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Markov decision model

To simulate the scenario of the FOB test screening project with a stop-screen design (Fig. 1), a Markov decision model underpinned by a five-state disease natural history model was constructed. In the control arm, the decision tree structure follows the five-state disease natural history (Fig. 2): normal, PCDP Dukes' stage A + B, PCDP Dukes' stage C + D, clinical Dukes' stage A + B, and clinical Dukes' stage C + D. Each state has a corresponding prognostic effect on death from CRC and death from a competing cause. In the screening arm or the control arm, offered a one-shot screen at the close of the trial, the "treated PCDP Dukes' A + B" and "treated Dukes' C + D" are added into the Markov cycle as a result of early detection by the screen.

Markov cycle for the screening arm

Attendance rate

In the screening arm, those who are in the "normal," "PCDP Dukes' A + B," or "PCDP Dukes' C + D" groups would be detected by uptake of the screen. The first parameter shown in Fig. S1 is thus attendance rate for uptake of screening, with a two-year cycle. Those who do not attend the screening follow Fig. S2 for normal, Fig. S3 for the PCDP Dukes' A + B, and Fig. S4 for the PCDP Dukes' C + D. For normal subjects without uptake of screening, the decision tree is subject to other causes of death, progressions to CRC death (very low chance), two occult states (PCDP Dukes' A + B and PCDP Dukes' C + D), and two symptomatic states (clinical Dukes' A + B and clinical Dukes' C+D) in each cycle (per year). Similar schema have been delineated for Fig. S3 and Fig. S4. Note that those in the normal, the PCDP Dukes' A + B, and the PCDP Dukes' C + D groups in the current cycle move back to the Markov cycle to start the next cycle. Those who have already progressed to clinical Dukes' A + B and clinical Dukes'

C + D follow Fig. S5 and Fig. S6, respectively.

Sensitivity, specificity, and compliance rate with colonoscopy

The tree structure for those who do not attend screening follows the disease natural history for normal (Fig. S2), PCDP Dukes' A + B (Fig. S3), and PCDP Dukes' C + D (Fig. S4) subjects when they are invited to screen. Those who attend the screening and are diagnosed as normal or as in either of the two occult PCDP stages require the assignment of the FOB test sensitivity and specificity for classification as true positives, true negatives, false positives, and false negatives. Whether FOB test-positive cases are false positives or true positives is subject to the compliance rate of colonoscopy. After the uptake of screening, normal subjects who are truly negative or false positive cases who do not comply with colonoscopy follow Fig. S2. The corresponding group complying with colonoscopy follows the surveillance model (see Fig. S9). Similarly, after the uptake of screening, those who are already in PCDP Dukes' A + B, complying with colonoscopy, are classified as treated PCDP Dukes' A + B (Fig. S7), whereas the corresponding group not complying with colonoscopy follow Fig. S3. False negative cases after the uptake of screening also follow Fig. S. A similar tree structure is also applied to screenees who are already in PCDP Dukes' C + D on the uptake of screening.

Prognosis

Surveillance mode (normal finding after colonoscopy)

Following the US Preventive Service Task Force (USPSTF) guidelines for colorectal cancer screening, false positive cases who have undergone colonoscopic examination with normal findings should be monitored by five-yearly colonoscopy screening. Alternatively, they may return to a two-year screening interval by the FOB test. In addition to those with normal findings, those who may be diagnosed as "PCDP Dukes' A, B," "PCDP Dukes' C, D," "clinical Dukes' A, B," and "clinical Dukes' C, D" should be subjected to five-year follow-up.

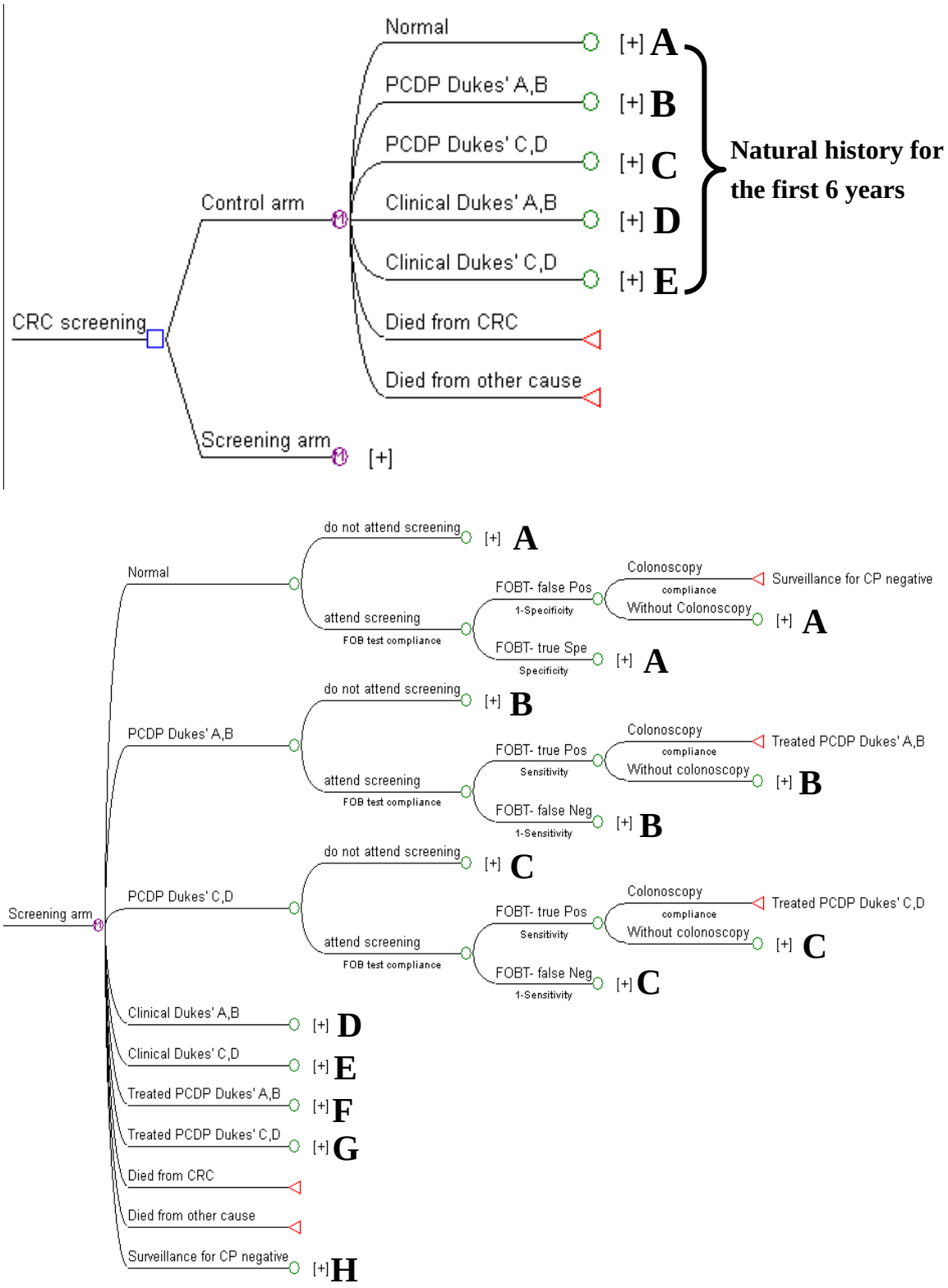

Figure S1. Markov cycle tree for colorectal cancer screening

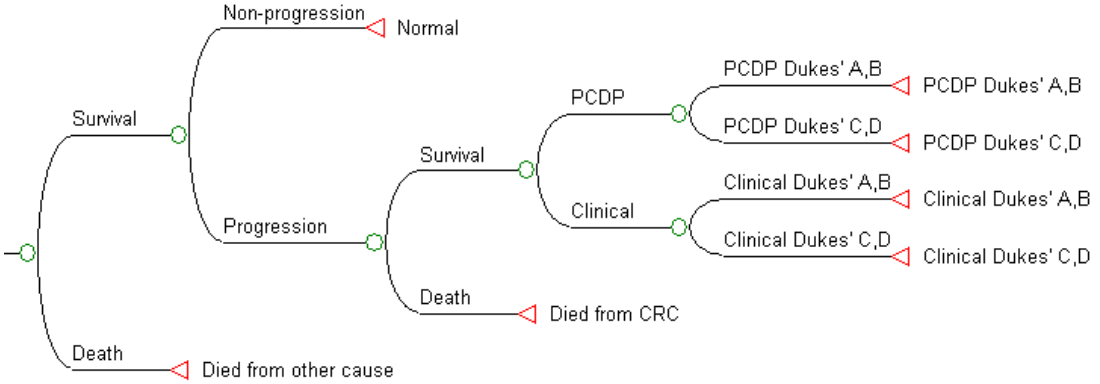

Figure S2. Normal

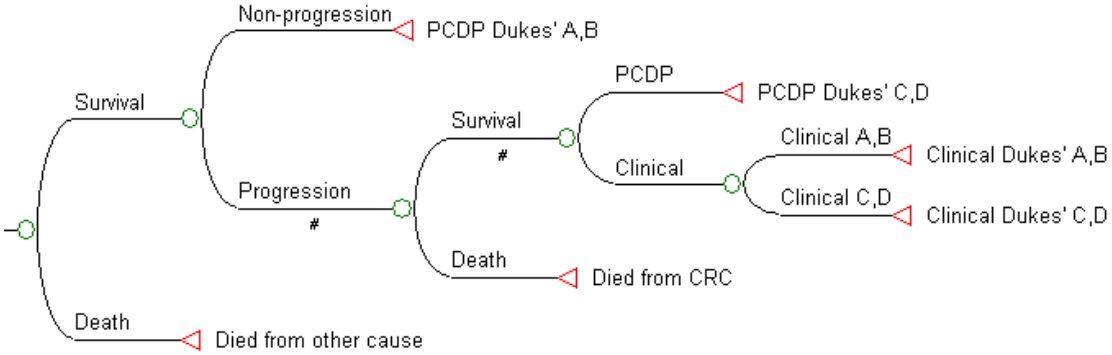

Figure S3. PCDP Dukes' A, B

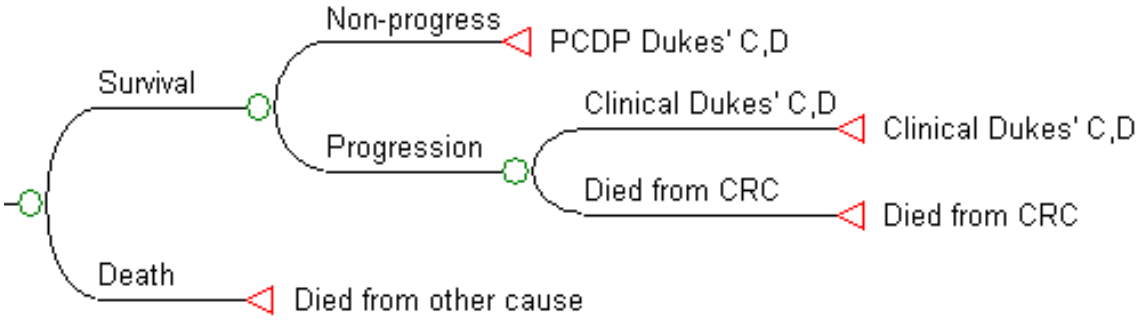

Figure S4. PCDP Dukes' C, D

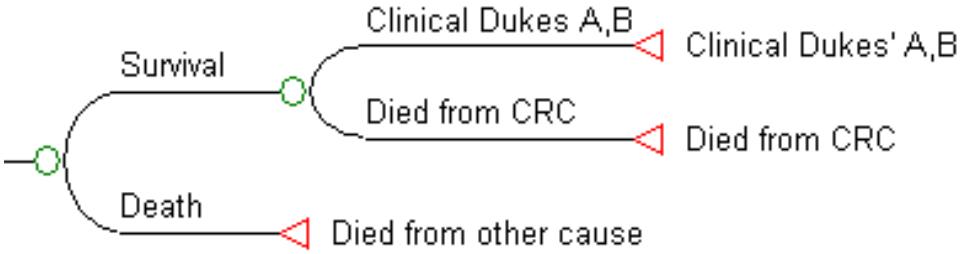

Figure S5. Clinical Dukes' A, B

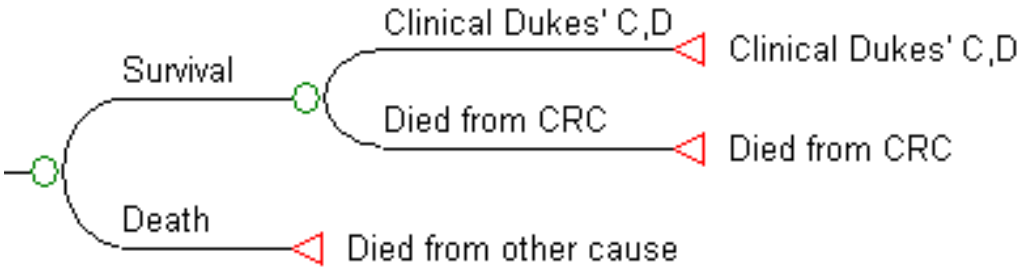

Figure S6. Clinical Dukes' C, D

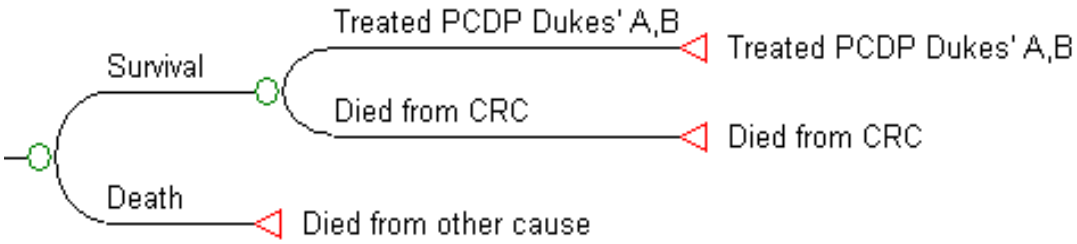

Figure S7. Treated PCDP Dukes' A, B

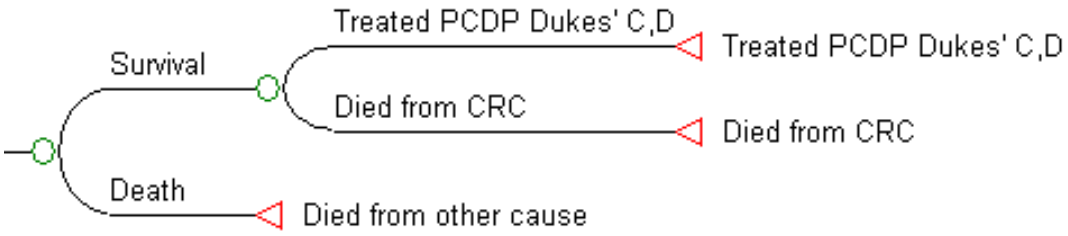

Figure S8. Treated PCDP Dukes' C, D

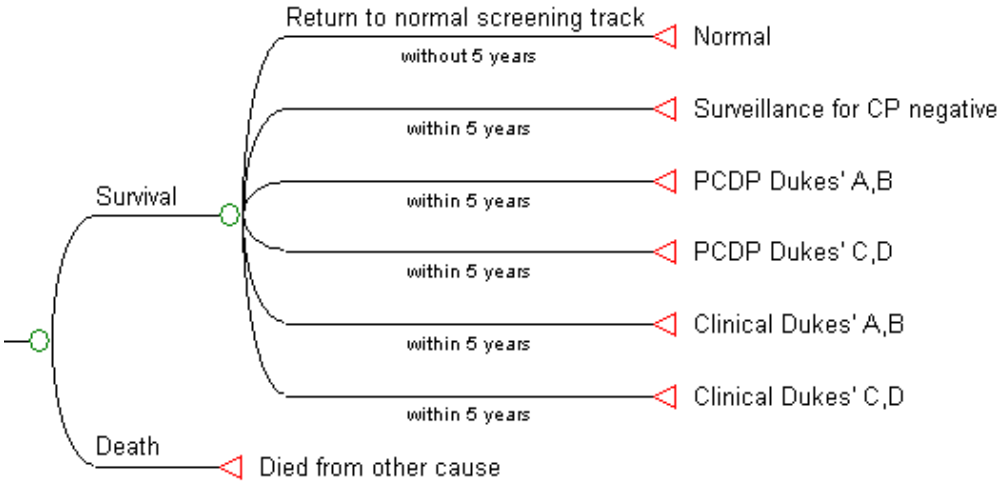

Figure S9. Surveillance for colonoscopy negative