

## Supplementary Online Content

Maret-Ouda J, Wahlin K, El-Serag HB, Lagergren J. Association between laparoscopic antireflux surgery and recurrence of gastroesophageal reflux. *JAMA*. doi:10.1001/jama.2017.10981

**eAppendix 1.** Inclusion and exclusion criteria

**eAppendix 2.** Definition of the study outcomes and defined daily doses of the medications

**eAppendix 3.** Risk factors for recurrence of reflux following primary laparoscopic antireflux surgery

This supplementary material has been provided by the authors to give readers additional information about their work.

## **eAppendix 1. Inclusion and Exclusion Criteria**

### **Inclusion Criteria**

#### **Gastroesophageal reflux disease:**

Heartburn/pyrosis: ICD-7: 78430; ICD-8: 78430; ICD-9: 787B; ICD-10: R12.

Hiatal hernia: ICD-7: 56040; ICD-8: 55130; ICD-9: 553D; ICD-10: K44.

Reflux and esophagitis: ICD-7: 53911 and 53912; ICD-8: 53093 and 53094; ICD-9: 530B-C; ICD-10: K20 and K21.

Barrett's esophagus: ICD-10: K227

#### **Laparoscopic antireflux surgery:**

JBC01 Laparoscopic surgery for gastroesophageal reflux

JBW97 Other laparoscopic surgery of the diaphragm or for gastroesophageal reflux

### **Exclusion Criteria**

#### **Any previous antireflux surgery (before 2005):**

Before 1997:

4272 Fundoplication

After 1997:

JBC00 Open surgery for gastroesophageal reflux

JBC01 Laparoscopic surgery for gastroesophageal reflux

JBW96 Other surgery of the diaphragm or for gastroesophageal reflux

JBW97 Other laparoscopic surgery of the diaphragm or for gastroesophageal reflux

## **eAppendix 2. Definition of the study outcomes and defined daily doses of the medications**

### **Proton-pump inhibitors:**

A02BC Proton-pump inhibitors (Includes: Omeprazol, Pantoprazol, Lansoprazol, Rabeprazol, and Esomeprazol)

### **Defined Daily Dose (DDD)**

<i>ATC code</i>	<i>Name</i>	<i>DDD</i>	<i>Unit</i>
A02BC01	Omeprazol	20	mg
A02BC02	Pantoprazol	40	mg
A02BC03	Lansoprazol	30	mg
A02BC04	Rabeprazol	20	mg
A02BC05	Esomeprazol	30	mg

### **Histamine<sub>2</sub>-receptor antagonists:**

A02BA Histamin-2-receptor antagonists (Includes: Ranitidin, Famotidin, Ranitidin in combination with Ca-carbonate)

### **Defined Daily Dose (DDD)**

<i>ATC code</i>	<i>Name</i>	<i>DDD</i>	<i>Unit</i>
A02BA02	Ranitidine	0.3	g
A02BA03	Famotidine	40	mg

### **Antireflux surgery:**

JBC00 Open surgery for gastroesophageal reflux

JBC01 Laparoscopic surgery for gastroesophageal reflux

JBW96 Other surgery of the diaphragm or for gastroesophageal reflux

JBW97 Other laparoscopic surgery of the diaphragm or for gastroesophageal reflux

**eAppendix 3.** Risk factors for recurrence of reflux following primary laparoscopic antireflux surgery in 2,655 patients, presented as adjusted hazard ratios (HR) with 95% confidence intervals (CI).

	<b>Patients, Number (%)</b>	<b>Overall recurrence (470 patients) HR (95% CI)*</b>	<b>Recurrence treated with medication (393 patients) HR (95% CI)*</b>	<b>Recurrence treated with surgery (77 patients) HR (95% CI)*</b>
<b>Sex</b>				
Male	1,354 (51.0)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Female	1,301 (49.0)	1.57 (1.29-1.90)	1.53 (1.24-1.89)	1.78 (1.10-2.87)
<b>Age (years)</b>				
≤45	989 (37.3)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
46-60	951 (35.8)	1.28 (1.02-1.61)	1.30 (1.01-1.68)	1.20 (0.71-2.04)
≥61	715 (26.9)	1.41 (1.10-1.81)	1.50 (1.14-1.97)	1.00 (0.53-1.87)
<b>Comorbidity score**</b>				
0	1,851 (69.7)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
≥1	804 (30.3)	1.36 (1.13-1.65)	1.48 (1.20-1.81)	0.87 (0.52-1.45)
<b>Year of surgery</b>				
2005-2006	1,098 (41.4)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
2007-2009	802 (30.2)	1.61 (1.27-2.03)	1.91 (1.46-2.49)	0.88 (0.52-1.48)
2010-2014	755 (28.4)	3.86 (2.98-5.02)	5.20 (3.86-7.01)	1.20 (0.64-2.24)
<b>Hospital volume</b>				
≤24	266 (10.0)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
25-75	863 (32.5)	1.13 (0.79-1.62)	1.25 (0.84-1.86)	0.65 (0.28-1.53)
≥76	1,526 (57.5)	1.09 (0.77-1.53)	1.08 (0.74-1.59)	1.14 (0.54-2.41)

\* Adjusted for sex, age, comorbidity, calendar year and hospital volume, other than the variable in that row.

\*\* Charlson Comorbidity Index Score, a measurement of chronic comorbidities based on specific diagnostic codes.