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Survival after surgery vs medication for gastroesophageal reflux disease in a Nordic registry-based study

Authors: Manar Yanes, Giola Santoni, John Maret-Ouda, Eivind Ness-Jensen, Martti Färkkilä, Elsebeth Lynge, Eero Pukkala, Pål Romundstad, Laufey Tryggvadóttir, My von Euler-Chelpin, Jesper Lagergren

Manar Yanes

MD | PhD-student

Upper Gastrointestinal Surgery

Department of Molecular Medicine and Surgery

Karolinska Institutet

OUTLINE



Background and hypothesis



Methods



Results and conclusions

Background and hypothesis

Background

Gastroesophageal reflux disease (GERD)

- Common
- Cardinal symptoms
 - Heartburn and regurgitation
- Disrupted antireflux barrier
- Risk factors
 - Heredity, obesity and tobacco smoking
- Severe GERD (objectively determined)
 - Reflux esophagitis
 - Inflammation of esophagus
 - Barrett's esophagus
 - Columnar cell metaplasia due to chronic acid exposure
- Supra-esophageal manifestations
 - Larynx, pharynx and lung
- Cancer



Background

Treatment of GERD

- Medication: Proton pump inhibitor
 - Reduces acidity
 - Relieves symptoms
 - Heals reflux esophagitis
- Surgery: Antireflux surgery by fundoplication
 - Revives antireflux barrier
 - Reduces reflux of both acidic and non-acidic gastric content

Survival

- Antireflux surgery vs antireflux medication

Hypothesis

- Antireflux surgery is followed by better long-term survival than antireflux medication in patients with severe and objectively determined GERD, i.e. reflux esophagitis or Barrett's esophagus

Methods

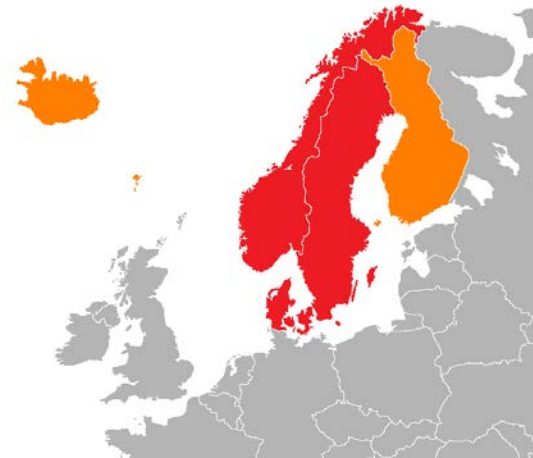
Source cohort

Nordic Antireflux Surgery Cohort (NordASCo)

Methods

NordASCo: Countries

- Denmark
- Finland
- Iceland
- Norway
- Sweden



Inclusion criteria:

GERD or antireflux surgery in the Nordic patient registries in 1964-2014



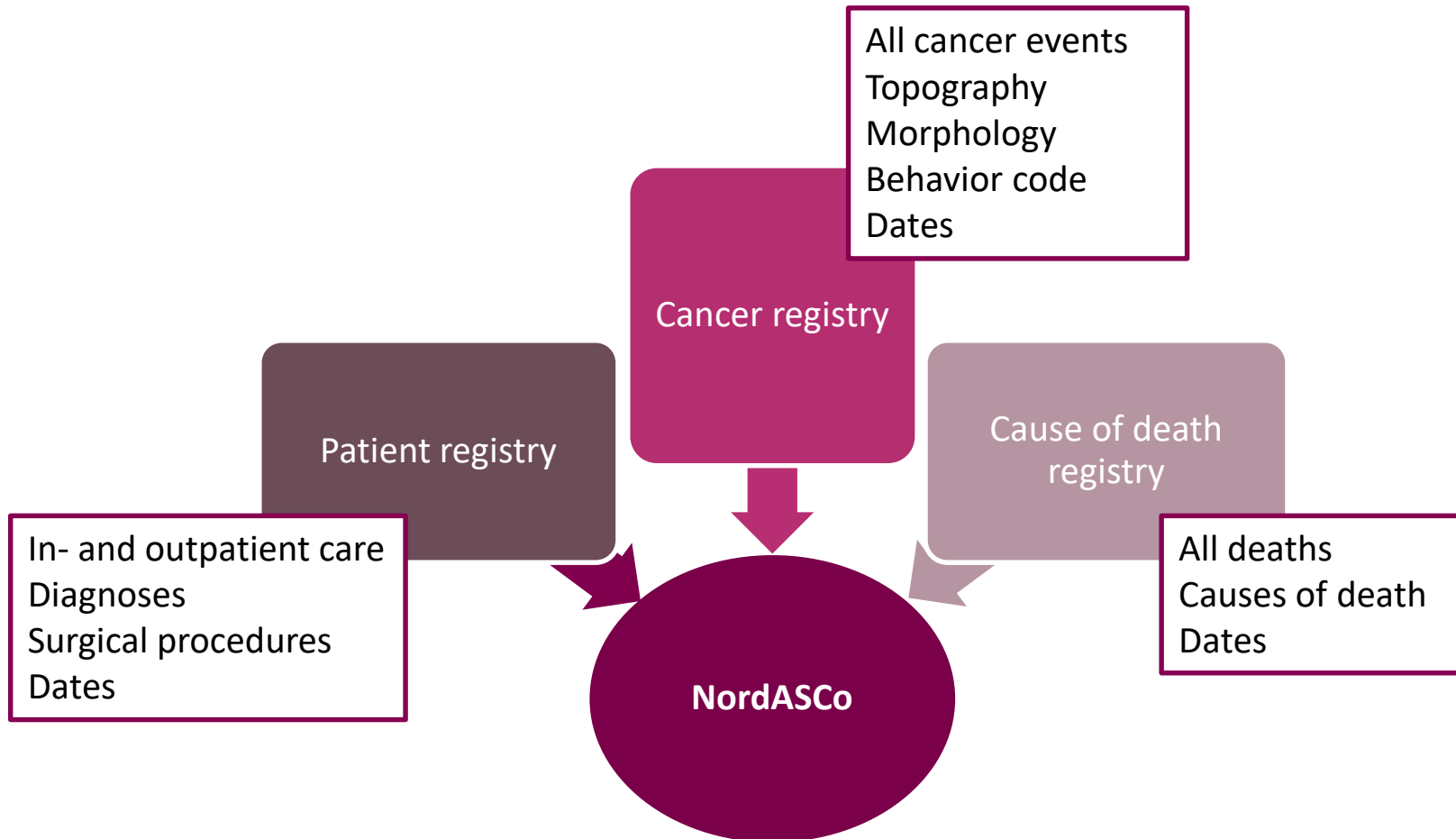
945 153
GERD



48 433
Antireflux surgery

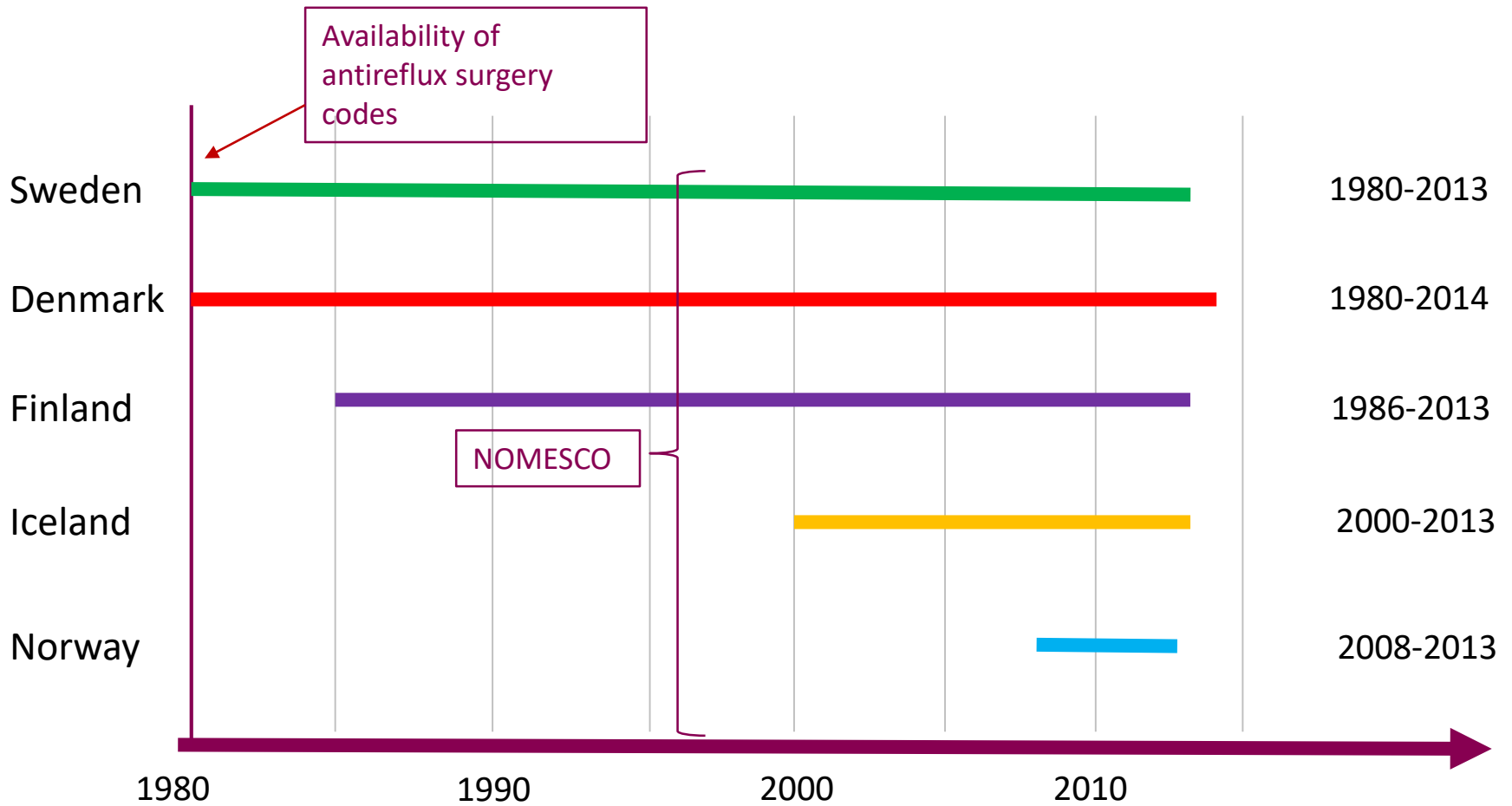
Methods

NordASCo: Data sources



Methods

NordASCo: Study period



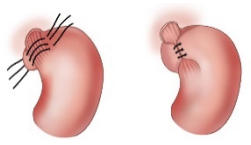

Methods

Design

Study design	<ul style="list-style-type: none">Population-based cohort study
Setting	<ul style="list-style-type: none">Denmark, Finland, Iceland, Sweden
Cohort	<ul style="list-style-type: none">Severe and objectively determined GERD: Reflux esophagitis or Barrett's esophagus
Exclusion	<ul style="list-style-type: none">Age <18 years or >70 years at the time of severe GERD diagnosis or antireflux surgeryAny GERD-related cancer before severe GERD diagnosis
Exposures	<ul style="list-style-type: none">Antireflux surgery versus antireflux medication
Outcomes	<ul style="list-style-type: none">All-cause mortalityDisease-specific mortality

Method

Statistical analyses

Comparison		Measure of effect	Adjustments
<p>Antireflux surgery</p> 	<p>Antireflux medication*</p> 	HR (95% CI)	Sex, age, calendar period, country, comorbidity

* Reference group

Results and conclusions

Results

Patient characteristics

Reflux esophagitis or Barrett's esophagus		
Total	Antireflux surgery Number (%)	Antireflux medication Number (%)
Participants	33,904 (100)	206,322 (100)
Person-years of follow-up	445,594 (100)	1,851,087 (100)
Causes of mortality		
All causes	4,496 (13.3)	39,390 (19.1)
Cardiovascular diseases	2,159 (6.4)	19,102 (9.3)
Respiratory diseases	1,154 (3.4)	10,229 (5.0)
Esophageal cancer	158 (0.5)	964 (0.5)
Laryngeal or pharyngeal cancer	13 (0.0)	270 (0.1)
Lung cancer	257 (0.8)	2,253 (1.1)

Results

All-cause mortality among patients with reflux esophagitis or Barrett's esophagus

	Antireflux medication	Antireflux surgery
	HR (95% CI)	Adjusted [†] HR (95% CI)
Follow-up (years)		
Overall	1.00 (Reference)	0.61 (0.58-0.63)
1-5	1.00 (Reference)	0.41 (0.38-0.45)
5-10	1.00 (Reference)	0.54 (0.50-0.58)
10-15	1.00 (Reference)	0.63 (0.59-0.68)
>15	1.00 (Reference)	0.76 (0.72-0.81)
Sex		
Men	1.00 (Reference)	0.59 (0.56-0.61)
Women	1.00 (Reference)	0.64 (0.61-0.68)
Age at inclusion		
<50	1.00 (Reference)	0.62 (0.57-0.66)
50-<65	1.00 (Reference)	0.59 (0.56-0.62)
≥65	1.00 (Reference)	0.65 (0.61-0.70)
Charlson Comorbidity Score		
0	1.00 (Reference)	0.62 (0.59-0.64)
1	1.00 (Reference)	0.48 (0.44-0.53)
≥2	1.00 (Reference)	0.47 (0.37-0.58)

[†] Adjusted for sex, age, calendar period, country of residence, and comorbidity

Results

All-cause mortality among patients with reflux esophagitis or Barrett's esophagus

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Results

Disease-specific mortality among patients with reflux esophagitis or Barrett's esophagus

Follow-up (years)	Antireflux medication	Antireflux surgery
	HR (95% CI)	Adjusted [†] HR (95% CI)
Cardiovascular disease		
Overall	1.00 (Reference)	0.58 (0.55-0.61)
1-5	1.00 (Reference)	0.37 (0.32-0.42)
5-10	1.00 (Reference)	0.49 (0.44-0.55)
10-15	1.00 (Reference)	0.59 (0.53-0.66)
>15	1.00 (Reference)	0.72 (0.66-0.78)
Respiratory disease		
Overall	1.00 (Reference)	0.62 (0.57-0.66)
1-5	1.00 (Reference)	0.36 (0.30-0.44)
5-10	1.00 (Reference)	0.48 (0.41-0.57)
10-15	1.00 (Reference)	0.60 (0.52-0.69)
>15	1.00 (Reference)	0.82 (0.74-0.92)

[†] Adjusted for sex, age, calendar period, country of residence, and comorbidity

Results

Disease-specific mortality among patients with reflux esophagitis or Barrett's esophagus

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Results

Disease-specific mortality among patients with reflux esophagitis or Barrett's esophagus

Follow-up (years)	Antireflux medication	Antireflux surgery
	HR (95% CI)	Adjusted [†] HR (95% CI)
Esophageal cancer		
Overall	1.00 (Reference)	1.05 (0.87-1.28)
1-5	1.00 (Reference)	0.56 (0.37-0.84)
5-10	1.00 (Reference)	1.25 (0.83-1.89)
10-15	1.00 (Reference)	1.82 (1.27-2.61)
>15	1.00 (Reference)	1.09 (0.74-1.60)
Laryngeal or pharyngeal cancer		
Overall	1.00 (Reference)	0.35 (0.19-0.65)
1-5	1.00 (Reference)	0.43 (0.13-1.48)
5-10	1.00 (Reference)	0.67 (0.27-1.67)
10-15	1.00 (Reference)	0.21 (0.05-0.80)
>15	1.00 (Reference)	0.18 (0.04-0.81)
Lung cancer		
Overall	1.00 (Reference)	0.67 (0.58-0.80)
1-5	1.00 (Reference)	0.41 (0.28-0.61)
5-10	1.00 (Reference)	0.75 (0.56-0.99)
10-15	1.00 (Reference)	0.76 (0.56-1.01)
>15	1.00 (Reference)	0.72 (0.54-0.94)

[†] Adjusted for sex, age, calendar period, country of residence, and comorbidity

Strengths and limitations



- Population-based design
- Large cohort
- Long follow-up
- Negligible loss to follow-up
- Objectively determined GERD



- Residual confounding
- Recurrence of GERD
- Partial lack of data on antireflux medication

Conclusions

- People with reflux esophagitis or Barrett's esophagus who undergo antireflux surgery may have decreased all-cause mortality compared to those who use antireflux medication
- Similar effects were present for disease-specific mortality due to cardiovascular disease, respiratory disease, laryngeal or pharyngeal cancer, or lung cancer
- Antireflux surgery might not decrease the risk of mortality from esophageal cancer better than antireflux medication

Funding

- Swedish Research Council



