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# International benchmarking in oesophageal and gastric cancer surgery

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**Background:** Benchmarking on an international level might lead to improved outcomes at a national level. The aim of this study was to compare treatment and surgical outcome data from the Swedish National Register for Oesophageal and Gastric Cancer (NREV) and the Dutch Upper Gastrointestinal Cancer Audit (DUCA).

**Methods:** All patients with primary oesophageal or gastric cancer who underwent a resection and were registered in NREV or DUCA between 2012 and 2014 were included. Differences in 30-day mortality were analysed using case mix-adjusted multivariable logistic regression.

**Results:** In total, 4439 patients underwent oesophagectomy (2509 patients) or gastrectomy (1930 patients). Estimated resection rates were comparable. Swedish patients were older but had less advanced disease and less co-morbidity than Dutch patients. Neoadjuvant treatment rates were lower in Sweden than in the Netherlands, both for patients who underwent oesophagectomy (68.6 *versus* 90.0 per cent respectively; P < 0.001) and for those having gastrectomy (38.3 *versus* 56.6 per cent; P < 0.001). In Sweden, transthoracic oesophagectomy was performed in 94.7 per cent of patients, whereas in the Netherlands, a transhiatal approach was undertaken in 35.8 per cent. Higher annual procedural volumes per hospital were observed in the Netherlands. Adjusted 30-day and/or in-hospital mortality after gastrectomy was statistically significantly lower in Sweden than in the Netherlands (odds ratio 0.53, 95 per cent c.i. 0.29 to 0.95).

**Conclusion:** For oesophageal and gastric cancer, there are differences in patient, tumour and treatment characteristics between Sweden and the Netherlands. Postoperative mortality in patients with gastric cancer was lower in Sweden.

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### Introduction

Clinical audit and other related quality improvement initiatives have been widely used in Western countries to measure and benchmark the quality of care delivered by individual hospitals<sup>1-4</sup>. Together with national treatment guidelines and quality standards, these initiatives are designed to improve the quality of cancer care. In Sweden, these registries are incorporated in daily clinical practice, and cancer care has an excellent reputation with high survival rates<sup>5–7</sup>. In the Netherlands, gastrointestinal cancer surgeons were among the first to embrace clinical audit at a national level.

The Swedish National Register for Oesophageal and Gastric Cancer (NREV) was launched in 2006. The completeness and accuracy of the register was assessed recently, and deemed to be high and valid<sup>8</sup>. The Dutch Upper Gastrointestinal Cancer Audit (DUCA) started with nationwide registration in 2011. Structural, process and

outcome data from the DUCA have also been reported, showing improvement of several important quality indicators between 2011 and 2014<sup>9</sup>. Both registries systematically and uniformly collect data, and use them to monitor and benchmark processes and outcomes for patients with oesophageal or gastric cancer.

In 2013, a study<sup>10</sup> comparing 30-day mortality and 2-year survival following oesophagogastric resection for cancer in the Netherlands, Sweden, Denmark and England between 2004 and 2009 showed that Sweden had the lowest 30-day mortality rate for oesophagectomy (1·9 per cent) and a significantly lower adjusted 30-day mortality rate after gastrectomy, compared with that in the Netherlands (3·5 *versus* 6·9 per cent respectively). Increasing hospital volumes were associated with lower 30-day mortality for both procedures.

The aim of the present study was to compare patient, tumour and treatment characteristics, and short-term outcomes between Sweden and the Netherlands, and to identify structural differences in the organization of care between the two countries that could be used for quality improvement initiatives.

#### **Methods**

#### Data source

# Swedish National Register for Oesophageal and Gastric Cancer (NREV)

The NREV is a nationwide quality registry with data acquired in surveys of all patients diagnosed with oesophageal or gastric cancer. Patients with non-epithelial tumours are excluded. The registry started in 2006, and since then more than 95 per cent of all patients with oesophageal or gastric cancers diagnosed in Sweden have been registered<sup>8</sup>. This was achieved by collaborating with the Swedish Cancer Register, mandated by law, which has close to complete coverage of the entire Swedish population<sup>11</sup>.

The diagnostic survey of NREV serves as a registration in both NREV and the Swedish Cancer Register. Accuracy of registered data is 91.1 per cent<sup>8</sup>. The physician responsible for treating the patient at each individual time point reports data to the central register. The first form is reported at the time of diagnosis, the second at the time of surgery, and the third at the first postoperative follow-up, no earlier than 30 days after surgery. Thereafter, only health-related quality-of-life assessment is undertaken, at 1 year after diagnosis. Six regional cancer centres monitor data, and regular follow-up is performed to complete the register. Registration in NREV is not mandatory. Sweden has several high-quality national registries administered by the Swedish Board of Health and Welfare. This allows for cross-matching between registers such as the Swedish Patient Register and Cause of Death Register, and simplifies data compilation. This study was approved by the regional ethics committee in Stockholm (numbers 2013/596-31/3 and 2016/891-32).

#### Dutch Upper Gastrointestinal Cancer Audit (DUCA)

The DUCA is a nationwide registry including all patients who had surgery with the intent of a resection for oesophageal or gastric cancer in the Netherlands from 20119. Patients with non-epithelial tumours and those undergoing non-surgical treatment (such as definitive chemoradiotherapy) are excluded from this registry. Nationwide coverage of the audit is stimulated via the Association of Surgeons of the Netherlands and the Health Care Inspectorate, as participation in the DUCA has been defined as a mandatory quality standard since 2012. Hospitals are free to decide who carries out data registration, but in all participating hospitals the final responsibility for data entry remains with the surgeon. Verification of randomly selected data registered in the DUCA in 2013 showed that case ascertainment was estimated at 97.8 per cent of all oesophageal cancer resections and 96.2 per cent of all gastric cancer resections<sup>9</sup>. The DUCA database consists of detailed information regarding patient, tumour and treatment factors, and short-term (surgical) outcomes up to 30 days after surgery or during the initial hospital admission. No long-term survival data are included. For the present study, no ethical approval or informed consent was required under Dutch law.

An overview of both registries is shown in Table 1.

# Patients

All patients with primary oesophageal or gastric cancer who underwent oesophagectomy or gastrectomy, and were registered in the NREV or the DUCA between 1 January 2012 and 31 December 2014 were included.

# Definitions

Clinical tumour staging was performed according to the seventh edition of the UICC TNM classification<sup>13</sup>, before neoadjuvant treatment. Tumour location was coded according to ICD-O. Annual hospital volume was defined separately for oesophagectomy and gastrectomy as the number of resections per hospital in each calendar year. Different definitions were used for postoperative complications in NREV and DUCA (*Table 1*; *Appendix S1*, supporting information). Two variables were combined to construct results for NREV data regarding pulmonary 
 Table 1 Comparison of Sweden and the Netherlands with regard to oesophageal and gastric cancer incidence and data captured in the respective national registries

|   | Sweden  | Netherlands   |
|---|---|---|
| Inhabitants ( $\times 10^{6}$ )                     | 10.00   | 17.06   |
| Incidence (2012–2014)*                              |   |   |
| Oesophageal cancer                                  | 2065  | 7760  |
| Gastric cancer                                      | 1433  | 3823  |
| Formal centralization of surgery                    |   |   |
| Oesophagectomy                                      | None  | 2006: 10/year/hospital                              |
|   |   | 2011: 20/year/hospital                              |
| Gastrectomy   | None  | 2012: 10/year/hospital                              |
|   |   | 2013: 20/year/hospital                              |
| Registry  |   |   |
| Registry used                                       | Swedish National Register for Oesophageal and | Dutch Upper Gastrointestinal Cancer                 |
|   | Gastric Cancer (NREV)                         | Audit (DUCA)  |
| Registry type                                       | Clinical audit                                | Clinical audit                                      |
| Registry active since                               | 2006  | 2011  |
| Data collection                                     | Physicians/regional cancer centre             | Surgeons  |
| Years of diagnosis in data set                      | 2012–2014                                     | 2012-2014   |
| Case ascertainment                                  | Nationwide                                    | Nationwide  |
| Mandatory   | Highly recommended                            | Yes   |
| Patients included                                   | All patients                                  | Intent of resection                                 |
| Data availability                                   |   |   |
| Patient characteristics                             |   |   |
| Age   | +   | +   |
| Sex   | +   | +   |
| BMI   | +   | +   |
| Co-morbidity  |   |   |
| Charlson index                                      | -   | +   |
| ASA grade   | +   | +   |
| Tumour characteristics                              |   |   |
| Location  | +   | +   |
| Histology/differentiation                           | +   | +   |
| TNM stage   | +   | +   |
| Neoadjuvant therapy                                 | +   | +   |
| Surgical treatment                                  |   |   |
| Resection type                                      | +   | +   |
| Level of anastomosis                                | +   | +   |
| Minimally invasive                                  | From 2014                                     | +   |
| Urgency of procedure                                | +   | +   |
| Pathology<br>Response to treatment                  |   |   |
| Response to treatment<br>No. of lymph nodes         |   | +   |
| Resected  |   |   |
| Positive  | +   | +   |
| Individual resection margins                        | +   | +   |
| Postoperative course                                | +   | +   |
| Postoperative course<br>Postoperative complications | + (within 30 days of surgery)                 | + (within 30 days of surgery/in hospital)           |
| Severity of complication                            | + (Clavien-Dindo classification)              | + (National Surgical Complication<br>Registration)† |
| 30-day mortality                                    | +   | +   |
| In-hospital mortality                               | (+)‡  | +   |
| 90-day mortality                                    | (+)§  | -   |
|   | ·   |   |

+, Yes; -, no. \*Including cardia tumours for oesophageal cancer; data obtained from the Central Cancer Registry and the Netherlands Cancer Registry. †Changed to Clavien–Dindo classification<sup>12</sup> from 2015. ‡Calculated by subtracting date of death from date of surgery and comparing it with length of postoperative stay. §By linkage with the Swedish Patient Registry.

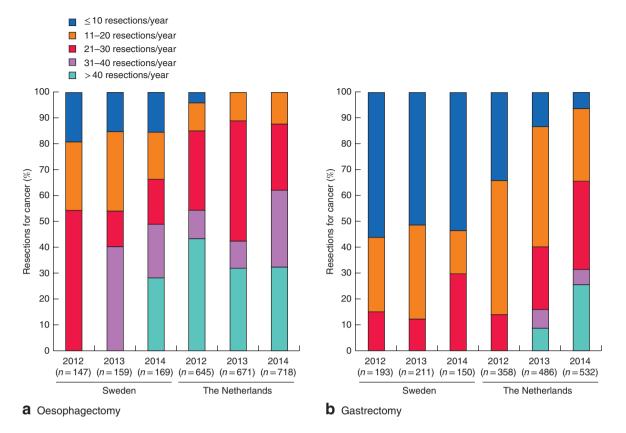


Fig. 1 Centralization of a oesophagectomy and b gastrectomy operations in Sweden and the Netherlands, 2012–2014

complications (pneumonia and pulmonary complications, specified under other complications) and thromboembolic complications (pulmonary embolus and thromboembolic complications, specified under other complications). In the first 3 years of the DUCA, the definition of the UK Royal College of Pathologists was used to describe a microscopically radical resection (R0)<sup>14</sup>. In 2014, this was changed to the definition of the College of American Pathologists (CAP)<sup>15,16</sup>. According to the CAP, resection margins are considered positive when tumour cells are present within the surgical margin, whereas the Royal College of Pathologists also includes tumour cells within 1 mm of this margin<sup>17</sup>. NREV used CAP definitions during the entire registration period. Both 30-day mortality and 30-day and/or in-hospital mortality rates were calculated using date of surgery, date of discharge and/or date of death. In the DUCA, 30-day and/or in-hospital mortality was also registered as a separate variable.

#### **Resection rates**

Resection rates were estimated using incidence rates (2012–2014) available from the Swedish Central Cancer

Registry and the Netherlands Cancer Registry. The Central Cancer Registry, maintained by the National Board of Health and Welfare, has close to complete coverage of the Swedish population<sup>11</sup>. The registry is based on notification of malignant and certain benign tumours. The Netherlands Cancer Registry uses a similar method and covers all hospitals in the Netherlands. Trained registrars routinely collect information on all newly diagnosed malignancies 6–18 months after diagnosis. Quality and completeness of the data are high<sup>18,19</sup>.

#### Statistical analysis

Differences regarding patient, tumour and treatment characteristics between the two countries were described using frequency tables. Categorical variables were compared using  $\chi^2$  tests. Changes over time were compared using  $\chi^2$  tests for trend. Statistical significance was set at a threshold of 0.05, with *P* values calculated by two-sided tests. Univariable analysis was performed to determine the correlation between country and 30-day mortality and 30-day and/or in-hospital mortality. Differences in 30-day and/or in-hospital mortality were also analysed

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 Table 2 Comparison of national data sets of patient and tumour characteristics of patients who underwent oesophagectomy or gastrectomy for cancer in Sweden and the Netherlands

|  | Oesopha                     | agectomy                 |         | Gastrectomy                 |                          |            |
|--|-----------------------------|--------------------------|---------|-----------------------------|--------------------------|------------|
|  | Sweden<br>( <i>n</i> = 475) | Netherlands $(n = 2034)$ | P*      | Sweden<br>( <i>n</i> = 554) | Netherlands $(n = 1376)$ | <i>P</i> * |
| Age (years)                              |                             |                          | < 0.001 |                             |                          | 0.017      |
| 0–59                                     | 112 (23.6)                  | 634 (31.2)               |         | 102 (18.4)                  | 295 (21.4)               |            |
| 60-75                                    | 303 (63.8)                  | 1248 (61.4)              |         | 273 (49.3)                  | 723 (52.5)               |            |
| > 75                                     | 60 (12.6)                   | 152 (7.5)                |         | 179 (32.3)                  | 358 (26.0)               |            |
| Median (i.g.r.)                          | 67.2 (60.8-72.5)            | 65.0 (59.0-71.0)         |         | 72.1 (64.8-78.7)            | 70.0 (62.0-77.0)         |            |
| Sex ratio (M : F)                        | 379:96                      | 1574:460                 | 0.256   | 317:237                     | 865:511                  | 0.021      |
| Median (i.g.r.) BMI (kg/m <sup>2</sup> ) | 25.4 (23.0–28.4)            | 25.5 (23.0–28.4)         | 0 200   | 24.7 (22.1–27.7)            | 25.9 (22.3–27.8)         | 0 02       |
| ASA grade                                | 20 . (20 0 20 .)            | 200 (200 20 ))           | < 0.001 | ()                          | 200 (22 0 2. 0)          | < 0.001    |
| I–II                                     | 411 (86.5)                  | 1550 (76-2)              |         | 412 (74-4)                  | 923 (67.1)               |            |
| ≥ III                                    | 60 (12.6)                   | 461 (22.7)               |         | 132 (23.8)                  | 436 (31.7)               |            |
| Not known                                | 4 (0.8)                     | 23 (1.1)                 |         | 10 (1.8)                    | 17 (1.2)                 |            |
| Histology                                | 4 (0.0)                     | 20 (11)                  | < 0.001 | 10 (1.0)                    | 17 (12)                  | < 0.001    |
| Adenocarcinoma                           | 222 (70 1)                  | 1/5/ (71 5)              | < 0.001 | F10 (00 1)                  | 1002 (04 0)              | < 0.001    |
|  | 333 (70.1)                  | 1454 (71.5)              |         | 510 (92.1)                  | 1293 (94.0)              |            |
| Squamous cell carcinoma                  | 80 (16.8)                   | 335 (16.5)               |         | 0 (0)                       | 3 (0.2)                  |            |
| Other                                    | 62 (13.1)                   | 209 (10.3)               |         | 44 (7.9)                    | 68 (4.9)                 |            |
| Not known                                | 0 (0)                       | 36 (1.8)                 |         | 0 (0)                       | 12 (0.9)                 |            |
| Tumour location (oesophagus)             |                             |                          | < 0.001 | -                           | -                        |            |
| C15.0 Cervical part                      | 3 (0.6)                     | 3 (0.1)                  |         | -                           | -                        |            |
| C15.3 Intrathoracic, proximal            | 6 (1.3)                     | 20 (1.0)                 |         | -                           | -                        |            |
| C15.4 Intrathoracic, middle              | 62 (13.1)                   | 229 (11.3)               |         | -                           | -                        |            |
| C15.5 Intrathoracic, distal              | 216 (45.5)                  | 1228 (60.4)              |         | -                           | -                        |            |
| C16.0 Cardia/GOJ                         | 176 (37.1)                  | 516 (25.4)               |         | -                           | -                        |            |
| Other/not known                          | 12 (2.5)                    | 38 (1.9)                 |         | -                           | -                        |            |
| Tumour location (stomach)                | -                           | -                        |         |                             |                          | < 0.001    |
| C16.0 Cardia/GOJ                         | -                           | -                        |         | 58 (10.5)                   | 47 (3.4)                 |            |
| C16.1 Fundus                             | -                           | -                        |         | 21 (3.8)                    | 101 (7.3)                |            |
| C16.2 Corpus                             | -                           | -                        |         | 155 (28.0)                  | 397 (28.9)               |            |
| C16.3 Antrum                             | -                           | -                        |         | 178 (32.1)                  | 542 (39.4)               |            |
| C16.4 Pylorus                            | -                           | -                        |         | 52 (9.4)                    | 95 (6.9)                 |            |
| C16.8 Stomach, overlapping               | _                           | -                        |         | 18 (3.2)                    | 72 (5.2)                 |            |
| Other/not known                          |                             |                          |         | 72 (13.0)                   | 122 (8.9)                |            |
| T category                               |                             |                          | < 0.001 | 12 (10 0)                   | 122 (0 0)                | < 0.001    |
| TO                                       | 9 (1.9)                     | 10 (0.5)                 | <0.001  | 11 (2.0)                    | 12 (0.9)                 |            |
| T1                                       | 31 (6.5)                    | 111 (5.5)                |         | 52 (9.4)                    | 106 (7.7)                |            |
| T2                                       | 126 (26.5)                  | 369 (18.1)               |         | 146 (26.4)                  | 256 (18.6)               |            |
| T3                                       | · · ·                       | 1362 (67.0)              |         | . ,                         |                          |            |
| T4                                       | 231 (48.6)                  | · · ·                    |         | 208 (37.5)                  | 549 (39·9)               |            |
|  | 15 (3.2)                    | 79 (3·9)                 |         | 34 (6.1)                    | 81 (5.9)                 |            |
| Not known                                | 63 (13.3)                   | 103 (5.1)                | 0.001   | 103 (18.6)                  | 372 (27.0)               | 0.004      |
| N category                               |                             |                          | < 0.001 |                             |                          | < 0.001    |
| NO                                       | 272 (57.3)                  | 706 (34.7)               |         | 358 (64.6)                  | 684 (49.7)               |            |
| N1                                       | 156 (32.8)                  | 792 (38.9)               |         | 107 (19.3)                  | 324 (23.5)               |            |
| N2                                       | 35 (7.4)                    | 377 (18.5)               |         | 30 (5.4)                    | 108 (7.8)                |            |
| N3                                       | 6 (1.3)                     | 55 (2.7)                 |         | 10 (1.8)                    | 22 (1.6)                 |            |
| Not known                                | 6 (1.3)                     | 104 (5.1)                |         | 49 (8.8)                    | 238 (17.3)               |            |
| M category                               |                             |                          | < 0.001 |                             |                          | < 0.001    |
| M0                                       | 466 (98.1)                  | 1936 (95.2)              |         | 528 (95.3)                  | 1264 (91.9)              |            |
| M1                                       | 8 (1.7)                     | 15 (0.7)                 |         | 23 (4.2)                    | 23 (1.7)                 |            |
| Not known                                | 1 (0.2)                     | 83 (4.1)                 |         | 3 (0.5)                     | 89 (6.5)                 |            |
|  |                             |                          |         |                             |                          |            |

Values in parentheses are percentages unless indicated otherwise. GOJ, gastro-oesophageal junction.  $\chi^2$  test.

in a multivariable logistic regression model, adjusting for available case mix factors (sex, age, ASA grade, BMI, type of neoadjuvant treatment, type of resection, location of anastomosis). Available case mix factors were selected on clinical grounds and literature. Co-variables such as smoking history or deprivation score were not included in both registries. All co-variables used for case mix in the multivariable analyses were analysed in discrete categories. For discrete co-variables with more than two categories, the lowest or normal value was chosen as reference level

|                           | Oesophagectomy |                 | Gastrectomy |            |                    |         |
|---------------------------|----------------|-----------------|-------------|------------|--------------------|---------|
|                           | Sweden         | The Netherlands | 0.          | Sweden     | The Netherlands    |         |
|                           | (n = 475)      | (n = 2034)      | P†          | (n = 554)  | ( <i>n</i> = 1376) | P†      |
| Neoadjuvant treatment     |                |                 | < 0.001     |            |                    | < 0.001 |
| None                      | 149 (31.4)     | 204 (10.0)      |             | 342 (61.7) | 597 (43.4)         |         |
| Chemotherapy              | 128 (26.9)     | 157 (7.7)       |             | 201 (36.3) | 745 (54.1)         |         |
| Chemoradiotherapy         | 195 (41.1)     | 1662 (81.7)     |             | 10 (1.8)   | 23 (1.7)           |         |
| Other/not known           | 3 (0.6)        | 11 (0.5)        |             | 1 (0.2)    | 11 (0.8)           |         |
| Type of resection         |                |                 | < 0.001     |            |                    |         |
| Transhiatal approach      | 25 (5.3)       | 729 (35.8)      |             | -          | -                  |         |
| Transthoracic approach    | 450 (94.7)     | 1305 (64.2)     |             | -          | -                  |         |
| Partial gastrectomy       | -              | -               |             | 282 (50.9) | 768 (55.8)         | 0.050   |
| Total gastrectomy         | -              | -               |             | 272 (49.1) | 608 (44.2)         |         |
| Reconstruction            |                |                 | < 0.001     |            |                    |         |
| Gastric tube/full stomach | 429 (90.3)     | 1996 (98.7)     |             | 2* (0.4)   | 14* (1·0)          | 0.092   |
| Oesophagojejunostomy      | 35 (7.4)       | 6 (0.3)         |             | 244 (44.0) | 596 (43.3)         |         |
| Gastroenterostomy         | 0 (0)          | 0 (0)           |             | 286 (51.6) | 677 (49.2)         |         |
| Other/not known           | 11 (2.3)       | 32 (1.6)        |             | 22 (4.0)   | 89 (6.5)           |         |
| Location anastomosis      |                |                 | < 0.001     |            |                    | < 0.001 |
| Intra-abdominal           | 6 (1.3)        | 2 (0.1)         |             | 520 (93.9) | 1183 (86.0)        |         |
| Intrathoracic             | 368 (77.5)     | 560 (27.5)      |             | 21 (3.8)   | 124 (9.0)          |         |
| Cervical                  |                | 1432 (70.4)     |             | 1 (0.2)    | 2 (0.1)            |         |
| Other/not known           | 4 (0.8)        | 40 (2.0)        |             | 12 (2.2)   | 67 (4.9)           |         |
| Annual procedural volume  |                |                 | < 0.001     |            |                    | < 0.001 |
| ≤10                       | 78 (16.4)      | 26 (1.3)        |             | 296 (53.4) | 219 (15.9)         |         |
| 11-20                     | 119 (25.1)     | 233 (11.5)      |             | 158 (28.5) | 562 (40.8)         |         |
| 21-30                     | 131 (27.6)     | 693 (34.1)      |             | 100 (18.1) | 349 (25.4)         |         |
| 31-40                     | 99 (20.8)      | 354 (17.4)      |             | 0 (0)      | 66 (4.8)           |         |
| > 40                      | 48 (10.1)      | 728 (35.8)      |             | 0 (0)      | 180 (13·1)         |         |

Table 3 Treatment and hospital characteristics of patients undergoing oesophagectomy and gastrectomy by country

Values in parentheses are percentages. \*Registration error.  $\dagger\chi^2$  test.

 Table 4 Postoperative complications following oesophagectomy and gastrectomy by country

|                                     | Oesop                       | Oesophagectomy               |                             | strectomy                    |
|-------------------------------------|-----------------------------|------------------------------|-----------------------------|------------------------------|
|                                     | Sweden<br>( <i>n</i> = 475) | The Netherlands $(n = 2034)$ | Sweden<br>( <i>n</i> = 554) | The Netherlands $(n = 1376)$ |
| Postoperative complications         |                             |                              |                             |                              |
| Pulmonary                           | 64 (13.5)                   | 674 (33.1)                   | 50 (9.0)                    | 193 (14.0)                   |
| Anastomotic leakage                 | 38 (8.0)                    | 273 (13.4)                   | 25 (4.5)                    | 57 (4.1)                     |
| Cardiovascular                      | 33 (6.9)                    | 266 (13.1)                   | 20 (3.6)                    | 78 (5.7)                     |
| Chylous leakage                     | 11 (2.3)                    | 151 (7.4)                    | 0 (0)                       | 28 (2.0)                     |
| Recurrence nerve injury             | 22 (4.6)                    | 98 (4.8)                     | 1 (0.2)                     | 0 (0)                        |
| Thromboembolic                      | 12 (2.5)                    | 50 (2.5)                     | 14 (2.5)                    | 20 (1.5)                     |
| Conduit necrosis                    | 16 (3.4)                    | 36 (1.8)                     | 1 (0.2)                     | 3 (0.2)                      |
| Bleeding                            | 4 (0.8)                     | 23 (1.1)                     | 13 (2.3)                    | 23 (1.7)                     |
| Intra-abdominal abscess             | 4 (0.8)                     | 15 (0.7)                     | 33 (6.0)                    | 51 (3.7)                     |
| Pathology                           |                             |                              |                             |                              |
| No. of lymph nodes*                 | 27 (15-47)                  | 18 (13–24)                   | 21 (10-39)                  | 19 (13–27)                   |
| Resection margins                   |                             |                              |                             |                              |
| Complete tumour removal (R0)        | 439 (92.4)                  | 1888 (92.8)                  | 458 (82.7)                  | 1170 (85.0)                  |
| Incomplete tumour removal/not known | 36 (7.6)                    | 146 (7·2)                    | 96 (17·3)                   | 206 (15.0)                   |

Values in parentheses are percentages unless indicated otherwise; \*values are median (i.q.r.). Some patients had multiple complications.

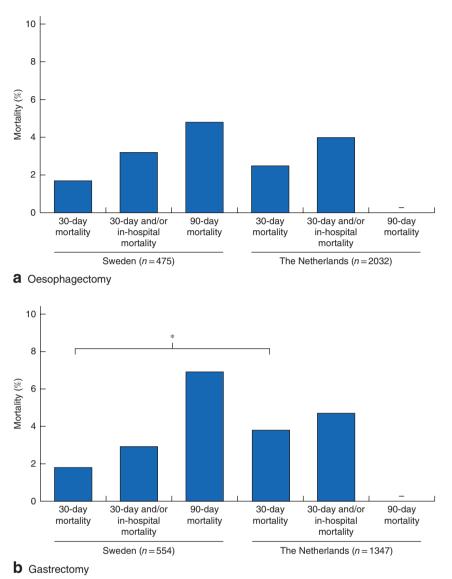


Fig. 2 Postoperative mortality (30-day, 30-day and/or in-hospital, and 90-day) after **a** oesophagectomy and **b** gastrectomy in Sweden and the Netherlands. Ninety-day mortality in Sweden was calculated by linkage with the Swedish Patient Registry; for the Netherlands,

90-day mortality is not included in the register. \* $P < 0.050 (\chi^2 \text{ test})$ 

(age, ASA grade, BMI). For non-ordinal co-variables with more than two categories, the reference category was based on guidelines or group size (neoadjuvant treatment, type of resection and location of anastomosis). Missing items were analysed in a separate group if they exceeded 5.0 per cent.

Statistical analyses were performed in PASW<sup>®</sup> Statistics version 21.0 (IBM, Armonk, New York, USA).

#### **Results**

Between January 2012 and December 2014, 4439 patients underwent oesophagectomy (2509 patients) or gastrectomy

(1930 patients) for oesophageal or gastric cancer. The number of patients who had an oesophagectomy was almost fourfold lower in Sweden: 475 *versus* 2034 in the Netherlands. Some 554 patients had a gastrectomy in Sweden compared with 1376 patients in the Netherlands. Estimated resection rates were almost similar for oesophageal cancer (23.0 per cent in Sweden *versus* 26.2 per cent in the Netherlands) and gastric cancer (38.7 and 36.0 per cent respectively). In both countries, the number of patients who underwent oesophagectomy for cancer increased during the study period. The number of gastrectomies for cancer decreased in Sweden, compared with an increase in the Netherlands (*Fig. 1*). In 2012, oesophagectomies and gastrectomies were performed in ten and 33 hospitals respectively in Sweden *versus* eight and 26 hospitals in 2014. The situation in the Netherlands was similar: in 2012, oesophagectomies and gastrectomies were performed in 23 and 44 hospitals *versus* 22 and 27 hospitals in 2014.

### Patient and tumour characteristics

Patient and tumour characteristics are shown in *Table 2*. The median age was 66 (i.q.r. 59–71) years in patients who had an oesophagectomy and 70.5 (62–77) years in those who had a gastrectomy. Patients registered in the NREV were older but had less co-morbidity, as reflected by lower ASA grades. No clinically relevant differences were seen for tumour location. Patients in the DUCA had a more advanced clinical tumour stage than those in the NREV. Incomplete clinical tumour staging (T, N and M categories) was observed more frequently in the DUCA, especially for patients with gastric cancer.

#### Treatment and hospital characteristics

Neoadjuvant chemotherapy or chemoradiotherapy was given to 85.9 per cent of patients who underwent oesophagectomy compared with 51.3 per cent who underwent gastrectomy (*Table 3*). Neoadjuvant treatment rates were significantly lower for oesophagectomy and gastrectomy in Sweden (68.6 and 38.3 per cent) than in the Netherlands (90.0 and 56.6 per cent).

In the Netherlands, chemoradiotherapy was the preferred neoadjuvant treatment modality in patients undergoing oesophagectomy (81·7 per cent). A transthoracic oesophagectomy (94·7 per cent) with an intrathoracic anastomosis (77·5 per cent) was chosen in the majority of patients who had an oesophagectomy in Sweden. In the Netherlands, a transhiatal approach (35·8 per cent) was also common, and a cervical anastomosis (70·4 per cent) was preferred (*Table 3*).

In both countries, the annual procedural hospital volume increased between 2012 and 2014 for oesophagectomy (P < 0.001 for Sweden; P = 0.550 for the Netherlands) and gastrectomy (P = 0.042 for Sweden; P < 0.001 for the Netherlands) (*Fig. 1*). Higher annual procedural volumes per hospital were observed in the Netherlands (*Table 3*). The median annual hospital volume for oesophagectomy was 26.0 (i.q.r. 14.0-31.0) in Sweden and 33.0 (25.0-49.0) in the Netherlands; for gastrectomy, the median volume was 10.0 (5.0-19.0) in Sweden and 18.0 (13.0-25.0) in the Netherlands.

**Table 5** Multivariable analysis of postoperative mortality inpatients who underwent oesophagectomy or gastrectomy forcancer in Sweden and the Netherlands

|                          | 30-day and/or in-hospital mortality |                           |  |
|--------------------------|-------------------------------------|---------------------------|--|
|                          | Oesophagectomy<br>Odds ratio        | Gastrectomy<br>Odds ratio |  |
| Age (years)              |                                     |                           |  |
| 60-75                    | 1.00 (reference)                    | 1.00 (reference)          |  |
| 0-59                     | 0.46 (0.26, 0.81)                   | 0.24 (0.09, 0.68)         |  |
| > 75                     | 1.63 (0.89, 2.99)                   | 0.78 (0.46, 1.32)         |  |
| Sex                      |                                     |                           |  |
| Μ                        | 1.00 (reference)                    | 1.00 (reference)          |  |
| F                        | 1.28 (0.79, 2.06)                   | 1.39 (0.87, 2.22)         |  |
| ASA grade                |                                     |                           |  |
| 1–11                     | 1.00 (reference)                    | 1.00 (reference)          |  |
| $\geq$ III               | 2.77 (1.80, 4.26)                   | 2.97 (1.84, 4.80)         |  |
| Unknown                  | 3.92 (0.87, 17.61)                  | 1.32 (0.17, 10.21)        |  |
| BMI (kg/m <sup>2</sup> ) |                                     |                           |  |
| 20-24                    | 1.00 (reference)                    | 1.00 (reference)          |  |
| < 20                     | 2.04 (1.04, 4.00)                   | 0.90 (0.44, 1.88)         |  |
| 25–29                    | 0.89 (0.55, 1.44)                   | 0.51 (0.29, 0.90)         |  |
| ≥ 30                     | 0.68 (0.35, 1.32)                   | 0.47 (0.21, 1.02)         |  |
| Unknown                  | 1.70 (0.21, 14.06)                  | 1.45 (0.40, 5.24)         |  |
| Neoadjuvant treatment    |                                     |                           |  |
| Chemoradiotherapy        | 1.00 (reference)                    | 2.57 (0.55, 11.99)        |  |
| None                     | 1.03 (0.56, 1.90)                   | 1.84 (1.05, 3.23)         |  |
| Chemotherapy             | 0.40 (0.14, 1.09)                   | 1.00 (reference)          |  |
| Other/unknown            | 1.58 (0.19, 13.04)                  | 2.57 (0.30, 22.03)        |  |
| Type of resection        |                                     |                           |  |
| Transthoracic approach   | 1.00 (reference)                    | -                         |  |
| Transhiatal approach     | 0.67 (0.40, 1.13)                   | -                         |  |
| Partial gastrectomy      | -                                   | 1.00 (reference)          |  |
| Total gastrectomy        | -                                   | 1.44 (0.88, 2.37)         |  |
| Location of anastomosis  |                                     |                           |  |
| Cervical                 | 1.00 (reference)                    | -                         |  |
| Intra-abdominal          | 4.12 (0.44, 38.20)                  | 1.00 (reference)          |  |
| Intrathoracic            | 0.89 (0.54, 1.49)                   | 1.56 (0.68, 3.57)         |  |
| Other/unknown            | 1.16 (0.27, 5.03)                   | 0.24 (0.03, 1.81)         |  |
| Country                  |                                     |                           |  |
| The Netherlands          | 1.00 (reference)                    | 1.00 (reference)          |  |
| Sweden                   | 0.79 (0.40, 1.56)                   | 0.53 (0.29, 0.95)         |  |

Values in parentheses are 95 per cent confidence intervals.

#### Surgical outcomes

Complication rates were higher for patients who underwent oesophagectomy (1432 of 2509, 57·1 per cent) than for those who had a gastrectomy (680 of 1930, 35·2 per cent) (P < 0.001). Complication rates were lower in Sweden than in the Netherlands for both oesophagectomy (42·5 *versus* 60·5 per cent respectively; P < 0.001) and gastrectomy (30·0 *versus* 37·4 per cent; P < 0.001) (*Table 4*). Univariable analysis revealed a statistically significant difference in the 30-day mortality rate between the two countries following gastrectomy (1·8 per cent in Sweden *versus* 3·8 per cent in the Netherlands; P = 0.026). After oesophagectomy, the 30-day mortality rate was 1.7 and 2.5 per cent respectively (P = 0.285) (*Fig. 2*).

#### Multivariable model

After adjustment for differences in case mix, the risk of 30-day and/or in-hospital mortality was lower for patients who underwent gastrectomy in Sweden than for those in the Netherlands (odds ratio 0.53, 95 per cent c.i. 0.29 to 0.95) (*Table 5*). There was no significant difference for 30-day and/or in-hospital mortality after oesophagectomy between the two countries. Other factors independently associated with 30-day and/or in-hospital mortality were age, ASA grade and BMI (only for gastrectomy). A lower BMI (below 20 kg/m<sup>2</sup>) was associated with worse outcome after oesophagectomy, whereas a BMI of 25-29 kg/m<sup>2</sup> indicated better outcome after gastrectomy, compared with a BMI of 20-24 kg/m<sup>2</sup> (*Table 5*).

#### **Discussion**

This study has demonstrated differences in patient, tumour and treatment characteristics as well as in 30-day and/or in-hospital mortality between Sweden and the Netherlands in patients undergoing resection for oesophageal or gastric cancer. A number of differences existed between the two countries. Patients in Sweden were older but had less advanced disease and less co-morbidity than those in the Netherlands. A lower proportion of patients underwent neoadjuvant treatment in Sweden. Surgical strategies differed. A transthoracic approach with intrathoracic anastomosis was performed predominantly in Sweden, whereas a transhiatal approach and cervical anastomosis were both used more frequently in the Netherlands. Adjusted 30-day and/or in-hospital mortality after gastrectomy in the Netherlands was twice as high as in Sweden.

Nationwide cancer registries and clinical audit systems give insight into the safety and effectiveness of the provided treatment. These quality initiatives also provide excellent opportunities for research including questions that are not easily investigated in RCTs<sup>20</sup>. In recent years, three studies<sup>10,21,22</sup> have shown variable outcomes for patients with oesophageal or gastric cancer across Europe. The present study confirms these country-dependent differences.

Centralization of oesophagogastric cancer surgery improves outcome<sup>23,24</sup>. In Sweden and the Netherlands, the process of centralization for both oesophagectomy and gastrectomy has taken place<sup>9,25,26</sup>. In the Netherlands, centralization accelerated after the introduction of quality standards, defined by the Health Care Inspectorate, the Association of Surgeons of the Netherlands and the Dutch Federation for Oncological Societies (SON-COS), describing a minimum annual hospital volume for each procedure<sup>9,27</sup>. In Sweden, no minimum annual procedural hospital volume has been defined. This is reflected by lower annual hospital volumes observed for both oesophagectomy and gastrectomy. However, the SKL (Sveriges Kommuner och Landsting), a central Swedish agency with impact on healthcare issues, recommended that oesophagogastric cancer surgery should be performed in only six hospitals from 2017 onwards.

Despite higher annual hospital volumes observed in the Netherlands, postoperative morbidity and mortality rates were higher than those in Sweden. These differences in mortality have already been described in a previous study<sup>10</sup> based on data covering the years 2004-2009. This was before the process of centralization was initiated in either country, indicating that other factors are involved. These differences are not likely to be explained by differences in resection rates between the two countries, as estimated resection rates were similar for both oesophageal cancer and gastric cancer. Previous data from NREV<sup>26</sup> showed significant differences between regions in Sweden in terms of resections rates. Similar hospital variation exists for the probability of receiving surgery for gastric or oesophageal cancer in the Netherlands<sup>28,29</sup>. Such cultural differences between surgical centres at a national level may contribute to disparities in patient selection. This might also be true on an international level.

Although this study found that patients in Sweden were significantly older, they had less advanced disease and less co-morbidity. The risk of postoperative complications and death may be determined by co-morbidity rather than age alone<sup>30,31</sup>. A higher proportion of patients in the Netherlands underwent neoadjuvant chemotherapy or radiotherapy. This could also have an impact on postoperative morbidity and mortality<sup>32</sup>. Higher neoadjuvant treatment rates in the Netherlands, in particular chemoradiotherapy before oesophagectomy, are likely due to the influence of a national RCT (CROSS) that showed improved survival with this treatment modality compared with surgery alone<sup>33</sup>. Two Swedish studies<sup>34,35</sup> demonstrated a higher risk of postoperative morbidity and mortality after neoadjuvant treatment and improved survival rates only for a subgroup of patients. Differences in pathological outcomes, such as higher lymph node yield in Sweden after oesophagectomy, could be explained by both differences in surgical approach, with a higher rate of transthoracic resections in Sweden, and a higher rate of neoadjuvant chemoradiotherapy observed in the Netherlands<sup>36,37</sup>. The higher proportion of patients with oesophageal cancer who received neoadjuvant chemoradiotherapy followed by a transhiatal resection and cervical anastomosis may also reflect the implementation of a Dutch RCT that reported fewer pulmonary complications and a shorter hospital/ICU stay in patients following transhiatal oesophagectiomy<sup>38</sup>.

In Sweden, the definitions of distal oesophageal cancer (C15.5) and gastro-oesophageal junctional cancer type I (C16.0A) are often used interchangeably. This might reflect the observed difference in the incidence of gastro-oesophageal junction cancer between the two countries, but have little effect on the choice of operative strategy as tumours in these locations are best treated with oesophagectomy. The present study showed a similar rate of postoperative recurrent nerve injury palsy in Sweden and the Netherlands, although more cervical anastomoses were performed in the Netherlands. This reflects the importance of adding nationwide population-based data to obtain a comprehensive and more complete view of the pros and cons of different therapeutic alternatives. In-depth investigation of preventive measures that lead to lower recurrent nerve injury palsy in Sweden might potentially result in further improvement in quality of care at an international level.

Differences between the countries in neither 90-day mortality nor long-term survival could be investigated in the present study. The univariable model showed that, compared with the Netherlands, Sweden had a significantly lower 30-day mortality rate after gastrectomy. The 90-day mortality rate in Sweden is known to be higher than the 30-day mortality rate, highlighting the importance of longer follow-up after surgery for oesophagogastric cancer to draw proper conclusions regarding patient selection, treatment and quality of postoperative care<sup>39</sup>. As all Swedish citizens are given a unique identification number at birth, cross-matching between registers such as the NREV, the Swedish Patient Register and the Cause of Death Register facilitates calculation of survival. In the Netherlands, collaborations between registers have failed due to legal and political obstacles, and linkage of all relevant databases for oesophagogastric cancer in the Netherlands has not yet been successful. Furthermore, in the NREV all patients diagnosed with oesophagogastric cancer are registered, whereas the DUCA is a surgical audit including only patients who had surgery with the intent of resection. On the other hand, registration in DUCA is mandatory, whereas registration in NREV is voluntary. At the beginning of each calendar year, data entry for the preceding year in the DUCA must be completed. This enables efficient data analysis and delivery of information to hospitals and specialists. Insight into differences between NREV and DUCA may help to increase the completeness

and validation of cancer patient registration systems in both countries.

The strengths of this study are its population-based design, using data from multiple years from two high-quality registries including in-depth information and near-complete coverage of all patients who underwent resection for oesophagogastric cancer in Sweden and the Netherlands. As healthcare in both countries is based on a public system, no private institutions are involved in oesophagogastric cancer surgery. This supports completeness of the data. Some limitations of the study are that it was possible to analyse only those variables included in both registries. For example, it was not possible to evaluate differences in patient selection, organization of care, use of minimally invasive techniques, severity of complications and long-term survival. In addition, different definitions of morbidity and mortality were used in the two registries, and these could influence results, although the accuracy of reporting both surgical and general postoperative complications in the NREV was found to be 90-93 per cent in a recent study<sup>8</sup>. A common data item list, as presented by the European Registration of Cancer Care in 2014, is of great value for international benchmarking in oesophageal and gastric cancer surgery. Standardization of registries, together with international consensus regarding definitions used in the registries, would allow easier comparisons between different countries and minimize reporting bias<sup>40</sup>. Both registries have now adopted registration of complications according to this format<sup>41</sup>.

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#### **Supporting information**

Additional supporting information can be found online in the Supporting Information section at the end of the article.