**Supplementary Material**

**Supplemental Digital Content 1.** Crude and age-standardized colorectal cancer incidence (per 100,000), proportion of advanced stages and distribution by location in persons ≥55 years determined based on GePaRD and, for comparison, based on data from the German Centre for Cancer Registry (Zentrum für Krebsregisterdaten, ZfKD).

**Supplemental Digital Content 2**. Flow chart illustrating the selection of the study population.

**Supplemental Digital Content 3**. Description ofcolorectal cancers (CRCs) occurring in cohort 1 and cohort 2 within the entire follow-up, stratified by sex.

**Supplemental Digital Content 4.** Distribution of colorectal cancers (CRC) occurring within 10 years after screening colonoscopy in cohort 1 and cohort 2according to location, stratified by age group and sex. Here, distal CRCs are subdivided into CRCs in the distal colon vs. the rectum.

**Supplemental Digital Content 5.** Colorectal cancers (CRCs) diagnosed at first repeat colonoscopy per 10,000 person-years in cohort 1 and cohort 2, overall and according to site and stage of the CRCs, stratified by sex and age at first repeat colonoscopy.

**Supplemental Digital Content 6.** Proportion of persons with a colorectal cancer (CRC) detected at first repeat colonoscopy according to years since baseline screening colonoscopy in cohort 1 and cohort 2: Stratification of the analyses underlying Figure 2 by site (A: Proximal, B: Distal) and sex (C: Men, D: Women).

**Supplemental Digital Content 7.** Number of persons (A), distribution of sex (B) and age (C) in the study populations underlying the proportions shown in Figure 2 (denominators).

**Supplemental Digital Content 8.** Proportion of persons with a colorectal cancer (CRC) detected at first repeat colonoscopy according to years since baseline screening colonoscopy in cohort 1 and cohort 2: Restriction of the analyses underlying Figure 2 to persons aged 70 years or younger.

**Supplemental Digital Content 1.** Crude and age-standardized colorectal cancer incidence (per 100,000), proportion of advanced stages and distribution by location in persons ≥55 years determined based on GePaRD and, for comparison, based on data from the German Centre for Cancer Registry (Zentrum für Krebsregisterdaten, ZfKD)1.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Incidence (crude) | Incidence (age-standardized2) | Advanced  | Site |
| Proximal | Distal |
| GePaRD | ZfKD | GePaRD | ZfKD | GePaRD | ZfKD | GePaRD | ZfKD | GePaRD | ZfKD |
| Men2008200920102011201220132014 | 252.2245.0245.3243.5220.3228.8216.6 | 286.9270.1260.3256.3248.9243.5229.6 | 258.8249.4247.2242.6219.4226.4212.6 | 296.4276.9265.1260.0250.7244.1228.9 | 36.4%37.7%40.0%40.6%41.2%42.1%44.0% | 37.8%38.6%38.9%40.7%40.8%41.6%39.8% | 27.9%29.2%28.1%30.0%29.8%29.7%30.0% | 24.7%26.1%26.8%27.4%27.8%28.2%28.9% | 65.9%63.5%60.4%59.5%60.3%60.6%60.9% | 65.6%64.6%64.9%64.4%64.5%63.9%63.4% |
| Women2008200920102011201220132014 | 175.9171.8180.5175.5168.6161.4160.1 | 193.4184.0178.4174.9167.9162.2154.0 | 191.3184.1190.6183.5176.4168.0166.2 | 196.1185.1179.2175.1167.9161.8153.4 | 37.0%36.6%38.6%36.6%39.6%41.1%40.8% | 37.4%38.1%38.3%39.2%40.1%38.8%38.0% | 36.8%38.7%34.7%37.2%36.3%38.5%39.8% | 32.3%34.4%35.0%36.0%36.4%37.0%38.2% | 54.8%54.0%48.9%46.2%48.7%47.7%47.9% | 54.9%53.6%53.3%52.5%52.1%51.9%51.3% |

1 Based on cancer registries from federal states with an estimated level of completeness ≥95% between 2008 and 2014 (covering ~32 million persons).

2 Using the German population of 2014 as the standard population.

Age-standardized1 incidence per 100,000 persons aged 55 years or older in GePaRD vs. ZfKD by year in males and females.

Males:

Females:

1 Using the German population of 2014 as the standard population.

**Supplemental Digital Content 2**. Flow chart illustrating the selection of the study population.

Persons with at least one colonoscopy between 2006 and 2017: N= 4,151,218

Continuous insurance before index colonoscopy <2 years: N=383,618

Residency outside of Germany: N=8,996

Non-valid information on age or sex: N=82

Colonoscopy coded as a diagnostic colonoscopy or person <55 years: N=2,646,513

Codes indicating a prevalent colorectal cancer: N=16,628

Persons with screening colonoscopy included into the study: N= 1,095,381

**Supplemental Digital Content 3.** Description ofcolorectal cancers (CRCs) occurring in cohort 1 and cohort 21 within the entire follow-up, stratified by sex.

|  |  |  |
| --- | --- | --- |
|  | Cohort 1  | Cohort 2 |
|  | Men | Women | Men | Women |
| Persons, n  | 110,658 | 83,087 | 302,862 | 421,018 |
| CRC incidence per 10,000 person-years | 14.3 (13.4-15.3) | 12.5 (11.5-13.6) | 5.9 (5.6-6.3) | 5.3 (5.1-5.6) |
| Number of incident CRC cases, n (% of all persons)*Of these,* Site Proximal, n (% of all CRCs)Distal, n (% of all CRCs)Both, n (% of all CRCs)Unknown, n (% of all CRCs)StageNon-advanced, n (% of all CRCs)Advanced, n (% of all CRCs) | 905 (0.8%)430 (47.5%)379 (41.9%)20 (2.2%)76 (8.4%)632 (69.8%)273 (30.2%) | 576 (0.7%)306 (53.1%)189 (32.8%)6 (1.0%) 75 (13.0%)383 (66.5%) 193 (33.5%) | 1,087 (0.4%)457 (42.0%)487 (44.8%)16 (1.5%)127 (4.8%)632 (58.1%)455 (41.9%) | 1,313 (0.3%)629 (47.9%)470 (35.8%)33 (2.5%)181 (13.8%)804 (61.2%)509 (38.8%) |

1 Cohort 1: persons with a snare polypectomy at baseline screening colonoscopy, cohort 2: persons without codes indicating polyps/polypectomy at baseline screening colonoscopy.

**Supplemental Digital Content 4.** Distribution of colorectal cancers (CRC) occurring within 10 years after screening colonoscopy in cohort 1 and cohort 2according to location, stratified by age group and sex. Here, distal CRCs are subdivided into CRCs in the distal colon vs. the rectum.

|  |  |
| --- | --- |
|  | Proportion of total CRC1 |
| Proximal | Distal |
| Distal colon2 | Rectum | Unknown whether distal colon or rectum  |
| **Men** |  |  |  |  |
| Cohort 1 |  |  |  |  |
| 55–64 y. | 48.0% | 26.8% | 22.8% | 2.4% |
| 65–74 y. | 54.4% | 22.4% | 22.2% | 1.0% |
| 75+ y. | 57.7% | 18.7% | 22.0% | 1.6% |
| Cohort 2 |   |  |  |  |
| 55–64 y. | 43.8% | 25.7% | 28.3% | 2.2% |
| 65–74 y. | 47.3% | 24.8% | 26.8% | 1.1% |
| 75+ y. | 55.3% | 21.7% | 21.7% | 1.3% |
| **Women** |   |  |  |  |
| Cohort 1 |   |  |  |  |
| 55–64 y. | 56.2% | 21.9% | 20.5% | 1.4% |
| 65–74 y. | 63.2% | 16.1% | 19.8% | 0.8% |
| 75+ y. | 66.7% | 14.9% | 18.4% | 0.0% |
| Cohort 2 |   |  |  |  |
| 55–64 y. | 53.2% | 20.8% | 24.6% | 1.5% |
| 65–74 y. | 58.0% | 18.7% | 21.3% | 2.0% |
| 75+ y. | 62.2% | 17.8% | 18.9% | 1.1% |

1 Excluding those in the category “Both/ Unknown” in the denominator.

2 Tumors located between splenic flexure and rectosigmoid junction.

**Supplemental Digital Content 5.** Colorectal cancers (CRCs) diagnosed at first repeat colonoscopy per 10,000 person-years in cohort 1 and cohort 21, overall and according to site and stage of the CRCs, stratified by sex and age at first repeat colonoscopy.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Total | Site | Stage |
| Proximal | Distal | Both/ Unknown | Non-advanced | Advanced |
| Cohort 1 (N=84,770)MenAll age groups55-<65 y.65-<75 y.75+ y.WomenAll age groups 55-<65 y. 65-<75 y. 75+ y. | 21.3 (19.8-23.0)22.7 (20.6-25.0)16.0 (12.8-19.7)22.3 (19.3-25.6)32.5 (27.3-38.4)19.4 (17.1-21.9)13.8 (10.5-17.7)17.1 (14.0-20.7)32.9 (26.6-40.3) | 9.3 (8.3-10.5)9.2 (7.9-10.7)5.9 (4.0-8.3)8.6 (6.8-10.7)14.9 (11.5-19.1)9.5 (7.9-11.3)5.0 (3.2-7.6)8.3 (6.2-10.9)18.9 (14.2-24.7) | 9.7 (8.6-10.8)11.5 (10.0-13.2)8.3 (6.0-11.0) 11.9 (9.8-14.4)14.9 (11.5-19.1)7.1 (5.7-8.7)6.2 (4.1-9.0)6.2 (4.4-8.5)10.5 (7.1-15.0) | 2.3 (1.8-2.9)2.0 (1.4-2.7)1.8 (0.9-3.4)1.8 (1.0-2.9)2.6 (1.3-4.7)2.8 (1.9-3.8)2.5 (1.3-4.5)2.6 (1.5-4.2)3.5 (1.7-6.4) | 15.5 (14.1-16.9)16.2 (14.5-18.2)11.4 (8.7-14.6) 16.4 (13.9-19.3)22.0 (17.8-27.0) 14.4 (12.5-16.6)11.5 (8.5-15.1)12.4 (9.7-15.5)23.5 (18.2-29.8) | 5.9 (5.0-6.8)6.5 (5.4-7.8)4.6 (3.0-6.8)5.8 (4.4-7.6)10.4 (7.6-14.0)4.9 (3.8-6.3)2.3 (1.1-4.2)4.7 (3.2-6.8)9.5 (6.2-13.8) |
| Cohort 2 (N=146,541)MenAll age groups55-<65 y.65-<75 y.75+ y.WomenAll age groups 55-<65 y. 65-<75 y. 75+ y. | 14.0 (13.2-14.9)15.0 (13.7-16.3)8.9 (6.9-11.4)14.7 (13.0-16.5)19.6 (17.0-22.5)13.3 (12.3-14.4)11.5 (9.5-13.7)11.9 (10.5-13.3)17.9 (15.6-20.4) | 6.1 (5.5-6.6)5.7 (4.9-6.5)2.8 (1.8-4.3)5.1 (4.1-6.2)8.7 (7.0-10.6) 6.4 (5.7-7.1)4.5 (3.4-6.0)5.1 (4.3-6.1)10.4 (8.6-12.3) | 6.3 (5.7-6.8)7.7 (6.8-8.6)5.1 (3.6-7.1)7.8 (6.6-9.2)9.1 (7.4-11.2)5.2(4.6-5.9)4.7 (3.5-6.2)5.0 (4.1-5.9)6.1 (4.8-7.6) | 1.7 (1.4-2.0)1.6 (1.2-2.1)0.9 (0.4-2.0)1.8 (1.3-2.5)1.8 (1.1-2.8)1.8 (1.4-2.2)2.2 (1.4-3.3)1.8 (1.3-2.4)1.5 (0.9-2.3) | 8.6 (8.0-9.3)9.0 (8.1-10.0)6.2 (4.6-8.3)8.5 (7.3-10.0)11.8 (9.8-14.0)8.4 (7.6-9.2)6.7 (5.2-8.4)7.1 (6.1-8.3)12.3 (10.4-14.4) | 5.4 (4.9 (5.9)5.9 (5.2-6.8)2.7 (1.7-4.2)6.1 (5.1-7.4)7.8 (6.2-9.7)5.0 (4.3-5.6)4.8 (3.6-6.3)4.7 (3.9-5.7)5.6 (4.3-7.1) |

1 Cohort 1: persons with a snare polypectomy at baseline screening colonoscopy, cohort 2: persons without codes indicating polyps/polypectomy at baseline screening colonoscopy.

**Supplemental Digital Content 6.** Proportion of persons with a colorectal cancer (CRC) detected at first repeat colonoscopy according to years since baseline screening colonoscopy in cohort 1 and cohort 21: Stratification of the analyses underlying Figure 2 by site (A: Proximal, B: Distal) and sex (C: Men, D: Women).

**A.** Proximal



**B.** Distal



**C.** Men



**D.** Women



1 Cohort 1: persons with a snare polypectomy at baseline screening colonoscopy, cohort 2: persons without codes indicating polyps/polypectomy at baseline screening colonoscopy.

**Supplemental Digital Content 7.** Number of persons (A),distribution of sex (B) and age (C) in the study populations underlying the proportions shown in Figure 2 (denominators).

**A.** N persons

|  |  |  |
| --- | --- | --- |
| Years between screening and repeat colonoscopy | Cohort 1 | Cohort 2 |
| 0.5-2 years | 23,138 | 15,124 |
| 2-4 years | 37,336 | 36,021 |
| 4-6 years | 16,313 | 41,847 |
| 6-8 years | 5,521 | 28,198 |
| >8 years | 2,462 | 25,351 |

**B.** Proportion of males [%].

|  |  |  |
| --- | --- | --- |
| Years between screening and repeat colonoscopy | Cohort 1 | Cohort 2 |
| 0.5-2 years | 58.1 | 43.3 |
| 2-4 years | 57.4 | 44.1 |
| 4-6 years | 58.6 | 42.7 |
| 6-8 years | 59.6 | 42.8 |
| >8 years | 60.9 | 44.5 |

**C.** Age [mean (SD)] at first repeat colonoscopy, stratified by sex

|  |  |  |
| --- | --- | --- |
| Years between screening and repeat colonoscopy | Cohort 1 | Cohort 2 |
| Male | Female | Male  | Female |
| 0.5-2 years | 66.9 (6.9) | 66.4 (7.1) | 67.7 (7.6) | 67.1 (7.6) |
| 2-4 years | 67.9 (6.6) | 67.4 (6.7) | 68.6 (7.1) | 68.0 (7.1) |
| 4-6 years | 69.4 (6.4) | 69.1 (6.6) | 69.5 (6.7) |  69.0 (6.6) |
| 6-8 years | 71.6 (6.3) | 71.4 (6.5) | 70.9 (6.3) | 70.6 (6.3) |
| >8 years | 73.4 (5.8) | 73.0 (5.9) | 72.4 (5.7) | 71.9 (5.6) |

**Supplemental Digital Content 8.** Proportion of persons with a colorectal cancer (CRC) detected at first repeat colonoscopy according to years since baseline screening colonoscopy in cohort 1 and cohort 21: Restriction of the analyses underlying Figure 2 to persons aged 70 years or younger.

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1 Cohort 1: persons with a snare polypectomy at baseline screening colonoscopy, cohort 2: persons without codes indicating polyps/polypectomy at baseline screening colonoscopy.