**Incidence of and Risk Factors for Systemic Adverse Events after Screening or Primary Diagnostic Colonoscopy: A Nationwide Cohort Study**

supplemental digital content

Supplemental Methods:

Presentation of the SNDS databases

Descriptive statistics

Supplemental Table 1: Procedure codes for colonoscopies, from French medical classification of medical procedures

Supplemental Table 2: Procedure codes for major colic or rectal surgery procedures leading to exclusion, from French medical classification of medical procedures

Supplemental Table 3: ICD-10 codes for definition of adverse events

Supplemental Table 4a: Standardized incidence ratios (SIRs) of serious adverse events after colonoscopy.

Supplemental Table 4b: Standardized incidence ratios (SIRs) of serious adverse events after colonoscopy, in the further selected population excluding colonoscopies performed on day 2 of hospitalization or without identified bowel preparation.

Supplemental Table 5: Characteristics associated with cardiovascular adverse events: unadjusted logistic regression models (N = 4,088,799)

Supplemental Table 6: Characteristics associated with renal adverse events: unadjusted logistic regression models (N = 4,088,799)

Supplemental Table 7: Characteristics associated with myocardial infarction: sensitivity analysis using a broader definition for myocardial infarction (4,088,799 patients, including 476 with myocardial infarction)

Supplemental Table 8: Characteristics associated with acute renal failure: sensitivity analysis using a more stringent definition for acute renal failure (4,088,799 patients, including 522 with acute renal failure)

Supplemental Methods

*Presentation of the SNDS databases*

The study was conducted using French medical administrative databases SNDS (*Système National des Données de Santé*, National Heath Data System), consisting of individual data from both the SNIIRAM (*Système National d’Information Inter-Régime de l’Assurance Maladie*, National Health Insurance claims information system) and PMSI (*Programme de Médicalisation des Systèmes d’Information*, national hospital discharge database). These databases were linked by means of a unique anonymous number allocated to each individual, providing detailed information on health insurance claims for inpatient (PMSI) and outpatient (SNIIRAM) care for 99% of the population living in France (about 67,000,000 people). Further description of these databases and their use is available in English in the papers by Bezin et al.1 and Moulis et al.2, and more extensively in the paper by Tuppin et al.3.

The database contains data about all outpatient services reimbursed by National Health Insurance, including drugs, physician visits, and laboratory investigations, but does not provide any information about the medical indications. Patients with chronic diseases (LTD: long-term diseases), such as cancer or Crohn’s disease, are 100% reimbursed for their health expenditure, and the diagnosis is recorded (coded according to International Classification of Diseases (ICD)-10 codes4). The accuracy of medication use estimated on the basis of SNDS data has been previously investigated: drugs with the best agreements between SNDS data and patient interviews were antidiabetic and cardiovascular drugs (Kappa values >0.80)5; the sensitivity of drug exposure was 85.3% with a specificity of 91% for antithrombotics6.

The database also contains the procedures performed during all hospital stays (notably, colonoscopies), and the principal (DP), related (DR), and associated (DAS) diagnoses (coded according to ICD-10). DP and DR correspond to the diseases justifying admission to hospital, and DAS are comorbidities or adverse events treated during the hospitalization. In order to be recorded as a hospitalization diagnosis in the database (DP, DR, or DAS), the diagnosis therefore had to have an impact on medical care. Procedures are coded according to the French medical classification for clinical procedures (CCAM, *Classification commune des actes médicaux*7). The database does not contain any information about the inpatient or outpatient status, which cannot be deduced from other data. Drugs used during hospitalization (notably, those used for sedation) are not available, except for certain expensive drugs (such as some types of cancer chemotherapy). Dates available for hospital stays are admission date, discharge date, and procedure (e.g. colonoscopy) date. For the purposes of this study, admission date was used as an approximation for the SAE date.

Almost all persons living in France are covered by one of the various national health insurance schemes. Each national health insurance scheme reimburses almost all medical care (including colonoscopies) at the same rate for both public and private care. Persons with limited income or LTD are 100% reimbursed. The general scheme is the largest health insurance scheme in France (covering 76% of the population living in France). This scheme includes employed workers, retired, unemployed, and disadvantaged people. Follow-up of beneficiaries is stable, as people rarely leave this scheme. Other schemes (mainly farmers and self-employed) are more specific. The present study was restricted to the general scheme, as reliable information (notably on death date) for the entire study period is only available for this scheme.

SNDS data are commonly used for non-interventional studies in various conditions. To date, more than 400 published studies have used these databases3 (see for example8–15). These comprehensive national databases are powerful tools to assess the prevalence of rare events. As the primary purpose of these databases is financial, any false statements constitute serious frauds, liable to legal proceedings, which also tends to ensure the accuracy of the data recorded. Furthermore, quality controls and audits are performed before transmission to National Health Insurance (CNAM, *Caisse Nationale de l’Assurance Maladie*), mainly for processing of aberrant or missing data.

***Descriptive statistics***

Crude SAE rates per 10,000 colonoscopies were calculated by dividing the total numbers of adverse events by the total number of colonoscopies in the cohort. Standardized incidence ratios (SIRs) were calculated to compare these incidence rates with the incidence rates of these events in 2013 in the general population (general scheme beneficiaries aged 30 years and over, i.e. 32,490,167 individuals), which served as the reference group (reference rates were stratified by gender and 5-year age-groups). More precisely, SIRs were estimated by dividing the observed number of SAEs by the expected number of SAEs, obtained by applying the incidence rate observed in the general population (in this case, the general scheme beneficiaries) to the number of individuals in our cohort in each age and gender group considered. Crude 5-day and 30-day mortality rates per 1,000 SAE were calculated for each SAE by dividing the total numbers of deaths occurring within 5 or 30 days after a SAE by the total number of SAE in the cohort. Crude 5-day and 30-day mortality rates per 100,000 procedures were also calculated for each SAE by dividing the total numbers of deaths occurring within 5 or 30 days after a SAE by the total number of colonoscopies in the cohort. Crude odds ratios (OR) for each SAE studied were estimated by logistic regression models for patient, colonoscopy, endoscopist, and facility characteristics.

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Supplemental Table 1: Procedure codes for colonoscopies, from French medical classification of medical procedures.

|  |  |
| --- | --- |
| **Procedure code** | **Wording** |
| ***Incomplete colonoscopies*** | |
| Without polypectomy | |
| HHQE004 | Incomplete colonoscopy beyond the sigmoid colon |
| With polypectomy | |
| HHFE001 | Resection of 1 to 3 polyps less than 1 cm in diameter from the colon and/or rectum, by recto-sigmoidoscopy or incomplete colonoscopy |
| HHFE005 | Resection of a polyp larger than 1 cm in diameter or 4 or more polyps from the colon and/or rectum, by recto-sigmoidoscopy or incomplete colonoscopy |
| ***Complete colonoscopies*** | |
| Without polypectomy | |
| HHQE002 | Complete colonoscopy, beyond the ileocecal valve |
| HHQE005 | Complete colonoscopy with visualization of the base of the caecum, without crossing the ileocecal valve |
| With polypectomy | |
| HHFE002 | Resection of 1 to 3 polyps less than 1 cm in diameter from the colon and/or rectum, by complete colonoscopy |
| HHFE004 | Resection of a polyp larger than 1 cm in diameter or 4 or more polyps from the colon and/or rectum, by complete colonoscopy |

CCAM (*Classification Commune des Actes Médicaux*).

Supplemental Table 2: Procedure codes for major colic or rectal surgery procedures leading to exclusion, from French medical classification of medical procedures.

|  |  |
| --- | --- |
| **Procedure code** | **Wording** |
| HHCC007 | Cutaneous colostomy, by laparoscopy |
| HHCA002 | Cutaneous colostomy, by laparotomy |
| HHCC011 | Colocolostomy diversion [Colocolic anastomosis without colonic resection], by laparoscopy |
| HHCA003 | Colocolostomy diversion [Colocolic anastomosis without colonic resection], by laparotomy |
| HHFA026 | Right colectomy without restoration of continuity, by laparotomy |
| HHFA009 | Right colectomy with restoration of continuity, by laparotomy |
| HHFA008 | Right colectomy with restoration of continuity, by laparoscopy, or laparotomy with laparoscopic preparation |
| HHFA018 | Transverse colectomy, by laparotomy |
| HHFA023 | Transverse colectomy, by laparoscopy, or laparotomy with laparoscopic preparation |
| HHFA014 | Left hemicolectomy without release of splenic flexure, without restoration of continuity, by laparotomy |
| HHFA017 | Left hemicolectomy without release of splenic flexure, with restoration of continuity, by laparotomy |
| HHFA010 | Left hemicolectomy without release of splenic flexure, with restoration of continuity, by laparoscopy, or laparotomy with laparoscopic preparation |
| HHFA024 | Left hemicolectomy with release of splenic flexure, without restoration of continuity, by laparotomy |
| HHFA006 | Left hemicolectomy with release of splenic flexure, with restoration of continuity, by laparotomy |
| HHFA002 | Left hemicolectomy with release of splenic flexure, with restoration of continuity, by laparoscopy, or laparotomy with laparoscopic preparation |
| HHFA021 | Complete colectomy with preservation of the rectum, without restoration of continuity, by laparotomy |
| HHFA005 | Complete colectomy with preservation of the rectum, without restoration of continuity, by laparoscopy, or laparotomy with laparoscopic preparation |
| HHFA022 | Complete colectomy with preservation of the rectum, with ileorectal anastomosis, by laparotomy |
| HHFA004 | Complete colectomy with preservation of the rectum, with ileorectal anastomosis, by laparoscopy, or laparotomy with laparoscopic preparation |
| HJFC031 | Recto-sigmoid resection extending beyond the pouch of Douglas, without restoration of continuity, by laparoscopy |
| HJFA011 | Recto-sigmoid resection extending beyond the pouch of Douglas, without restoration of continuity, by laparotomy |
| HJFA002 | Recto-sigmoid resection with infraperitoneal colorectal anastomosis, by laparotomy |
| HJFA004 | Recto-sigmoid resection with infraperitoneal colorectal anastomosis, by laparoscopy, or by laparotomy with laparoscopic preparation |
| HJFA006 | Recto-sigmoid resection by laparotomy, with coloanal anastomosis by anal or trans-sphincter approach |
| HJFA017 | Laparoscopic or open recto-sigmoid resection with laparoscopic preparation, with coloanal anastomosis by anal approach |
| HJFA001 | Retrocolic resection with retrorectal lowering of the colon by laparotomy, with colorectal anastomosis by anal approach |
| HJFA005 | Amputation of the rectum, by perineal approach |
| HJFA007 | Amputation of the rectum, by laparotomy and perineal approach |
| HJFA019 | Amputation of the rectum, by laparoscopy, or laparotomy with preparation by laparoscopy and perineal approach |

CCAM (*Classification Commune des Actes Médicaux*).

Supplemental Table 3: ICD10 codes for definition of adverse events.

|  |  |
| --- | --- |
| **ICD10 code** | **Wording** |
| ***Cardiovascular adverse events*** | |
| Shock | |
| R57.0 | Cardiogenic shock |
| R57.1 | Hypovolemic shock |
| R57.9 | Shock, unspecified |
| Myocardial infarction | |
| I21 | Acute myocardial infarction |
| I22 | Subsequent myocardial infarction |
| Stroke | |
| I63 | Cerebral infarction |
| I64 | Stroke, not specified as hemorrhage or infarction |
| Pulmonary embolism | |
| I26 | Pulmonary embolism |
| ***Acute renal failure*** | |
| N17 | Acute renal failure |
| ***Urolithiasis*** | |
| N20 | Calculus of kidney and ureter |
| N21 | Calculus of lower urinary tract |
| N22 | Calculus of urinary tract in diseases classified elsewhere |
| N23 | Unspecified renal colic |

ICD10: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision.

Supplemental Table 4a: Standardized incidence ratios (SIRs) of serious adverse events after colonoscopy (n=4,088,799).

|  |  |  |
| --- | --- | --- |
|  | **SIR** | **95% CI** |
| **Cardiovascular adverse events** |  |  |
| shock | 15.8 | [14.9-16.7] |
| myocardial infarction | 3.3 | [3.0-3.7] |
| stroke | 5.1 | [4.7-5.5] |
| pulmonary embolism | 12.8 | [12.1-13.6] |
| **Renal adverse events** |  |  |
| acute renal failure | 11.8 | [11.4-12.3] |
| urolithiasis | 7.3 | [6.9-7.7] |

Standard population: general scheme beneficiaries aged 30 years and over.

CI: confidence interval.

Supplemental Table 4b: Rates and standardized incidence ratios (SIRs) of serious adverse events after colonoscopy, in the further selected population excluding colonoscopies performed on day 2 of hospitalization or without identified bowel preparation (n=3,549,206).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Number** | **per 10,000 procedures** | **SIR** | **95% CI** |
| **Cardiovascular adverse events** |  |  |  |  |
| shock | 116 | 0.33 | 1.9 | [1.6-2.3] |
| myocardial infarction | 136 | 0.38 | 1.5 | [1.3-1.8] |
| stroke | 214 | 0.60 | 1.8 | [1.6-2.1] |
| pulmonary embolism | 378 | 1.1 | 5.0 | [4.6-5.6] |
| **Renal adverse events** |  |  |  |  |
| acute renal failure | 316 | 0.89 | 2.1 | [1.8-2.3] |
| urolithiasis | 924 | 2.6 | 5.6 | [5.3-6.0] |

Standard population: general scheme beneficiaries aged 30 years and over.

CI: confidence interval.

Patients excluded from this analysis were older (14.3% aged 80 or older) and had a higher number of pre-existing conditions (27.9% with a Charlson index score ≥2).

Supplemental Table 5: Characteristics associated with cardiovascular adverse events: unadjusted logistic regression models (N = 4,088,799).

|  | **Shock** | |  | **Myocardial infarction** | |  | **Stroke** | |  | **Pulmonary embolism** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |
| ***Year*** |  |  |  |  |  |  |  |  |  |  |  |
| 2010 | 1.13 [0.93-1.38] | 0.23 |  | 1.01 [0.73-1.40] | 0.93 |  | 1.39 [1.1-1.74] | 0.005 |  | 1.14 [0.94-1.37] | 0.18 |
| 2011 | 1.00 [0.82-1.23] | 1.00 |  | 0.76 [0.54-1.08] | 0.13 |  | 1.10 [0.87-1.4] | 0.42 |  | 0.98 [0.81-1.19] | 0.83 |
| 2012 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| 2013 | 1.26 [1.04-1.53] | 0.02 |  | 0.86 [0.61-1.21] | 0.38 |  | 1.08 [0.84-1.38] | 0.56 |  | 1.01 [0.83-1.23] | 0.94 |
| 2014 | 1.05 [0.85-1.29] | 0.64 |  | 0.72 [0.50-1.04] | 0.083 |  | 1.04 [0.81-1.34] | 0.74 |  | 1.03 [0.84-1.26] | 0.77 |
| 2015 | 1.31 [1.07-1.61] | 0.009 |  | 0.85 [0.59-1.23] | 0.39 |  | 0.74 [0.55-0.98] | 0.037 |  | 1.05 [0.85-1.29] | 0.65 |
| **Patient characteristics** |  |  |  |  |  |  |  |  |  |  |  |
| ***Sex*** |  |  |  |  |  |  |  |  |  |  |  |
| male | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| female | 0.45 [0.40-0.50] | <.0001 |  | 0.38 [0.31-0.48] | <.0001 |  | 0.68 [0.59-0.79] | <.0001 |  | 0.85 [0.76-0.96] | 0.0062 |
| ***Age*** |  |  |  |  |  |  |  |  |  |  |  |
| 30-39 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| 40-49 | 0.96 [0.66-1.40] | 0.85 |  | 4.77 [1.46-15.5] | 0.0096 |  | 1.54 [0.73-3.22] | 0.25 |  | 1.57 [1.10-2.25] | 0.013 |
| 50-59 | 1.20 [0.85-1.69] | 0.31 |  | 5.91 [1.86-18.8] | 0.0026 |  | 3.28 [1.66-6.47] | 0.0006 |  | 1.44 [1.02-2.04] | 0.041 |
| 60-69 | 1.97 [1.41-2.74] | <.0001 |  | 8.81 [2.79-27.8] | 0.0002 |  | 5.45 [2.79-10.7] | <.0001 |  | 1.88 [1.34-2.64] | 0.0003 |
| 70-79 | 3.93 [2.83-5.47] | <.0001 |  | 15.1 [4.78-47.8] | <.0001 |  | 14.0 [7.19-27.2] | <.0001 |  | 4.64 [3.32-6.49] | <.0001 |
| 80 and older | 13.6 [9.78-19.0] | <.0001 |  | 50.1 [15.8-158] | <.0001 |  | 43.3 [22.2-84.3] | <.0001 |  | 11.4 [8.10-16.1] | <.0001 |
| ***Pre-existing conditions*** |  |  |  |  |  |  |  |  |  |  |  |
| myocardial infarction | 10.7 [9.41-12.1] | <.0001 |  | 74.6 [58.8-94.7] | <.0001 |  | 4.90 [4.04-5.95] | <.0001 |  | 2.59 [2.13-3.15] | <.0001 |
| congestive heart failure | 33.4 [29.5-37.9] | <.0001 |  | 26.8 [21.2-33.8] | <.0001 |  | 16.1 [13.4-19.3] | <.0001 |  | 8.60 [7.15-10.4] | <.0001 |
| peripheral vascular disease | 14.4 [12.7-16.2] | <.0001 |  | 21.0 [17.0-25.9] | <.0001 |  | 7.35 [6.15-8.77] | <.0001 |  | 3.46 [2.88-4.17] | <.0001 |
| cerebrovascular disease | 9.18 [7.84-10.8] | <.0001 |  | 5.79 [4.14-8.11] | <.0001 |  | 241 [199-291] | <.0001 |  | 3.77 [3.02-4.70] | <.0001 |
| dementia | 8.81 [6.68-11.6] | <.0001 |  | 7.50 [4.39-12.8] | <.0001 |  | 15.7 [12.1-20.5] | <.0001 |  | 8.12 [6.11-10.8] | <.0001 |
| chronic pulmonary disease | 2.43 [2.15-2.75] | <.0001 |  | 1.79 [1.42-2.27] | <.0001 |  | 1.68 [1.42-1.98] | <.0001 |  | 1.73 [1.52-1.98] | <.0001 |
| connective tissue disease | 2.53 [1.83-3.50] | <.0001 |  | 2.16 [1.15-4.04] | 0.017 |  | 1.19 [0.67-2.11] | <.0001 |  | 2.55 [1.85-3.50] | <.0001 |
| ulcer disease | 8.75 [7.39-10.4] | <.0001 |  | 3.19 [2.01-5.06] | <.0001 |  | 3.22 [2.35-4.41] | <.0001 |  | 3.19 [2.47-4.11] | <.0001 |
| moderate or severe renal disease | 46.3 [41.1-52.2] | <.0001 |  | 20.3 [15.6-26.4] | <.0001 |  | 16.2 [13.3-19.6] | <.0001 |  | 9.22 [7.63-11.2] | <.0001 |
| hemiplegia | 10.2 [7.98-13.0] | <.0001 |  | 7.67 [4.64-12.7] | <.0001 |  | 49.7 [42.0-58.8] | <.0001 |  | 4.69 [3.32-6.63] | <.0001 |
| HIV/AIDS | 2.94 [1.58-5.48] | 0.0007 |  | 2.86 [0.92-8.92] | 0.07 |  | 2.23 [0.93-5.38] | 0.073 |  | 3.76 [2.17-6.49] | <.0001 |
| liver disease | 8.09 [6.84-9.57] | <.0001 |  | 2.72 [1.69-4.37] | <.0001 |  | 2.54 [1.82-3.55] | <.0001 |  | 2.88 [2.24-3.72] | <.0001 |
| *mild liver disease* | 4.64 [3.63-5.93] | <.0001 |  | 3.02 [1.80-5.07] | <.0001 |  | 2.07 [1.35-3.16] | 0.0008 |  | 2.20 [1.58-3.06] | <.0001 |
| *moderate or severe liver disease* | 18.5 [14.9-22.9] | <.0001 |  | 1.81 [0.58-5.65] | 0.31 |  | 3.95 [2.33-6.70] | <.0001 |  | 4.94 [3.37-7.24] | <.0001 |
| diabetes | 3.88 [3.41-4.41] | <.0001 |  | 3.91 [3.10-4.92] | <.0001 |  | 4.20 [3.60-4.91] | <.0001 |  | 2.10 [1.80-2.44] | <.0001 |
| *diabetes without end-organ damage* | 1.70 [1.40-2.05] | <.0001 |  | 1.40 [0.97-2.04] | 0.074 |  | 1.41 [1.09-1.82] | 0.0093 |  | 1.79 [1.51-2.12] | <.0001 |
| *diabetes with end-organ damage* | 18.6 [15.9-21.7] | <.0001 |  | 20.7 [15.8-27.0] | <.0001 |  | 23.0 [19.3-27.5] | <.0001 |  | 4.16 [3.15-5.50] | <.0001 |
| cancera | 3.34 [2.94-3.80] | <.0001 |  | 2.31 [1.79-2.98] | <.0001 |  | 2.64 [2.23-3.12] | <.0001 |  | 4.04 [3.58-4.57] | <.0001 |
| *non metastatic cancerb* | 2.78 [2.41-3.20] | <.0001 |  | 2.16 [1.65-2.82] | <.0001 |  | 2.22 [1.85-2.67] | <.0001 |  | 2.93 [2.55-3.37] | <.0001 |
| *metastatic solid tumor* | 10.8 [8.50-13.7] | <.0001 |  | 4.32 [2.30-8.11] | <.0001 |  | 8.12 [5.87-11.2] | <.0001 |  | 18.8 [15.6-22.7] | <.0001 |

Supplemental Table 5: Characteristics associated with cardiovascular adverse events: unadjusted logistic regression models (N = 4,088,799) (continued).

|  | **Shock** | |  | **Myocardial infarction** | |  | **Stroke** | |  | **Pulmonary embolism** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |
| **Patient characteristics (continued)** |  |  |  |  |  |  |  |  |  |  |  |
| ***Charlson index*** |  |  |  |  |  |  |  |  |  |  |  |
| 0 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| 1 | 4.34 [3.50-5.39] | <.0001 |  | 3.42 [2.49-4.68] | <.0001 |  | 11.7 [8.66-15.8] | <.0001 |  | 2.08 [1.75-2.47] | <.0001 |
| ≥2 | 22.7 [19.3-26.8] | <.0001 |  | 10.2 [7.92-13.0] | <.0001 |  | 42.7 [32.7-55.8] | <.0001 |  | 6.49 [5.72-7.36] | <.0001 |
| ***Medical history of urolithiasis*** |  |  |  |  |  |  |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| yes | 1.23 [0.73-2.09] | 0.43 |  | 1.44 [0.6-3.47] | 0.42 |  | 1.07 [0.54-2.15] | 0.84 |  | 0.60 [0.29-1.26] | 0.1795 |
| ***Previous treatment (during previous 6 months)*** |  |  |  |  |  |  |  |  |  |  |  |
| antiplatelet drugs | 4.85 [4.32-5.45] | <.0001 |  | 6.84 [5.56-8.42] | <.0001 |  | 7.61 [6.60-8.78] | <.0001 |  | 2.05 [1.79-2.34] | <.0001 |
| anticoagulants | 8.96 [7.92-10.1] | <.0001 |  | 3.43 [2.57-4.57] | <.0001 |  | 8.64 [7.41-10.1] | <.0001 |  | 22.5 [20.0-25.2] | <.0001 |
| **Colonoscopy characteristics** |  |  |  |  |  |  |  |  |  |  |  |
| ***Bowel preparation*** |  |  |  |  |  |  |  |  |  |  |  |
| polyethylene glycol | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| phosphate preparation | 0.69 [0.41-1.15] | 0.16 |  | 0.74 [0.45-1.21] | 0.23 |  | 0.62 [0.42-0.92] | 0.016 |  | 0.47 [0.34-0.66] | <.0001 |
| magnesium preparation | 0.78 [0.52-1.16] | 0.22 |  | 0.79 [0.54-1.17] | 0.25 |  | 0.53 [0.38-0.74] | 0.0002 |  | 0.61 [0.48-0.77] | <.0001 |
| not retrieved | 50.3 [40.8-61.9] | <.0001 |  | 9.66 [7.61-12.3] | <.0001 |  | 12.7 [10.8-15.1] | <.0001 |  | 10.5 [9.20-11.9] | <.0001 |
| ***Polypectomy*** |  |  |  |  |  |  |  |  |  |  |  |
| no polypectomy | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| polyp <1 cm | 0.15 [0.12-0.20] | <.0001 |  | 0.46 [0.35-0.62] | <.0001 |  | 0.62 [0.51-0.74] | <.0001 |  | 0.44 [0.37-0.52] | <.0001 |
| polyp >1 cm | 0.65 [0.49-0.87] | 0.0032 |  | 0.91 [0.57-1.45] | 0.70 |  | 1.30 [0.98-1.72] | 0.066 |  | 0.92 [0.71-1.18] | 0.51 |
| ***Sedation*** |  |  |  |  |  |  |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| yes | 0.04 [0.04-0.05] | <.0001 |  | 0.08 [0.06-0.10] | <.0001 |  | 0.13 [0.11-0.16] | <.0001 |  | 0.17 [0.14-0.20] | <.0001 |
| ***Complete colonoscopy*** |  |  |  |  |  |  |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| yes | 0.05 [0.05-0.06] | <.0001 |  | 0.09 [0.07-0.11] | <.0001 |  | 0.14 [0.11-0.16] | <.0001 |  | 0.16 [0.14-0.19] | <.0001 |

Supplemental Table 5: Characteristics associated with cardiovascular adverse events: unadjusted logistic regression models (N = 4,088,799) (continued).

|  | **Shock** | |  | **Myocardial infarction** | |  | **Stroke** | |  | **Pulmonary embolism** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |  | **OR [95% CI]** | **p value** |
| **Endoscopist characteristics** |  |  |  |  |  |  |  |  |  |  |  |
| ***Number of years since MD graduation*** |  |  |  |  |  |  |  |  |  |  |  |
| <5 | *included in the next modality* |  |  | 0.89 [0.12-6.46] | 0.91 |  | 1.19 [0.29-4.88] | 0.81 |  | 1.08 [0.34-3.41] | 0.89 |
| 5-14 | 1.01 [0.60-1.71] | 0.96 |  | 0.91 [0.50-1.67] | 0.76 |  | 1.62 [1.07-2.43] | 0.021 |  | 1.21 [0.86-1.72] | 0.28 |
| 15-24 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| 25-34 | 1.25 [0.88-1.78] | 0.22 |  | 0.96 [0.64-1.44] | 0.84 |  | 1.08 [0.78-1.50] | 0.65 |  | 0.88 [0.67-1.14] | 0.33 |
| ≥35 | 0.81 [0.44-1.49] | 0.50 |  | 1.41 [0.82-2.44] | 0.21 |  | 1.40 [0.90-2.19] | 0.14 |  | 0.97 [0.65-1.44] | 0.87 |
| not retrieved | 19.8 [14.8-26.3] | <.0001 |  | 5.45 [3.91-7.59] | <.0001 |  | 8.72 [6.7-11.36] | <.0001 |  | 8.50 [6.92-10.4] | <.0001 |
| ***Number of procedures performed during the previous year*** |  |  |  |  |  |  |  |  |  |  |  |
| <150 | 0.67 [0.15-2.94] | 0.59 |  | 1.80 [0.64-5.05] | 0.26 |  | 1.62 [0.76-3.46] | 0.21 |  | 1.25 [0.57-2.72] | 0.58 |
| 150-299 | 1.03 [0.48-2.22] | 0.95 |  | 1.01 [0.45-2.26] | 0.97 |  | 0.88 [0.49-1.58] | 0.66 |  | 1.04 [0.62-1.76] | 0.89 |
| 300-599 | 1.29 [0.73-2.27] | 0.39 |  | 0.89 [0.48-1.63] | 0.70 |  | 0.68 [0.44-1.06] | 0.092 |  | 1.04 [0.70-1.54] | 0.86 |
| 600-999 | 0.92 [0.51-1.66] | 0.78 |  | 0.85 [0.46-1.57] | 0.59 |  | 0.74 [0.48-1.16] | 0.19 |  | 0.76 [0.50-1.14] | 0.18 |
| ≥1,000 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| not retrieved | 19.7 [11.6-33.4] | <.0001 |  | 4.89 [2.80-8.56] | <.0001 |  | 5.83 [3.93-8.64] | <.0001 |  | 8.15 [5.67-11.73] | <.0001 |
| **Hospital/clinic characteristics** |  |  |  |  |  |  |  |  |  |  |  |
| ***Type of health facility*** |  |  |  |  |  |  |  |  |  |  |  |
| for-profit private clinic | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |
| not-for-profit private clinic | 4.69 [3.60-6.12] | <.0001 |  | 2.11 [1.38-3.23] | 0.0005 |  | 1.51 [1.04-2.19] | 0.030 |  | 2.71 [2.11-3.47] | <.0001 |
| local public hospital | 13.3 [11.2-15.8] | <.0001 |  | 5.06 [3.96-6.47] | <.0001 |  | 6.59 [5.52-7.87] | <.0001 |  | 7.59 [6.56-8.79] | <.0001 |
| university public hospital | 63.8 [53.3-76.4] | <.0001 |  | 16.5 [12.4-22.0] | <.0001 |  | 27.9 [23.1-33.8] | <.0001 |  | 29.6 [25.3-34.7] | <.0001 |
| ***Number of procedures performed in the facility each year*** |  |  |  |  |  |  |  |  |  |  |  |
| <400 | 3.79 [3.07-4.67] | <.0001 |  | 3.42 [2.24-5.22] | <.0001 |  | 4.05 [3.10-5.31] | <.0001 |  | 4.68 [3.75-5.84] | <.0001 |
| 400-2000 | 0.84 [0.70-1.00] | 0.055 |  | 0.98 [0.68-1.40] | 0.90 |  | 0.86 [0.68-1.09] | 0.21 |  | 0.96 [0.78-1.17] | 0.66 |
| 2000-4999 | 0.23 [0.19-0.29] | <.0001 |  | 0.44 [0.30-0.65] | <.0001 |  | 0.37 [0.28-0.48] | <.0001 |  | 0.40 [0.32-0.49] | <.0001 |
| ≥5000 | 1.00 |  |  | 1.00 |  |  | 1.00 |  |  | 1.00 |  |

OR [95% CI]: Odds ratio (95% confidence interval).

a except non-melanoma skin cancer

b including lymphoma and leukemia

Supplemental Table 6: Characteristics associated with renal adverse events: unadjusted logistic regression models (N = 4,088,799).

|  | **Acute renal failure** | |  | **Urolithiasis** | |
| --- | --- | --- | --- | --- | --- |
|  | **OR [95%CI]** | **p value** |  | **OR [95%CI]** | **p value** |
| ***Year*** |  |  |  |  |  |
| 2010 | 1.31 [1.15-1.51] | <.0001 |  | 1.31 [1.10-1.55] | 0.0016 |
| 2011 | 1.15 [1.00-1.33] | 0.045 |  | 1.35 [1.14-1.60] | 0.0004 |
| 2012 | 1.00 |  |  | 1.00 |  |
| 2013 | 1.11 [0.96-1.29] | 0.14 |  | 0.86 [0.71-1.04] | 0.13 |
| 2014 | 1.07 [0.92-1.24] | 0.37 |  | 0.79 [0.65-0.97] | 0.024 |
| 2015 | 1.09 [0.93-1.27] | 0.27 |  | 0.73 [0.59-0.90] | 0.0041 |
| **Patient characteristics** |  |  |  |  |  |
| ***Sex*** |  |  |  |  |  |
| male | 1.00 |  |  | 1.00 |  |
| female | 0.49 [0.45-0.54] | <.0001 |  | 0.47 [0.42-0.52] | <.0001 |
| ***Age*** |  |  |  |  |  |
| 30-39 | 1.00 |  |  | 1.00 |  |
| 40-49 | 1.24 [0.91-1.69] | 0.17 |  | 1.14 [0.91-1.44] | 0.24 |
| 50-59 | 1.66 [1.25-2.22] | 0.0005 |  | 1.04 [0.84-1.30] | 0.68 |
| 60-69 | 3.04 [2.30-4.02] | <.0001 |  | 0.96 [0.77-1.20] | 0.77 |
| 70-79 | 5.87 [4.44-7.76] | <.0001 |  | 0.95 [0.74-1.21] | 0.69 |
| 80 and older | 19.6 [14.8-26.0] | <.0001 |  | 1.56 [1.17-2.09] | 0.002 |
| ***Pre-existing conditions*** |  |  |  |  |  |
| myocardial infarction | 7.78 [7.06-8.58] | <.0001 |  | 1.52 [1.21-1.91] | 0.0003 |
| congestive heart failure | 28.4 [25.9-31.1] | <.0001 |  | 2.30 [1.69-3.13] | <.0001 |
| peripheral vascular disease | 11.3 [10.3-12.4] | <.0001 |  | 1.74 [1.38-2.20] | <.0001 |
| cerebrovascular disease | 7.91 [7.02-8.91] | <.0001 |  | 1.46 [1.07-2.00] | 0.020 |
| dementia | 9.96 [8.26-12.0] | <.0001 |  | 2.18 [1.33-3.56] | 0.002 |
| chronic pulmonary disease | 2.16 [1.97-2.36] | <.0001 |  | 1.12 [0.97-1.29] | 0.10 |
| connective tissue disease | 2.45 [1.93-3.10] | <.0001 |  | 1.16 [0.75-1.79] | 0.50 |
| ulcer disease | 6.04 [5.25-6.95] | <.0001 |  | 2.11 [1.58-2.80] | <.0001 |
| moderate or severe renal disease | 82.8 [76.2-90.0] | <.0001 |  | 2.70 [1.99-3.66] | <.0001 |
| hemiplegia | 10.5 [8.88-12.5] | <.0001 |  | 2.18 [1.37-3.47] | 0.001 |
| HIV/AIDS | 3.92 [2.66-5.78] | <.0001 |  | 2.99 [1.69-5.28] | 0.0002 |
| liver disease |  |  |  |  |  |
| *mild liver disease* | 5.97 [5.10-6.99] | <.0001 |  | 3.17 [2.45-4.11] | <.0001 |
| *moderate or severe liver disease* | 19.7 [16.9-22.9] | <.0001 |  | 2.22 [1.31-3.76] | 0.003 |
| diabetes |  |  |  |  |  |
| *diabetes without end-organ damage* | 2.53 [2.24-2.85] | <.0001 |  | 1.78 [1.52-2.08] | <.0001 |
| *diabetes with end-organ damage* | 24.6 [22.2-27.4] | <.0001 |  | 1.89 [1.30-2.75] | 0.0009 |
| cancera |  |  |  |  |  |
| *non-metastatic cancerb* | 2.92 [2.64-3.22] | <.0001 |  | 0.95 [0.79-1.14] | 0.62 |
| *metastatic solid tumor* | 11.3 [9.62-13.4] | <.0001 |  | 1.68 [1.04-2.72] | 0.030 |
| ***Charlson index*** |  |  |  |  |  |
| 0 | 1.00 |  |  | 1.00 |  |
| 1 | 6.27 [5.34-7.36] | <.0001 |  | 1.25 [1.08-1.44] | 0.003 |
| ≥2 | 29.4 [25.8-33.5] | <.0001 |  | 1.53 [1.33-1.75] | <.0001 |
| ***Medical history of urolithiasis*** |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |
| yes | 1.03 [0.68-1.56] | 0.86 |  | 29.1 [25.6-33.0] | <.0001 |
| ***Previous treatment (during previous 6 months)*** |  |  |  |  |  |
| antiplatelet drugs | 4.53 [4.17-4.93] | <.0001 |  | 1.20 [1.04-1.40] | 0.01 |
| anticoagulants | 7.10 [6.47-7.79] | <.0001 |  | 1.50 [1.22-1.83] | <.0001 |

Supplemental Table 6: Characteristics associated with renal adverse events: unadjusted logistic regression models (N = 4,088,799) (continued).

|  | **Acute renal failure** | |  | **Urolithiasis** | |
| --- | --- | --- | --- | --- | --- |
|  | **OR [95%CI]** | **p value** |  | **OR [95%CI]** | **p value** |
| **Colonoscopy characteristics** |  |  |  |  |  |
| ***Polypectomy*** |  |  |  |  |  |
| no polypectomy | 1.00 |  |  | 1.00 |  |
| polyp <1 cm | 0.27 [0.23-0.31] | <.0001 |  | 0.83 [0.73-0.94] | 0.004 |
| polyp >1 cm | 0.54 [0.43-0.67] | <.0001 |  | 1.09 [0.86-1.37] | 0.46 |
| ***Bowel preparation*** |  |  |  |  |  |
| polyethylene glycol | 1.00 |  |  | 1.00 |  |
| phosphate preparation | 0.43 [0.30-0.61] | <.0001 |  | 1.04 [0.87-1.25] | 0.61 |
| magnesium preparation | 0.50 [0.38-0.66] | <.0001 |  | 1.07 [0.92-1.24] | 0.36 |
| not retrieved | 29.8 [26.4-33.7] | <.0001 |  | 3.25 [2.85-3.70] | <.0001 |
| ***Sedation*** |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |
| yes | 0.05 [0.05-0.06] | <.0001 |  | 0.60 [0.46-0.78] | 0.0002 |
| ***Complete colonoscopy*** |  |  |  |  |  |
| no | 1.00 |  |  | 1.00 |  |
| yes | 0.06 [0.05-0.06] | <.0001 |  | 0.45 [0.37-0.56] | <.0001 |
| **Endoscopist characteristics** |  |  |  |  |  |
| ***Number of years since MD graduation*** |  |  |  |  |  |
| <5 | 1.63 [0.72-3.69] | 0.24 |  | 0.81 [0.36-1.83] | 0.62 |
| 5-14 | 1.03 [0.75-1.42] | 0.84 |  | 1.28 [1.04-1.58] | 0.020 |
| 15-24 | 1.00 |  |  | 1.00 |  |
| 25-34 | 0.77 [0.61-0.98] | 0.039 |  | 1.12 [0.96-1.31] | 0.14 |
| ≥35 | 1.09 [0.78-1.52] | 0.60 |  | 1.16 [0.92-1.45] | 0.20 |
| not retrieved | 13.6 [11.4-16.3] | <.0001 |  | 1.67 [1.43-1.94] | <.0001 |
| ***Number of procedures performed during the previous year*** |  |  |  |  |  |
| <150 | 1.20 [0.55-2.62] | 0.63 |  | 1.77 [1.16-2.70] | 0.0073 |
| 150-299 | 1.08 [0.65-1.80] | 0.76 |  | 1.30 [0.96-1.77] | 0.087 |
| 300-599 | 1.20 [0.82-1.76] | 0.34 |  | 1.03 [0.81-1.31] | 0.80 |
| 600-999 | 1.10 [0.74-1.62] | 0.62 |  | 1.03 [0.81-1.32] | 0.79 |
| ≥1,000 | 1.00 |  |  | 1.00 |  |
| not retrieved | 16.8 [11.8-24.0] | <.0001 |  | 1.61 [1.27-2.05] | <.0001 |
| **Hospital/clinic characteristics** |  |  |  |  |  |
| ***Type of health facility*** |  |  |  |  |  |
| for-profit private clinic | 1.00 |  |  | 1.00 |  |
| not-for-profit private clinic | 3.49 [2.87-4.24] | <.0001 |  | 1.12 [0.91-1.38] | 0.25 |
| local public hospital | 10.9 [9.74-12.3] | <.0001 |  | 1.46 [1.28-1.67] | <.0001 |
| university public hospital | 54.5 [48.2-61.5] | <.0001 |  | 2.48 [1.98-3.10] | <.0001 |
| ***Number of procedures performed in the facility each year*** |  |  |  |  |  |
| <400 | 4.60 [3.95-5.35] | <.0001 |  | 1.13 [0.88-1.44] | 0.32 |
| 400-2000 | 0.84 [0.73-0.96] | 0.012 |  | 0.55 [0.47-0.65] | <.0001 |
| 2000-4999 | 0.29 [0.24-0.34] | <.0001 |  | 0.46 [0.39-0.55] | <.0001 |
| ≥5000 | 1.00 |  |  | 1.00 |  |

OR [95% CI]: Odds ratio [95% confidence interval].

a except non-melanoma skin cancer

b including lymphoma and leukemia

Supplemental Table 7: Characteristics associated with myocardial infarction: sensitivity analysis using a broader definition for myocardial infarction (4,088,799 patients, including 476 with myocardial infarction).

|  |  |  |
| --- | --- | --- |
|  | **aOR [95% CI]** | **p value** |
| **Patient characteristics** |  |  |
| ***Sex*** |  |  |
| male | 1.00 |  |
| female | 0.80 [0.65-0.99] | 0.037 |
| ***Age*** |  |  |
| 30-39 | 1.00 |  |
| 40-49 | 3.13 [1.11-8.79] | 0.031 |
| 50-59 | 2.65 [0.96-7.31] | 0.060 |
| 60-69 | 2.79 [1.01-7.66] | 0.047 |
| 70-79 | 2.83 [1.02-7.82] | 0.045 |
| 80 and older | 4.59 [1.65-12.8] | 0.0035 |
| ***Pre-existing conditions*** |  |  |
| myocardial infarct | 95.4 [70.5-129] | <.0001 |
| congestive heart failure | 2.05 [1.61-2.60] | <.0001 |
| peripheral vascular disease | 2.09 [1.69-2.59] | <.0001 |
| moderate or severe renal disease | 1.55 [1.19-2.02] | 0.0010 |
| hemiplegia | 1.96 [1.25-3.07] | 0.0033 |
| ***Previous treatment (within 6 months)*** |  |  |
| antiplatelet drugs | 0.32 [0.25-0.40] | <.0001 |
| anticoagulants | 0.46 [0.35-0.60] | <.0001 |
| ***Polypectomy*** |  |  |
| no polypectomy | 1.00 |  |
| polyp <1 cm | 0.55 [0.42-0.71] | <.0001 |
| polyp >1 cm | 0.68 [0.46-1.01] | 0.056 |
| **Hospital/clinic characteristics** |  |  |
| ***Type of health facility*** |  |  |
| for-profit private clinic | 1.00 |  |
| not-for-profit private clinic | 1.61 [0.98-2.63] | 0.059 |
| local public hospital | 2.41 [1.74-3.34] | <.0001 |
| university public hospital | 7.62 [4.66-12.5] | <.0001 |
| ***Number of procedures performed in the facility each year*** |  |  |
| <400 | 2.01 [0.86-4.69] | 0.11 |
| 400-2000 | 1.30 [0.60-2.81] | 0.51 |
| 2000-4999 | 1.04 [0.48-2.28] | 0.92 |
| ≥5000 | 1.00 |  |

Multilevel logistic regression model accounting for patients nested within facility, adjusted for yearly calendar effect.

aOR [95% CI]: Adjusted odds ratio [95% confidence interval].

Supplemental Table 8: Characteristics associated with acute renal failure: sensitivity analysis using a more stringent definition for acute renal failure (4,088,799 patients, including 522 with acute renal failure).

|  |  |  |
| --- | --- | --- |
|  | **aOR [95% CI]** | **p value** |
| **Patient characteristics** |  |  |
| ***Sex*** |  |  |
| male | 1.00 |  |
| female | 0.91 [0.76-1.11] | 0.36 |
| ***Age*** |  |  |
| 30-39 | 1.00 |  |
| 40-49 | 0.84 [0.48-1.46] | 0.54 |
| 50-59 | 0.88 [0.53-1.47] | 0.63 |
| 60-69 | 0.86 [0.52-1.42] | 0.56 |
| 70-79 | 0.73 [0.44-1.22] | 0.23 |
| 80 and older | 0.27 [0.16-0.46] | <.0001 |
| ***Pre-existing conditions*** |  |  |
| congestive heart failure | 1.46 [1.18-1.80] | 0.0004 |
| peripheral vascular disease | 1.46 [1.19-1.80] | 0.0003 |
| moderate or severe renal disease | 185 [132-261] | <.0001 |
| hemiplegia | 1.86 [1.31-2.65] | 0.0006 |
| liver disease |  |  |
| *mild* | 0.87 [0.64-1.19] | 0.39 |
| *moderate or severe* | 1.68 [1.20-2.37] | 0.0027 |
| diabetes |  |  |
| *without end-organ damage* | 0.91 [0.65-1.28] | 0.60 |
| *with end-organ damage* | 0.72 [0.58-0.89] | 0.0026 |
| cancer |  |  |
| *non metastatica* | 1.08 [0.85-1.36] | 0.53 |
| *metastaticb* | 1.18 [0.71-1.95] | 0.52 |
| ***Previous treatment (within 6 months)*** |  |  |
| anticoagulants | 0.78 [0.62-0.97] | 0.027 |
| ***Bowel preparation*** |  |  |
| polyethylene glycol | 1.00 |  |
| phosphate preparation | 0.45 [0.11-1.90] | 0.28 |
| magnesium preparation | 1.01 [0.46-2.21] | 0.98 |
| not retrieved | 12.1 [8.40-17.5] | <.0001 |
| ***Polypectomy*** |  |  |
| no polypectomy | 1.00 |  |
| polyp <1 cm | 0.26 [0.18-0.39] | <.0001 |
| polyp >1 cm | 0.20 [0.09-0.43] | <.0001 |
| **Hospital/clinic characteristics** |  |  |
| ***Type of health facility*** |  |  |
| for-profit private clinic | 1.00 |  |
| not-for-profit private clinic | 2.86 [1.37-5.96] | 0.005 |
| local public hospital | 2.43 [1.39-4.25] | 0.0019 |
| university public hospital | 6.03 [2.71-13.4] | <.0001 |
| ***Number of procedures performed in the facility each year*** |  |  |
| <400 | 2.41 [0.44-13.1] | 0.31 |
| 400-2000 | 2.09 [0.42-10.5] | 0.37 |
| 2000-4999 | 1.90 [0.37-9.68] | 0.44 |
| ≥5000 | 1.00 |  |

Multilevel logistic regression model accounting for patients nested within facility, adjusted for yearly calendar effect.

aOR [95% CI]: Adjusted odds ratio [95% confidence interval].

a except non-melanoma skin cancer

b including lymphoma and leukemia