**SUPPLEMENTARY DATA**

**Supplementary Table 1. Patient and colonoscopy characteristics by index colonoscopy findings**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Findings on index colonoscopy | | | | | | | | |
|  | No adenoma | | | NAA | | | AA | | |
|  | 40-49yo  n=1,507 (29.5%) | 50-59yo  n=3,597 (70.5%) | p-value | 40-49yo  n=610 (14.9%) | 50-59yo  n=3,497 (85.1%) | p-value | 40-49yo  n=279 (12.9%) | 50-59yo  n=1,884 (87.1%) | p-value |
| Age (Years)  Mean (STD)  Median (IQR) | 45.2 (2.8)  46.0 (43.0-48.0) | 54.2 (3.0)  54.0 (51.0-57.0) | <0.0001 | 45.7 (2.8)  46.0 (44.0-48.0) | 54.3 (3.0)  54.0 (52.0-57.0) | <0.0001 | 45.9 (2.8)  47.0 (44.0-48.0) | 54.0 (2.9)  54.0 (51.0-57.0) | <0.0001 |
| Sex  Male  Female | 636 (42.2)  871 (57.8) | 1,447 (40.2)  2,150 (59.8) | 0.19 | 301 (49.3)  309 (50.7) | 2,061 (58.9)  1,436 (41.1) | <0.0001 | 134 (48.0)  145 (52.0) | 1,098 (58.3)  786 (41.7) | 0.001 |
| Race/ethnicity  Non-Hispanic white  Hispanic  Black  Asian  Other/Unknown | 767 (50.9)  241 (16.0)  133 (8.8)  270 (17.9)  96 (6.4) | 2,078 (57.8)  470 (13.1)  269 (7.5)  545 (15.1)  235 (6.5) | 0.0001 | 284 (46.6)  118 (19.3)  26 (4.3)  143 (23.4)  39 (6.4) | 1,913 (54.7)  520 (14.9)  197 (5.6)  668 (19.1)  199 (5.7) | 0.0004 | 141 (50.5)  57 (20.4)  31 (11.1)  38 (13.6)  12 (4.3) | 1,102 (58.5)  228 (12.1)  161 (8.5)  296 (15.7)  97 (5.2) | 0.001 |
| Body mass index  < 25.0  25-29.9  ≥ 30.0  Median (IQR) | 494 (32.8)  522 (34.7)  489 (32.5)  27.4 (24.0-31.5) | 1,106 (30.9)  1,328 (37.1)  1,148 (32.0)  27.4 (24.2-31.3) | 0.22 | 182 (29.8)  207 (33.9)  221 (36.2)  27.8 (24.3-32.4) | 907 (26.0)  1,349 (38.8)  1,225 (35.2)  28.0 (24.9-31.8) | 0.05 | 81 (29.0)  99 (35.5)  99 (35.5)  28.1 (24.5-32.1) | 461 (24.7)  693 (37.1)  715 (38.2)  28.1 (25.0-32.2) | 0.29 |
| Smoking  Ever  Never  Unknown | 391 (26.0)  1,084 (71.9)  32 (2.1) | 1,206 (33.5)  2,332 (64.8)  59 (1.6) | <0.0001 | 191 (31.3)  408 (66.9)  11 (1.8) | 1,205 (34.5)  2,205 (63.0)  87 (2.5) | 0.15 | 95 (34.0)  181 (64.9)  3 (1.1) | 684 (36.3)  1,156 (61.4)  44 (2.3) | 0.27 |
| Family history of CRC  Yes  No  Unknown | 519 (34.4)  263 (17.5)  725 (48.1) | 850 (23.6)  691 (19.2)  2,056 (57.2) | <0.0001 | 128 (21.0)  128 (21.0)  354 (58.0) | 358 (10.2)  800 (22.9)  2,339 (66.9) | <0.0001 | 34 (12.2)  81 (29.0)  164 (58.8) | 119 (6.3)  482 (25.6)  1,283 (68.1) | 0.0003 |
| Index colonoscopy indication  Screening  FIT positive  Non-screening | 692 (45.9)  32 (2.1)  783 (52.0) | 1,585 (44.1)  550 (15.3)  1,462 (40.6) | <0.0001 | 218 (35.7)  20 (3.3)  372 (61.0) | 1,218 (34.8)  1,176 (33.6)  1,103 (31.5) | <0.0001 | 54 (19.4)  28 (10.0)  197 (70.6) | 321 (17.0)  1,148 (60.9)  415 (22.0) | <0.0001 |
| Follow-up time, median y (IQR) | 7.4 (6.4-8.1) | 7.4 (6.3-8.1) | 0.832 | 7.1 (6.1-7.9) | 7.0 (6.1-7.9) | 0.392 | 6.8 (5.7-7.8) | 6.8 (5.6-7.9) | 0.592 |

AA = advanced adenoma, IQR = interquartile range, NAA = non-advanced adenoma, STD = standard deviation

1 P-value for the Chi-Square Test of Association for categorical variables, and t-test for continuous variables unless noted otherwise.

2 P-value for Median Test.

**Supplementary Table 2. Numbers of patients by age and outcome on index and surveillance colonoscopy**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Index colonoscopy | |  | Surveillance colonoscopy | |  |
| 40-49yo  n (%) | 50-59yo  n (%) | p-value\* | 40-49yo  n (%) | 50-59yo  n (%) | p-value\* |
| No Adenoma | 1,507 (62.9) | 3,597 (40.1) | <0.0001 | 1,606 (67.0) | 4,908 (54.7) | <0.0001 |
| NAA | 610 (25.4) | 3,497 (39.0) | <0.0001 | 706 (29.5) | 3,449 (38.4) | <0.0001 |
| AA | 279 (11.6) | 1,884 (21.0) | <0.0001 | 84 (3.5) | 621 (6.9) | <0.0001 |
| Total | 2,396 (100) | 8,978 (100) |  | 2,396 (100) | 8,978 (100) |  |

AA = advanced adenoma, CRC = colorectal cancer, NAA = non-advanced adenoma

\*P-value for Test of Two Independent Proportions

**Supplementary Table 3A. Time until surveillance colonoscopy after adenoma detection on index colonoscopy by age group**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Years until surveillance colonoscopy, median (IQR) | | p-value |
| 40-49yo | 50-59yo |
| NAA on index colonoscopy | 5.1 (4.8-5.7) | 5.2 (4.9-5.7) | 0.16 |
| AA on index colonoscopy | 3.6 (3.1-4.9) | 3.7 (3.1-5.1) | 0.66 |

AA = advanced adenoma, IQR = interquartile range, NAA = non-advanced adenoma

**Supplementary Table 3B. Time until metachronous advanced neoplasia after adenoma detection on index colonoscopy by age group**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Years until metachronous AN, median (IQR) | | p-value |
| 40-49yo | 50-59yo |
| NAA on index colonoscopy | 5.1 (4.7-5.6) | 5.3 (5.0-5.9) | 0.12 |
| AA on index colonoscopy | 4.0 (3.1-5.4) | 3.7 (3.0-5.2) | 0.49 |

AA = advanced adenoma, AN = advanced neoplasia IQR = interquartile range, NAA = non-advanced adenoma

**Supplementary Table 4A. Unadjusted hazard ratios for CRC in patients aged 40-49 years compared to 50-59 years based on index colonoscopy findings when stratified by sex, race, BMI, smoking, and index colonoscopy indication**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | HR for CRC (95% CI) with no adenoma on index colonoscopy | P-value\* | HR for CRC (95% CI) with NAA on index colonoscopy | P-value\* | HR for CRC (95% CI) with AA on index colonoscopy | P-value\* |
| Sex  Male  Female | Cannot calculate  0.51 (0.08-2.03) |  | 1.23 (0.06-8.08)  Cannot calculate |  | 0.66 (0.03-4.13)  Cannot calculate |  |
| Race/ethnicity    Black Non-Hispanic  Not Black Non-Hispanic | Cannot calculate  0.34 (0.05-1.22) |  | Cannot calculate  0.94 (0.05-5.77) |  | Cannot calculate  Cannot calculate |  |
| BMI  < 25.0  ≥ 25.0 | 1.47 (0.19-7.78)  Cannot calculate |  | Cannot calculate  1.02 (0.05-6.57) |  | Cannot calculate  0.82 (0.04-5.45) |  |
| Smoking  Ever  Never/Unknown | 1.10 (0.05-8.78)  0.15 (0.08-0.75) | 0.18 | Cannot calculate  1.58 (0.08-11.7) |  | Cannot calculate  0.92 (0.04-7.31) |  |
| Index colonoscopy indication  Screening  FIT positive  Non-screening | Cannot calculate  Cannot calculate  0.47 (0.07-1.95) |  | Cannot calculate  Cannot calculate  3.46 (0.14-87.5) |  | Cannot calculate  Cannot calculate  0.78 (0.04-6.42) |  |

\*P-value for the test of interaction between age group and stratification variable.

**Supplementary Table 4B. (with family hx\*indication interaction) Adjusted hazard ratios for advanced adenoma, CRC, and AN in patients aged 40-49 years compared to 50-59 years by index colonoscopy findings**

|  |  |  |  |
| --- | --- | --- | --- |
|  | HR for AA (95% CI)\* | HR for CRC (95% CI)\* | HR for AN (95% CI)\* |
| No adenoma on index colonoscopy | 0.64 (0.42-0.94) | 0.26 (0.04-0.91) | 0.59 (0.40-0.85) |
| NAA on index colonoscopy | 0.85 (0.55-1.27) | 1.03 (0.05-6.10) | 0.86 (0.56-1.27) |
| AA on index colonoscopy | 0.84 (0.50-1.33) | 0.62 (0.03-3.84) | 0.82 (0.50-1.30) |

AA = advanced adenoma, AN = advanced neoplasia, CRC = colorectal cancer, HR = hazard ratio, CI = Confidence Interval, NAA = non-advanced adenoma

\* HR is for 40-49yo group with referent being the 50-59yo group, and is adjusted for sex, race/ethnicity, BMI, smoking, family history of CRC, index colonoscopy indication, and family history of CRC\*index colonoscopy indication

**Supplementary Table 5. Adjusted hazard ratios for advanced adenoma, CRC, and AN in patients aged 40-49 years compared to 50-59 years by index colonoscopy findings excluding surveillance colonoscopies occurring 0-12 months after index colonoscopy**

|  |  |  |  |
| --- | --- | --- | --- |
|  | HR for AA (95% CI)\* | HR for CRC (95% CI)\* | HR for AN (95% CI)\* |
| No adenoma on index colonoscopy | 0.64 (0.42-0.93) | 0.28 (0.04-0.98) | 0.59 (0.40-0.85) |
| NAA on index colonoscopy | 0.84 (0.54-1.25) | 0.86 (0.05-5.05) | 0.84 (0.55-1.24) |
| AA on index colonoscopy | 0.87 (0.51-1.42) | \*\* | 0.83 (0.49-1.35) |

AA = advanced adenoma, AN = advanced neoplasia, CRC = colorectal cancer, HR = hazard ratio, CI = Confidence Interval, NAA = non-advanced adenoma

\* HR is for 40-49yo group with referent being the 50-59yo group, and is adjusted for sex, race/ethnicity, BMI, smoking, family history of CRC, and index colonoscopy indication

\*\* Insufficient number of people with AA on index colonoscopy who had CRC detected on surveillance to calculate HR

**Supplementary Table 6. Surveillance colonoscopy findings and adjusted hazard ratios for AN and CRC in patients aged 40-49 years compared to 50-59 years when serrated polyp concurrent with conventional adenoma detected on index colonoscopy**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Number of patients | | Number of AN cases on surveillance | | Number of CRC cases on surveillance | | Adjusted HR for AN\* (95% CI) | Adjusted HR for CRC\* (95% CI) |
| 40-49yo | 50-59yo | 40-49yo | 50-59yo | 40-49yo | 50-59yo |
| 451 | 3260 | 27 | 301 | 3 | 6 | 0.86 (0.56-1.27) | 4.70 (0.88-21.98) |

AN = advanced neoplasia, CI = confidence interval, CRC = colorectal cancer, HR = hazard ratio

\* HR is for 40-49yo group with referent group being the 50-59yo group, and is adjusted for sex, race/ethnicity, BMI, smoking, family history of CRC, and index colonoscopy indication