\beta=1}^{k-\ell} [1 - \theta(v_{j_\beta}, n_2/V_2)], & z = 0, \\ \displaystyle\sum_{C_{z,k-\ell}} \prod_{\alpha \in \{\alpha_1, \ldots, \alpha_z\}} \theta(v_{j_\alpha}, n_2/V_2) \prod_{\beta \in \overline{\{\alpha_1, \ldots, \alpha_z\}}_{k-\ell}} [1 - \theta(v_{j_\beta}, n_2/V_2)], & 1 \le z \le k - \ell. \end{cases}$$

Using (A.7), (A.8), (A.9), and (A.10) in (A.4), (A.5), and (A.6), and then in turn using (A.4), (A.5), and (A.6) in (A.3), we obtain the joint probabilities $P(L_1 = y, M_1 = z)$, for $y, z = 0, \ldots, k$ with $y + z \le k$.

Joint probability distribution of (L_0, M_0)

Because $L_0 \le L_1 \le L \le k$, $M_0 \le M_1 \le M \le k$, and $M = k - L$, we have $0 \le L_0 + M_0 \le k$. Also, $L_0 \le n_1$ and $M_0 \le n_2$ must hold. For $s = 0, \ldots, \min\{k, n_1\}$ and $t = 0, \ldots, \min\{k, n_2\}$ with $s + t \le k$, and letting

$$\sum_{\{(y,z)\ge(s,t)\}_k} \text{denote} \sum_{\{(y,z):\ 0\le s\le y\le k,\ 0\le t\le z\le k,\ y+z\le k\}},$$

we thus have

$$\begin{aligned} &P(L_0 = s, M_0 = t) \qquad (A.11)\\ &= \sum_{\{(y,z)\ge(s,t)\}_k} P(L_1 = y, M_1 = z)\, P(L_0 = s, M_0 = t \,|\, L_1 = y, M_1 = z)\\ &= \sum_{\{(y,z)\ge(s,t)\}_k} P(L_1 = y, M_1 = z)\, P(L_0 = s \,|\, L_1 = y)\, P(M_0 = t \,|\, M_1 = z). \end{aligned}$$

In the last step we use that, conditional on L_1, the variable L_0 is independent of M_0 and M_1, and, conditional on M_1, the variable M_0 is independent of L_0 and L_1.

For a term in (A.11), the factor $P(L_1 = y, M_1 = z)$ is available from above. The other two factors we recognize to be special cases of probabilities arising in classical occupancy problems. In particular, we use (e.g., [29, Table 6A])

Lemma 2 *For distribution of n indistinguishable balls into M distinguishable urns, the probability that exactly m of N specified urns will be empty, where $N \le M$, is*

$$\frac{\binom{N}{m}\binom{M-N+n-1}{M-m-1}}{\binom{M+n-1}{n}},\ m = 0, 1, \ldots, N. \qquad (A.12)$$

This is used with $n \ge 1$, $M \ge N \ge 1$, and the convention, for $w = -1, 0, 1, \ldots$, that $\binom{w}{u} = 1$ in the cases $u = 0 \le w$ and $u = w$, and $= 0$ in the cases $u < 0$ with $w \ge 0$ and $u > w$ (in particular, $\binom{0}{0} = \binom{1}{0} = \binom{-1}{-1} = 1$ and $\binom{0}{-1} = 0$).

To evaluate $P(L_0 = s \,|\, L_1 = y)$, we first note that for the case $y = 0$ we have $P(L_0 = 0 \,|\, L_1 = 0) = 1$. For $y \ge 1$, we apply (A.12) by considering the $L_1 = y$ hits of the n_1 cores in the PZ to represent y "balls" distributed into n_1 "urns" and the number $L_0 = s$ of distinct cores hit to correspond to exactly $n_1 - s$ urns remaining empty. Thus, for $0 \le s \le \min\{y, n_1\}$, we apply (A.12) with $n = y$, $M = n_1$, $N = n_1$, and $m = n_1 - s$, obtaining

$$P(L_0 = s \,|\, L_1 = y) = \frac{\binom{n_1}{n_1-s}\binom{y-1}{s-1}}{\binom{n_1+y-1}{y}} = \frac{\binom{n_1}{s}\binom{y-1}{s-1}}{\binom{n_1+y-1}{y}},\ 0 \le s \le \min\{y, n_1\}, \qquad (A.13)$$

which includes the case $s = y = 0$. Similarly, $P(M_0 = 0 \,|\, M_1 = 0) = 1$ and we apply (A.12) for $z \ge 1$, obtaining

$$P(M_0 = t \,|\, M_1 = z) = \frac{\binom{n_2}{n_2-t}\binom{z-1}{t-1}}{\binom{n_2+z-1}{z}} = \frac{\binom{n_2}{t}\binom{z-1}{t-1}}{\binom{n_2+z-1}{z}},\ 0 \le t \le \min\{z, n_2\}. \qquad (A.14)$$

Inserting these into (A.11), we obtain as the joint probability distribution of the numbers (L_0, M_0) of *distinct cores* hit in the PZ and TZ the following transform of the joint probability distribution of (L_1, M_1):

$$P(L_0 = s, M_0 = t) = \binom{n_1}{s}\binom{n_2}{t} \sum_{\{(y,z)\geq(s,t)\}_k} \frac{\binom{y-1}{s-1}\binom{z-1}{t-1}}{\binom{n_1+y-1}{y}\binom{n_2+z-1}{z}} P(L_1 = y, M_1 = z), \tag{A.15}$$

for $s = 0, \ldots, \min\{k, n_1\}$ and $t = 0, \ldots, \min\{k, n_2\}$ with $s + t \leq k$.

Results for the case of no partition into PZ and TZ

Suppose, without distinguishing between the peripheral and transition zones, that k spherical tumor nodules are distributed independently into a prostate of volume V and that n biopsy cores are used. Again index the tumor nodules in order of decreasing volume with $v_1 \geq v_2 \geq \ldots \geq v_k$. Also, put $R = \frac{n}{V}$. We develop analogues of the preceding results. Let L_1^* = number of hits by the k nodules and L_0^* = number of distinct cores hit by the k nodules.

Probability distributions of L_1^* and L_0^*

Specializing results for L_1, M_1, and L to $L = k$, $M_1 = 0$, and $L_1 = L_1^*$, we obtain

$$\begin{aligned}
&P(L_1^* = y) \\
&\quad = \quad P(L_1 = y, M_1 = 0) \\
&\quad \overset{\text{via } (A.3)}{=} \quad P(L_1 = y, M_1 = 0, L = k) \\
&\quad \overset{\text{via } (A.6)}{=} \quad p(y \,|\, v_1, \ldots, v_k, R) \\
&\quad \overset{\text{via } (A.2)}{=} \quad \begin{cases} \displaystyle\prod_{j=1}^{k} [1 - \theta(v_j, R)], & y = 0, \\ \displaystyle\sum_{C_{y,k}} \prod_{i\in\{i_1,\ldots,i_y\}} \theta(v_i, R) \prod_{j\in\overline{\{i_1,\ldots,i_y\}}_k} [1 - \theta(v_j, R)], & 1 \leq y \leq k, \end{cases}
\end{aligned} \tag{A.16}$$

$$\overset{\text{via } (A.1)}{=} \quad \begin{cases} \displaystyle\prod_{j=1}^{k} (1 - R\,V_{\text{eff}}(v_j))^+, & y = 0, \\ \displaystyle\sum_{C_{y,k}} \prod_{i\in\{i_1,\ldots,i_y\}} [1 - (1 - R\,V_{\text{eff}}(v_i))^+] \prod_{j\in\overline{\{i_1,\ldots,i_y\}}_k} (1 - R\,V_{\text{eff}}(v_j))^+, & 1 \leq y \leq k. \end{cases} \tag{A.17}$$

Using (A.15) with $L_0 = L_0^*$ and $M_0 = 0$, we obtain

$$P(L_0^* = s) = \binom{n}{s} \sum_{y=s}^{k} \frac{\binom{y-1}{s-1}}{\binom{n+y-1}{y}} P(L_1^* = y), \tag{A.18}$$

for $s = 0, \ldots, \min\{k, n\}$. (For $P(L_1^* = y)$ in (A.18), we use (A.16) or (A.17).) This establishes Theorem 1.

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Table 1. Probability distribution of number of positive cores (*D*), by prostate volume (*V*) and number of cores (*n*), for total tumor volume **0.25** cc.

		V												
n	*D*	10	20	30	40	50	60	80	100	120	140	160	180	200
6	0	0.18	0.47	0.61	0.69	0.75	0.79	0.84	0.87	0.89	0.90	0.92	0.92	0.93
	1	0.49	0.43	0.34	0.28	0.20	0.20	0.16	0.13	0.11	0.09	0.08	0.07	0.07
	2	0.28	0.10	0.05	0.03	0.01	0.01	0.01	0.01	0	0	0	0	0
	3	0.05	0.01	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0.18	0.35	0.47	0.55	0.61	0.69	0.75	0.79	0.82	0.84	0.85	0.87
	1	0.15	0.44	0.45	0.41	0.37	0.33	0.27	0.23	0.20	0.17	0.15	0.14	0.13
	2	0.43	0.30	0.17	0.11	0.08	0.06	0.03	0.02	0.02	0.01	0.01	0.01	0.01
	3	0.32	0.07	0.03	0.01	0.01	0	0	0	0	0	0	0	0
	4	0.09	0.01	0	0	0	0	0	0	0	0	0	0	0
	5	0.01	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0.05	0.18	0.30	0.39	0.47	0.57	0.64	0.69	0.73	0.76	0.79	0.81
	1	0.02	0.29	0.43	0.45	0.43	0.40	0.35	0.30	0.27	0.24	0.22	0.20	0.18
	2	0.21	0.41	0.30	0.21	0.15	0.11	0.07	0.05	0.03	0.03	0.02	0.02	0.01
	3	0.43	0.21	0.08	0.04	0.02	0.01	0.01	0	0	0	0	0	0
	4	0.27	0.04	0.01	0	0	0	0	0	0	0	0	0	0
	5	0.06	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0.08	0.18	0.27	0.35	0.47	0.55	0.61	0.66	0.69	0.72	0.75
	1	0	0.12	0.33	0.42	0.44	0.44	0.40	0.36	0.32	0.29	0.27	0.25	0.23
	2	0.08	0.38	0.38	0.30	0.23	0.18	0.12	0.08	0.06	0.05	0.04	0.03	0.02
	3	0.33	0.36	0.17	0.09	0.05	0.03	0.01	0.01	0	0	0	0	0
	4	0.40	0.13	0.03	0.01	0.01	0	0	0	0	0	0	0	0
	5	0.17	0.02	0	0	0	0	0	0	0	0	0	0	0
	6	0.02	0	0	0	0	0	0	0	0	0	0	0	0

Table 2. Probability distribution of number of positive cores (*D*), by prostate volume (*V*) and number of cores (*n*), for total tumor volume **2.0** cc.

		V												
n	*D*	10	20	30	40	50	60	80	100	120	140	160	180	200
6	0	0	0	0.09	0.20	0.29	0.37	0.49	0.57	0.63	0.68	0.71	0.74	0.76
	1	0.07	0.27	0.46	0.51	0.50	0.48	0.42	0.37	0.33	0.29	0.26	0.24	0.22
	2	0.40	0.51	0.37	0.26	0.18	0.14	0.09	0.06	0.04	0.03	0.02	0.02	0.02
	3	0.41	0.20	0.08	0.04	0.02	0.01	0.01	0	0	0	0	0	0
	4	0.11	0.02	0	0	0	0	0	0	0	0	0	0	0
	5	0.01	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0.04	0.09	0.20	0.29	0.37	0.44	0.49	0.53	0.57
	1	0	0.02	0.09	0.19	0.32	0.40	0.46	0.47	0.45	0.43	0.40	0.38	0.36
	2	0.07	0.23	0.39	0.46	0.44	0.38	0.28	0.20	0.15	0.12	0.10	0.08	0.07
	3	0.30	0.45	0.39	0.28	0.18	0.12	0.06	0.03	0.02	0.01	0.01	0.01	0
	4	0.42	0.25	0.12	0.06	0.03	0.01	0	0	0	0	0	0	0
	5	0.19	0.05	0.01	0	0	0	0	0	0	0	0	0	0
	6	0.02	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0.05	0.13	0.20	0.26	0.32	0.37	0.42
	1	0	0	0.01	0.03	0.10	0.17	0.33	0.41	0.45	0.46	0.45	0.44	0.43
	2	0.01	0.06	0.17	0.29	0.39	0.44	0.41	0.34	0.28	0.23	0.19	0.16	0.14
	3	0.12	0.30	0.43	0.44	0.37	0.31	0.18	0.10	0.07	0.04	0.03	0.02	0.02
	4	0.36	0.42	0.31	0.21	0.12	0.08	0.03	0.01	0.01	0	0	0	0
	5	0.39	0.19	0.08	0.03	0.01	0	0	0	0	0	0	0	0
	6	0.12	0.02	0.01	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0.04	0.09	0.15	0.20	0.25	0.29
	1	0	0	0	0.01	0.01	0.06	0.16	0.28	0.37	0.41	0.44	0.45	0.45
	2	0	0.02	0.05	0.14	0.22	0.32	0.42	0.42	0.38	0.33	0.28	0.24	0.21
	3	0.05	0.14	0.29	0.40	0.44	0.41	0.32	0.21	0.14	0.10	0.07	0.05	0.04
	4	0.25	0.40	0.43	0.35	0.26	0.18	0.09	0.04	0.02	0.01	0.01	0	0
	5	0.45	0.36	0.20	0.10	0.05	0.03	0.01	0	0	0	0	0	0
	6	0.25	0.08	0.02	0.01	0	0	0	0	0	0	0	0	0

Table 3. Model-based specificity (SP) and sensitivity (SE) for selected insignificant CaP thresholds (x_0), by prostate volume (*V*) and number of biopsy cores (*n*). *Cases in bold prioritize on high SP with favorable n versus SE tradeoff.*

	n							
	6		12		18		24	
V	x_0	(SP, SE)	x_0	(SP, SE)	x_0	(SP, SE)	x_0	(SP, SE)
10	1	(67, 93)	2	(58, 93)	3	(66, 87)	4	(81, 70)
	2	**(95, 53)**	3	(91, 63)	4	(93, 51)	5	(98, 25)
20	0	(47, 100)	1	(62, 98)	2	(74, 94)	3	(85, 84)
	1	**(89, 73)**	2	(92, 75)	3	(95, 64)	4	(98, 44)
30	0	(61, 91)	1	(80, 91)	1	(61, 99)	2	(79, 95)
	1	**(95, 45)**	2	(97, 52)	2	(91, 82)	3	(96, 65)
40	0	(69, 80)	0	(47,100)	1	(75, 97)	2	(90, 86)
	1	**(97, 29)**	**1**	**(88, 81)**	**2**	**(96, 68)**	3	(99, 45)
50	0	(75, 71)	0	(55, 96)	1	(82, 90)	1	(71, 99)
	1	**(98, 21)**	**1**	**(92, 65)**	**2**	**(98, 51)**	2	(94, 76)
60	0	(79, 63)	0	(61, 91)	1	(87, 83)	1	(79, 94)
	1	(99, 15)	**1**	**(94, 51)**	**2**	**(99,39)**	2	(97, 62)
70	0	(82, 56)	0	(66, 85)	0	(52, 98)	1	(83, 89)
	1	(99, 12)	**1**	**(96, 41)**	**1**	**(90, 72)**	2	(98, 51)
80	0	(84, 51)	0	(69, 80)	0	(57, 95)	1	(87, 84)
	1	(100, 9)	**1**	**(97, 34)**	**1**	**(92, 62)**	2	(98, 42)
90	0	(85, 47)	0	(72, 75)	0	(61, 91)	0	(51, 99)
	1	(100, 7)	**1**	**(97, 28)**	**1**	**(94, 53)**	1	(89, 77)
100	0	(87, 43)	0	(75, 71)	0	(64, 87)	0	(55, 96)
	1	100, 6)	**1**	**(98, 24)**	**1**	**(95, 46)**	1	(91, 68)
110	0	(88, 40)	0	(77, 66)	0	(67, 84)	0	(58, 94)
	1	(100, 5)	1	(98, 20)	**1**	**(96, 40)**	**1**	**(92, 61)**
120	0	(89, 37)	0	(79, 63)	0	(69, 80)	0	(61, 91)
	1	(100, 4)	1	(98, 18)	**1**	**(96, 35)**	**1**	**(94, 54)**
130	0	(90, 34)	0	(80, 59)	0	(72, 77)	0	(64, 88)
	1	(100, 4)	1	(99, 15)	**1**	**(97, 31)**	**1**	**(94, 49)**
140	0	(90, 32)	0	(82, 56)	0	(73, 74)	0	(66, 85)
	1	(100, 3)	1	(99, 13)	**1**	**(97, 28)**	**1**	**(95, 44)**
150	0	(91, 30)	0	(83, 54)	0	(75, 71)	0	(68, 83)
	1	(100, 3)	1	(99, 12)	**1**	**(98, 25)**	**1**	**(96, 40)**
160	0	(92, 29)	0	(84, 51)	0	(76, 68)	0	(69, 80)
	1	(100, 3)	1	(100, 11)	**1**	**(98, 22)**	**1**	**(96, 36)**
170	0	(92, 27)	0	(85, 49)	0	(78, 65)	0	(71, 78)
	1	(100, 2)	1	(100, 10)	**1**	**(98, 20)**	**1**	**(97, 33)**
180	0	(92, 26)	0	(85, 47)	0	(79, 63)	0	(72, 75)
	1	(100, 2)	1	(100, 9)	**1**	**(98, 18)**	**1**	**(97, 30)**
190	0	(93, 25)	0	(86, 45)	0	(80, 60)	0	(74, 73)
	1	(100, 2)	1	(100, 8)	**1**	**(98, 17)**	**1**	**(97, 28)**
200	0	(93, 24)	0	(87, 43)	0	(81, 58)	0	(75, 71)
	1	(100, 2)	1	(100, 7)	**1**	**(99, 15)**	**1**	**(98, 26)**

Table 4A. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 0-2 ng/dl, by number of cores (*n*), for prostate volumes (*V*) = 10 cc, …, 90 cc. Compare PPI with SEER prior probability 0.36 for T = 0.5 cc, and PM with SEER prior median 1.37, not adjusted for *n* and *V*. *Cases in bold prioritize on SP with favorable n versus SE tradeoffs.*

	n			
V	6	12	18	24
10	x_0 = 1: (SP, SE) = (67, 93) **x_0 = 2: (SP, SE) = (95, 53)** *D* = 1: PPI .81, PM 0.30 *D* = 2: PPI .34, PM 1.25 *D* = 3: PPI .07, PM 3.09	x_0 = 2: (SP, SE) = (58, 93) x_0 = 3: (SP, SE) = (91, 63) *D* = 2: PPI .76, PM 0.32 *D* = 3: PPI .38, PM 1.07 *D* = 4: PPI .11, PM 2.55	x_0 = 3: (SP, SE) = (66, 87) x_0 = 4: (SP, SE) = (93, 51) *D* = 3: PPI .65, PM 0.37 *D* = 4: PPI .30, PM 1.43 *D* = 5: PPI .08, PM 2.97	x_0 = 4: (SP, SE) = (81, 70) x_0 = 5: (SP, SE) = (98, 25) *D* = 4: PPI .46, PM 0.70 *D* = 5: PPI .17, PM 1.96 *D* = 6: PPI .04, PM 3.36
20	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (89, 73)** *D* = 1: PPI .63, PM 0.39 *D* = 2: PPI .18, PM 1.99	x_0 = 1: (SP, SE) = (62, 98) x_0 = 2: (SP, SE) = (92, 75) *D* = 1: PPI .90, PM 0.27 *D* = 2: PPI .49, PM 0.55 *D* = 3: PPI .11, PM 2.09	x_0 = 2: (SP, SE) = (74, 94) x_0 = 3: (SP, SE) = (95, 64) *D* = 2: PPI .77, PM 0.32 *D* = 3: PPI .31, PM 1.22 *D* = 4: PPI .06, PM 2.82	x_0 = 3: (SP, SE) = (85, 84) x_0 = 4: (SP, SE) = (98, 44) *D* = 3: PPI .57, PM 0.43 *D* = 4: PPI .17, PM 1.76 *D* = 5: PPI .03, PM 3.74
30	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (95, 45)** *D* = 1: PPI .53, PM 0.46 *D* = 2: PPI .14, PM 2.98	x_0 = 1: (SP, SE) = (80, 91) x_0 = 2: (SP, SE) = (97, 52) *D* = 1: PPI .78, PM 0.31 *D* = 2: PPI .31, PM 1.29 *D* = 3: PPI .05, PM 3.43	x_0 = 1: (SP, SE) = (61, 99) x_0 = 2: (SP, SE) = (91, 82) *D* = 1: PPI .92, PM 0.27 *D* = 2: PPI .56, PM 0.44 *D* = 3: PPI .14, PM 1.82	x_0 = 2: (SP, SE) = (79, 95) x_0 = 3: (SP, SE) = (96, 65) *D* = 2: PPI .76, PM 0.32 *D* = 3: PPI .29, PM 1.25 *D* = 4: PPI .05, PM 2.94
40	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 29)** *D* = 1: PPI .47, PM 0.66 *D* = 2: PPI .13, PM 3.33	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (88, 81)** *D* = 1: PPI .69, PM 0.35 *D* = 2: PPI .23, PM 1.67	x_0 = 1: (SP, SE) = (75, 97) **x_0 = 2: (SP, SE) = (96, 68)** *D* = 1: PPI .84, PM 0.29 *D* = 2: PPI .41, PM 0.87 *D* = 3: PPI .08, PM 2.74	x_0 = 2: (SP, SE) = (90, 86) x_0 = 3: (SP, SE) = (99, 45) *D* = 2: PPI .60, PM 0.41 *D* = 3: PPI .16, PM 1.70 *D* = 4: PPI .02, PM 3.75
50	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 21)** *D* = 1: PPI .44, PM 0.86 *D* = 2: PPI .12, PM 3.43	x_0 = 0: (SP, SE) = (55, 96) **x_0 = 1: (SP, SE) = (92, 65)** *D* = 1: PPI .62, PM 0.40 *D* = 2: PPI .19, PM 1.99	x_0 = 1: (SP, SE) = (82, 90) **x_0 = 2: (SP, SE) = (98, 51)** *D* = 1: PPI .78, PM 0.31 *D* = 2: PPI .31, PM 1.28 *D* = 3: PPI .05, PM 3.45	x_0 = 1: (SP, SE) = (71, 99) x_0 = 2: (SP, SE) = (94, 76) *D* = 1: PPI .87, PM 0.28 *D* = 2: PPI .48, PM 0.59 *D* = 3: PPI .10, PM 2.16
60	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .42, PM 0.99 *D* = 2: PPI .12, PM 3.48	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 51)** *D* = 1: PPI .57, PM 0.43 *D* = 2: PPI .16, PM 2.55	x_0 = 1: (SP, SE) = (87, 83) **x_0 = 2: (SP, SE) = (99, 39)** *D* = 1: PPI .71, PM 0.34 *D* = 2: PPI .25, PM 1.54 *D* = 3: PPI .04, PM 4.0+	x_0 = 1: (SP, SE) = (79, 94) x_0 = 2: (SP, SE) = (97, 62) *D* = 1: PPI .82, PM 0.30 *D* = 2: PPI .38, PM 1.02 *D* = 3: PPI .07, PM 2.98
70	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .41, PM 1.06 *D* = 2: PPI .12, PM 3.51	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (96, 41)** *D* = 1: PPI .53, PM 0.46 *D* = 2: PPI .15, PM 2.88	x_0 = 0: (SP, SE) = (52, 98) **x_0 = 1: (SP, SE) = (90, 72)** *D* = 1: PPI .66, PM 0.37 *D* = 2: PPI .21, PM 1.78	x_0 = 1: (SP, SE) = (83, 89) x_0 = 2: (SP, SE) = (98, 51) *D* = 1: PPI .77, PM 0.32 *D* = 2: PPI .31, PM 1.27 *D* = 3: PPI .05, PM 3.48
80	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .40, PM 1.11 *D* = 2: PPI .12, PM 3.53	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 34)** *D* = 1: PPI .50, PM 0.52 *D* = 2: PPI .14, PM 3.06	x_0 = 0: (SP, SE) = (57, 95) **x_0 = 1: (SP, SE) = (92, 62)** *D* = 1: PPI .62, PM 0.40 *D* = 2: PPI .19, PM 1.97	x_0 = 1: (SP, SE) = (87, 84) x_0 = 2: (SP, SE) = (98, 42) *D* = 1: PPI .72, PM 0.34 *D* = 2: PPI .27, PM 1.47 *D* = 3: PPI .04, PM 3.91
90	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .39, PM 1.14 *D* = 2: PPI .12, PM 3.55	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .47, PM 0.65 *D* = 2: PPI .13, PM 3.17	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 53)** *D* = 1: PPI .58, PM 0.42 *D* = 2: PPI .17, PM 2.34	x_0 = 0: (SP, SE) = (51, 99) x_0 = 1: (SP, SE) = (89, 77) *D* = 1: PPI .68, PM 0.36 *D* = 2: PPI .23, PM 1.66

Table 4B. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 0-2 ng/dl, by number of cores (*n*), for prostate volumes (*V*) = 100 cc, …, 200 cc. Compare PPI with SEER prior probability 0.36 for T = 0.5 cc, and PM with SEER prior median 1.37, not adjusted for *n* and *V*. *Cases in bold prioritize on SP with favorable n versus SE tradeoffs.*

V	*n*			
	6	12	18	24
100	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 6) *D* = 1: PPI .39, PM 1.17 *D* = 2: PPI .12, PM 3.55	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 24)** *D* = 1: PPI .46, PM 0.75 *D* = 2: PPI .13, PM 3.25	x_0 = 0: (SP, SE) = (64, 87) **x_0 = 1: (SP, SE) = (95, 46)** *D* = 1: PPI .55, PM 0.44 *D* = 2: PPI .16, PM 2.62	x_0 = 0: (SP, SE) = (55, 96) x_0 = 1: (SP, SE) = (91, 68) *D* = 1: PPI .64, PM 0.38 *D* = 2: PPI .21, PM 1.82
110	x_0 = 0: (SP, SE) = (88, 40) x_0 = 1: (SP, SE) = (100, 5) *D* = 1: PPI .39, PM 1.19 *D* = 2: PPI .12, PM 3.56	x_0 = 0: (SP, SE) = (77, 66) x_0 = 1: (SP, SE) = (98, 20) *D* = 1: PPI .44, PM 0.83 *D* = 2: PPI .13, PM 3.31	x_0 = 0: (SP, SE) = (67, 84) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .53, PM 0.47 *D* = 2: PPI .15, PM 2.82	x_0 = 0: (SP, SE) = (58, 94) **x_0 = 1: (SP, SE) = (92, 61)** *D* = 1: PPI .61, PM 0.40 *D* = 2: PPI .19, PM 1.96
120	x_0 = 0: (SP, SE) = (89, 37) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .38, PM 1.21 *D* = 2: PPI .12, PM 3.57	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (98, 18) *D* = 1: PPI .43, PM 0.90 *D* = 2: PPI .13, PM 3.35	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 35)** *D* = 1: PPI .50, PM 0.49 *D* = 2: PPI .14, PM 2.95	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 54)** *D* = 1: PPI .59, PM 0.42 *D* = 2: PPI .18, PM 2.23
130	x_0 = 0: (SP, SE) = (90, 34) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .38, PM 1.22 *D* = 2: PPI .11, PM 3.57	x_0 = 0: (SP, SE) = (80, 59) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .43, PM 0.95 *D* = 2: PPI .12, PM 3.38	x_0 = 0: (SP, SE) = (72, 77) **x_0 = 1: (SP, SE) = (97, 31)** *D* = 1: PPI .49, PM 0.57 *D* = 2: PPI .14, PM 3.04	x_0 = 0: (SP, SE) = (64, 88) **x_0 = 1: (SP, SE) = (94, 49)** *D* = 1: PPI .56, PM 0.43 *D* = 2: PPI .17, PM 2.46
140	x_0 = 0: (SP, SE) = (90, 32) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .38, PM 1.23 *D* = 2: PPI .11, PM 3.57	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 13) *D* = 1: PPI .42, PM 1 *D* = 2: PPI .12, PM 3.40	x_0 = 0: (SP, SE) = (73, 74) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .47, PM 0.65 *D* = 2: PPI .14, PM 3.12	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (95, 44)** *D* = 1: PPI .55, PM 0.45 *D* = 2: PPI .16, PM 2.65
150	x_0 = 0: (SP, SE) = (91, 30) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .38, PM 1.24 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (83, 54) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .41, PM 1.03 *D* = 2: PPI .12, PM 3.42	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 25)** *D* = 1: PPI .46, PM 0.72 *D* = 2: PPI .13, PM 3.17	x_0 = 0: (SP, SE) = (68, 83) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .53, PM 0.47 *D* = 2: PPI .15, PM 2.78
160	x_0 = 0: (SP, SE) = (92, 29) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .38, PM 1.25 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 11) *D* = 1: PPI .41, PM 1.06 *D* = 2: PPI .12, PM 3.44	x_0 = 0: (SP, SE) = (76, 68) **x_0 = 1: (SP, SE) = (98, 22)** *D* = 1: PPI .45, PM 0.77 *D* = 2: PPI .13, PM 3.22	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 36)** *D* = 1: PPI .51, PM 0.48 *D* = 2: PPI .15, PM 2.88
170	x_0 = 0: (SP, SE) = (92, 27) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .37, PM 1.26 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (85, 49) x_0 = 1: (SP, SE) = (100, 10) *D* = 1: PPI .41, PM 1.08 *D* = 2: PPI .12, PM 3.45	x_0 = 0: (SP, SE) = (78, 65) **x_0 = 1: (SP, SE) = (98, 20)** *D* = 1: PPI .45, PM 0.82 *D* = 2: PPI .13, PM 3.26	x_0 = 0: (SP, SE) = (71, 78) **x_0 = 1: (SP, SE) = (97, 33)** *D* = 1: PPI .50, PM 0.52 *D* = 2: PPI .14, PM 2.97
180	x_0 = 0: (SP, SE) = (92, 26) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .37, PM 1.27 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .40, PM 1.10 *D* = 2: PPI .12, PM 3.47	x_0 = 0: (SP, SE) = (79, 63) **x_0 = 1: (SP, SE) = (98, 18)** *D* = 1: PPI .44, PM 0.87 *D* = 2: PPI .13, PM 3.29	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 30)** *D* = 1: PPI .48, PM 0.59 *D* = 2: PPI .14, PM 3.03
190	x_0 = 0: (SP, SE) = (93, 25) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .37, PM 1.27 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (86, 45) x_0 = 1: (SP, SE) = (100, 8) *D* = 1: PPI .40, PM 1.12 *D* = 2: PPI .12, PM 3.48	x_0 = 0: (SP, SE) = (80, 60) **x_0 = 1: (SP, SE) = (98, 17)** *D* = 1: PPI .43, PM 0.90 *D* = 2: PPI .13, PM 3.32	x_0 = 0: (SP, SE) = (74, 73) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .47, PM 0.65 *D* = 2: PPI .14, PM 3.09
200	x_0 = 0: (SP, SE) = (93, 24) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .37, PM 1.28 *D* = 2: PPI .11, PM 3.58	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .40, PM 1.13 *D* = 2: PPI .12, PM 3.49	x_0 = 0: (SP, SE) = (81, 58) **x_0 = 1: (SP, SE) = (99, 15)** *D* = 1: PPI .43, PM 0.94 *D* = 2: PPI .13, PM 3.34	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 26)** *D* = 1: PPI .47, PM 0.70 *D* = 2: PPI .14, PM 3.13

Table 5A. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 2-4 ng/dl, by number of cores (*n*), for prostate volumes (*V*) = 10 cc, …, 90 cc. Compare PPI with SEER prior probability 0.24 for T = 0.5 cc, and PM with SEER prior median 1.86, not adjusted for *n* and *V*. C*ases in bold prioritize on SP with favorable n versus SE tradeoffs.*

	n			
V	6	12	18	24
10	x_0 = 1: (SP, SE) = (67, 93) **x_0 = 2: (SP, SE) = (95, 53)** *D* = 1: PPI .72, PM 0.34 *D* = 2: PPI .23, PM 1.62 *D* = 3: PPI .04, PM 3.38	x_0 = 2: (SP, SE) = (58, 93) x_0 = 3: (SP, SE) = (91, 63) *D* = 2: PPI .66, PM 0.37 *D* = 3: PPI .27, PM 1.48 *D* = 4: PPI .06, PM 3	x_0 = 3: (SP, SE) = (66, 87) x_0 = 4: (SP, SE) = (93, 51) *D* = 3: PPI .53, PM 0.46 *D* = 4: PPI .20, PM 1.79 *D* = 5: PPI .05, PM 3.31	x_0 = 4: (SP, SE) = (81, 70) x_0 = 5: (SP, SE) = (98, 25) *D* = 4: PPI .34, PM 1.32 *D* = 5: PPI .11, PM 2.63 *D* = 6: PPI .03, PM 3.56
20	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (89, 73)** *D* = 1: PPI .51, PM 0.48 *D* = 2: PPI .11, PM 2.68	x_0 = 1: (SP, SE) = (62, 98) x_0 = 2: (SP, SE) = (92, 75) *D* = 1: PPI .85, PM 0.29 *D* = 2: PPI .37, PM 0.97 *D* = 3: PPI .07, PM 2.63	x_0 = 2: (SP, SE) = (74, 94) x_0 = 3: (SP, SE) = (95, 64) *D* = 2: PPI .68, PM 0.36 *D* = 3: PPI .21, PM 1.51 *D* = 4: PPI .04, PM 3.14	x_0 = 3: (SP, SE) = (85, 84) x_0 = 4: (SP, SE) = (98, 44) *D* = 3: PPI .45, PM 0.69 *D* = 4: PPI .11, PM 1.98 *D* = 5: PPI .02, PM 3.85
30	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (95, 45)** *D* = 1: PPI .40, PM 0.95 *D* = 2: PPI .09, PM 3.41	x_0 = 1: (SP, SE) = (80, 91) x_0 = 2: (SP, SE) = (97, 52) *D* = 1: PPI .70, PM 0.35 *D* = 2: PPI .22, PM 1.57 *D* = 3: PPI .03, PM 3.62	x_0 = 1: (SP, SE) = (61, 99) x_0 = 2: (SP, SE) = (91, 82) *D* = 1: PPI .89, PM 0.28 *D* = 2: PPI .44, PM 0.68 *D* = 3: PPI .09, PM 2.07	x_0 = 2: (SP, SE) = (79, 95) x_0 = 3: (SP, SE) = (96, 65) *D* = 2: PPI .67, PM 0.37 *D* = 3: PPI .20, PM 1.49 *D* = 4: PPI .03, PM 3.21
40	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 29)** *D* = 1: PPI .35, PM 1.25 *D* = 2: PPI .08, PM 3.69	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (88, 81)** *D* = 1: PPI .59, PM 0.42 *D* = 2: PPI .15, PM 1.95	x_0 = 1: (SP, SE) = (75, 97) **x_0 = 2: (SP, SE) = (96, 68)** *D* = 1: PPI .77, PM 0.32 *D* = 2: PPI .30, PM 1.22 *D* = 3: PPI .05, PM 3.08	x_0 = 2: (SP, SE) = (90, 86) x_0 = 3: (SP, SE) = (99, 45) *D* = 2: PPI .49, PM 0.53 *D* = 3: PPI .10, PM 1.89 *D* = 4: PPI .01, PM 3.84
50	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 21)** *D* = 1: PPI .32, PM 1.41 *D* = 2: PPI .07, PM 3.77	x_0 = 0: (SP, SE) = (55, 96) **x_0 = 1: (SP, SE) = (92, 65)** *D* = 1: PPI .50, PM 0.49 *D* = 2: PPI .12, PM 2.66	x_0 = 1: (SP, SE) = (82, 90) **x_0 = 2: (SP, SE) = (98, 51)** *D* = 1: PPI .69, PM 0.35 *D* = 2: PPI .22, PM 1.55 *D* = 3: PPI .03, PM 3.63	x_0 = 1: (SP, SE) = (71, 99) x_0 = 2: (SP, SE) = (94, 76) *D* = 1: PPI .82, PM 0.30 *D* = 2: PPI .36, PM 0.97 *D* = 3: PPI .06, PM 2.63
60	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .30, PM 1.51 *D* = 2: PPI .07, PM 3.81	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 51)** *D* = 1: PPI .44, PM 0.75 *D* = 2: PPI .10, PM 3.08	x_0 = 1: (SP, SE) = (87, 83) **x_0 = 2: (SP, SE) = (99, 39)** *D* = 1: PPI .61, PM 0.40 *D* = 2: PPI .17, PM 1.81 *D* = 3: PPI .02, PM 4.0+	x_0 = 1: (SP, SE) = (79, 94) x_0 = 2: (SP, SE) = (97, 62) *D* = 1: PPI .74, PM 0.33 *D* = 2: PPI .27, PM 1.31 *D* = 3: PPI .04, PM 3.26
70	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .29, PM 1.57 *D* = 2: PPI .07, PM 3.84	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (96, 41)** *D* = 1: PPI .40, PM 0.95 *D* = 2: PPI .09, PM 3.35	x_0 = 0: (SP, SE) = (52, 98) **x_0 = 1: (SP, SE) = (90, 72)** *D* = 1: PPI .55, PM 0.45 *D* = 2: PPI .14, PM 2.18	x_0 = 1: (SP, SE) = (83, 89) x_0 = 2: (SP, SE) = (98, 51) *D* = 1: PPI .69, PM 0.36 *D* = 2: PPI .22, PM 1.54 *D* = 3: PPI .03, PM 3.65
80	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .28, PM 1.61 *D* = 2: PPI .07, PM 3.85	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 34)** *D* = 1: PPI .37, PM 1.13 *D* = 2: PPI .09, PM 3.49	x_0 = 0: (SP, SE) = (57, 95) **x_0 = 1: (SP, SE) = (92, 62)** *D* = 1: PPI .50, PM 0.51 *D* = 2: PPI .12, PM 2.63	x_0 = 1: (SP, SE) = (87, 84) x_0 = 2: (SP, SE) = (98, 42) *D* = 1: PPI .62, PM 0.39 *D* = 2: PPI .18, PM 1.74 *D* = 3: PPI .03, PM 4.0+
90	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .28, PM 1.65 *D* = 2: PPI .07, PM 3.86	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .35, PM 1.24 *D* = 2: PPI .08, PM 3.58	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 53)** *D* = 1: PPI .46, PM 0.68 *D* = 2: PPI .11, PM 2.93	x_0 = 0: (SP, SE) = (51, 99) x_0 = 1: (SP, SE) = (89, 77) *D* = 1: PPI .57, PM 0.43 *D* = 2: PPI .15, PM 1.94

Table 5B. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 2-4 ng/dl, by number of cores (n), for prostate volumes (*V*) = 100 cc, …, 200 cc. Compare PPI with SEER prior probability 0.24 for T = 0.5 cc, and PM with SEER prior median 1.86, not adjusted for *n* and *V*. C*ases in bold prioritize on SP with favorable n versus SE tradeoffs.*

	n			
V	6	12	18	24
100	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 6) *D* = 1: PPI .27, PM 1.67 *D* = 2: PPI .07, PM 3.87	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 24)** *D* = 1: PPI .33, PM 1.32 *D* = 2: PPI .08, PM 3.64	x_0 = 0: (SP, SE) = (64, 87) **x_0 = 1: (SP, SE) = (95, 46)** *D* = 1: PPI .43, PM 0.82 *D* = 2: PPI .10, PM 3.15	x_0 = 0: (SP, SE) = (55, 96) x_0 = 1: (SP, SE) = (91, 68) *D* = 1: PPI .53, PM 0.46 *D* = 2: PPI .13, PM 2.30
110	x_0 = 0: (SP, SE) = (88, 40) x_0 = 1: (SP, SE) = (100, 5) *D* = 1: PPI .27, PM 1.69 *D* = 2: PPI .07, PM 3.87	x_0 = 0: (SP, SE) = (77, 66) x_0 = 1: (SP, SE) = (98, 20) *D* = 1: PPI .32, PM 1.39 *D* = 2: PPI .08, PM 3.68	x_0 = 0: (SP, SE) = (67, 84) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .40, PM 0.96 *D* = 2: PPI .09, PM 3.30	x_0 = 0: (SP, SE) = (58, 94) **x_0 = 1: (SP, SE) = (92, 61)** *D* = 1: PPI .50, PM 0.52 *D* = 2: PPI .12, PM 2.61
120	x_0 = 0: (SP, SE) = (89, 37) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .27, PM 1.71 *D* = 2: PPI .07, PM 3.88	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (98, 18) *D* = 1: PPI .31, PM 1.44 *D* = 2: PPI .08, PM 3.71	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 35)** *D* = 1: PPI .38, PM 1.08 *D* = 2: PPI .09, PM 3.40	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 54)** *D* = 1: PPI .47, PM 0.64 *D* = 2: PPI .11, PM 2.84
130	x_0 = 0: (SP, SE) = (90, 34) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .27, PM 1.72 *D* = 2: PPI .07, PM 3.88	x_0 = 0: (SP, SE) = (80, 59) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .31, PM 1.48 *D* = 2: PPI .08, PM 3.73	x_0 = 0: (SP, SE) = (72, 77) **x_0 = 1: (SP, SE) = (97, 31)** *D* = 1: PPI .36, PM 1.17 *D* = 2: PPI .09, PM 3.48	x_0 = 0: (SP, SE) = (64, 88) **x_0 = 1: (SP, SE) = (94, 49)** *D* = 1: PPI .44, PM 0.76 *D* = 2: PPI .10, PM 3.02
140	x_0 = 0: (SP, SE) = (90, 32) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .26, PM 1.73 *D* = 2: PPI .07, PM 3.88	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 13) *D* = 1: PPI .30, PM 1.52 *D* = 2: PPI .07, PM 3.75	x_0 = 0: (SP, SE) = (73, 74) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .35, PM 1.24 *D* = 2: PPI .08, PM 3.53	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (95, 44)** *D* = 1: PPI .42, PM 0.86 *D* = 2: PPI .10, PM 3.17
150	x_0 = 0: (SP, SE) = (91, 30) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .26, PM 1.74 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (83, 54) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .30, PM 1.54 *D* = 2: PPI .07, PM 3.77	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 25)** *D* = 1: PPI .34, PM 1.29 *D* = 2: PPI .08, PM 3.58	x_0 = 0: (SP, SE) = (68, 83) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .40, PM 0.97 *D* = 2: PPI .09, PM 3.27
160	x_0 = 0: (SP, SE) = (92, 29) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .26, PM 1.75 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 11) *D* = 1: PPI .29, PM 1.57 *D* = 2: PPI .07, PM 3.78	x_0 = 0: (SP, SE) = (76, 68) **x_0 = 1: (SP, SE) = (98, 22)** *D* = 1: PPI .33, PM 1.34 *D* = 2: PPI .08, PM 3.61	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 36)** *D* = 1: PPI .38, PM 1.06 *D* = 2: PPI .09, PM 3.35
170	x_0 = 0: (SP, SE) = (92, 27) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .26, PM 1.75 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (85, 49) x_0 = 1: (SP, SE) = (100, 10) *D* = 1: PPI .29, PM 1.59 *D* = 2: PPI .07, PM 3.79	x_0 = 0: (SP, SE) = (78, 65) **x_0 = 1: (SP, SE) = (98, 20)** *D* = 1: PPI .32, PM 1.38 *D* = 2: PPI .08, PM 3.64	x_0 = 0: (SP, SE) = (71, 78) **x_0 = 1: (SP, SE) = (97, 33)** *D* = 1: PPI .37, PM 1.13 *D* = 2: PPI .09, PM 3.42
180	x_0 = 0: (SP, SE) = (92, 26) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .26, PM 1.76 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .28, PM 1.61 *D* = 2: PPI .07, PM 3.80	x_0 = 0: (SP, SE) = (79, 63) **x_0 = 1: (SP, SE) = (98, 18)** *D* = 1: PPI .32, PM 1.42 *D* = 2: PPI .08, PM 3.67	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 30)** *D* = 1: PPI .36, PM 1.19 *D* = 2: PPI .09, PM 3.47
190	x_0 = 0: (SP, SE) = (93, 25) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .26, PM 1.77 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (86, 45) x_0 = 1: (SP, SE) = (100, 8) *D* = 1: PPI .28, PM 1.62 *D* = 2: PPI .07, PM 3.81	x_0 = 0: (SP, SE) = (80, 60) **x_0 = 1: (SP, SE) = (98, 17)** *D* = 1: PPI .31, PM 1.45 *D* = 2: PPI .08, PM 3.69	x_0 = 0: (SP, SE) = (74, 73) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .35, PM 1.23 *D* = 2: PPI .08, PM 3.51
200	x_0 = 0: (SP, SE) = (93, 24) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .26, PM 1.77 *D* = 2: PPI .07, PM 3.89	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .28, PM 1.64 *D* = 2: PPI .07, PM 3.82	x_0 = 0: (SP, SE) = (81, 58) **x_0 = 1: (SP, SE) = (99, 15)** *D* = 1: PPI .31, PM 1.47 *D* = 2: PPI .08, PM 3.70	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 26)** *D* = 1: PPI .34, PM 1.28 *D* = 2: PPI .08, PM 3.55

Table 6A. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 4-10 ng/dl, by number of cores (*n*), for prostate volumes (*V*) = 10 cc, …, 90 cc. Compare PPI with SEER prior probability 0.19 for T = 0.5 cc, and PM with SEER prior median 2.99, not adjusted for *n* and *V*. C*ases in bold prioritize on SP with favorable n versus SE tradeoffs.*

	n			
V	6	12	18	24
10	x_0 = 1: (SP, SE) = (67, 93) **x_0 = 2: (SP, SE) = (95, 53)** *D* = 1: PPI .68, PM 0.36 *D* = 2: PPI .18, PM 2.11 *D* = 3: PPI .03, PM 4.0+	x_0 = 2: (SP, SE) = (58, 93) x_0 = 3: (SP, SE) = (91, 63) *D* = 2: PPI .61, PM 0.40 *D* = 3: PPI .22, PM 1.89 *D* = 4: PPI .05, PM 4.0+	x_0 = 3: (SP, SE) = (66, 87) x_0 = 4: (SP, SE) = (93, 51) *D* = 3: PPI .47, PM 0.67 *D* = 4: PPI .16, PM 2.69 *D* = 5: PPI .04, PM 4.0+	x_0 = 4: (SP, SE) = (81, 70) x_0 = 5: (SP, SE) = (98, 25) *D* = 4: PPI .28, PM 1.85 *D* = 5: PPI .08, PM 3.74 *D* = 6: PPI .02, PM 4.0+
20	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (89, 73)** *D* = 1: PPI .47, PM 0.65 *D* = 2: PPI .08, PM 3.70	x_0 = 1: (SP, SE) = (62, 98) x_0 = 2: (SP, SE) = (92, 75) *D* = 1: PPI .84, PM 0.29 *D* = 2: PPI .32, PM 1.26 *D* = 3: PPI .05, PM 3.62	x_0 = 2: (SP, SE) = (74, 94) x_0 = 3: (SP, SE) = (95, 64) *D* = 2: PPI .65, PM 0.38 *D* = 3: PPI .18, PM 1.83 *D* = 4: PPI .03, PM 4.0+	x_0 = 3: (SP, SE) = (85, 84) x_0 = 4: (SP, SE) = (98, 44) *D* = 3: PPI .40, PM 0.93 *D* = 4: PPI .08, PM 3.04 *D* = 5: PPI .01, PM 4.0+
30	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (95, 45)** *D* = 1: PPI .35, PM 1.29 *D* = 2: PPI .06, PM 4.0+	x_0 = 1: (SP, SE) = (80, 91) x_0 = 2: (SP, SE) = (97, 52) *D* = 1: PPI .68, PM 0.36 *D* = 2: PPI .17, PM 1.88 *D* = 3: PPI .02, PM 4.0+	x_0 = 1: (SP, SE) = (61, 99) x_0 = 2: (SP, SE) = (91, 82) *D* = 1: PPI .88, PM 0.28 *D* = 2: PPI .40, PM 0.86 *D* = 3: PPI .07, PM 3.09	x_0 = 2: (SP, SE) = (79, 95) x_0 = 3: (SP, SE) = (96, 65) *D* = 2: PPI .64, PM 0.38 *D* = 3: PPI .16, PM 1.75 *D* = 4: PPI .02, PM 4.0+
40	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 29)** *D* = 1: PPI .29, PM 1.64 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (47, 100) **x_0 = 1: (SP, SE) = (88, 81)** *D* = 1: PPI .56, PM 0.44 *D* = 2: PPI .12, PM 2.92	x_0 = 1: (SP, SE) = (75, 97) **x_0 = 2: (SP, SE) = (96, 68)** *D* = 1: PPI .76, PM 0.32 *D* = 2: PPI .26, PM 1.44 *D* = 3: PPI .03, PM 3.98	x_0 = 2: (SP, SE) = (90, 86) x_0 = 3: (SP, SE) = (99, 45) *D* = 2: PPI .46, PM 0.65 *D* = 3: PPI .08, PM 2.69 *D* = 4: PPI .01, PM 4.0+
50	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 21)** *D* = 1: PPI .26, PM 1.86 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (55, 96) **x_0 = 1: (SP, SE) = (92, 65)** *D* = 1: PPI .46, PM 0.70 *D* = 2: PPI .09, PM 3.66	x_0 = 1: (SP, SE) = (82, 90) **x_0 = 2: (SP, SE) = (98, 51)** *D* = 1: PPI .68, PM 0.36 *D* = 2: PPI .18, PM 1.84 *D* = 3: PPI .02, PM 4.0+	x_0 = 1: (SP, SE) = (71, 99) x_0 = 2: (SP, SE) = (94, 76) *D* = 1: PPI .81, PM 0.30 *D* = 2: PPI .32, PM 1.16 *D* = 3: PPI .04, PM 3.53
60	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .24, PM 2 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 51)** *D* = 1: PPI .39, PM 1.05 *D* = 2: PPI .07, PM 4.0+	x_0 = 1: (SP, SE) = (87, 83) **x_0 = 2: (SP, SE) = (99, 39)** *D* = 1: PPI .59, PM 0.42 *D* = 2: PPI .13, PM 2.50 *D* = 3: PPI .02, PM 4.0+	x_0 = 1: (SP, SE) = (79, 94) x_0 = 2: (SP, SE) = (97, 62) *D* = 1: PPI .73, PM 0.33 *D* = 2: PPI .23, PM 1.53 *D* = 3: PPI .03, PM 4.0+
70	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .23, PM 2.20 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (96, 41)** *D* = 1: PPI .35, PM 1.27 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (52, 98) **x_0 = 1: (SP, SE) = (90, 72)** *D* = 1: PPI .51, PM 0.48 *D* = 2: PPI .10, PM 3.19	x_0 = 1: (SP, SE) = (83, 89) x_0 = 2: (SP, SE) = (98, 51) *D* = 1: PPI .67, PM 0.37 *D* = 2: PPI .18, PM 1.82 *D* = 3: PPI .02, PM 4.0+
80	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .22, PM 2.34 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (97, 34)** *D* = 1: PPI .31, PM 1.49 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (57, 95) **x_0 = 1: (SP, SE) = (92, 62)** *D* = 1: PPI .46, PM 0.71 *D* = 2: PPI .09, PM 3.63	x_0 = 1: (SP, SE) = (87, 84) x_0 = 2: (SP, SE) = (98, 42) *D* = 1: PPI .60, PM 0.41 *D* = 2: PPI .14, PM 2.24 *D* = 3: PPI .02, PM 4.0+
90	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .22, PM 2.43 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .29, PM 1.64 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 53)** *D* = 1: PPI .41, PM 0.95 *D* = 2: PPI .08, PM 3.93	x_0 = 0: (SP, SE) = (51, 99) x_0 = 1: (SP, SE) = (89, 77) *D* = 1: PPI .54, PM 0.45 *D* = 2: PPI .12, PM 2.86

Table 6B. Model-based specificity (SP) and sensitivity (SE) for selected thresholds (x_0), and Bayesian posterior probability of insignificance (PPI) and posterior median (PM) for selected number of positive cores (*D*), using SEER priors for age 40-75 years and PSA 4-10 ng/dl, by number of cores (*n*), for prostate volumes (*V*) = 100 cc, …, 200 cc. Compare PPI with SEER prior probability 0.19 for T = 0.5 cc, and PM with SEER prior median 2.99, not adjusted for *n* and *V*. C*ases in bold prioritize on SP with favorable n versus SE tradeoffs.*

	n			
V	6	12	18	24
100	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 6) *D* = 1: PPI .22, PM 2.51 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 24)** *D* = 1: PPI .27, PM 1.75 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (64, 87) **x_0 = 1: (SP, SE) = (95, 46)** *D* = 1: PPI .38, PM 1.13 *D* = 2: PPI .07, PM 4.0+	x_0 = 0: (SP, SE) = (55, 96) x_0 = 1: (SP, SE) = (91, 68) *D* = 1: PPI .49, PM 0.53 *D* = 2: PPI .10, PM 3.30
110	x_0 = 0: (SP, SE) = (88, 40) x_0 = 1: (SP, SE) = (100, 5) *D* = 1: PPI .21, PM 2.56 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (77, 66) x_0 = 1: (SP, SE) = (98, 20) *D* = 1: PPI .26, PM 1.84 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (67, 84) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .35, PM 1.29 *D* = 2: PPI .07, PM 4.0+	x_0 = 0: (SP, SE) = (58, 94) **x_0 = 1: (SP, SE) = (92, 61)** *D* = 1: PPI .45, PM 0.72 *D* = 2: PPI .09, PM 3.60
120	x_0 = 0: (SP, SE) = (89, 37) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .21, PM 2.60 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (79, 63) x_0 = 1: (SP, SE) = (98, 18) *D* = 1: PPI .25, PM 1.90 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 35)** *D* = 1: PPI .32, PM 1.43 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (61, 91) **x_0 = 1: (SP, SE) = (94, 54)** *D* = 1: PPI .42, PM 0.90 *D* = 2: PPI .08, PM 3.84
130	x_0 = 0: (SP, SE) = (90, 34) x_0 = 1: (SP, SE) = (100, 4) *D* = 1: PPI .21, PM 2.64 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (80, 59) x_0 = 1: (SP, SE) = (99, 15) *D* = 1: PPI .25, PM 1.96 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (72, 77) **x_0 = 1: (SP, SE) = (97, 31)** *D* = 1: PPI .31, PM 1.54 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (64, 88) **x_0 = 1: (SP, SE) = (94, 49)** *D* = 1: PPI .39, PM 1.06 *D* = 2: PPI .07, PM 4.0+
140	x_0 = 0: (SP, SE) = (90, 32) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .21, PM 2.67 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (82, 56) x_0 = 1: (SP, SE) = (99, 13) *D* = 1: PPI .24, PM 2.03 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (73, 74) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .29, PM 1.63 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (66, 85) **x_0 = 1: (SP, SE) = (95, 44)** *D* = 1: PPI .37, PM 1.17 *D* = 2: PPI .07, PM 4.0+
150	x_0 = 0: (SP, SE) = (91, 30) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .20, PM 2.70 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (83, 54) x_0 = 1: (SP, SE) = (99, 12) *D* = 1: PPI .24, PM 2.12 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 25)** *D* = 1: PPI .28, PM 1.71 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (68, 83) **x_0 = 1: (SP, SE) = (96, 40)** *D* = 1: PPI .35, PM 1.30 *D* = 2: PPI .07, PM 4.0+
160	x_0 = 0: (SP, SE) = (92, 29) x_0 = 1: (SP, SE) = (100, 3) *D* = 1: PPI .20, PM 2.72 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (84, 51) x_0 = 1: (SP, SE) = (100, 11) *D* = 1: PPI .23, PM 2.20 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (76, 68) **x_0 = 1: (SP, SE) = (98, 22)** *D* = 1: PPI .27, PM 1.77 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (69, 80) **x_0 = 1: (SP, SE) = (96, 36)** *D* = 1: PPI .33, PM 1.40 *D* = 2: PPI .06, PM 4.0+
170	x_0 = 0: (SP, SE) = (92, 27) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .20, PM 2.73 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (85, 49) x_0 = 1: (SP, SE) = (100, 10) *D* = 1: PPI .23, PM 2.26 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (78, 65) **x_0 = 1: (SP, SE) = (98, 20)** *D* = 1: PPI .26, PM 1.83 *D* = 2: PPI .06, PM 4.0+	x_0 = 0: (SP, SE) = (71, 78) **x_0 = 1: (SP, SE) = (97, 33)** *D* = 1: PPI .31, PM 1.49 *D* = 2: PPI .06, PM 4.0+
180	x_0 = 0: (SP, SE) = (92, 26) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .20, PM 2.75 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (85, 47) x_0 = 1: (SP, SE) = (100, 9) *D* = 1: PPI .23, PM 2.32 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (79, 63) **x_0 = 1: (SP, SE) = (98, 18)** *D* = 1: PPI .26, PM 1.87 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (72, 75) **x_0 = 1: (SP, SE) = (97, 30)** *D* = 1: PPI .30, PM 1.57 *D* = 2: PPI .06, PM 4.0+
190	x_0 = 0: (SP, SE) = (93, 25) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .20, PM 2.77 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (86, 45) x_0 = 1: (SP, SE) = (100, 8) *D* = 1: PPI .22, PM 2.37 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (80, 60) **x_0 = 1: (SP, SE) = (98, 17)** *D* = 1: PPI .25, PM 1.91 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (74, 73) **x_0 = 1: (SP, SE) = (97, 28)** *D* = 1: PPI .29, PM 1.63 *D* = 2: PPI .06, PM 4.0+
200	x_0 = 0: (SP, SE) = (93, 24) x_0 = 1: (SP, SE) = (100, 2) *D* = 1: PPI .20, PM 2.78 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (87, 43) x_0 = 1: (SP, SE) = (100, 7) *D* = 1: PPI .22, PM 2.41 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (81, 58) **x_0 = 1: (SP, SE) = (99, 15)** *D* = 1: PPI .25, PM 1.95 *D* = 2: PPI .05, PM 4.0+	x_0 = 0: (SP, SE) = (75, 71) **x_0 = 1: (SP, SE) = (98, 26)** *D* = 1: PPI .28, PM 1.69 *D* = 2: PPI .06, PM 4.0+