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| **Supplemental Table 7. Model Performance at Different Sensitivity Thresholds for CRC and HRA Detection Among Patients Aged 50 to 74****(Sequential Models for CRC and Residual ACNs)** |
| **Performance Characteristic** | **Sensitivity of CRC Detection (Model #1)** | **Sensitivity of CRC or HRA Detection in Residual Cohort (Model #2)** |
| **100%** | **99%** | **95%** |
| % missed CRC  | 0 | 0 | 0 | **80%** |
| % missed HRA | 7.6 | 8.1 | 12.4 |
| % colonoscopies potentially avoided | 19.0 | 19.6 | 28.5 |
| % missed CRC  | 0 | 0.95 | 0.95 | **70%** |
| % missed HRA | 11.1 | 12.3 | 18.6 |
| % colonoscopies potentially avoided | 25.4 | 27.4 | 38.2 |
| % missed CRC  | 0 | 0.95 | 1.9 | **60%** |
| % missed HRA | 15.0 | 16.8 | 24.9 |
| % colonoscopies potentially avoided | 30.9 | 33.9 | 46.2 |

Example of Interpretation (100% Column):

At 100% sensitivity threshold for CRC detection in Model #1 (entire cohort) and 80% sensitivity for CRC or HRA detection in Model #2 (residual cohort), the sequential modelling strategy would lead to a miss rate of 0% for CRC and 7.6% for HRA while permitting avoidance of up to 19.0% of colonoscopies