Appendix

1. Drugs included in the study

| Proton-pump inhibitors | Drug name      | ATC code | Defined daily dose |
|------------------------|----------------|----------|--------------------|
|                        | Omeprazole     | A02BC01  | 20 mg              |
|                        | Pantoprazole   | A02BC02  | 40 mg              |
|                        | Lansoprazole   | A02BC03  | 30 mg              |
|                        | Rabeprazole    | A02BC04  | 20 mg              |
|                        | Esomeprazole   | A02BC05  | 30 mg              |

| Anti-inflammatory medication | Drug name                  | ATC code | Defined daily dose                  |
|------------------------------|----------------------------|----------|-------------------------------------|
|                              | Non-steroidal anti-inflammatory drugs | M01A     | N/A                                 |
|                              | Acetylsalicylic acid        | B01AC06  | 1 tablet (independent of strength)  |

2. ICD-codes included in the study

| Charlson comorbidity index | Disease                          | ICD-10 codes                        |
|----------------------------|----------------------------------|-------------------------------------|
|                            | Myocardial infarction            | I21-I22, I12, I252                  |
|                            | Heart failure                    | I11, I13, I255, I43, I50, I517      |
|                            | Peripheral vascular disease      | I70-I73, I770, I771, K558, K559, Z958, Z959, K551, R02 |
|                            | Cerebrovascular disease          | G45-G46, I60-I69                    |
|                            | Dementia                         | F00-F03, G30-G31, A810, F051        |
|                            | Chronic obstructive pulmonary disease | I26-I27, J40-J47, J60-J67, J684, J701, J703 |
|                            | Rheumatic disease                | M05-M06, M32-M36, M09, M120, M315   |
|                            | Liver disease                    | K70-K71, B18, I85, I864, I982, K721, K29, K76, R162, Z944 |
|                            | Diabetes (type 1 and 2)          | E10-E14                             |
|                            | Hemi/paraplegia                  | G81-G83, G114                       |
|                            | Renal disease                    | N01, N03, N05, N07-N08, N171, N172, N18, N19, N25, Z49, Z940, Z992 |
|                            | AIDS/HIV                         | B20-B24                             |
|                            | Malignancy                       | C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C76, C80-C85, C88, C90-C97 |
|                            | Metastatic tumor                 | C77-C79                             |
| Disease                               | ICD-7 codes    | WHO/HS/CANC/C24.1 histology code |
|--------------------------------------|----------------|----------------------------------|
| Esophageal adenocarcinoma            | 150, 1511      | 096                              |
| Esophageal squamous cell carcinoma    | 150            | 146                              |
| Gastric adenocarcinoma               | 1510, 1518, 1519 | 096                            |
Cohort entry

1st PPI dispensation

2nd PPI dispensation

1 year

<180 PPI dispensed

≥180 PPI dispensed
Dispensed no PPI for 1 year

Time dependent analysis

Resumed PPI

1 year

Cohort entry

Study end

Unexposed person-time

Exposed person-time
Study end
No dispensed PPI during 1 year

Outcome scenarios

Cohort entry

1 year

Unexposed person-time
Exposed person-time

Case scenarios
Case 1: censored case
Case 2: unexposed case
Case 3: exposed case

Cohort entry

1 year

No dispensed PPI during 1 year

Study end