Supplementary Data

Appendix 1: Description of the 25 studies excluded from the meta-analysis of Sensitivity and Specificity.

Below we list each study excluded from our meta-analysis of the sensitivity and specificity of Hemoccult SENSA. Each study is listed only once. If a study was excluded for multiple reasons, we used the following hierarchy for assign a reason for exclusion: 1) No primary data reported (simulation study); 2) Insufficient data provided for calculation of sensitivity and specificity; 3) Evaluation of a population at high risk for colorectal cancer; 4) Study sample overlapped with another study included in our analysis.

Papers excluded because they report no primary data (simulation studies, two papers):


Papers excluded because they report insufficient data to calculate sensitivity and specificity (17 papers)


Papers excluded because they studied a population at high risk for colorectal cancer (five papers).


Papers excluded because the study sample overlapped with another included study (one paper)

Appendix 2: Contribution of cohort data to estimates of sensitivity and mean sojourn time

Figure A2 demonstrates the information used to estimate the sensitivity and MST associated with Hemoccult SENSA.

Screen-positive patients (types A, B, and C) are associated with screen detection and contribute information to the first component of the likelihood, L1. False positive tests (patient type A) are identified based on six months of follow-up, and implicitly assume that all people with a positive test undergo additional work-up or within six months. Between 1997 and 2004, approximately 90% of patients with a positive FOBT had some follow-up within a year, and most underwent colonoscopy(1). Screen-detected cancers (patient types B and C) occur with probability $S \times P(\lambda, J, L, T)$. We assume that the probability of testing positive and then transitioning from the normal to preclinical state before disease confirmation is negligible. We treated 17 patients who were diagnosed with CRC more than six months after a positive FOBT test as having false positive tests (13 of these patients were diagnosed more than one year after a positive test). That is, we assume that had these 17 patients been assessed within 6 months of their positive FOBT, they would resemble type “A” patients rather than type “B” patients.

Screen-negative patients (types D, E, F, G, and H) are associated with symptom detection and contribute information to the second component of the likelihood, L2. Follow-up of patient types D, E, and F ends before cancer detection (the outcome is censored); These cases provide denominator information about the population at risk for developing symptom-detected (clinical) cancer. Follow-up of patient types G and H ends with clinical cancer detection. We expect $y$ newly developed cancers (patient type G, and these have sojourn time that is that is less than follow-up time $1 - \exp(-\hat{\lambda}(t - 0.5))$. We expect $c(t - S)/S$ missed cancers (patient type H), and these have sojourn time is greater than follow-up time $\exp(-\hat{\lambda}(t - 0.5))$. 

References

Appendix 3: Winbugs code used for primary analysis

Below we provide the algorithms and winbugs code fragments used to estimate

We estimated sensitivity (S) and mean sojourn time in the proximal and distal colorectum (mst.proxi, and mst.distal, respectively for each of the three age groups within the same model statement using a similar block of code for each each age-group, shown below for an arbitrary age group (e.g., for age group 45-50 age=50, J.proxi=1.08 per 10,000 and J.distal=2.95 per 10,000):

\[
p.scr[1] <- \frac{(S \cdot J.proxi \cdot (exp(-age/mst.proxi) - exp(-J.proxi*age)) \cdot (exp(-J.proxi*age) + (J.proxi*(exp(-age/mst.proxi)-exp(-J.proxi*age))/(J.proxi-1/mst.proxi))))}{\frac{(exp(-J.proxi*age) + (J.proxi*(exp(-age/mst.proxi)-exp(-J.proxi*age))/(J.proxi-1/mst.proxi)))}{}}\]

\[
p.scr[2] <- \frac{(S \cdot J.distal \cdot (exp(-age/mst.distal) - exp(-J.distal*age)) \cdot (exp(-J.distal*age) + (J.distal*(exp(-age/mst.distal)-exp(-J.distal*age))/(J.distal-1/mst.distal)))}{\frac{(exp(-J.distal*age) + (J.distal*(exp(-age/mst.distal)-exp(-J.distal*age))/(J.distal-1/mst.distal)))}{}}\]

\[

\[
can.scr[1:3] \sim \text{dmulti}(p.scr[1:3], \text{n.scr})\]

for(i in 1:N){
    can.int[i, 1:3] \sim \text{dmulti}(p.int[i, 1:3], \text{py[i]})
    p.int[i, 1] <- ( \text{py[i]}*J.proxi*(1-exp(-(time[i]-0.5)/mst.proxi)) + can.scr[1]*((1-S)/S)*exp(-(time[i]-0.5)/mst.proxi) )/py[i]
    p.int[i, 2] <- ( \text{py[i]}*J.distal*(1-exp(-(time[i]-0.5)/mst.distal)) + can.scr[2]*((1-S)/S)*exp(-(time[i]-0.5)/mst.distal) )/py[i]
    p.int[i, 3] <- 1-p.int[i, 1]-p.int[i, 2]
}

S \sim \text{dnorm}(0.748, 366.29)(0.001, 0.999)
mst.proxi \sim \text{dunif}(0.05, 10)
mst.distal \sim \text{dunif}(0.05, 10)

For each age group, the data vector can.scr contains the number of cancers detected after a positive FOBT (proximal, distal, and none) and the matrix can.int: contains the number of cancers detected after a negative FOBT; the i-th row corresponds to the i-th year after the index FOBT with three columns for proximal, distal, and no cancers detected. The probability of screen-detected cancer, p.scr, and the probability of clinically-detected cancer after a negative test, p.int, are each calculated from data and unknown parameters.