**Adenomas and Sessile Serrated Lesions in 45-49- Year-Old Individuals Undergoing Colonoscopy: A Systematic Review and Meta-Analysis**

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**Running title:** **Adenoma and SSLs in 45-49- Year-Old Individuals**

**Supplementary Figures:**

***Supplementary Figure 1-A:*** *Forest plots summarizing the pooled overall adenoma detection rate (ADR) in 45-49-year-old individuals undergoing colonoscopies for all indications in North America*



***Supplementary Figure 1-B:*** *Forest plots summarizing the pooled adenoma detection rate (ADR) in 45-49-year-old individuals undergoing colonoscopies for all indications in Asia.*



***Supplementary Figure 1-C:*** *Sensitivity analysis for the pooled overall adenoma detection rate (ADR) in 45-49-year-old individuals undergoing colonoscopies for all indications in the 45-49 age group.*



***Supplementary Figure 1-D:*** *Funnel plot for evaluation of publication bias in the pooled overall adenoma detection rate (ADR) in 45-49-year-old individuals undergoing colonoscopies for all indications.*



***Supplementary Figure 2:*** *Sensitivity analysis for the pooled overall sessile serrated lesions (SSLs) detection rate in 45-49-year-old individuals undergoing colonoscopies for all indications*



***Supplementary Figure 3:*** *Sensitivity analysis for pooled adenoma detection rate (ADR) in 45-49-year-old individuals undergoing screening colonoscopies.*



**Supplementary Tables:**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study / Year** | **Country** | **Study Period** | **Study Design** | **Number of patients / colonoscopies** | **Inclusion Criteria**  | **Exclusion Criteria** | **Primary outcome of study/Secondary outcomes**  |
| Hong 2010 | South Korea | 2005-2009 | Retrospective, single center | 568 (patients) | Asymptomatic average risk patients aged 40 to 59 years undergoing first screening colonoscopy.  | Individuals with a history of previous colonoscopy, sigmoidoscopy, or barium enema, incomplete questionnaire answers, incomplete colonoscopies; and individuals with personal or family history of CRC or IBD | - Prevalence and clinicopathological characteristics of colorectal neoplasms, with a specific focus on potentially premalignant adenomas.- Analyze risk factors associated with colorectal neoplasms, mainly advanced neoplasms as the primary target for screening. |
| Friedenberg 2013 | United States | 2007-2010 | Retrospective, single center | 304 (patients) | Complete screening colonoscopy examinations with good to excellent preparation in average-risk Black American or non-Hispanic White patients aged 45-49. | Patients who exhibit signs, symptoms of lower gastrointestinal bleeding, have a family history of CRC, prior history of a screening colonoscopy, colon adenomas, or IBD.  | Anatomic distribution of adenomas in average-risk Black and White patients, and the yield CRC screening in Black patients under the age of 50 years. |
| Xirasagar 2014 | United States | 2009-2010 | Retrospective, multicenter | 77 (patients) | US citizens, no health insurance, income equal to or less than 200% of the federal poverty limit, age eligibility (50–64 years for Whites without CRC family history, 45–49 years for Whites with a CRC family history, and 45–64 years for African Americans irrespective of family history), absence of gastrointestinal symptoms, and not being up to date with CRC screening | ADR, ADR among African Americans, advanced neoplasm rate, cancer rates, cecum intubation rate, adverse event rate, |
| Lee 2016 | South Korea | 2012-2014 | Retrospective, single center | 491 (patients) | Average- risk patients undergoing routine colonoscopy.  | Incomplete examinations, colonoscopies for surveillance or diagnostic indications, prior colonoscopy in the last 10 years, individuals with familial syndromes (such as hereditary nonpolyposis CRC or familial adenomatous polyposis), or IBD.  | Prevalence of any colorectal neoplasia, African American, advanced neoplasia (AN) including CRC, and clinically significant serrated polyps (CSSPs) in average-risk patients younger than 50 years of age, and comparison to asymptomatic average-risk screening patients aged 50 and older. |
| Hong 2018 | China | 2013-2014 | Retrospective, single center | 2565 (patients) | Patients aged 13 years and older undergoing either screening colonoscopy or colonoscopy for symptoms. | Colonoscopy within the past year, incomplete colonoscopy, inadequate bowel preparation, a history of CRC, individuals who have undergone prior colonic resection, therapeutic colonoscopy, or incomplete polyp details. | Prevalence and characteristicsof colonic polyps, adenoma, and advanced adenoma |
| Eberth 2018 | United States | 2014-1016 | Retrospective, multicenter | 47 (patients) | Cost-free colonoscopy screening for uninsured, asymptomatic individuals aged 50–64 (with eligibility extended to African Americans aged 45–64) living at or below 150% of the poverty line | Individuals with prior colonoscopy within the past 10 years, history of colorectal neoplasia, recent onset CRC-related symptoms, inherited CRC disorder, inflammatory bowel disease, or personal history of cancer (excluding non-melanoma skin cancer). | Overall PDR and ADT and stratified by patient characteristics.: |
| Chen 2019 | China | 2010-2018 | Retrospective, multicenter | 6141 (patients) | Patients under the age of 50 who had undergone colonoscopy.  | Patients who were under the age of 18, those diagnosed with CRC without polyps, individuals with a diagnosis of familial adenomatous polyposis orIBD, and those who underwent colonoscopy after bowel surgery. | Polyp location in colonoscopies among patients under the age of 50 and the correlation between polyp features and their respective locations. |
| Karsenti 2019 | France | 2016 | Retrospective, single center | 515 (patients) | All patients who were scheduled for colonoscopy. | Partial colonoscopy or interventional colonoscopy | ADR and advanced neoplasia detection rate (ANDR) based on age. |
| Bilal 2020 | United States | 2010-2017 | Retrospective, single center | 931 (patients) |  Patients undergoing their first colonoscopy | (i) Previous colonoscopies (ii) History of IBD(iii) History of FAP or hereditary non-polyposis colorectal cancer (HNPCC), (iv) Overt gastrointestinal bleeding upon hospital presentation, (v) Incomplete colonoscopies aborted before reaching the splenic flexure. | **Main:** ADR in patients aged 40-49 undergoing first colonoscopy.**Others:** - Compare ADR between patients with and without family history of first-degree relatives with CRC - Evaluate outcomes in patients without family history of CRC, aged 40-44 vs. 45-49.- Identify predictors of increased ADR in the 40-49 age group. |
| Butterly 2021 | United States | 2004-2018 | Retrospective, New Hampshire Colonoscopy Registry (NHCR) | 1869 (patients) | Average-risk individuals undergoing their first screening colonoscopy. | Colonoscopies for surveillance and diagnostic indications in individuals younger than 50 years, excluded individuals with familial syndromes, IBD, incomplete examinations, and poor bowel preparation. | The prevalence of any colorectal neoplasia, AA, AA including CRC, and CSSP) and compare these findings to asymptomatic average-risk patients aged 50 and older**.** |
| Imperiale 2021 | United States | 2018-2019 | Prospective, multicenter | 816 (patients) | Average risk individuals aged 45 to 49 years  | Exclude individuals with overt rectal bleeding, positive fecal occult blood test or fecal immunochemical test in the last 6 months, previous colonoscopy, recent double-contrast barium enema, CT colonography, or flexible sigmoidoscopy, prior colorectal resection, personal history of CRC or hereditary syndromes, history of aerodigestive tract cancer, two or more first-degree relatives with colorectal cancer, a first-degree relative diagnosed before age 60, family history of FAP or Lynch syndrome, Cronkhite–Canada Syndrome, and inflammatory bowel disease. | **Primary Outcome:**- Specificity of the mt-sDNA test for advanced colorectal neoplasia using colonoscopy as the reference standard.**Secondary Outcomes:**- Specificity for any precancerous lesion (both advanced and non-advanced). - Reporting advanced precancerous lesion sensitivity (APL) as a secondary outcome**.** |
| Bilal 2022 | United States | 2014-2020 | Retrospective, GI Quality Improvement Consortium (GIQuIC) database | 47,213 (colonoscopies) | Average-risk screening colonoscopies with adequate bowel preparation, and photo-documentation of the cecum among individuals aged 45–75 years. | N/A | ADR in men and women aged 45–49 undergoing screening colonoscopy and comparison with those aged 50–75. |
| Pang 2022 | Canada | 2014-2019 | Retrospective, single center | 1725 (patients) | Patients aged <50 years who underwent a colonoscopy.  |  - Adults >50 years of age at the time of colonoscopy, personal history of IBD or CRC, personal history of genetic cancer syndromes (e.g., familial adenomatous polyposis, Lynch syndrome, etc) and  incomplete colonoscopy. |  - Characterize the incidence, location, and histology of colorectal polyps in young adults aged <50 years. - Explore predictors of colorectal adenoma detection in this population. |
| Liang 2022 | United States | 2010-2020 | Retrospective, GI Quality Improvement Consortium (GIQuIC) database | 129,173 (colonoscopies) | Outpatient screening colonoscopies  | Procedures performed for indications other than screening, patients outside the age range of 18 to 89 years, inadequate bowel preparation, and procedures without reported photo documentation of the appendiceal orifice or terminal ileum, family history of CRC or advanced adenomas in a first-degree relative before age 60 years. |  **Primary Outcome:** - Prevalence of advanced neoplasia in age groups younger than 50 years. **Secondary Outcomes:** - Prevalence of adenomas (excluding SSLs). - Prevalence ratio of advanced neoplasia and adenomas compared with 50- to 54-year-olds undergoing screening. - Prevalence of advanced neoplasia and adenomas stratified by sex and race**.**- Predictors of advanced neoplasia and adenomas in those younger vs older than 50 years |
| Shaukat 2022 | United States | 2015-2019 | Retrospective, single center | 4841 (colonoscopies) | All screening colonoscopies. | Family history of CRC or advanced polyps. | - Assess ADR in men and women aged 45–49 during screening colonoscopy. - Compare ADR in the 45- to 49-year-old group with two other groups: 50- to 54-year-old and 50- to 75-year-old men and women from the same population.- Examine adenomas per colonoscopy and the detection rate of advanced neoplasia across these age groups. |
| Ladabaum 2022 | United States | 2017-2021 | Retrospective, multicenter (database study) | 391 (colonoscopies) | All screening colonoscopies | Cases with nonadherence to documentation requirements, no clear documentation of the examination extent to the cecum or a Boston Bowel Preparation Score ≥2 in each segment. | 1. Assess the impact of updated guidelines on screening colonoscopy volumes in 45- to 50-year-old patients.2. Compare detection rates in 45- to 50-year-old patients at first-time screening colonoscopy for SSL, advanced SSL, ADR, advanced ADR, APC in periods before and after new guidelines.3. Contextualize contemporary detection rates in 45- to 50-year-olds by comparing them with 50- to 54-year-olds and older individuals undergoing rescreening. |

*ADR: adenoma detection rate, PDR: polyp detection rates, AA; advanced adenoma, SSL: sessile serrated lesion, CRC: Colorectal cancer, IBD: inflammatory bowel disease, CCSP: clinically significant serrated polyps*

**Supplementary Table 1.** Baseline characteristics of included studies for patients who underwent colonoscopy in the 45-49 age group.

**AAs, African Americans; GI, Gastrointestinal; NR, not reported; CAD, computer aided detection.**

Search Strategy

Updated 10/10/2022

Databases:

1. Ovid Medline - 906
2. Embase - 2828
3. Scopus - 1773
4. Web of Science - 1026
5. Cochrane - 825
6. ClinicalTrials.gov - 338

**Searches executed:** 10/10/2022

**Total before duplicates removed:** 7696

**Total after duplicates removed:**  4335

Ovid Medline (906)

|  |  |  |
| --- | --- | --- |
| **#** | **Search Statement** | **Results** |
| 1 | exp Colonoscopy/ | 34067 |
| 2 | colonoscop\*.ti,ab,kw,kf. | 35400 |
| 3 | 1 or 2 | 50844 |
| 4 | ((adenoma or adenomas or (sessile serrated adj (lesion\* or polyp\*))) adj4 detect\*).ti,ab,kw,kf. | 3746 |
| 5 | age\*.ti,ab,kw,kf. | 4357846 |
| 6 | 3 and 4 and 5 | 906 |

Embase (2828)

|  |  |  |
| --- | --- | --- |
| **#** | **Search Statement** | **Results** |
| 1 | exp Colonoscopy/ | 96919 |
| 2 | colonoscop\*.ti,ab,kw,kf. | 71777 |
| 3 | 1 or 2 | 107378 |
| 4 | ((adenoma or adenomas or (sessile serrated adj (lesion\* or polyp\*))) adj4 detect\*).ti,ab,kw,kf. | 7724 |
| 5 | age\*.ti,ab,kw,kf. | 6355856 |
| 6 | 3 and 4 and 5 | 2828 |

Scopus (1773)

( ( INDEXTERMS ( colonoscopy ) ) OR ( TITLE-ABS-KEY ( colonoscop\* ) ) ) AND ( TITLE-ABS-KEY ( ( adenoma OR adenomas OR ( sessile AND serrated W/1 ( lesion\* OR polyp\* ) ) ) W/4 detect\* ) )

Web of Science (1026)

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years

|  |  |  |
| --- | --- | --- |
| **#** | **Results** | **Search Statement** |
| # 1 | 3271 | (ts=(colonoscop\*)) AND (ts=((adenoma or adenomas or (sessile serrated NEAR/1 (lesion\* or polyp\*))) NEAR/4 detect\*)) |

Cochrane (825)

|  |  |  |
| --- | --- | --- |
| **ID** | **Search** | **Hits** |
| #1 | MeSH descriptor: [Colonoscopy] explode all trees | 2293 |
| #2 | colonoscop\* | 8084 |
| #3 | #1 OR #2 | 8286 |
| #4 | ((adenoma or adenomas or (sessile serrated NEAR/1 (lesion\* or polyp\*))) NEAR/4 detect\*) | 1400 |
| #5 | age\* | 897114 |
| #6 | #3 AND #4 AND #5 | 827 |
|  | Limited to reviews, protocols, and trials | 825 |

ClinicalTrials.gov (338)

**Condition or Disease:** n/a

**Other terms:** age AND colonoscopy