**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 |
| Men  2008  2009  2010  2011  2012  2013  2014 | 252.2  245.0  245.3  243.5  220.3  228.8  216.6 | 286.9  270.1  260.3  256.3  248.9  243.5  229.6 | 258.8  249.4  247.2  242.6  219.4  226.4  212.6 | 296.4  276.9  265.1  260.0  250.7  244.1  228.9 | 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% |
| Women  2008  2009  2010  2011  2012  2013  2014 | 175.9  171.8  180.5  175.5  168.6  161.4  160.1 | 193.4  184.0  178.4  174.9  167.9  162.2  154.0 | 191.3  184.1  190.6  183.5  176.4  168.0  166.2 | 196.1  185.1  179.2  175.1  167.9  161.8  153.4 | 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)  Stage  Non-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.

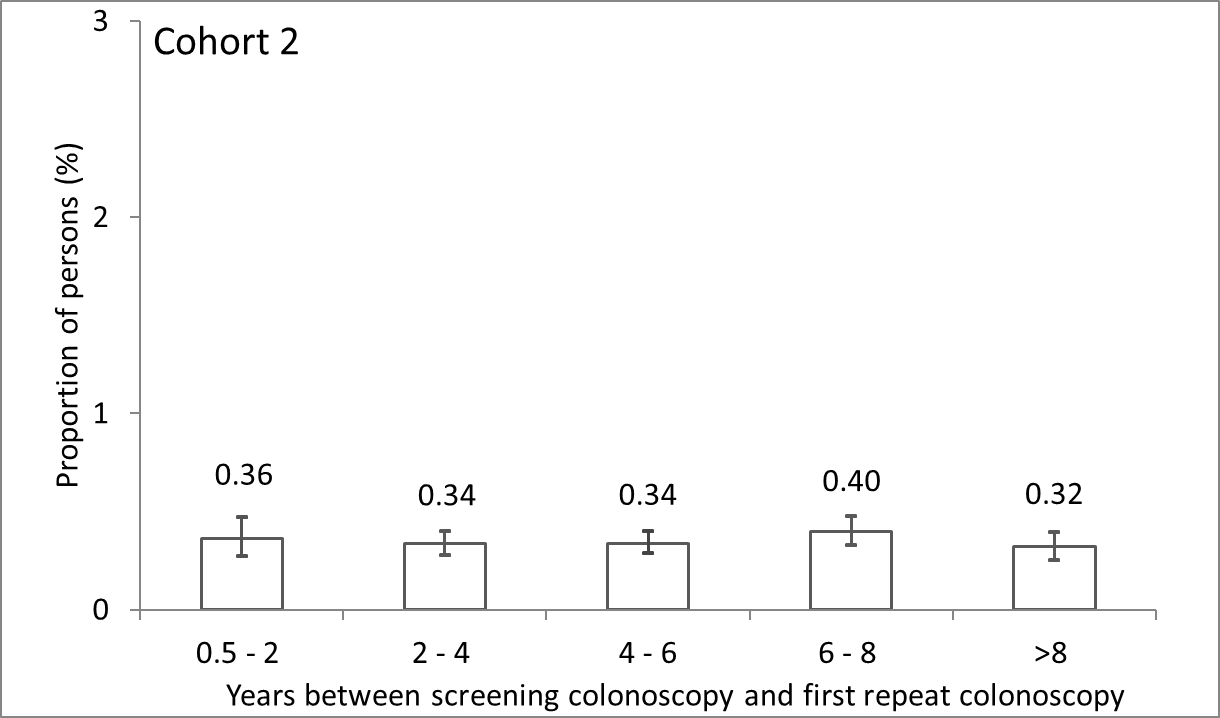
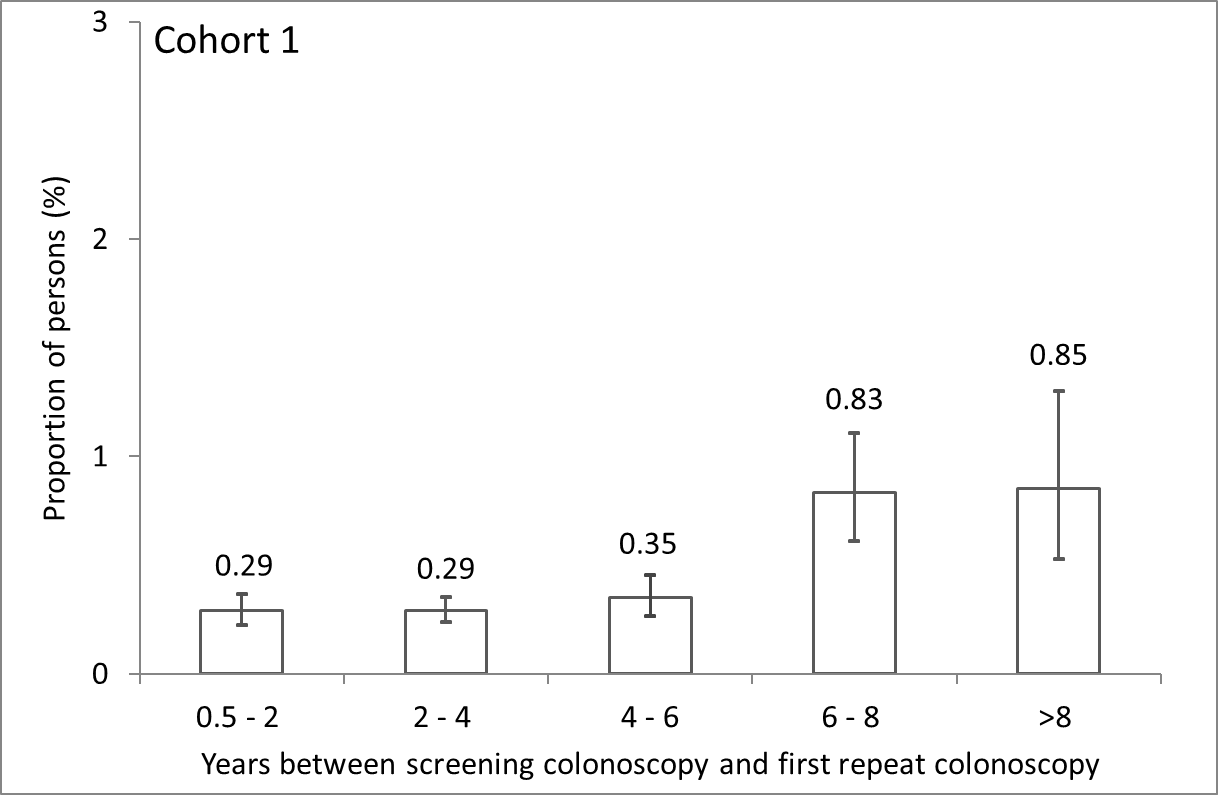
**Supplemental Digital Content 5.** Colorectal cancers (CRCs) diagnosed at first repeat colonoscopy per 10,000 person-years in cohort 1 and cohort 21, overall and according to site and stage of the CRCs, stratified by sex and age at first repeat colonoscopy.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Total | Site | | | Stage | |
| Proximal | Distal | Both/ Unknown | Non-advanced | Advanced |
| Cohort 1 (N=84,770)  Men  All age groups  55-<65 y.  65-<75 y.  75+ y.  Women  All 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)  Men  All age groups  55-<65 y.  65-<75 y.  75+ y.  Women  All 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) |

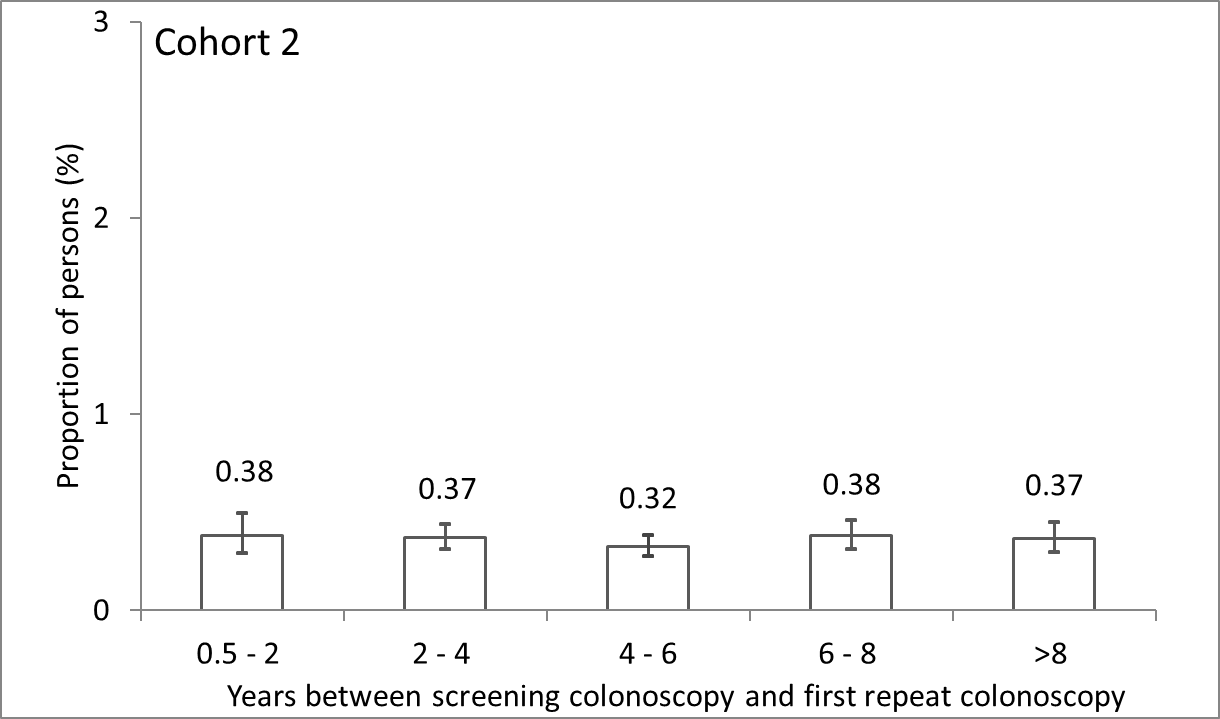
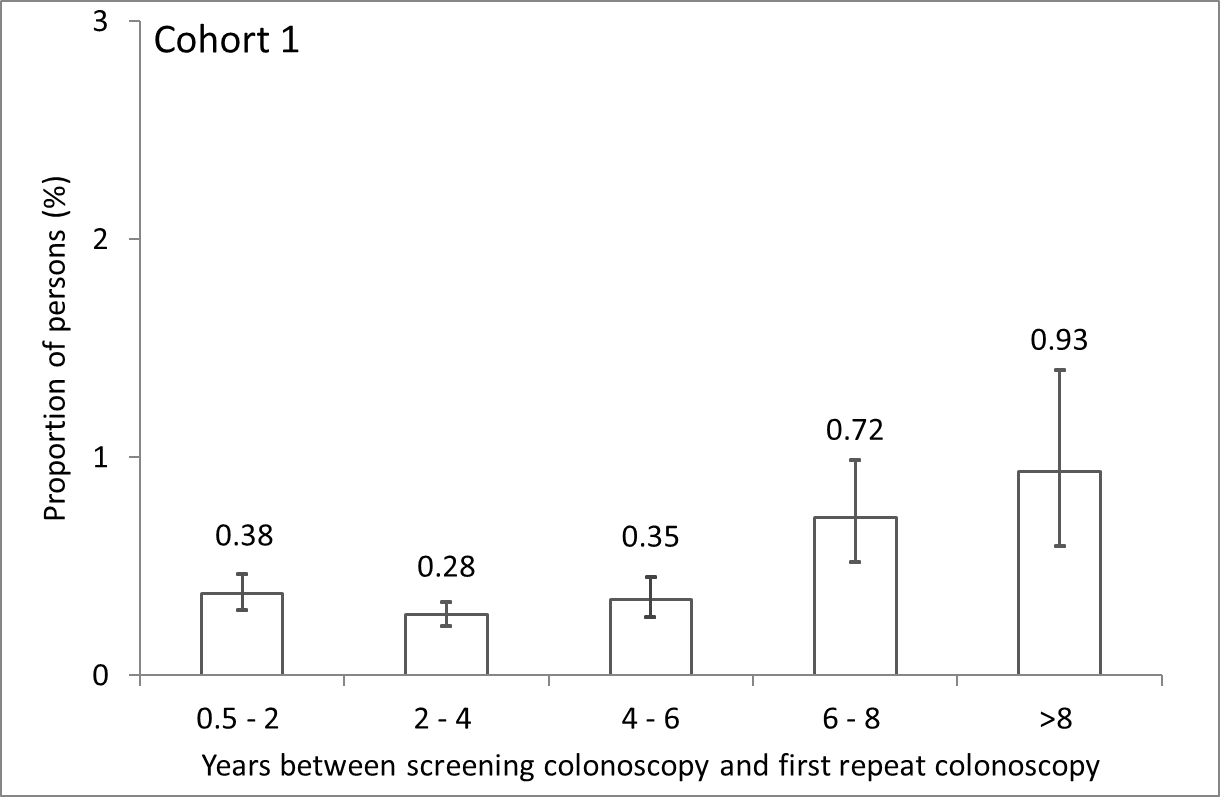
1 Cohort 1: persons with a snare polypectomy at baseline screening colonoscopy, cohort 2: persons without codes indicating polyps/polypectomy at baseline screening colonoscopy.

**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).

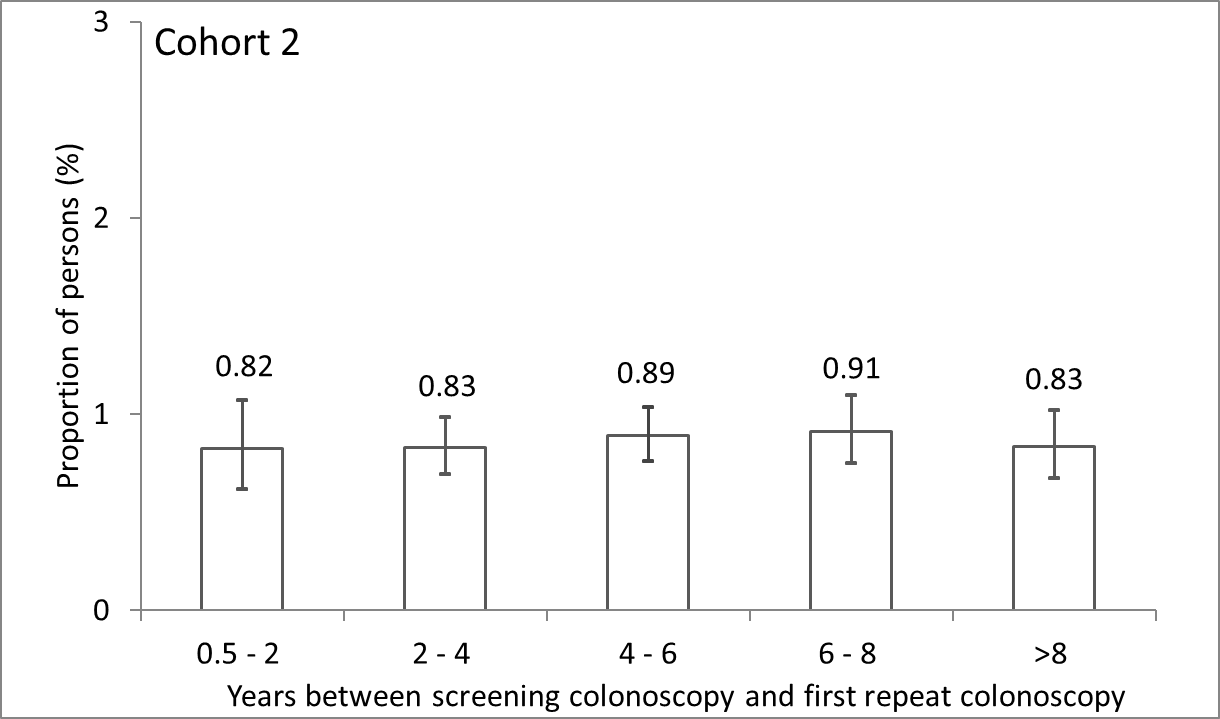
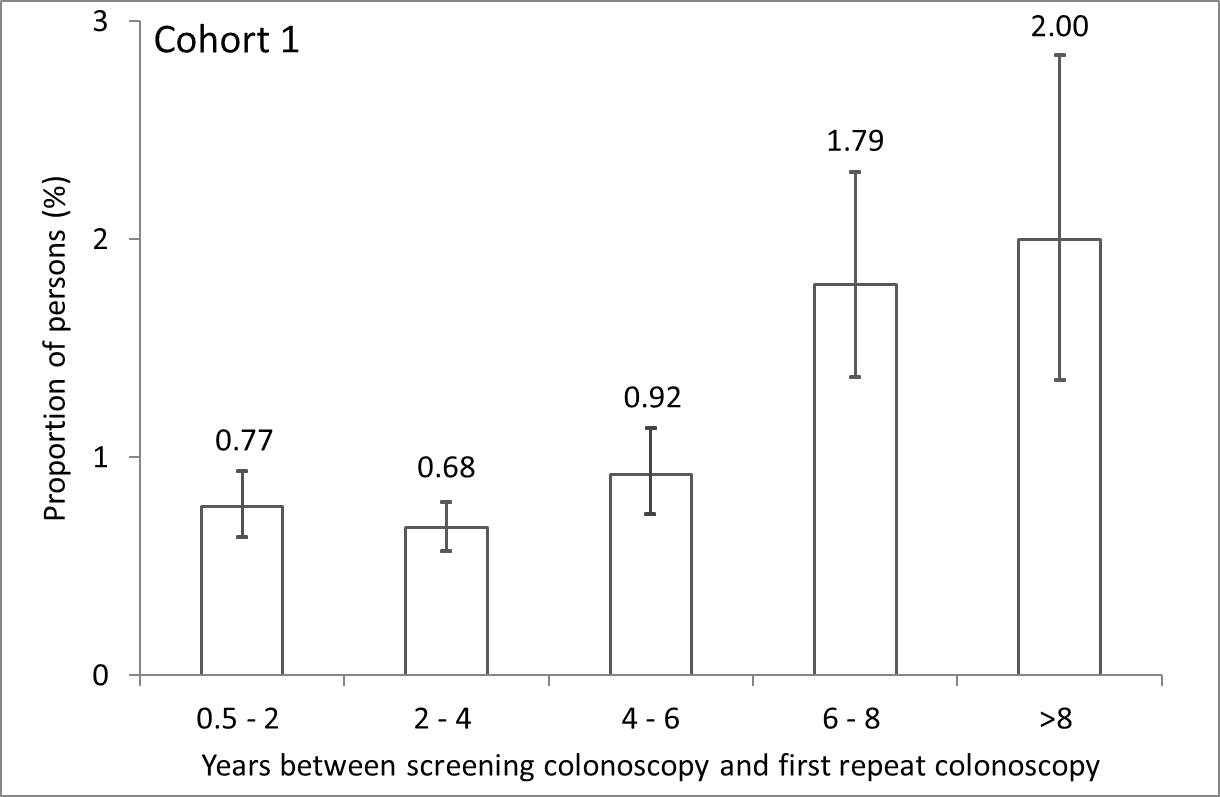
**A.** Proximal



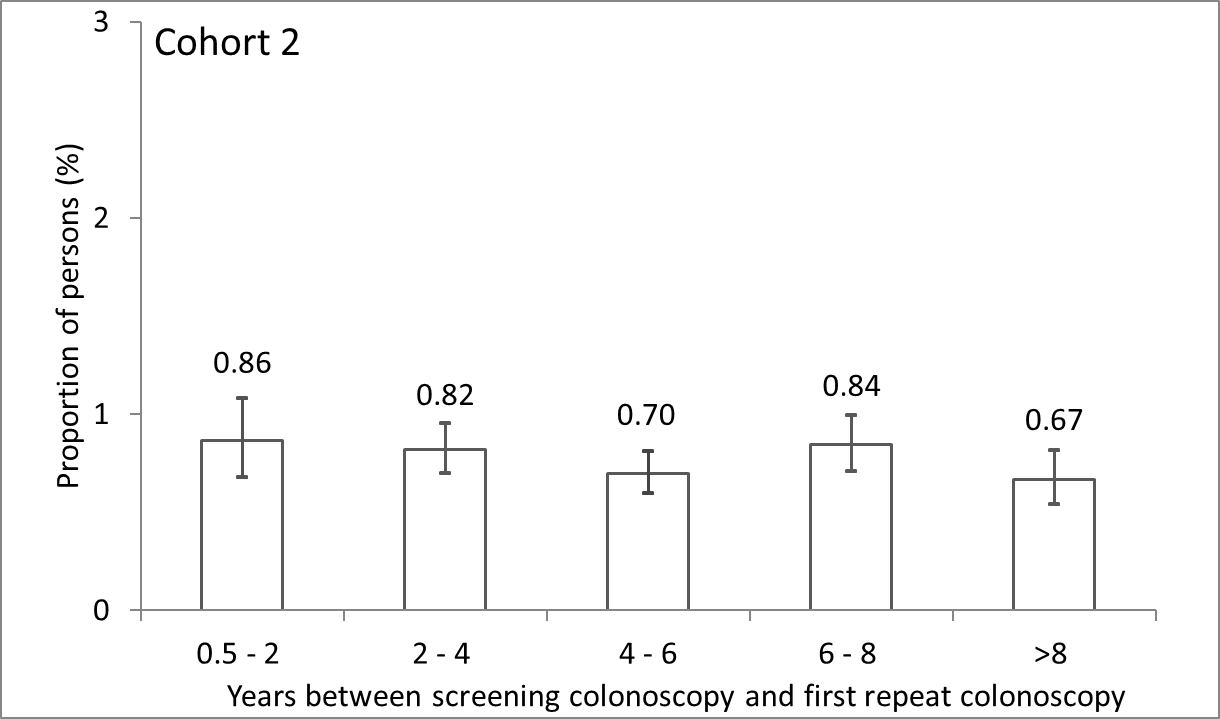
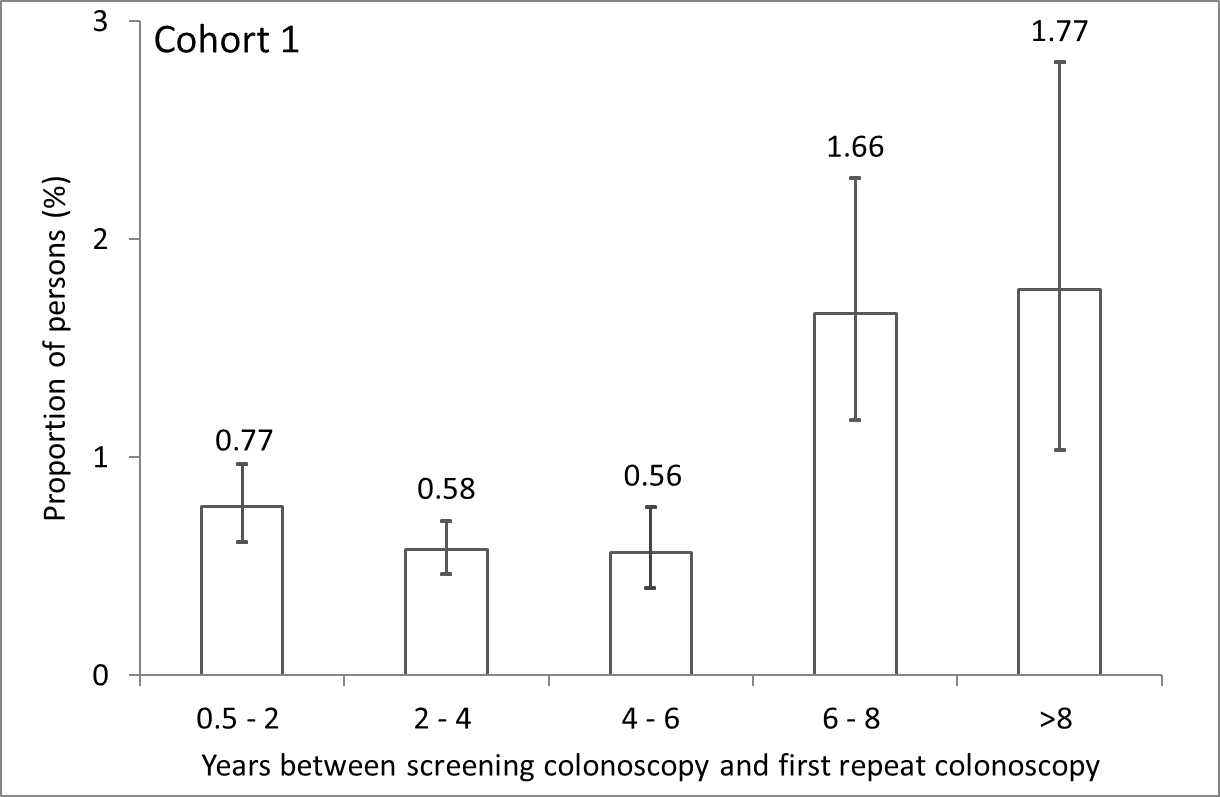
**B.** Distal



**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 |

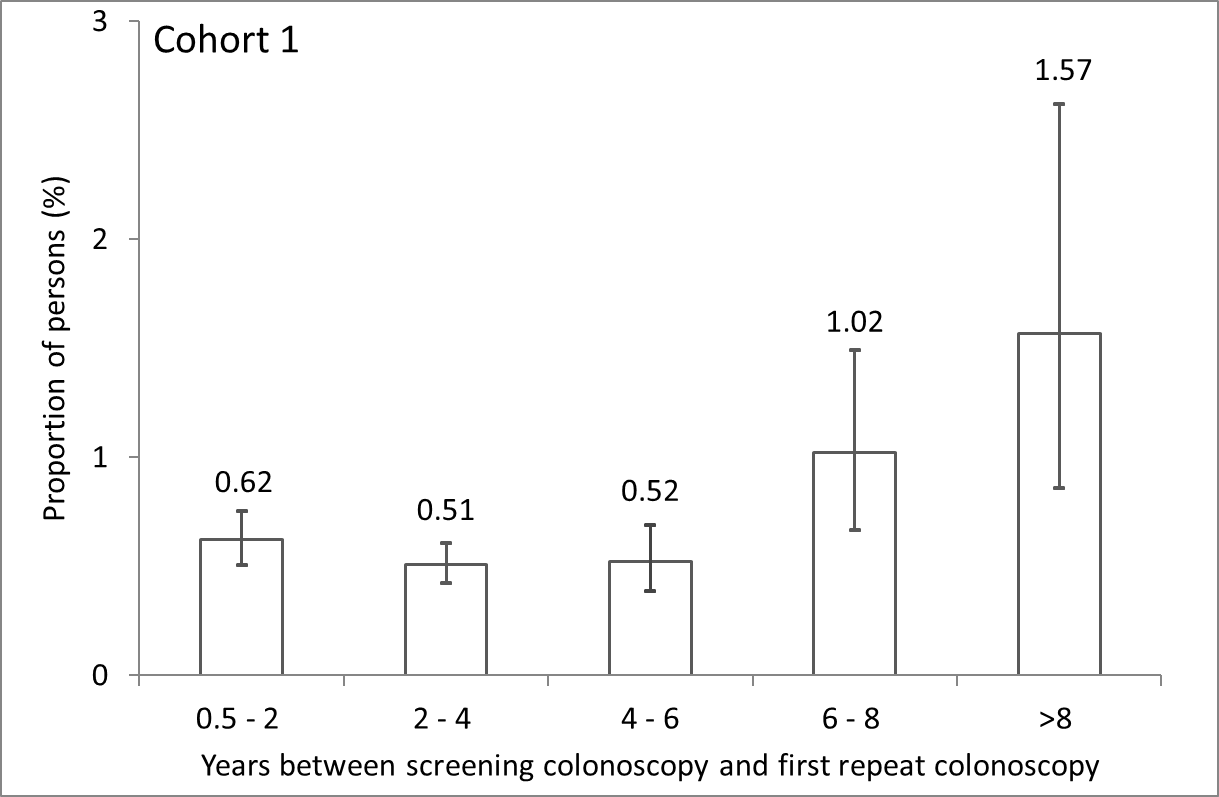
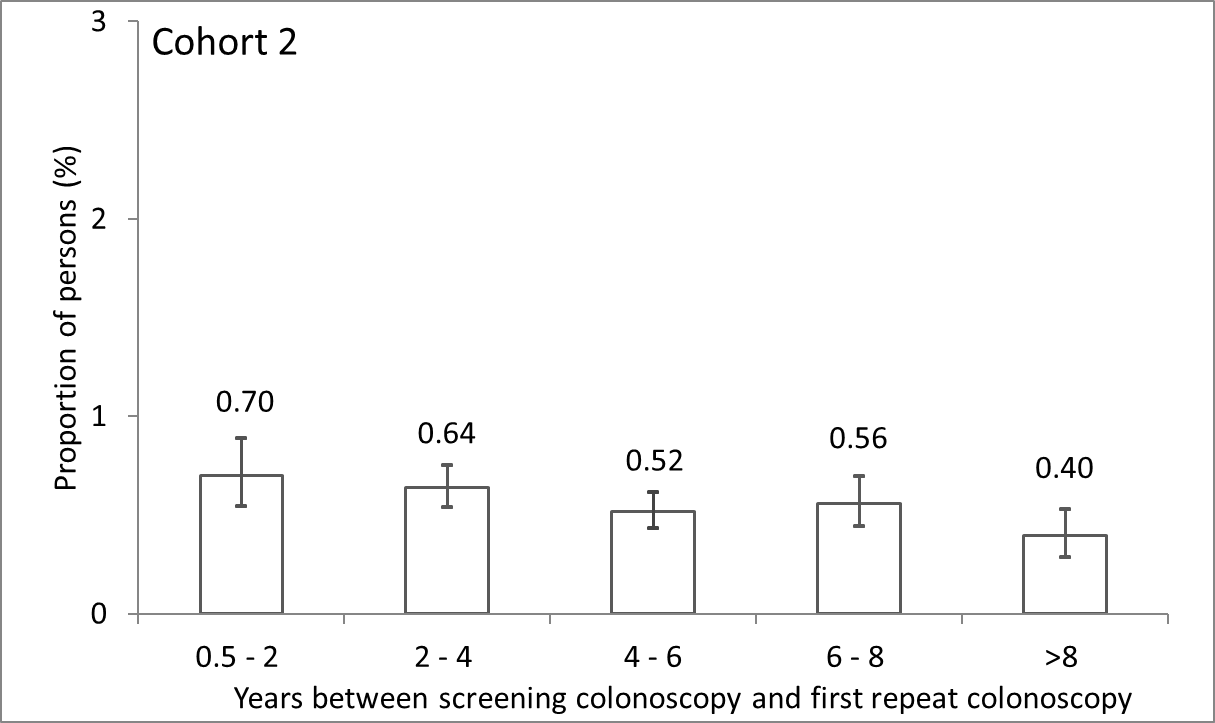
**B.** Proportion of males [%].

|  |  |  |
| --- | --- | --- |
| 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.