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| **Supplemental Table 5. Model Performance at Different Sensitivity Thresholds for CRC and HRA Detection Among Patients with Signs or Symptoms****(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 | 3.5 | 10.7 | 13.8 |
| % colonoscopies potentially avoided | 13.1 | 21.8 | 30.5 |
| % missed CRC  | 0 | 0 | 0 | **70%** |
| % missed HRA | 5.4 | 16.2 | 20.4 |
| % colonoscopies potentially avoided | 18.3 | 31.5 | 38.7 |
| % missed CRC  | 0 | 0 | 0 | **60%** |
| % missed HRA | 7.1 | 21.2 | 27.2 |
| % colonoscopies potentially avoided | 21.0 | 37.6 | 46.7 |

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 3.5% for HRA while permitting avoidance of up to 13.1% of colonoscopies