

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

BMJ Open

The completeness of follow-up, a previously unrecognized quality indicator for outcome analyses in registry-based studies?

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-019551
Article Type:	Research
Date Submitted by the Author:	15-Sep-2017
Complete List of Authors:	Enochsson, Lars; Umea University, Surgical and Perioperative Sciences Blohm, My; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Sandblom, Gabriel; Karolinska Institute, Center for Digestive Disease; Karolinska Institutet Department for Clinical Intervention and Technology, Jonas, Eduard; University of Cape Town, Health Sciences Faculty Hallerbäck, Bengt; Goteborgs Universitet, Department of Surgery Lundell, Lars; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Österberg, Johanna; Karolinska institutet Department of Clinical Sciences Intervention and Technology
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Epidemiology
Keywords:	Adult surgery < SURGERY, Hepatobiliary surgery < SURGERY, QUALITATIVE RESEARCH, Endoscopy < GASTROENTEROLOGY

SCHOLARONE™
Manuscripts

The completeness of follow-up, a previously unrecognized quality indicator for outcome analyses in registry-based studies?

Lars Enochsson¹, My Blohm^{2,3}, Gabriel Sandblom^{2,4}, Eduard Jonas⁵, Bengt Hallerbäck⁶, Lars Lundell², Johanna Österberg^{2,3}

¹Department of Surgical and Perioperative Sciences, Sunderby Research Unit, Umeå University, Sweden

²Division of Surgery, CLINTEC, Karolinska Institutet, Stockholm, Sweden

³Department of Surgery, Mora Hospital, Mora, Sweden

⁴Center for Digestive Diseases, Karolinska University Hospital, Huddinge, Stockholm, Sweden

⁵Surgical Gastroenterology Unit, Department of Surgery, Groote Schuur Hospital, University of Cape Town Health Sciences Faculty, Cape Town, South Africa

⁶Department of Surgery, Norra Älvsborg County Hospital, Trollhättan, Sweden

Correspondence to:

Lars Enochsson, MD, PhD

Department of Surgical and Perioperative Sciences, Umeå University, Umeå,

Sunderby Hospital

97180 Luleå,

Sweden

E-mail: lars.enochsson@umu.se

Phone: +46 920 28 31 05

Fax: +46 920 28 33 20

ABSTRACT

OBJECTIVE

To analyse factors that may affect the validity of follow-up data in a national quality registry.

DESIGN

Population-based register study.

SETTING

Data from the Swedish national registry of gallstone surgery and endoscopic retrograde cholangiopancreatography (ERCP), GallRiks.

POPULATION

All cholecystectomies and ERCPs recorded in GallRiks between 1 Jan 2006 and 31 Dec 2014.

MAIN OUTCOME MEASURES

Outcomes for intra- as well as post-procedural adverse events between units with either a 30-day follow-up of $\geq 90\%$ compared to those with a less frequent follow-up ($< 90\%$).

RESULTS

Between 2006 and 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of non-index procedures and those with incomplete data 152 827 procedures remained for final analyses. In patients having a cholecystectomy, there were no differences regarding the adverse event rates, irrespective of the follow-up frequency. However, in the more complicated endoscopic ERCP procedures, the postoperative adverse event rates were significantly higher in those with a more frequent and complete 30-day follow-up (OR 1.92; 95% CI 1.76-2.11).

CONCLUSIONS

Differences in the follow-up frequency in registries affects the reported outcomes as exemplified by the complicated endoscopic ERCP procedures. A high follow-up rate shall serve as an additional quality indicator for surgical registries.

Strengths and limitations of this study

-The prospectively collected data from over 90% of the registered cholecystectomies and ERCP in nearly all Swedish hospitals is a major strength of this study.

-Self-reported data always have the inherent risk of being subjected to certain bias.

-Another limitation of this study is that it presents data from a period of nine years (2006-2014) where the national coverage rate increased from 73% to 90%.

Funding

This study was made possible by a grant from the Umeå University ALF research funding.

The funding body had no role in the study. The GallRiks Registry is funded by the Swedish National Board of Health and Welfare.

No competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Data sharing statement

There is no additional unpublished data from this study. The data in this study are taken from Swedish registry of Cholecystectomy and ERCP (GallRiks) and are available via the corresponding author on request.

INTRODUCTION

National quality registry studies have been presented as a complement to Randomized controlled trials (RCTs). Registry based studies usually require less financial resources and enable data collection from large-scale patient cohorts without the unavoidable selection bias among those enrolled into clinical trials and always carry valid statistical power. Databases with long-term follow-up open up for conduct of studies focusing on rare events and effects occurring late in the clinical course. There are several instances where registry-based studies have improved the management of patients, for example in the treatment of non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS),¹ the elimination of sub-standard orthopaedic prostheses from clinical use² and the effects of different surgical approaches and suture materials on the outcome of hernia surgery.^{3,4} Accordingly registry studies can address clinical questions that due to statistical power issues, time and financial constraints would never have been studied under the design of a RCTs such as the value of intraoperative cholangiography in preventing bile duct injury in association with gallstone surgery^{5,6} and the question whether and why women with inguinal herniorrhaphies have a significantly higher reoperation rate compared to males.⁷ Furthermore, in a randomized clinical trial published in Lancet 2016 the outcome of closure of mesenteric defects in gastric bypass surgery was evaluated by analysing registry data from the Scandinavian Obesity Surgery Registry (SOREG).⁸

Thus, registry-based studies have a definite role in addressing many of the questions that arise in and have relevance for everyday clinical practice.

However, although population-based registry studies have high external validity, reflecting real-life data and the clinical routines as they are practised in the community at large, they are often hampered by the lack of uniform protocols and standardised routines for registering relevant data. This may skew the outcome since units, in which a limited awareness for

1
2
3 quality of care is prevailing, may well report data with incomplete accuracy, leading to a risk
4
5 for lower coverage concerning the self-reported registrations on adverse events. Hence such a
6
7 heterogeneity in the validity of data may seriously limit the options for correct interpretations
8
9 in respective outcome analyses.

10
11 The aim of this study was therefore to analyse factors that may affect the validity of follow-up
12
13 data in a national quality registry.
14
15

16 17 18 **METHODS**

19 20 **The Swedish National Registry for Gallstone Surgery and Endoscopic retrograde** 21 22 **cholangiopancreatography (ERCP) (www.gallriks.se)**

23
24 The Swedish National Registry for Gallstone Surgery and ERCP (GallRiks) was established
25
26 on 1 May 2005 as a registry for cholecystectomy and ERCP procedures.⁹ The aim of the
27
28 registry is to obtain a comprehensive database of individuals subjected to these interventions,
29
30 including information on patient demographics and the indications and outcomes of
31
32 interventions. All data entering are online. The initial procedures, including information on
33
34 perioperative complications, are usually registered by operating clinicians. At a 30-day
35
36 follow-up all medical records are reviewed for post-procedural adverse events and data are
37
38 entered, usually by a local coordinator (nurse or a medical secretary).⁹ GallRiks data are
39
40 compared to patients' records on a regular basis by a dedicated independent validation team. A
41
42 complete match between overall registry data and medical records has been reported in 98.2%
43
44 of subjects with a 100% match for bile duct injury.¹⁰
45
46
47
48
49

50 51 *Data extraction*

52
53 Data on cholecystectomy and ERCP procedures performed between 1 January 2006 and 31
54
55 December 2014 and entered into the GallRiks registry were assessed. Non-index procedures
56
57
58
59

1
2
3 and procedures with incomplete data were excluded from the analysis. The complete 30-day
4 follow-up frequency of cholecystectomy and ERCP procedures for individual units
5 participating in the registry was calculated. We arbitrary chose the 90% limit for the 30-day
6 complete follow-up in order to compare groups with sufficient number of procedures to reach
7 enough statistical power to compare good follow-up ($\geq 90\%$) with a less complete follow-up
8 ($< 90\%$). Outcomes for peri- and postoperative complications were studied.
9
10
11
12
13
14
15

16 17 18 *Definitions*

19 For the purpose of this paper, and in accordance with the descriptions in the GallRiks
20 database, adverse events are defined and described per consensus agreement.
21
22

23
24 *Cholecystectomy*: Surgical removal of the gallbladder in patients with an indication for
25 removing the organ including symptomatic gallstone disease, neoplasms, and acalculous
26 gallbladder conditions.
27
28

29
30
31 *Endoscopic retrograde cholangiopancreatography (ERCP)*: An endoscopic technique for
32 transpapillary access to the common bile duct and/or pancreatic duct including accessing the
33 mentioned ducts through bilio- or pancreatico-digestive anastomoses, with diagnostic or
34 therapeutic intent.
35
36
37

38
39
40 *Index procedures*: The first cholecystectomy and/or ERCP-procedure for each patient per in-
41 hospital treatment period.
42

43
44 *Intra-procedural adverse events for cholecystectomy*: Bile duct injury, gut perforation,
45 bleeding requiring intervention or other complications that adversely affected the operation.
46
47

48
49 *Intra-procedural adverse events for ERCP*: Bleeding, extravasation of contrast, perforation or
50 any other reason for the ERCP being terminated prematurely.
51

52
53 *Post-procedural adverse events*: Complications during the 30-day follow-up period that
54 require some form of medical or surgical intervention, including readmission and death.
55
56
57

1
2
3 *Pancreatitis*: Abdominal pain and an elevated amylase at least three times above normal at a
4 time point more than 24 hours after terminating the procedure, as defined by Cotton.¹¹
5
6
7

8 9 *Statistical analysis*

10
11 Statistical analyses were performed using JMP 12.2.0 (SAS, Cary, NC, USA). Comparisons
12 of patient and procedure characteristics are presented in contingency tables, with pairwise
13 differences analysed with Pearson Chi-square test. The influence of $\leq 90\%$ follow-up on the
14 risk of adverse events, pancreatitis and bleeding was analysed using multivariable logistic
15 regression modelling. Each variable was tested in univariate and multivariate analyses for
16 statistical significance, according to purposeful selection as described by Hosmer et al.¹² In
17 the multivariate analysis the outcome was adjusted for sex, age (treated as a continuous
18 variable in the models but presented dichotomized into $<$ or \geq than 60 years (median)),
19 comorbidity dichotomized into ASA 1-2 and ASA 3-5, acute or elective procedure and
20 indication. The models were tested for multicollinearity and effect modification and were
21 finally assessed for goodness of fit. The effects of analysed variables are presented as odds
22 ratios for adverse events with 95% confidence intervals.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

RESULTS

Between January 1 2006 and December 31 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of 9328 non-index procedures and 57 procedures with incomplete data, 152 827 procedures remained for final analyses (95840 cholecystectomies and 56987 ERCPs) (figure 1). In total, 96.0% of the cholecystectomies and 95.4% of the ERCP procedures had a complete 30-day follow-up. The distribution of complete 30-day follow-up per hospital, for cholecystectomies and ERCP procedures are depicted in figure 2. For the cholecystectomy group, 20% of the hospitals had a 30-day follow-up frequency of less than 90% compared to 17% for ERCPs (figure 2). The demographics, physical status assessment and urgency of intervention of included patients are given in table 1. Patients that were operated on with a cholecystectomy or underwent an ERCP in centres with incomplete follow-up were older and had a higher ASA-score compared to those with a more complete 30-day follow-up. The adverse event rates for cholecystectomy and ERCP (intraoperative and total postoperative, with pancreatitis and bleeding showed separately) are given in figure 3. The overall total postoperative adverse event rate for ERCP during the study period was 13.2% and the pancreatitis frequency 3.8%. The incidence of these post-intervention adverse event rates was rather stable over the study period, except for pancreatitis where a small but significant increase was noted (figure 3). The reported risk of post procedural complications as well as pancreatitis and bleeding per se after ERCP was significantly increased in those hospitals with a more frequent follow-up, both in absolute terms as well as when adjusted for confounders (table 3). The reported risk of postoperative adverse events, including post-ERCP pancreatitis, was twice as high compared to the group with less complete follow-up. The risk of bleeding within the 30-day follow-up period was 38% higher in the group with a better follow-up. On the contrary, the risk of intra-

1
2
3 operative adverse events was significantly reduced in the centres included in the $\geq 90\%$ 30-day
4 follow-up group (table 3).
5
6
7

8
9 The incidence of recorded adverse events for cholecystectomies during the corresponding
10 period was 8.1% for postoperative adverse events, including 0.5% for pancreatitis. Although
11 the absolute frequency of total postoperative adverse events after cholecystectomy was
12 significantly higher in hospitals with a less complete 30-day follow-up, the risk of
13 complications did not differ between the two groups when adjusted for confounders (table 2).
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

DISCUSSION

The results of this study, analysing data from the Swedish national registry for gallstone surgery and ERCP (GallRiks), emphasize the importance of considering a thorough follow-up as an important confounder when analysing the outcome of registry-based studies.

Furthermore, differences in the follow-up frequency seemed to have a greater impact as a confounder in the more complicated interventional procedure ERCP than in the often technically less complicated procedure cholecystectomy.

Strengths and limitations of the study

The prospectively collected data in GallRiks from over 90% of the registered procedures in nearly all Swedish hospitals is a major strength of this study. The data registered in GallRiks have also been verified to have a high validity of over 98%.¹⁰ Another strength is that this report includes data from University Hospitals, County Hospitals, District Hospitals and private units as well. The quality of data has been a concern already from the start of the registry and is guaranteed by continuous quality controls of the data-validity. However, due to financial and time constraints this prospective and integrated part of the registry has to be limited to approximately 30 randomly selected, cross-matches between patient records and GallRiks registrations at each hospital completed every third year.

Self-reported data always have the inherent risk of being subjected to certain bias. When analysing the results of quality registry data, factors like coverage of the relevant population by the registry data as well as the follow-up rate have to be taken into consideration. Another limitation of this study is that it presents data from a period of nine years (2006-2014) where the national coverage rate increased from 73% to 90%. There is, however, no systematic reason why the proportion of those with incomplete versus complete follow up shall depend

1
2
3 on the coverage rate as such. It must also be emphasized that, although we found significant
4 differences between units with a high ($\geq 90\%$) and units with $< 90\%$ complete follow-up, the
5 overall completeness must be considered excellent since only 4.0 % of the cholecystectomies
6 and 4.6 % of the ERCs have an incomplete follow-up. Nevertheless the absence of uniform
7 study protocols makes it impossible to fully guarantee overall quality of data in population-
8 based registers. Even if these data are considered to have high external validity the
9 population-based registers may still produce some skewness of the data. The care for accuracy
10 of reporting, and providing healthcare of high quality, may result in a positive correlation
11 between self-reported adverse outcome and completeness of data. On the other hand centres,
12 where the quality of care is poorer, may also have insufficient routines for scrutinising
13 treatment outcome. The only way of avoiding this is a meticulous validation of all registered
14 data, preferably with careful selective assessment of data from units with low coverage as
15 well as to provide continuous education and support from the registry to the participating
16 units with less complete follow-up routines.
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34

35 *Comparison with other studies*

36
37 RCTs are considered one of the cornerstones of modern, evidence based medical science. It is
38 regarded as the most accurate method to answer key clinical questions and to offer the highest
39 levels of evidence that can be translated into the strongest treatment recommendations.¹³
40
41 However, RCTs are also associated with definite drawbacks and logistic challenges^{14 15} In
42 addition, in the case of industry-funded research, and particularly so when study data are
43 owned by the sponsoring body, study results that might have negative economic implications
44 are sometimes withheld from publication, leading to publication bias.¹⁶ Furthermore, the
45 number of included patients necessary for creating sufficient power for testing of hypotheses
46 in RCTs may preclude the completion of trials within reasonable time limits.¹⁷ Moreover,
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 treatment methods that in RCTs originating from large academic institutions from which
4 excellent results are reported, cannot always be repeated by and implemented in smaller and
5 more resource-challenged facilities. It has also been shown that the outcome for patients
6 excluded from randomisation often differs significantly from those enrolled in the randomised
7 trial co-hort.¹⁸ Thus, registry-based studies can and shall be looked upon as offering a
8 complement to RCTs data, since they can more closely mirror the effect of a certain
9 treatment-intervention in the entire population, given that good coverage is prevailing.
10
11
12
13
14
15
16
17
18
19

20 Several national quality registries have reported good coverage which is a prerequisite for a
21 well-functioning quality registry, particularly so for cancer registries and in the paediatric
22 population.^{19 20} As for Sweden, there are 53 national quality registries that report their
23 coverage to the Swedish National Board of Health and Welfare
24 (<http://www.socialstyrelsen.se/publikationer2015/2015-12-8>). Of these 53 registries 19 cover
25 specific interventional procedures, for example gynaecological operations, hip-replacement,
26 hernia surgery, and cholecystectomy, to mention a few. The national coverage of these
27 registries varies from 46% to 98%. In fact, some of these registries have a better coverage
28 than the Swedish National Patient Registry (NPR) because many of the procedures are done
29 by private hospitals that do not report to NPR as diligently as the government-funded
30 hospitals.
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45

46 Besides having good coverage, it is of vital importance for quality registries to contain valid
47 data. Dedicated validation processes should be in place for assessing and reporting the
48 correctness of the included data at regular intervals. The issue of a complete follow-up is
49 especially challenging in registries with focus on the management of benign diseases, since
50
51
52
53
54
55
56
57
58
59
60

1
2
3 these procedures do not have the same rigorous demands of a compulsory follow-up as those
4
5 for malignant conditions (<http://www.socialstyrelsen.se/publikationer2015/2015-12-8>).

6
7 The impact of the level of completeness of the follow-up for the validity of reported outcomes
8
9 in registries covering benign conditions, has not been previously probed and elucidated in the
10
11 literature. A survey by Rystedt et al, based on the validation of GallRiks, showed a high
12
13 completeness and correctness of entered data with an overall correctness of data of 98.2% and
14
15 100% for bile duct injuries.¹⁰ However, in this publication the completeness of follow-up was
16
17 not specifically addressed.
18
19

20
21
22 The compelling finding of this paper is that the reported incidence of postoperative adverse
23
24 events after ERCP is significantly lower in hospitals with an incomplete 30-day follow-up
25
26 frequency (<90%) as compared to those with a more complete follow-up ($\geq 90\%$). Although
27
28 these results could mirror true outcomes, it is more likely to be the result of failure to report
29
30 some of the adverse events by the hospitals with a less stringent documentation system for
31
32 follow-up. This assumption is supported by the finding that the reported incidence of intra-
33
34 operative adverse event is significantly higher in the group with $\geq 90\%$ 30-day follow-up,
35
36 implying that hospitals with an immaculate and accurate information accrual system also
37
38 follow up patients more diligently and report adverse events to a higher degree. This
39
40 discrepancy, where a less frequent 30-day follow-up significantly affected the reported
41
42 outcome in ERCP but not in cholecystectomy could imply that the effect of a complete 30-
43
44 day follow-up is more pronounced in procedures with a higher complication profile, since
45
46 ERCPs have a more congested post-operative complication profile compared to
47
48 cholecystectomies.
49
50
51
52
53
54
55
56
57
58
59
60

Conclusions and implications

Our findings may have significant general implications on how we shall interpret outcome data from registry studies. Differences in the follow-up rate seemed to significantly affect the reported outcome. The findings suggest that the validation process has to include the completeness of follow-up. Differences in the follow-up frequency in registries affect the reported outcomes as exemplified by the complicated endoscopic ERCP procedures. The study emphasises the importance of complete follow-up, since this variable may well act as a quality indicator for the respective registry.

Future research

Future research should focus on how the degree of complete follow-up in quality registers can correlate to more objectively and not self-reported quality indicators.

Contributors

LE conceived the study, created the study design, participated in the statistical analysis, analysed the data, and drafted and revised the paper. He is guarantor. MB participated in the analysis and interpretation of data, and revised the paper. GS participated in the statistical analysis and interpretation of data, and drafted and revised the paper. EJ interpreted the data and revised the manuscript. BH conceived the study and reviewed the manuscript. LL interpreted data and reviewed the manuscript. JÖ conceived the study, created the study design, and drafted and revised the paper.

All authors have approved of the final draft submitted.

Ethical approval

The regional research ethics committee at Karolinska Institutet, Stockholm, Sweden, approved the study.

Transparency

The first author (LE) confirms that the manuscript is an honest, accurate, and transparent account of the study; that no important aspects of the study have been omitted.

REFERENCES

1. Damman P, Jernberg T, Lindahl B, et al. Invasive strategies and outcomes for non-ST-segment elevation acute coronary syndromes: a twelve-year experience from SWEDHEART. *EuroIntervention* 2016;12(9):1108-16.
2. Graves SE. The value of arthroplasty registry data. *Acta Orthop* 2010;81(1):8-9.
3. Dahlstrand U, Wollert S, Nordin P, et al. Emergency femoral hernia repair: a study based on a national register. *Ann Surg* 2009;249(4):672-6.
4. Novik B, Nordin P, Skullman S, et al. More recurrences after hernia mesh fixation with short-term absorbable sutures: A registry study of 82 015 Lichtenstein repairs. *Arch Surg* 2011;146(1):12-7.
5. Tornqvist B, Stromberg C, Akre O, et al. Selective intraoperative cholangiography and risk of bile duct injury during cholecystectomy. *Br J Surg* 2015;102(8):952-8.
6. Tornqvist B, Stromberg C, Persson G, et al. Effect of intended intraoperative cholangiography and early detection of bile duct injury on survival after cholecystectomy: population based cohort study. *BMJ* 2012;345:e6457.
7. Bay-Nielsen M, Kehlet H. Inguinal herniorrhaphy in women. *Hernia* 2006;10(1):30-3.
8. Stenberg E, Szabo E, Agren G, et al. Closure of mesenteric defects in laparoscopic gastric bypass: a multicentre, randomised, parallel, open-label trial. *Lancet* 2016;387(10026):1397-404.
9. Enochsson L, Thulin A, Osterberg J, et al. The Swedish Registry of Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks): A nationwide registry for quality assurance of gallstone surgery. *JAMA Surg* 2013;148(5):471-8.

10. Rystedt J, Montgomery A, Persson G. Completeness and correctness of cholecystectomy data in a national register--GallRiks. *Scand J Surg* 2014;103(4):237-44.
11. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. *Gastrointest Endosc* 1991;37(3):383-93.
12. Hosmer DW, Taber S, Lemeshow S. The importance of assessing the fit of logistic regression models: a case study. *Am J Public Health* 1991;81(12):1630-5.
13. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328(7454):1490.
14. Carter AJ, Nguyen CN. A comparison of cancer burden and research spending reveals discrepancies in the distribution of research funding. *BMC Public Health* 2012;12:526.
15. Lundh A, Sismondo S, Lexchin J, et al. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2012;12:MR000033.
16. Doucet M, Sismondo S. Evaluating solutions to sponsorship bias. *J Med Ethics* 2008;34(8):627-30.
17. van den Broek MA, van Dam RM, Malago M, et al. Feasibility of randomized controlled trials in liver surgery using surgery-related mortality or morbidity as endpoint. *Br J Surg* 2009;96(9):1005-14.
18. Ros A, Carlsson P, Rahmqvist M, et al. Non-randomised patients in a cholecystectomy trial: characteristics, procedures, and outcomes. *BMC Surg* 2006;6:17.

- 1
2
3 19. Larsen IK, Smastuen M, Johannesen TB, et al. Data quality at the Cancer Registry
4 of Norway: an overview of comparability, completeness, validity and timeliness.
5 *Eur J Cancer* 2009;45(7):1218-31.
6
7
8
9 20. Steliarova-Foucher E, Kaatsch P, Lacour B, et al. Quality, comparability and
10 methods of analysis of data on childhood cancer in Europe (1978-1997): report
11 from the Automated Childhood Cancer Information System project. *Eur J Cancer*
12 2006;42(13):1915-51.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 **LEGEND TO FIGURES**

4
5 **Figure 1**

6
7 The procedures included in the analyses.
8
9

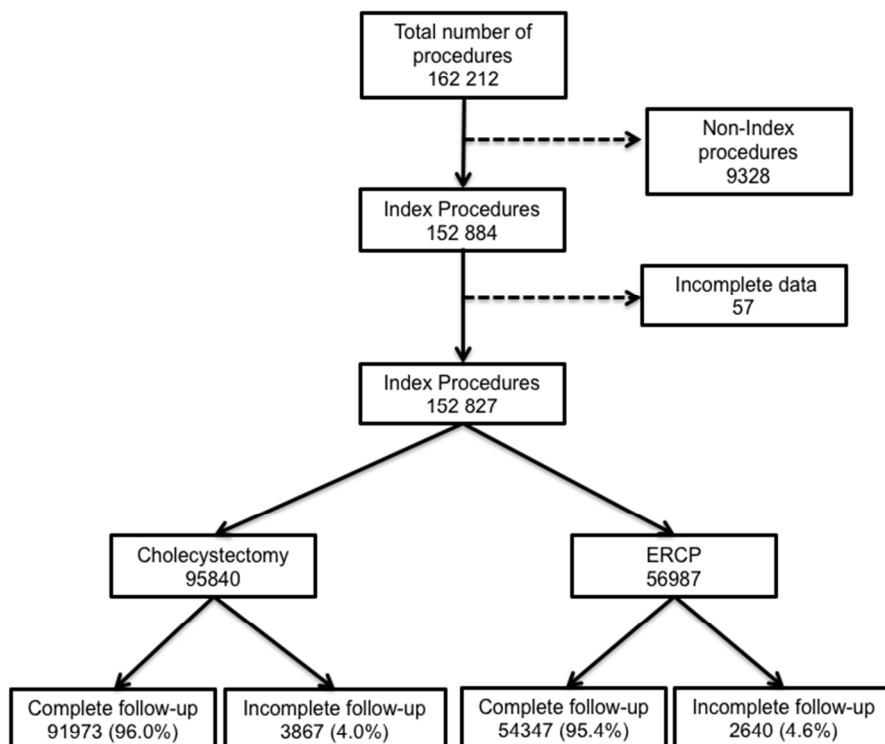
10
11 **Figure 2**

12
13 Complete 30-day follow-up frequencies following cholecystectomies and ERCP.
14
15

16
17 **Figure 3**

18
19 Adverse event rates after cholecystectomies and ERCP.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

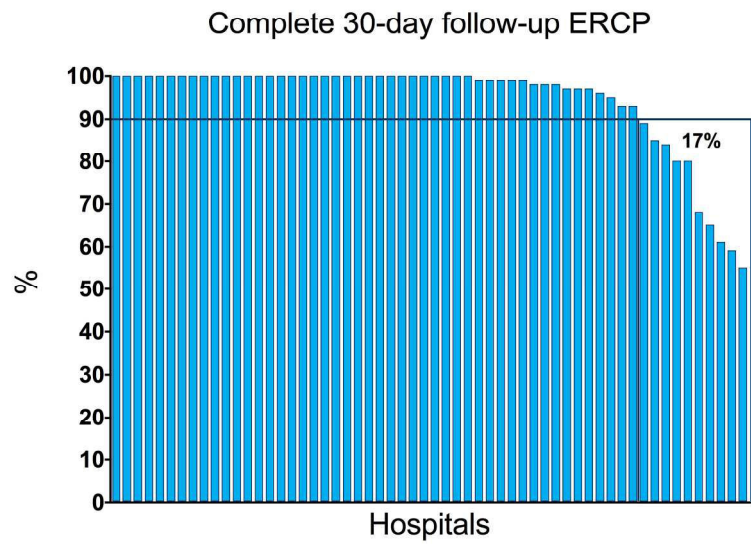
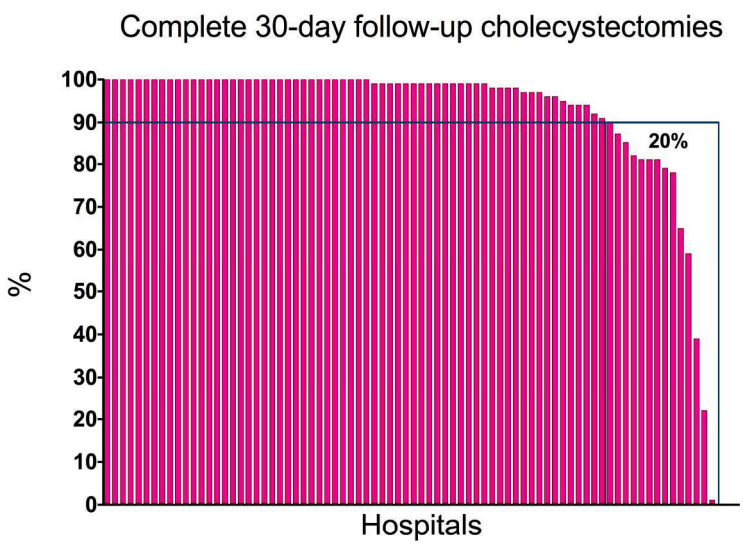
For peer review only



The procedures included in the analyses.

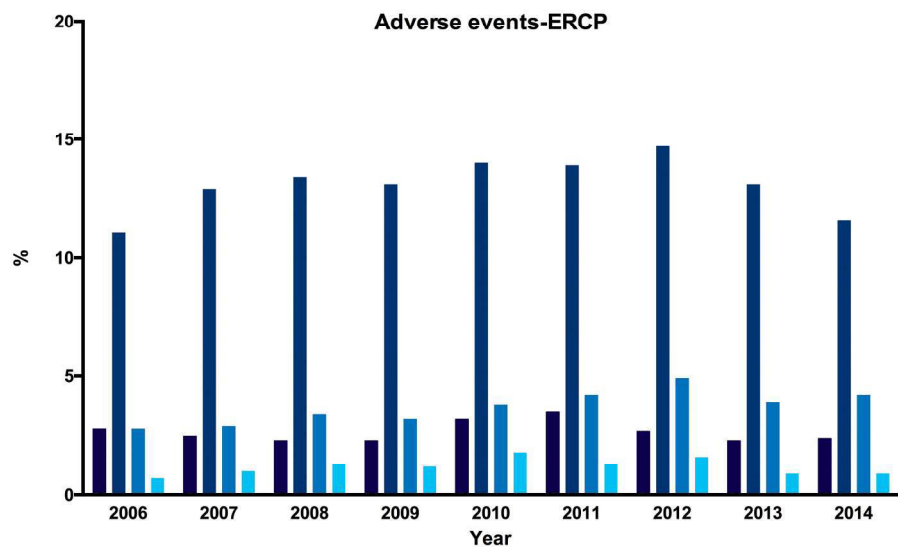
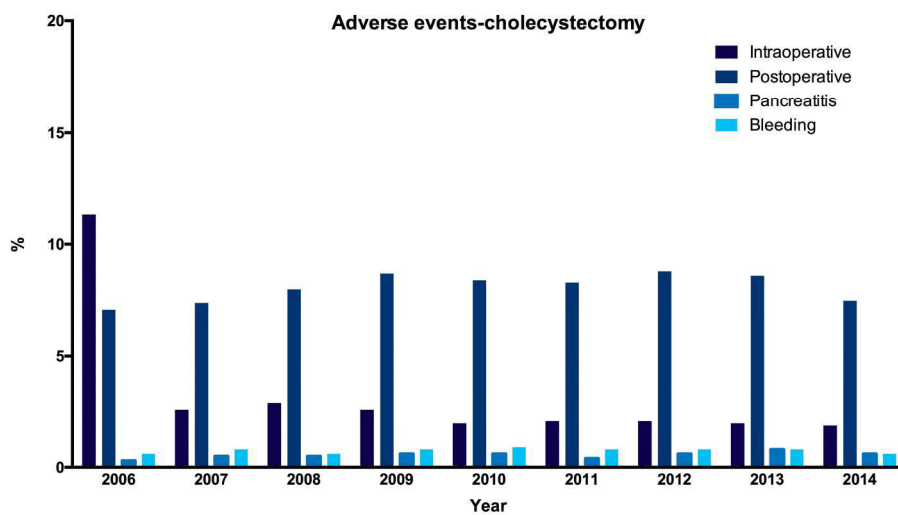
190x254mm (96 x 96 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Complete 30-day follow-up frequencies following cholecystectomies and ERCP.

668x1042mm (72 x 72 DPI)



Adverse event rates after cholecystectomies and ERCP.

809x1007mm (72 x 72 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Table 1
Demographics, physical status assessment and urgency of intervention stratification of examinations for the 152 827 patients included in the study

		30-day follow-up of cholecystectomies					30-day follow-up of ERCP				
		≥90%		<90%		<i>P</i>	≥90%		<90%		<i>P</i>
		<i>n</i>	%	<i>n</i>	%		<i>n</i>	%	<i>n</i>	%	
Gender	Female	55908	67.3	8311	65.1	<.0001	25673	53.0	4460	52.0	0.0906
	Male	27159	32.7	4462	34.9		22743	47.0	4111	48.0	
Age (years)	≥60	26442	31.9	4462	35.0	<.0001	35532	73.6	6724	78.5	<.0001
	<60	56461	68.1	8290	65.0		12767	26.4	1843	21.5	
ASA	ASA 1-2	76478	92.1	11124	87.1	<.0001	33457	69.1	4748	55.4	<.0001
	ASA ≥3	6589	7.9	1649	12.9		14959	30.9	3823	44.6	
Acute/Scheduled	Acute	24237	29.2	4433	34.7	<.0001	30093	62.2	5055	59.0	<.0001
	Scheduled	58830	70.8	8340	65.3		18323	37.8	3516	41.0	

Table 2

Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of cholecystectomies \geq 90%

	Adverse events				
	$\geq 90\%$ n=83067		<90% n=12773		P
	n	%	n	%	
Intraoperative	2548	3.0	381	3.0	0.8826
Total postoperative	6681	8.0	1119	8.8	0.0057
Pancreatitis	455	0.6	66	0.5	0.6570
Bleeding	629	0.8	96	0.8	0.9454

	Adverse events				
	Pancreatic duct cannulation vs. no cannulation				
	Unadjusted		Adjusted*		P
Odds Ratio	(95% CI)	Odds Ratio	(95% CI)		
Intraoperative	0.99	(0.89-1.11)	0.93	(0.84-1.04)	0.2298
Total postoperative	0.91	(0.85-0.97)	0.98	(0.91-1.05)	0.5067
Pancreatitis	1.06	(0.83-1.39)	1.30	(0.99-1.75)	0.0606
Bleeding	1.01	(0.82-1.26)	0.97	(0.78-1.21)	0.7821

*Adjusted for sex, age, ASA class, acute interventions and indications.

Table 3

Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of ERCPs $\geq 90\%$

	Adverse events				<i>P</i>
	$\geq 90\%$ n=48416		<90% n=8571		
	n	%	n	%	
Intraoperative	1267	2.6	252	2.9	0.0868
Total postoperative	6821	14.1	689	8.0	<.0001
Pancreatitis	1978	4.1	178	2.1	<.0001
Bleeding	591	1.2	76	0.9	0.0081

	Adverse events				<i>P</i>
	$\geq 90\%$ vs <90% 30-day follow-up				
	Unadjusted		Adjusted*		
	Odds Ratio	(95% CI)	Odds Ratio	(95% CI)	
Intraoperative	0.89	(0.77-1.02)	0.76	(0.66-0.87)	0.0002
Total postoperative	1.88	(1.73-2.04)	1.92	(1.76-2.11)	<.0001
Pancreatitis	2.01	(1.73-2.35)	2.04	(1.72-2.43)	<.0001
Bleeding	1.38	(1.09-1.77)	1.38	(1.08-1.79)	0.0100

*Adjusted for sex, age, ASA class, acute interventions and indications.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 2	Population-based register study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pages 4-5	
Objectives	3	State specific objectives, including any prespecified hypotheses	Abstract and page 5	
Methods				
Study design	4	Present key elements of study design early in the paper	Page 4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 5-6	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Pages 5-6	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 6-7	
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 5-7	
Bias	9	Describe any efforts to address potential sources of bias	Pages 10-11	
Study size	10	Explain how the study size was arrived at	Pages 5-6	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 7
		(b) Describe any methods used to examine subgroups and interactions	Page 7
		(c) Explain how missing data were addressed	Partly described on page 7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	The article is about this subject
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Described in results.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	That is what this article is all about
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Tables 2-3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2-3
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	In Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Inversed relationship between completeness of follow-up and coverage of postoperative complications. A potential source of bias in patient registers.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-019551.R1
Article Type:	Research
Date Submitted by the Author:	01-Nov-2017
Complete List of Authors:	Enochsson, Lars; Umea University, Surgical and Perioperative Sciences Blohm, My; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Sandblom, Gabriel; Karolinska Institute, Center for Digestive Disease; Karolinska Institutet Department for Clinical Intervention and Technology, Jonas, Eduard; University of Cape Town, Health Sciences Faculty Hallerbäck, Bengt; Goteborgs Universitet, Department of Surgery Lundell, Lars; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Österberg, Johanna; Karolinska institutet Department of Clinical Sciences Intervention and Technology
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Epidemiology
Keywords:	Adult surgery < SURGERY, Hepatobiliary surgery < SURGERY, QUALITATIVE RESEARCH, Endoscopy < GASTROENTEROLOGY

SCHOLARONE™
Manuscripts

1
2
3 **Inversed relationship between completeness of follow-up and**
4
5 **coverage of postoperative complications. A potential source of**
6
7 **bias in patient registers.**
8
9

10
11
12
13 Lars Enochsson¹, My Blohm^{2,3}, Gabriel Sandblom^{2,4}, Eduard Jonas⁵, Bengt Hallerbäck⁶, Lars
14
15 Lundell², Johanna Österberg^{2,3}
16
17

18
19
20 ¹Department of Surgical and Perioperative Sciences, Sunderby Research Unit, Umeå
21
22 University, Sweden
23

24 ²Division of Surgery, CLINTEC, Karolinska Institutet, Stockholm, Sweden
25

26 ³Department of Surgery, Mora Hospital, Mora, Sweden
27

28 ⁴Center for Digestive Diseases, Karolinska University Hospital, Huddinge, Stockholm,
29
30 Sweden
31

32
33 ⁵Surgical Gastroenterology Unit, Department of Surgery, Groote Schuur Hospital,
34
35 University of Cape Town Health Sciences Faculty, Cape Town, South Africa
36

37 ⁶Department of Surgery, Norra Älvsborg County Hospital, Trollhättan, Sweden
38
39

40
41
42 ***Correspondence to:***

43
44 Lars Enochsson, MD, PhD

45
46 Department of Surgical and Perioperative Sciences, Umeå University, Umeå,
47
48 Sunderby Hospital

49
50 97180 Luleå,

51
52 Sweden

53
54 E-mail: lars.enochsson@umu.se

55
56 Phone: +46 920 28 31 05

57
58 Fax: +46 920 28 33 20
59
60

ABSTRACT

OBJECTIVE

To analyse factors that may affect the validity of follow-up data in a national quality registry.

DESIGN

Population-based register study.

SETTING

Data from the national Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (ERCP), GallRiks.

POPULATION

All cholecystectomies and ERCPs recorded in GallRiks between 1 Jan 2006 and 31 Dec 2014.

MAIN OUTCOME MEASURES

Outcomes for intra- as well as post-procedural adverse events between units with either a 30-day follow-up of $\geq 90\%$ compared to those with a less frequent follow-up ($< 90\%$).

RESULTS

Between 2006 and 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of non-index procedures and those with incomplete data 152 827 procedures remained for final analyses. In patients having a cholecystectomy, there were no differences regarding the adverse event rates, irrespective of the follow-up frequency. However, in the more complicated endoscopic ERCP procedures, the postoperative adverse event rates were significantly higher in those with a more frequent and complete 30-day follow-up (OR 1.92; 95% CI 1.76-2.11).

CONCLUSIONS

Differences in the follow-up frequency in registries affect the reported outcomes as exemplified by the complicated endoscopic ERCP procedures. A high and complete follow-up rate shall serve as an additional quality indicator for surgical registries.

Strengths and limitations of this study

-The prospectively collected data from over 90% of the registered cholecystectomies and ERCP in nearly all Swedish hospitals is a major strength of this study.

-Data reported by the medical professional performing the procedure always have the inherent risk of being subjected to certain bias. However, the 30-day follow-up data are collected by coordinators that have not met the patients.

-Another limitation of this study is that it presents data from a period of nine years (2006-2014) where the national coverage rate increased from 73% to 90%.

Funding

This study was made possible by a grant from the Umeå University ALF research funding. The funding body had no role in the study. The GallRiks Registry is funded by the Swedish National Board of Health and Welfare.

No competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Data sharing statement

There are no additional unpublished data from this study. The data in this study are extracted from the Swedish Registry for Gallstone Surgery and ERCP (GallRiks) and are available via the corresponding author on request.

INTRODUCTION

National quality registry studies have been presented as a complement to Randomized Controlled Trials (RCTs). Registry based studies usually require less financial resources and enable data collection from large-scale patient cohorts without the unavoidable selection bias among those enrolled into clinical trials and most often carry valid statistical power.

Databases with long-term follow-up open up for conduct of studies focusing on rare events harms and effects occurring late in the clinical course. There are several instances where registry-based studies have improved the management of patients, for example in the treatment of non-ST-segment elevation acute coronary syndrome (NSTE-ACS),¹ the elimination of sub-standard orthopaedic prostheses from clinical use² and the effects of different surgical approaches and suture materials on the outcome of hernia surgery.^{3,4}

Accordingly registry studies can address clinical questions, that due to statistical power issues, time and financial constraints would never have been studied under the design of a RCTs such as the value of intraoperative cholangiography in preventing bile duct injury in association with gallstone surgery^{5,6} with data from the Swedish Registry for Gallstone Surgery and ERCP (GallRiks) or the question whether and why women with inguinal herniorrhaphies have a significantly higher reoperation rate compared to males (data from the Swedish Hernia Registry).⁷ Furthermore, in a randomized clinical trial published in Lancet 2016 the outcome of closure of mesenteric defects in gastric bypass surgery was evaluated by analysing registry data from the Scandinavian Obesity Surgery Registry (SOREG).⁸

Thus, registry-based studies have a definite role in addressing many of the questions that arise in and have relevance for everyday clinical practice.

However, although population-based registry studies have high external validity, reflecting real-life data and the clinical routines as they are practised in the community at large, they are often hampered by the lack of uniform protocols and standardised routines for registering

1
2
3 relevant data. This may skew the outcome since units, in which a limited awareness for
4
5 quality of care is prevailing, may well report data with incomplete accuracy, leading to a risk
6
7 for lower coverage concerning the registrations on adverse events by the participating units in
8
9 the respective registers. Hence such a heterogeneity in the validity of data may seriously limit
10
11 the options for correct interpretations in respective outcome analyses.
12
13
14

15 16 **Aims**

17
18 The aim of this study was to analyse the completeness in GallRiks of the follow-up frequency
19
20 in relation to the intra- and postoperative outcome of reported complications.
21
22
23

24 25 **METHODS**

26 27 **The Swedish National Registry for Gallstone Surgery and Endoscopic Retrograde** 28 29 **Cholangiopancreatography (ERCP)**⁹

30
31 The national Swedish Registry for Gallstone Surgery and ERCP (GallRiks) was established
32
33 on 1 May 2005 as a registry for cholecystectomy and ERCP procedures.¹⁰ The aim of the
34
35 registry is to obtain a comprehensive database of individuals subjected to these interventions,
36
37 including information on patient demographics and the indications and outcomes of
38
39 interventions. All data entering are online. The initial procedures, including information on
40
41 perioperative complications, are usually registered by operating clinicians. At a 30-day
42
43 follow-up all medical records are reviewed for post-procedural adverse events and data are
44
45 entered, usually by a local coordinator (nurse or a medical secretary).¹⁰ If a 30-day follow-up
46
47 protocol of a cholecystectomy or ERCP is not complete or is missing it is noted by the system
48
49 and these procedures can easily be assessed when analyzing the data. GallRiks data are
50
51 compared to patients' records on a regular basis by a dedicated independent validation team.
52
53
54
55
56
57
58
59
60

1
2
3 A complete match between overall registry data and medical records has been reported in
4
5 98.2% of subjects with a 100% match for bile duct injury.¹¹
6
7

8 9 *Data extraction*

10
11 Data on cholecystectomy and ERCP procedures performed between 1 January 2006 and 31
12
13 December 2014 and entered into the GallRiks registry were assessed. Non-index procedures
14
15 and procedures with incomplete data were excluded from the analysis. The complete 30-day
16
17 follow-up frequency of cholecystectomy and ERCP procedures for individual units
18
19 participating in the registry was calculated. We arbitrary chose the 90% limit for the 30-day
20
21 complete follow-up in order to compare groups with sufficient number of procedures to reach
22
23 enough statistical power to compare good follow-up ($\geq 90\%$) with a less complete follow-up
24
25 ($< 90\%$). Outcomes for peri- and postoperative complications were studied.
26
27
28
29

30 31 *Definitions*

32
33 For the purpose of this paper, and in accordance with the descriptions in the GallRiks
34
35 database, adverse events are defined and described per consensus agreement.
36

37
38 *Cholecystectomy*: Surgical removal of the gallbladder in patients with an indication for
39
40 removing the organ including symptomatic gallstone disease, neoplasms, and acalculous
41
42 gallbladder conditions.
43

44
45 *Endoscopic retrograde cholangiopancreatography (ERCP)*: An endoscopic technique for
46
47 transpapillary access to the common bile duct and/or pancreatic duct including accessing the
48
49 mentioned ducts through bilio- or pancreatico-digestive anastomoses, with diagnostic or
50
51 therapeutic intent.

52
53 *Index procedures*: The first cholecystectomy and/or ERCP-procedure for each patient per in-
54
55 hospital treatment period.
56
57
58

1
2
3 *Intra-procedural adverse events for cholecystectomy:* Bile duct injury, gut perforation,
4
5 bleeding requiring intervention or other complications that adversely affected the operation.

6
7 *Intra-procedural adverse events for ERCP:* Bleeding, extravasation of contrast, perforation or
8
9 any other reason for the ERCP being terminated prematurely.

10
11 *Post-procedural adverse events:* Complications during the 30-day follow-up period that
12
13 require some form of medical or surgical intervention, including readmission or death.

14
15 *Pancreatitis:* Abdominal pain and an elevated amylase at least three times above normal at a
16
17 time point more than 24 hours after terminating the procedure, as defined by Cotton.¹²

21 22 *Statistical analysis*

23
24 Statistical analyses were performed using JMP 12.2.0 (SAS, Cary, NC, USA). Comparisons
25
26 of patient and procedure characteristics are presented in contingency tables, with pairwise
27
28 differences analysed with Pearson Chi-square test. The influence of $\leq 90\%$ follow-up on the
29
30 risk of adverse events, pancreatitis and bleeding was analysed using multivariable logistic
31
32 regression modelling. Each variable was tested in univariate and multivariate analyses for
33
34 statistical significance, according to purposeful selection as described by Hosmer et al.¹³ In
35
36 the multivariate analysis the outcome was adjusted for sex, age (treated as a continuous
37
38 variable in the models but presented dichotomized into $<$ or \geq than 60 years (median)),
39
40 comorbidity dichotomized into ASA 1-2 and ASA 3-5, acute or elective procedure and
41
42 indication. The models were tested for multicollinearity and effect modification and were
43
44 finally assessed for goodness of fit. The effects of analysed variables are presented as odds
45
46 ratios for adverse events with 95% confidence intervals.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

RESULTS

Between January 1 2006 and December 31 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of 9328 non-index procedures and 57 procedures with incomplete data, 152 827 procedures remained for final analyses (95840 cholecystectomies and 56987 ERCPs) (figure 1). In total, 96.0% of the cholecystectomies and 95.4% of the ERCP procedures had a complete 30-day follow-up. The distribution of complete 30-day follow-up per hospital, for cholecystectomies and ERCP procedures are depicted in figure 2. For the cholecystectomy group, 20% of the hospitals had a 30-day follow-up frequency of less than 90% compared to 17% for ERCPs (figure 2). The demographics, physical status assessment and urgency of intervention of included patients are given in table 1. Patients that were operated on with a cholecystectomy or underwent an ERCP in centres with incomplete follow-up were older and had a higher ASA-score compared to those with a more complete 30-day follow-up. The adverse event rates for cholecystectomy and ERCP (intraoperative and total postoperative, with pancreatitis and bleeding showed separately) are given in figure 3. The overall total postoperative adverse event rate for cholecystectomies was significantly higher for the hospitals with a less complete 30-day follow-up. However, these differences disappeared when adjustments were made for sex, age, ASA-class and whether the operations were acute or scheduled (table 2). The overall total postoperative adverse event rate for ERCP during the study period was 13.2% and the pancreatitis frequency 3.8%. The incidence of these post-intervention adverse event rates was rather stable over the study period, except for pancreatitis where a small but significant increase was noted (figure 3). The reported risk of post procedural complications as well as pancreatitis and bleeding per se after ERCP was significantly increased in those hospitals with a more frequent and complete follow-up, both in absolute terms as well as when adjusted for confounders (table 3). The reported risk of postoperative adverse events,

1
2 including post-ERCP pancreatitis, was nearly twice as high compared to the group with less
3 complete follow-up. The risk of bleeding within the 30-day follow-up period was 38% higher
4 in the group with a better follow-up. On the contrary, the risk of intra-operative adverse
5 events was significantly reduced in the centres included in the $\geq 90\%$ 30-day follow-up group
6 (table 3).
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

DISCUSSION

The results of this study, analysing data from the nationwide Swedish Registry for Gallstone Surgery and ERCP (GallRiks), emphasize the importance of considering a thorough follow-up as an important confounder when analysing the outcome of registry-based studies.

Furthermore, differences in the follow-up frequency seemed to have a greater impact as a confounder in the technically more complicated procedures like ERCP where complications like pancreatitis and cholangitis, usually are detected postoperatively in contrast to cholecystectomies where the adverse events and complications usually are detected intraoperatively. Thus, since the ERCP procedures to a higher extent are marred by postoperative complications, the demands for a thorough and logistically well designed follow-up organization with adequate resources are mandatory.

Strengths and limitations of the study

The prospectively collected data in GallRiks from over 90% of the registered procedures in nearly all Swedish hospitals is a major strength of this study. The data registered in GallRiks have also been verified to have a high validity of over 98%.¹¹ Another strength is that this report includes data from University Hospitals, County Hospitals, District Hospitals and private units as well. The quality of data has been a concern already from the start of the registry and is guaranteed by continuous quality controls of the data-validity. However, due to financial and time constraints this prospective and integrated part of the registry has to be limited to approximately 50 randomly selected, cross-matches between patient records and GallRiks registrations at each hospital completed every third year.

Data reported by the medical professionals performing the respective intervention or data assessment always have the inherent risk of being subjected to certain bias. When analysing

1
2
3 the results of quality registry data, factors like coverage of the relevant population by the
4 registry data as well as the follow-up rate have to be taken into consideration. Another
5
6 limitation of this study is that it presents data from a period of nine years (2006-2014) where
7
8 the national coverage increased from 73% to 90%. However, there is no systematic reason
9
10 why the proportion of those with incomplete versus complete follow up shall depend on the
11
12 coverage rate as such. It must also be emphasized that, although we found significant
13
14 differences between units with a high ($\geq 90\%$) and units with $< 90\%$ complete follow-up, the
15
16 overall completeness must be considered excellent since only 4.0 % of the cholecystectomies
17
18 and 4.6 % of the ERCs have an incomplete follow-up. Nevertheless the absence of uniform
19
20 study protocols makes it impossible to fully guarantee overall quality of data in population-
21
22 based registers. Even if these data are considered to have high external validity the
23
24 population-based registers may still produce some skewness of the data. The care for accuracy
25
26 of reporting, and providing healthcare of high quality, may result in a positive correlation
27
28 between self-reported adverse outcome and completeness of data. On the other hand centres,
29
30 where the quality of care is poorer, may also have insufficient routines for scrutinising
31
32 treatment outcome. The only way of avoiding this is a meticulous validation of all registered
33
34 data, preferably with careful selective assessment of data from units with low coverage as
35
36 well as to provide continuous education and support from the registry to the participating
37
38 units with less complete follow-up routines.
39
40
41
42
43
44
45

46 *Comparison with other studies*

47
48 RCTs are considered one of the cornerstones of modern, evidence based medical science. It is
49
50 regarded as the most accurate method to answer key clinical questions and to offer the highest
51
52 levels of evidence that can be translated into the strongest treatment recommendations.¹⁴

53
54 However, RCTs are also associated with definite drawbacks and logistic challenges.^{15 16} In
55
56
57
58
59
60

1
2
3 addition, in the case of industry-funded research, and particularly so when study data are
4 owned by the sponsoring body, study results that might have negative economic implications
5 are sometimes withheld from publication, leading to publication bias.¹⁷ Furthermore, the
6 number of included patients necessary for creating sufficient power for testing of hypotheses
7 in RCTs may preclude the completion of trials within reasonable time limits.¹⁸ Moreover,
8 treatment methods that in RCTs originating from large academic institutions from which
9 excellent results are reported, cannot always be repeated by and implemented in smaller and
10 more resource-challenged facilities. It has also been shown that the outcome for patients
11 excluded from randomisation often differs significantly from those enrolled in the randomised
12 trial co-hort.¹⁹ Thus, registry-based studies can and shall be looked upon as offering a
13 complement to RCTs data, since they can more closely mirror the effect of a certain
14 treatment-intervention in the entire population, given that good coverage is prevailing.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

31 Several national quality registries have reported good coverage which is a prerequisite for a
32 well-functioning quality registry, particularly so for cancer registries and in the paediatric
33 population.^{20 21} As for Sweden, there are 53 national quality registries that report their
34 coverage to the Swedish National Board of Health and Welfare²². Of these 53 registries 19
35 cover specific interventional procedures, for example gynaecological operations, hip-
36 replacement, hernia surgery, and cholecystectomy, to mention a few. The national coverage of
37 these registries varies from 46% to 98%. In fact, some of these registries have a better
38 coverage than the Swedish National Patient Registry (NPR) because many of the procedures
39 are done by private hospitals that do not report to NPR as diligently as the government-funded
40 hospitals.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Besides having good coverage, it is of vital importance for quality registries to contain valid
4 data. Dedicated validation processes should be in place for assessing and reporting the
5 correctness of the included data at regular intervals. The issue of a complete follow-up is
6 especially challenging in registries with focus on the management of benign diseases, since
7 these procedures do not have the same rigorous demands of a compulsory follow-up as those
8 for malignant conditions.
9

10
11 The impact of the level of completeness of the follow-up for the validity of reported outcomes
12 in registries covering benign conditions, has not been previously probed and elucidated in the
13 literature. A survey by Rystedt et al, based on the validation of GallRiks, showed a high
14 completeness and correctness of entered data with an overall correctness of data of 98.2% and
15 100% for bile duct injuries.¹¹ However, in this publication the completeness of the 30-day
16 follow-up was not specifically addressed.
17
18
19
20
21
22
23
24
25
26
27
28
29
30

31 The compelling finding of this paper is that the reported incidence of postoperative adverse
32 events after ERCP is significantly lower in hospitals with an incomplete 30-day follow-up
33 frequency (<90%) as compared to those with a more complete follow-up (≥90%). Although
34 these results could mirror true outcomes, it is more likely to be the result of failure to report
35 some of the adverse events by the hospitals with a less stringent documentation system for
36 follow-up and/or a lack of coordinators. The coordinator has the liability, together with the
37 GallRiks responsible surgeon, that the patient's data are registered and monitored. A contract
38 is signed with the head of the department that ≥90% follow-up in GallRiks should be done.
39 The agreement is broken at the units that have <90% 30-day follow-up.
40
41
42
43
44
45
46
47
48
49

50 These assumptions of less stringent reporting are supported by the finding that the reported
51 incidence of intra-operative adverse events is significantly higher in the group with ≥90% 30-
52 day follow-up, implying that hospitals with an immaculate and accurate information accrual
53
54
55
56
57
58
59
60

1
2
3 system also follow up patients more diligently and report adverse events to a higher degree.
4
5 This discrepancy, where a less frequent 30-day follow-up significantly affected the reported
6
7 outcome in ERCP but not in cholecystectomy could imply that the effect of a complete 30-
8
9 day follow-up is more pronounced in procedures with a higher complication profile, since
10
11 ERCPs have a more congested post-operative complication profile compared to
12
13 cholecystectomies.
14
15

16 17 18 *Conclusions and implications*

19
20 Our findings may have significant general implications on how we shall interpret outcome
21
22 data from registry studies. Differences in the follow-up rate seemed to significantly affect the
23
24 reported outcome. The findings suggest that the validation process has to include the
25
26 completeness of follow-up. Differences in the follow-up frequency in registries affect the
27
28 reported outcomes as exemplified by the complicated endoscopic ERCP procedures. The
29
30 study emphasises the importance of complete follow-up, since this variable may well act as a
31
32 quality indicator for the respective registry.
33
34
35

36 37 38 *Future research*

39
40 Future research should focus on how the degree of complete follow-up in quality registers can
41
42 correlate to more objectively and not self-reported quality indicators.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributors

LE conceived the study, created the study design, participated in the statistical analysis, analysed the data, and drafted and revised the paper. He is guarantor. MB participated in the analysis and interpretation of data, and revised the paper. GS participated in the statistical analysis and interpretation of data, and drafted and revised the paper. EJ interpreted the data and revised the manuscript. BH conceived the study and reviewed the manuscript. LL interpreted data and reviewed the manuscript. JÖ conceived the study, created the study design, and drafted and revised the paper.

All authors have approved of the final draft submitted.

Ethical approval

The regional research ethics committee at Karolinska Institutet, Stockholm, Sweden, approved the study.

Transparency

The first author (LE) confirms that the manuscript is an honest, accurate, and transparent account of the study; that no important aspects of the study have been omitted.

REFERENCES

1. Damman P, Jernberg T, Lindahl B, et al. Invasive strategies and outcomes for non-ST-segment elevation acute coronary syndromes: a twelve-year experience from SWEDHEART. *EuroIntervention* 2016;12(9):1108-16. doi: 10.4244/EIJY15M11_05
2. Graves SE. The value of arthroplasty registry data. *Acta Orthop* 2010;81(1):8-9. doi: 10.3109/17453671003667184
3. Dahlstrand U, Wollert S, Nordin P, et al. Emergency femoral hernia repair: a study based on a national register. *Ann Surg* 2009;249(4):672-6. doi: 10.1097/SLA.0b013e31819ed943
4. Novik B, Nordin P, Skullman S, et al. More recurrences after hernia mesh fixation with short-term absorbable sutures: A registry study of 82 015 Lichtenstein repairs. *Arch Surg* 2011;146(1):12-7. doi: 10.1001/archsurg.2010.302 [published Online First: 2011/01/19]
5. Tornqvist B, Stromberg C, Persson G, et al. Effect of intended intraoperative cholangiography and early detection of bile duct injury on survival after cholecystectomy: population based cohort study. *BMJ* 2012;345:e6457. doi: 10.1136/bmj.e6457 [published Online First: 2012/10/13]
6. Tornqvist B, Stromberg C, Akre O, et al. Selective intraoperative cholangiography and risk of bile duct injury during cholecystectomy. *Br J Surg* 2015;102(8):952-8. doi: 10.1002/bjs.9832 [published Online First: 2015/04/29]
7. Bay-Nielsen M, Kehlet H. Inguinal herniorrhaphy in women. *Hernia* 2006;10(1):30-3. doi: 10.1007/s10029-005-0029-3 [published Online First: 2005/09/01]
8. Stenberg E, Szabo E, Agren G, et al. Closure of mesenteric defects in laparoscopic gastric bypass: a multicentre, randomised, parallel, open-label trial. *Lancet* 2016;387(10026):1397-404. doi: 10.1016/S0140-6736(15)01126-5 [published Online First: 2016/02/21]
9. Gallriks 2017 [Available from: www.gallriks.se].
10. Enochsson L, Thulin A, Osterberg J, et al. The Swedish Registry of Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks): A nationwide registry for quality assurance of gallstone surgery. *JAMA Surg*

- 1
2
3 2013;148(5):471-8. doi: 10.1001/jamasurg.2013.1221 [published Online First:
4 2013/01/18]
5
6 11. Rystedt J, Montgomery A, Persson G. Completeness and correctness of
7 cholecystectomy data in a national register--GallRiks. *Scand J Surg*
8 2014;103(4):237-44. doi: 10.1177/1457496914523412 [published Online First:
9 2014/04/17]
10
11 12. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications
12 and their management: an attempt at consensus. *Gastrointest Endosc*
13 1991;37(3):383-93.
14
15 13. Hosmer DW, Taber S, Lemeshow S. The importance of assessing the fit of logistic
16 regression models: a case study. *Am J Public Health* 1991;81(12):1630-5.
17
18 14. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of
19 recommendations. *BMJ* 2004;328(7454):1490. doi: 10.1136/bmj.328.7454.1490
20
21 15. Carter AJ, Nguyen CN. A comparison of cancer burden and research spending
22 reveals discrepancies in the distribution of research funding. *BMC Public Health*
23 2012;12:526. doi: 10.1186/1471-2458-12-526
24
25 16. Lundh A, Sismondo S, Lexchin J, et al. Industry sponsorship and research outcome.
26 *Cochrane Database Syst Rev* 2012;12:MR000033. doi:
27 10.1002/14651858.MR000033.pub2
28
29 17. Doucet M, Sismondo S. Evaluating solutions to sponsorship bias. *J Med Ethics*
30 2008;34(8):627-30. doi: 10.1136/jme.2007.022467
31
32 18. van den Broek MA, van Dam RM, Malago M, et al. Feasibility of randomized
33 controlled trials in liver surgery using surgery-related mortality or morbidity as
34 endpoint. *Br J Surg* 2009;96(9):1005-14. doi: 10.1002/bjs.6663
35
36 19. Ros A, Carlsson P, Rahmqvist M, et al. Non-randomised patients in a
37 cholecystectomy trial: characteristics, procedures, and outcomes. *BMC Surg*
38 2006;6:17. doi: 10.1186/1471-2482-6-17
39
40 20. Larsen IK, Smastuen M, Johannesen TB, et al. Data quality at the Cancer Registry
41 of Norway: an overview of comparability, completeness, validity and timeliness.
42 *Eur J Cancer* 2009;45(7):1218-31. doi: 10.1016/j.ejca.2008.10.037
43
44 21. Steliarova-Foucher E, Kaatsch P, Lacour B, et al. Quality, comparability and
45 methods of analysis of data on childhood cancer in Europe (1978-1997): report
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 from the Automated Childhood Cancer Information System project. *Eur J Cancer*
4 2006;42(13):1915-51. doi: 10.1016/j.ejca.2006.05.007
5
6 22. The Swedish National Board of Health and Welfare 2017 [Available from:
7 <http://www.socialstyrelsen.se/english/compare>.
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3 **LEGEND TO FIGURES**

4
5 **Figure 1**

6
7 The procedures included in the analyses.
8
9

10
11 **Figure 2**

12
13 Complete 30-day follow-up frequencies following cholecystectomies and ERCP.
14
15

16
17
18 **Figure 3**

19
20 Adverse event rates after cholecystectomies and ERCP.
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1

Demographics, physical status assessment and urgency of interventions for the 152 827 patients included in the study

		30-day follow-up of cholecystectomies				
		≥90%		<90%		<i>P</i>
		<i>n</i>	%	<i>n</i>	%	
Gender	Female	55908	67.3	8311	65.1	<.0001
	Male	27159	32.7	4462	34.9	
Age (years)	≥60	26442	31.9	4462	35.0	<.0001
	<60	56461	68.1	8290	65.0	
ASA	ASA 1-2	76478	92.1	11124	87.1	<.0001
	ASA ≥3	6589	7.9	1649	12.9	
Acute/ Scheduled	Acute	24237	29.2	4433	34.7	<.0001
	Scheduled	58830	70.8	8340	65.3	

		30-day follow-up of ERCP				
		≥90%		<90%		<i>P</i>
		<i>n</i>	%	<i>n</i>	%	
Gender	Female	25673	53.0	4460	52.0	0.0906
	Male	22743	47.0	4111	48.0	
Age (years)	≥60	35532	73.6	6724	78.5	<.0001
	<60	12767	26.4	1843	21.5	
ASA	ASA 1-2	33457	69.1	4748	55.4	<.0001
	ASA ≥3	14959	30.9	3823	44.6	
Acute/ Scheduled	Acute	30093	62.2	5055	59.0	<.0001
	Scheduled	18323	37.8	3516	41.0	

Table 2

Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of cholecystectomies $\geq 90\%$

	Adverse events				<i>P</i>
	$\geq 90\%$ n=83067		<90% n=12773		
	n	%	n	%	
Intraoperative	2548	3.0	381	3.0	0.8826
Total postoperative	6681	8.0	1119	8.8	0.0057
Pancreatitis	455	0.6	66	0.5	0.6570
Bleeding	629	0.8	96	0.8	0.9454

	Adverse events		
	$\geq 90\%$ vs <90% 30-day follow-up Adjusted*		
	Odds Ratio	(95% CI)	<i>P</i>
Intraoperative	0.93	(0.84-1.04)	0.2298
Total postoperative	0.98	(0.91-1.05)	0.5067
Pancreatitis	1.30	(0.99-1.75)	0.0606
Bleeding	0.97	(0.78-1.21)	0.7821

*Adjusted for sex, age, ASA class, acute interventions and indications.

Table 3

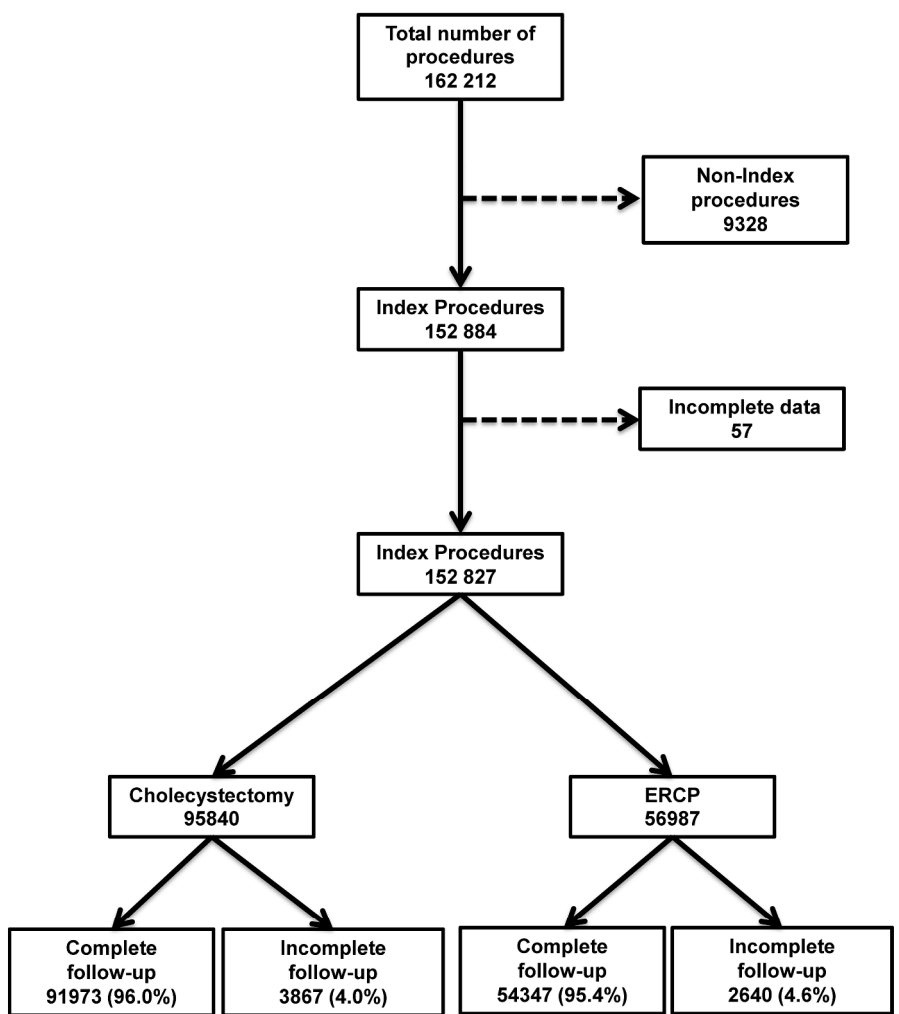
Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of ERCPs $\geq 90\%$

	Adverse events				<i>P</i>
	$\geq 90\%$ n=48416		$< 90\%$ n=8571		
	n	%	n	%	
Intraoperative	1267	2.6	252	2.9	0.0868
Total	6821	14.1	689	8.0	<.0001
postoperative	1978	4.1	178	2.1	<.0001
Pancreatitis	591	1.2	76	0.9	0.0081
Bleeding					

	Adverse events		
	$\geq 90\%$ vs $< 90\%$ 30-day follow-up Adjusted*		
	Odds Ratio	(95% CI)	<i>P</i>
Intraoperative	0.76	(0.66-0.87)	0.0002
Total	1.92	(1.76-2.11)	<.0001
postoperative	2.04	(1.72-2.43)	<.0001
Pancreatitis	1.38	(1.08-1.79)	0.0100
Bleeding			

*Adjusted for sex, age, ASA class, acute interventions and indications.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

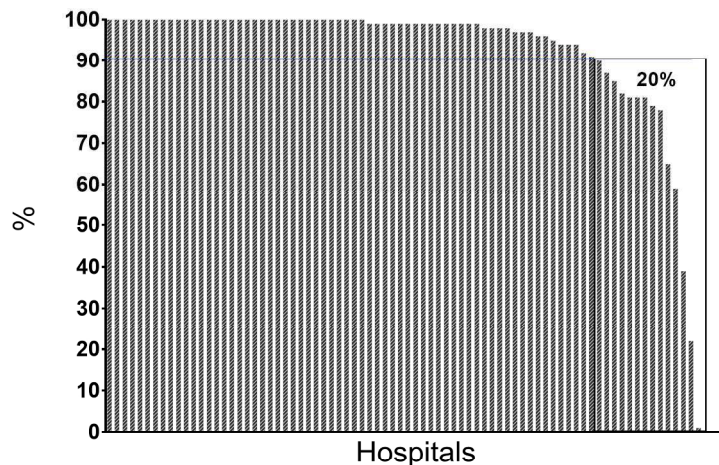


The procedures included in the analyses.

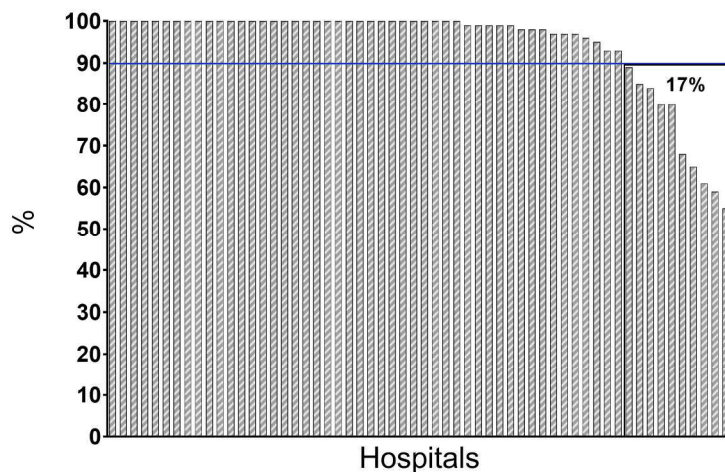
254x338mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Complete 30-day follow-up cholecystectomies



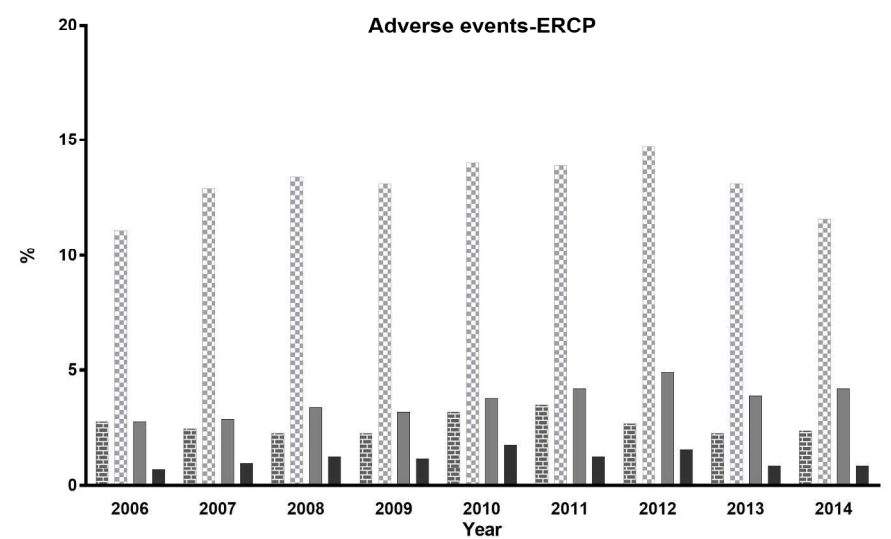
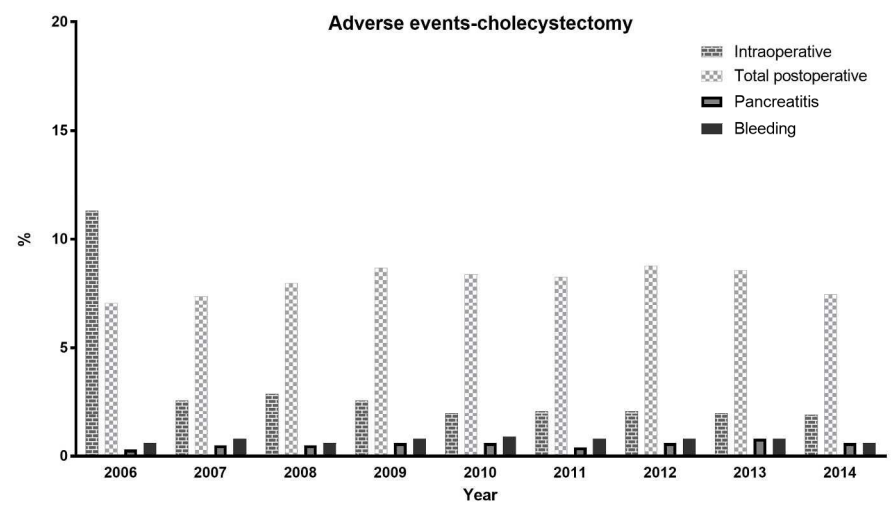
Complete 30-day follow-up ERCP



Complete 30-day follow-up frequencies following cholecystectomies and ERCP.

167x256mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Adverse event rates after cholecystectomies and ERCP.

198x247mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 2	Population-based register study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pages 4-5	
Objectives	3	State specific objectives, including any prespecified hypotheses	Abstract and page 5	
Methods				
Study design	4	Present key elements of study design early in the paper	Page 4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 5-6	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Pages 5-6	
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls		
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants		
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed		
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 6-7	
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 5-7	
Bias	9	Describe any efforts to address potential sources of bias	Pages 10-11	
Study size	10	Explain how the study size was arrived at	Pages 5-6	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 7
		(b) Describe any methods used to examine subgroups and interactions	Page 7
		(c) Explain how missing data were addressed	Partly described on page 7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	The article is about this subject
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Described in results.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	That is what this article is all about
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Tables 2-3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2-3
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	In Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Inversed relationship between completeness of follow-up and coverage of postoperative complications in gallstone surgery and ERCP. A potential source of bias in patient registers.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-019551.R2
Article Type:	Research
Date Submitted by the Author:	09-Dec-2017
Complete List of Authors:	Enochsson, Lars; Umea University, Surgical and Perioperative Sciences Blohm, My; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Sandblom, Gabriel; Karolinska Institute, Center for Digestive Disease; Karolinska Institutet Department for Clinical Intervention and Technology, Jonas, Eduard; University of Cape Town, Health Sciences Faculty Hallerbäck, Bengt; Goteborgs Universitet, Department of Surgery Lundell, Lars; Karolinska institutet Department of Clinical Sciences Intervention and Technology, Division of Surgery, CLINTEC Österberg, Johanna; Karolinska institutet Department of Clinical Sciences Intervention and Technology
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Epidemiology
Keywords:	Adult surgery < SURGERY, Hepatobiliary surgery < SURGERY, QUALITATIVE RESEARCH, Endoscopy < GASTROENTEROLOGY

SCHOLARONE™
Manuscripts

1
2
3 **Inversed relationship between completeness of follow-up and**
4
5
6 **coverage of postoperative complications in gallstone surgery and**
7
8 **ERCP. A potential source of bias in patient registers.**
9

10
11
12
13 Lars Enochsson¹, My Blohm^{2,3}, Gabriel Sandblom^{2,4}, Eduard Jonas⁵, Bengt Hallerbäck⁶, Lars
14
15 Lundell², Johanna Österberg^{2,3}

16
17
18
19
20 ¹Department of Surgical and Perioperative Sciences, Sunderby Research Unit, Umeå
21
22 University, Sweden

23
24 ²Division of Surgery, CLINTEC, Karolinska Institutet, Stockholm, Sweden

25
26 ³Department of Surgery, Mora Hospital, Mora, Sweden

27
28 ⁴Center for Digestive Diseases, Karolinska University Hospital, Huddinge, Stockholm,
29
30 Sweden

31
32 ⁵Surgical Gastroenterology Unit, Department of Surgery, Groote Schuur Hospital,
33
34 University of Cape Town Health Sciences Faculty, Cape Town, South Africa

35
36 ⁶Department of Surgery, Norra Älvsborg County Hospital, Trollhättan, Sweden

37
38
39
40
41
42 ***Correspondence to:***

43
44 Lars Enochsson, MD, PhD

45
46 Department of Surgical and Perioperative Sciences, Umeå University, Umeå,
47
48 Sunderby Hospital

49
50 97180 Luleå,

51
52 Sweden

53
54 E-mail: lars.enochsson@umu.se

55
56 Phone: +46 920 28 31 05

57
58 Fax: +46 920 28 33 20

ABSTRACT

OBJECTIVE

To analyse the completeness in GallRiks of the follow-up frequency in relation to the intra- and postoperative outcome.

DESIGN

Population-based register study.

SETTING

Data from the national Swedish Registry for Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (ERCP), GallRiks.

POPULATION

All cholecystectomies and ERCPs recorded in GallRiks between 1 Jan 2006 and 31 Dec 2014.

MAIN OUTCOMEMEASURES

Outcomes for intra- as well as post-procedural adverse events between units with either a 30-day follow-up of $\geq 90\%$ compared to those with a less frequent follow-up ($< 90\%$).

RESULTS

Between 2006 and 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of non-index procedures and those with incomplete data 152 827 procedures remained for final analyses. In patients having a cholecystectomy, there were no differences regarding the adverse event rates, irrespective of the follow-up frequency. However, in the more complicated endoscopic ERCP procedures, the postoperative adverse event rates were significantly higher in those with a more frequent and complete 30-day follow-up (OR 1.92; 95% CI 1.76-2.11).

CONCLUSIONS

Differences in the follow-up frequency in registries affect the reported outcomes as exemplified by the complicated endoscopic ERCP procedures. A high and complete follow-up rate shall serve as an additional quality indicator for surgical registries.

Strengths and limitations of this study

-The prospectively collected data from over 90% of the registered cholecystectomies and ERCP in nearly all Swedish hospitals is a major strength of this study.

-Data reported by the medical professional performing the procedure always have the inherent risk of being subjected to certain bias. However, the 30-day follow-up data are collected by coordinators that have not met the patients.

-Another limitation of this study is that it presents data from a period of nine years (2006-2014) where the national coverage rate increased from 73% to 90%.

Funding

This study was made possible by a grant from the Umeå University ALF research funding. The funding body had no role in the study. The GallRiks Registry is funded by the Swedish National Board of Health and Welfare.

No competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Data sharing statement

There are no additional unpublished data from this study. The data in this study are extracted from the Swedish Registry for Gallstone Surgery and ERCP (GallRiks) and are available via the corresponding author on request.

INTRODUCTION

National quality registry studies have been presented as a complement to Randomized Controlled Trials (RCTs). Registry based studies usually require less financial resources and enable data collection from large-scale patient cohorts without the unavoidable selection bias among those enrolled into clinical trials and most often carry valid statistical power. Databases with long-term follow-up open up for conduct of studies focusing on rare events harms and effects occurring late in the clinical course. There are several instances where registry-based studies have improved the management of patients, for example in the treatment of non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS),¹ the elimination of sub-standard orthopaedic prostheses from clinical use² and the effects of different surgical approaches and suture materials on the outcome of hernia surgery.^{3,4} Accordingly registry studies can address clinical questions, that due to statistical power issues, time and financial constraints would never have been studied under the design of a RCTs such as the value of intraoperative cholangiography in preventing bile duct injury in association with gallstone surgery^{5,6} with data from the Swedish Registry for Gallstone Surgery and ERCP (GallRiks) or the question whether and why women with inguinal herniorrhaphies have a significantly higher reoperation rate compared to males (data from the Swedish Hernia Registry).⁷ Furthermore, in a randomized clinical trial published in Lancet 2016 the outcome of closure of mesenteric defects in gastric bypass surgery was evaluated by analysing registry data from the Scandinavian Obesity Surgery Registry (SOREG).⁸

Thus, registry-based studies have a definite role in addressing many of the questions that arise in and have relevance for everyday clinical practice.

However, although population-based registry studies have high external validity, reflecting real-life data and the clinical routines as they are practised in the community at large, they are often hampered by the lack of uniform protocols and standardised routines for registering

1
2 relevant data. This may skew the outcomes since units, in which a limited awareness for quality
3 of care is prevailing, may well report data with incomplete accuracy, leading to a risk for lower
4 coverage concerning the registrations on adverse events by the participating units in the
5 respective registers. Hence such a heterogeneity in the validity of data may seriously limit the
6 options for correct interpretations in respective outcome analyses.
7
8
9
10
11
12

13 14 15 **Aims**

16 To analyse the completeness in GallRiks of the follow-up frequency in relation to the intra-
17 and postoperative outcome.
18
19
20
21
22
23
24
25

26 **METHODS**

27 28 29 **The Swedish National Registry for Gallstone Surgery and Endoscopic Retrograde** 30 **Cholangiopancreatography (ERCP)⁹**

31 The national Swedish Registry for Gallstone Surgery and ERCP (GallRiks) was established on
32 1 May 2005 as a registry for cholecystectomy and ERCP procedures.¹⁰ The aim of the registry
33 is to obtain a comprehensive database of individuals subjected to these interventions,
34 including information on patient demographics and the indications and outcomes of
35 interventions. All data entering are online. The initial procedures, including information on
36 perioperative complications, are usually registered by operating clinicians. At a 30-day follow-
37 up all medical records are reviewed for post-procedural adverse events and data are entered,
38 usually by a local coordinator (nurse or a medical secretary).¹⁰ If a 30-day follow-up protocol
39 of a cholecystectomy or ERCP is not complete or is missing it is noted by the system and
40 these procedures can easily be assessed when analyzing the data. GallRiks data are compared
41 to patients' records on a regular basis by a dedicated independent validation team. A complete
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 match between overall registry data and medical records has been reported in 98.2% of
4
5 subjects with a 100% match for bile duct injury.¹¹
6
7

8 9 *Data extraction*

10
11 Data on cholecystectomy and ERCP procedures performed between 1 January 2006 and 31
12
13 December 2014 and entered into the GallRiks registry were assessed. Non-index
14
15 procedures and procedures with incomplete data were excluded from the analysis. The
16
17 complete 30-day follow-up frequency of cholecystectomy and ERCP procedures for
18
19 individual units participating in the registry was calculated. We arbitrarily chose the 90% limit
20
21 for the 30-day complete follow-up in order to compare groups with sufficient number of
22
23 procedures to reach enough statistical power to compare good follow-up ($\geq 90\%$) with a less
24
25 complete follow-up ($< 90\%$). Outcomes for peri- and postoperative complications were studied.
26
27
28
29

30 31 *Definitions*

32
33 For the purpose of this paper, and in accordance with the descriptions in the GallRiks
34
35 database, adverse events are defined and described per consensus agreement.
36

37
38 *Cholecystectomy*: Surgical removal of the gallbladder in patients with an indication for
39
40 removing the organ including symptomatic gallstone disease, neoplasms, and acalculous
41
42 gallbladder conditions.

43
44 *Endoscopic retrograde cholangiopancreatography (ERCP)*: An endoscopic technique for
45
46 transpapillary access to the common bile duct and/or pancreatic duct including
47
48 accessing the mentioned ducts through bilio- or pancreatico-digestive anastomoses, with
49
50 diagnostic or therapeutic intent.

51
52 *Index procedures*: The first cholecystectomy and/or ERCP-procedure for each patient per in-
53
54 hospital treatment period.
55
56
57
58

1
2
3 *Intra-procedural adverse events for cholecystectomy:* Bile duct injury, gut perforation,
4
5 bleeding requiring intervention or other complications that adversely affected the operation.

6
7 *Intra-procedural adverse events for ERCP:* Bleeding, extravasation of contrast, perforation or
8
9 any other reason for the ERCP being terminated prematurely.

10
11 *Post-procedural adverse events:* Complications during the 30-day follow-up period that
12
13 require some form of medical or surgical intervention, including readmission or death.

14
15 *Pancreatitis:* Abdominal pain and an elevated amylase at least three times above normal at a
16
17 time point more than 24 hours after terminating the procedure, as defined by Cotton.¹²

21 22 *Statistical analysis*

23
24 Statistical analyses were performed using JMP 12.2.0 (SAS, Cary, NC, USA). Comparisons
25
26 of patient and procedure characteristics are presented in contingency tables, with pairwise
27
28 differences analysed with Pearson Chi-square test. The influence of $\leq 90\%$ follow-up on the
29
30 risk of adverse events, pancreatitis and bleeding was analysed using multivariable logistic
31
32 regression modelling. Each variable was tested in univariate and multivariate analyses for
33
34 statistical significance, according to purposeful selection as described by Hosmer et al.¹³ In the
35
36 multivariate analysis the outcome was adjusted for sex, age (treated as a continuous variable
37
38 in the models but presented dichotomized into $<$ or \geq than 60 years (median)), comorbidity
39
40 dichotomized into ASA 1-2 and ASA 3-5, acute or elective procedure and indication. The
41
42 models were tested for multicollinearity and effect modification and were finally assessed for
43
44 goodness of fit. The effects of analysed variables are presented as odds ratios for adverse
45
46 events with 95% confidence intervals.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

RESULTS

Between January 1 2006 and December 31 2014, 162 212 cholecystectomies and ERCP procedures were registered in GallRiks. After the exclusion of 9328 non-index procedures and 57 procedures with incomplete data, 152 827 procedures remained for final analyses (95840 cholecystectomies and 56987 ERCPs) (figure 1). In total, 96.0% of the cholecystectomies and 95.4% of the ERCP procedures had a complete 30-day follow-up. The distribution of complete 30-day follow-up per hospital, for cholecystectomies and ERCP procedures are depicted in figure 2. For the cholecystectomy group, 20% of the hospitals had a 30-day follow-up frequency of less than 90% compared to 17% for ERCPs (figure 2). The demographics, physical status assessment and urgency of intervention of included patients are given in table 1. Patients that were operated on with a cholecystectomy or underwent an ERCP in centres with incomplete follow-up were older and had a higher ASA-score compared to those with a more complete 30-day follow-up. The adverse event rates for cholecystectomy and ERCP (intraoperative and total postoperative, with pancreatitis and bleedings showed separately) are given in figure 3. The overall total postoperative adverse event rate for cholecystectomies was significantly higher for the hospitals with a less complete 30-day follow-up. However, these differences disappeared when adjustments were made for sex, age, ASA-class and whether the operations were acute or scheduled (table 2). The overall total postoperative adverse event rate for ERCP during the study period was 13.2% and the pancreatitis frequency 3.8%. The incidence of these post-intervention adverse event rates was rather stable over the study period, except for pancreatitis where a small but significant increase was noted (figure 3). The reported risk of post procedural complications as well as pancreatitis and bleeding per se after ERCP was significantly increased in those hospitals with a more frequent and complete follow-up, both in absolute terms as well as when adjusted for confounders (table 3). The reported risk of postoperative adverse events,

1
2
3 including post-ERCP pancreatitis, was nearly twice as high compared to the group with less
4 complete follow-up. The risk of bleeding within the 30-day follow-up period was 38% higher
5 in the group with a better follow-up. On the contrary, the risk of intra-operative adverse
6 events was significantly reduced in the centres included in the $\geq 90\%$ 30-day follow-up group
7 (table 3). The overall 30-day mortality of cholecystectomies and ERCP in this study was 2.3%.
8
9 However, since mortality figures are automatically transferred to the register from the
10 Swedish Central Death Register they are not affected by the local routines and management of
11 the reporting hospitals.
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

DISCUSSION

The results of this study, analysing data from the nationwide Swedish Registry for Gallstone Surgery and ERCP (GallRiks), emphasize the importance of considering a thorough follow-up as an important confounder when analysing the outcome of registry-based studies.

Furthermore, differences in the follow-up frequency seemed to have a greater impact as a confounder in the technically more complicated procedures like ERCP where complications like pancreatitis and cholangitis, usually are detected postoperatively in contrast to cholecystectomies where the adverse events and complications usually are detected intraoperatively. Thus, since the ERCP procedures to a higher extent are marred by postoperative complications, the demands for a thorough and logistically well designed follow-up organization with adequate resources are mandatory.

Strengths and limitations of the study

The prospectively collected data in GallRiks from over 90% of the registered procedures in nearly all Swedish hospitals is a major strength of this study. The data registered in GallRiks have also been verified to have a high validity of over 98%.¹¹ Another strength is that this report includes data from University Hospitals, County Hospitals, District Hospitals and private units as well. The quality of data has been a concern already from the start of the registry and is guaranteed by continuous quality controls of the data-validity. However, due to financial and time constraints this prospective and integrated part of the registry has to be limited to approximately 50 randomly selected, cross-matches between patient records and GallRiks registrations at each hospital completed every third year.

Data reported by the medical professionals performing the respective intervention or data assessment always have the inherent risk of being subjected to certain bias. When analysing

1
2
3 the results of quality registry data, factors like coverage of the relevant population by the
4 registry data as well as the follow-up rate have to be taken into consideration. Another
5
6 limitation of this study is that it presents data from a period of nine years (2006-2014) where
7
8 the national coverage increased from 73% to 90%. However, there is no systematic reason why
9
10 the proportion of those with incomplete versus complete follow up shall depend on the
11
12 coverage rate as such. It must also be emphasized that, although we found significant
13
14 differences between units with a high ($\geq 90\%$) and units with $< 90\%$ complete follow-up, the
15
16 overall completeness must be considered excellent since only 4.0 % of the cholecystectomies
17
18 and 4.6% of the ERCs have an incomplete follow-up. Nevertheless the absence of uniform
19
20 study protocols makes it impossible to fully guarantee overall quality of data in population-
21
22 based registers. Even if these data are considered to have high external validity the population-
23
24 based registers may still produce some skewness of the data. The care for accuracy of
25
26 reporting, and providing healthcare of high quality, may result in a positive correlation
27
28 between self-reported adverse outcome and completeness of data. On the other hand centres,
29
30 where the quality of care is poorer, may also have insufficient routines for scrutinising
31
32 treatment outcome. The only way of avoiding this is a meticulous validation of all registered
33
34 data, preferably with careful selective assessment of data from units with low coverage as
35
36 well as to provide continuous education and support from the registry to the participating
37
38 units with less complete follow-up routines.
39
40
41
42
43
44
45

46 *Comparison with other studies*

47
48 RCTs are considered one of the cornerstones of modern, evidence based medical science. It is
49
50 regarded as the most accurate method to answer key clinical questions and to offer the highest
51
52 levels of evidence that can be translated into the strongest treatment recommendations.¹⁴
53
54 However, RCTs are also associated with definite drawbacks and logistic challenges.^{15 16} In
55
56
57
58
59
60

1
2
3 addition, in the case of industry-funded research, and particularly so when study data are
4 owned by the sponsoring body, study results that might have negative economic
5 implications are sometimes withheld from publication, leading to publication bias.¹⁷
6
7 Furthermore, the number of included patients necessary for creating sufficient power for
8 testing of hypotheses in RCTs may preclude the completion of trials within reasonable time
9 limits.¹⁸ Moreover, treatment methods that in RCTs originating from large academic
10 institutions from which excellent results are reported, cannot always be repeated by and
11 implemented in smaller and more resource-challenged facilities. It has also been shown that
12 the outcome for patients excluded from randomisation often differs significantly from those
13 enrolled in the randomised trial cohort.¹⁹ Thus, registry-based studies can and shall be looked
14 upon as offering a complement to RCTs data, since they can more closely mirror the effect of
15 a certain treatment-intervention in the entire population, given that good coverage is prevailing.
16
17

18
19
20
21
22
23
24
25
26
27
28
29
30
31 Several national quality registries have reported good coverage which is a prerequisite for a
32 well-functioning quality registry, particularly so for cancer registries and in the paediatric
33 population.^{20 21} As for Sweden, there are 53 national quality registries that report their coverage
34 to the Swedish National Board of Health and Welfare²². Of these 53 registries 19 cover
35 specific interventional procedures, for example gynaecological operations, hip-replacement,
36 hernia surgery, and cholecystectomy, to mention a few. The national coverage of these
37 registries varies from 46% to 98%. In fact, some of these registries have a better coverage
38 than the Swedish National Patient Registry (NPR) because many of the procedures are done
39 by private hospitals that do not report to NPR as diligently as the government-funded
40 hospitals.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Besides having good coverage, it is of vital importance for quality registries to contain valid
4 data. Dedicated validation processes should be in place for assessing and reporting the
5 correctness of the included data at regular intervals. The issue of a complete follow-up is
6 especially challenging in registries with focus on the management of benign diseases, since
7 these procedures do not have the same rigorous demands of a compulsory follow-up as those
8 for malignant conditions.

9
10 The impact of the level of completeness of the follow-up for the validity of reported outcomes
11 in registries covering benign conditions, has not been previously probed and elucidated in the
12 literature. A survey by Rystedt et al, based on the validation of GallRiks, showed a high
13 completeness and correctness of entered data with an overall correctness of data of 98.2% and
14 100% for bile duct injuries.¹¹ However, in this publication the completeness of the 30-day
15 follow-up was not specifically addressed. There may also be a relative preponderance of
16 smaller units among those with low completeness. It is often more difficult to organise
17 standardised routines when the volumes are low. This could explain the relatively high
18 completeness on the national level despite the very low completeness at a few hospitals.

19
20 The compelling finding of this paper is that the reported incidence of postoperative adverse
21 events after ERCP is significantly lower in hospitals with an incomplete 30-day follow-up
22 frequency (<90%) as compared to those with a more complete follow-up (≥90%). Although
23 these results could mirror true outcomes, it is more likely to be the result of failure to
24 report some of the adverse events by the hospitals with a less stringent documentation system
25 for follow-up and/or a lack of coordinators. The coordinator has the liability, together with the
26 GallRiks responsible surgeon, that the patient's data are registered and monitored. A contract
27 is signed with the head of the department that ≥90% follow-up in GallRiks should be done.
28 The agreement is broken at the units that have <90% 30-day follow-up.

1
2
3 These assumptions of less stringent reporting are supported by the finding that the reported
4 incidence of intra-operative adverse events is significantly higher in the group with $\geq 90\%$ 30-
5 day follow-up, implying that hospitals with an immaculate and accurate information
6 accrual system also follow up patients more diligently and report adverse events to a higher
7 degree. This discrepancy, where a less frequent 30-day follow-up significantly affected the
8 reported outcome in ERCP but not in cholecystectomy could imply that the effect of a
9 complete 30-day follow-up is more pronounced in procedures with a higher complication
10 profile, since ERCPs have a more congested post-operative complication profile compared to
11 cholecystectomies.
12
13
14
15
16
17
18
19
20
21
22
23

24 *Conclusions and implications*

25
26 Our findings may have significant general implications on how we shall interpret outcome
27 data from registry studies. Differences in the follow-up rate seemed to significantly affect the
28 reported outcome. The findings suggest that the validation process has to include the
29 completeness of follow-up. Differences in the follow-up frequency in registries affect the
30 reported outcomes as exemplified by the complicated endoscopic ERCP procedures. The
31 study emphasises the importance of complete follow-up, since this variable may well act as a
32 quality indicator for the respective registry.
33
34
35
36
37
38
39
40
41
42
43

44 *Future research*

45
46 Future research should focus on how the degree of complete follow-up in quality registers can
47 correlate to more objectively and not self-reported quality indicators.
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributors

LE conceived the study, created the study design, participated in the statistical analysis, analysed the data, and drafted and revised the paper. He is guarantor. MB participated in the analysis and interpretation of data, and revised the paper. GS participated in the statistical analysis and interpretation of data, and drafted and revised the paper. EJ interpreted the data and revised the manuscript. BH conceived the study and reviewed the manuscript. LL interpreted data and reviewed the manuscript. JÖ conceived the study, created the study design, and drafted and revised the paper.

All authors have approved of the final draft submitted.

Ethical approval

The regional research ethics committee at KarolinskaInstitutet, Stockholm, Sweden, approved the study.

Transparency

The first author (LE) confirms that the manuscript is an honest, accurate, and transparent account of the study; that no important aspects of the study have been omitted.

1
2
3 **REFERENCES**
4

- 5 1. Damman P, Jernberg T, Lindahl B, et al. Invasive strategies and outcomes for non-
6 ST-segment elevation acute coronary syndromes: a twelve-year experience from
7 SWEDEHEART. *EuroIntervention* 2016;12(9):1108-16. doi:
8 10.4244/EIJY15M11_05
9
- 10 2. Graves SE. The value of arthroplasty registry data. *Acta Orthop* 2010;81(1):8-9.
11 doi: 10.3109/17453671003667184
12
- 13 3. Dahlstrand U, Wollert S, Nordin P, et al. Emergency femoral hernia repair: a study
14 based on a national register. *Ann Surg* 2009;249(4):672-6. doi:
15 10.1097/SLA.0b013e31819ed943
16
- 17 4. Novik B, Nordin P, Skullman S, et al. More recurrences after hernia mesh fixation
18 with short-term absorbable sutures: A registry study of 82 015 Lichtenstein
19 repairs. *Arch Surg* 2011;146(1):12-7. doi: 10.1001/archsurg.2010.302 [published
20 Online First: 2011/01/19]
21
- 22 5. Tornqvist B, Stromberg C, Persson G, et al. Effect of intended intraoperative
23 cholangiography and early detection of bile duct injury on survival after
24 cholecystectomy: population based cohort study. *BMJ* 2012;345:e6457. doi:
25 10.1136/bmj.e6457 [published Online First: 2012/10/13]
26
- 27 6. Tornqvist B, Stromberg C, Akre O, et al. Selective intraoperative cholangiography
28 and risk of bile duct injury during cholecystectomy. *Br J Surg* 2015;102(8):952-8.
29 doi: 10.1002/bjs.9832 [published Online First: 2015/04/29]
30
- 31 7. Bay-Nielsen M, Kehlet H. Inguinal herniorrhaphy in women. *Hernia*
32 2006;10(1):30-3. doi: 10.1007/s10029-005-0029-3 [published Online First:
33 2005/09/01]
34
- 35 8. Stenberg E, Szabo E, Agren G, et al. Closure of mesenteric defects in laparoscopic
36 gastric bypass: a multicentre, randomised, parallel, open-label trial. *Lancet*
37 2016;387(10026):1397-404. doi: 10.1016/S0140-6736(15)01126-5 [published
38 Online First: 2016/02/21]
39
- 40 9. Gallriks 2017 [Available from: www.gallriks.se.]
41
- 42 10. Enochsson L, Thulin A, Osterberg J, et al. The Swedish Registry of Gallstone
43 Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks): A
44 nationwide registry for quality assurance of gallstone surgery. *JAMA*
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 *Surg*2013;148(5):471-8. doi: 10.1001/jamasurg.2013.1221 [published Online
4 First: 2013/01/18]
5
- 6 11. Rystedt J, Montgomery A, Persson G. Completeness and correctness of
7 cholecystectomy data in a national register--GallRiks. *Scand J Surg*
8 2014;103(4):237-44. doi: 10.1177/1457496914523412 [published Online First:
9 2014/04/17]
10
- 11 12. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications
12 and their management: an attempt at consensus. *Gastrointest Endosc*
13 1991;37(3):383-93.
14
- 15 13. Hosmer DW, Taber S, Lemeshow S. The importance of assessing the fit of logistic
16 regression models: a case study. *Am J Public Health* 1991;81(12):1630-5.
17
- 18 14. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of
19 recommendations. *BMJ* 2004;328(7454):1490. doi: 10.1136/bmj.328.7454.1490
20
- 21 15. Carter AJ, Nguyen CN. A comparison of cancer burden and research spending
22 reveals discrepancies in the distribution of research funding. *BMC Public Health*
23 2012;12:526. doi: 10.1186/1471-2458-12-526
24
- 25 16. Lundh A, Sismondo S, Lexchin J, et al. Industry sponsorship and research outcome.
26 *Cochrane Database Syst Rev* 2012;12:MR000033. doi:
27 10.1002/14651858.MR000033.pub2
28
- 29 17. Doucet M, Sismondo S. Evaluating solutions to sponsorship bias. *J Med Ethics*
30 2008;34(8):627-30. doi: 10.1136/jme.2007.022467
31
- 32 18. van den Broek MA, van Dam RM, Malago M, et al. Feasibility of randomized
33 controlled trials in liver surgery using surgery-related mortality or morbidity as
34 endpoint. *Br J Surg* 2009;96(9):1005-14. doi: 10.1002/bjs.6663
35
- 36 19. Ros A, Carlsson P, Rahmqvist M, et al. Non-randomised patients in a
37 cholecystectomy trial: characteristics, procedures, and outcomes. *BMC Surg*
38 2006;6:17. doi: 10.1186/1471-2482-6-17
39
- 40 20. Larsen IK, Smastuen M, Johannesen TB, et al. Data quality at the Cancer Registry
41 of Norway: an overview of comparability, completeness, validity and timeliness.
42 *Eur J Cancer* 2009;45(7):1218-31. doi: 10.1016/j.ejca.2008.10.037
43
- 44 21. Steliarova-Foucher E, Kaatsch P, Lacour B, et al. Quality, comparability and
45 methods of analysis of data on childhood cancer in Europe (1978-1997): report
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 from the Automated Childhood Cancer Information System project. *Eur J Cancer*
4 2006;42(13):1915-51. doi: 10.1016/j.ejca.2006.05.007
5
6 22. The Swedish National Board of Health and Welfare 2017 [Available from:
7 <http://www.socialstyrelsen.se/english/compare>.
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3 **LEGEND TO FIGURES**

4
5 **Figure 1**

6
7 The procedures included in the analyses.
8
9

10
11 **Figure 2**

12
13 Complete 30-day follow-up frequencies following cholecystectomies and ERCP. The
14 hospitals are ordered on the x-axis by level of completeness.
15
16
17

18
19
20 **Figure 3**

21
22 Adverse event rates after cholecystectomies and ERCP.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1

Demographics, physical status assessment and urgency of interventions for the 152 827 patients included in the study

		30-day follow-up of cholecystectomies				
		≥90%		<90%		<i>P</i>
		<i>n</i>	%	<i>n</i>	%	
Gender	Female	55908	67.3	8311	65.1	<.0001
	Male	27159	32.7	4462	34.9	
Age (years)	≥60	26442	31.9	4462	35.0	<.0001
	<60	56461	68.1	8290	65.0	
ASA	ASA 1-2	76478	92.1	11124	87.1	<.0001
	ASA ≥3	6589	7.9	1649	12.9	
Acute/ Scheduled	Acute	24237	29.2	4433	34.7	<.0001
	Scheduled	58830	70.8	8340	65.3	

		30-day follow-up of ERCP				
		≥90%		<90%		<i>P</i>
		<i>n</i>	%	<i>n</i>	%	
Gender	Female	25673	53.0	4460	52.0	0.0906
	Male	22743	47.0	4111	48.0	
Age (years)	≥60	35532	73.6	6724	78.5	<.0001
	<60	12767	26.4	1843	21.5	
ASA	ASA 1-2	33457	69.1	4748	55.4	<.0001
	ASA ≥3	14959	30.9	3823	44.6	
Acute/ Scheduled	Acute	30093	62.2	5055	59.0	<.0001
	Scheduled	18323	37.8	3516	41.0	

Table 2

Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of cholecystectomies $\geq 90\%$

	Adverse events				<i>P</i>
	$\geq 90\%$ n=83067		<90% n=12773		
	n	%	n	%	
Intraoperative	2548	3.0	381	3.0	0.8826
Total postoperative	6681	8.0	1119	8.8	0.0057
Pancreatitis	455	0.6	66	0.5	0.6570
Bleeding	629	0.8	96	0.8	0.9454

	Adverse events		
	$\geq 90\%$ vs <90% 30-day follow-up Adjusted*		
	Odds Ratio	(95% CI)	<i>P</i>
Intraoperative	0.93	(0.84-1.04)	0.2298
Total postoperative	0.98	(0.91-1.05)	0.5067
Pancreatitis	1.30	(0.99-1.75)	0.0606
Bleeding	0.97	(0.78-1.21)	0.7821

*Adjusted for sex, age, ASA class, acute interventions and indications.

Table 3

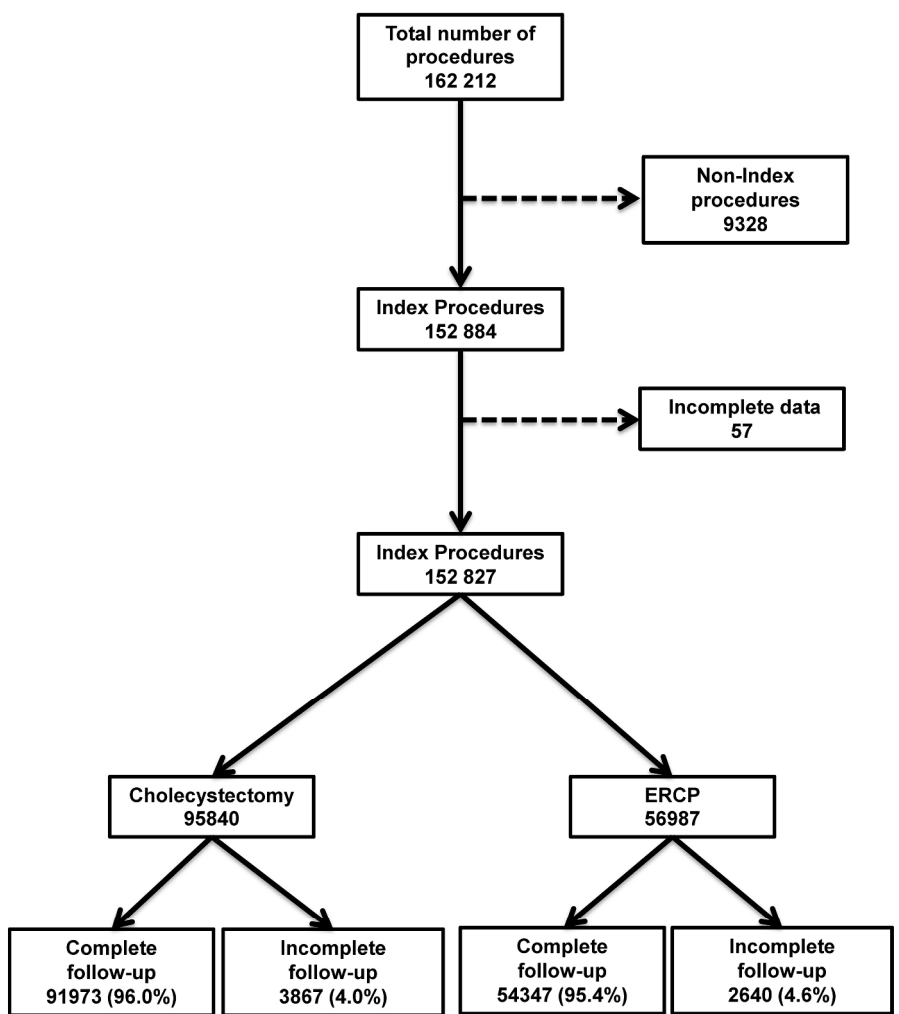
Adverse event rates, Odds Ratios (OR) and 95% confidence intervals of hospitals with or without a 30-day follow-up frequency of ERCPs $\geq 90\%$

	Adverse events				<i>P</i>
	$\geq 90\%$ n=48416		$< 90\%$ n=8571		
	n	%	n	%	
Intraoperative	1267	2.6	252	2.9	0.0868
Total	6821	14.1	689	8.0	<.0001
postoperative	1978	4.1	178	2.1	<.0001
Pancreatitis	591	1.2	76	0.9	0.0081
Bleeding					

	Adverse events		
	$\geq 90\%$ vs $< 90\%$ 30-day follow-up Adjusted*		
	Odds Ratio	(95% CI)	<i>P</i>
Intraoperative	0.76	(0.66-0.87)	0.0002
Total	1.92	(1.76-2.11)	<.0001
postoperative	2.04	(1.72-2.43)	<.0001
Pancreatitis	1.38	(1.08-1.79)	0.0100
Bleeding			

*Adjusted for sex, age, ASA class, acute interventions and indications.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

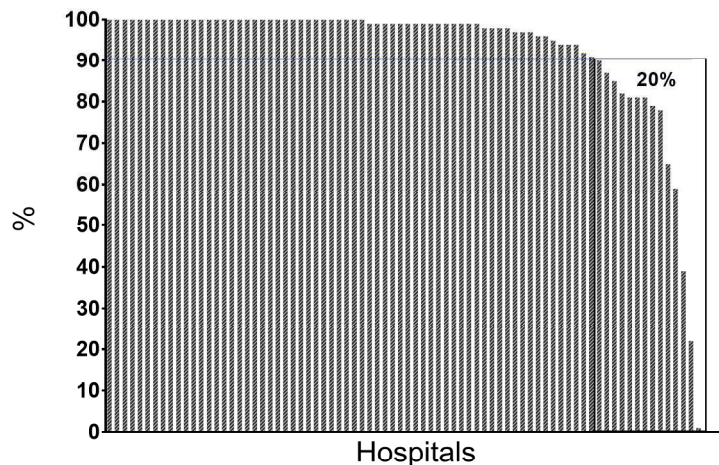


The procedures included in the analyses.

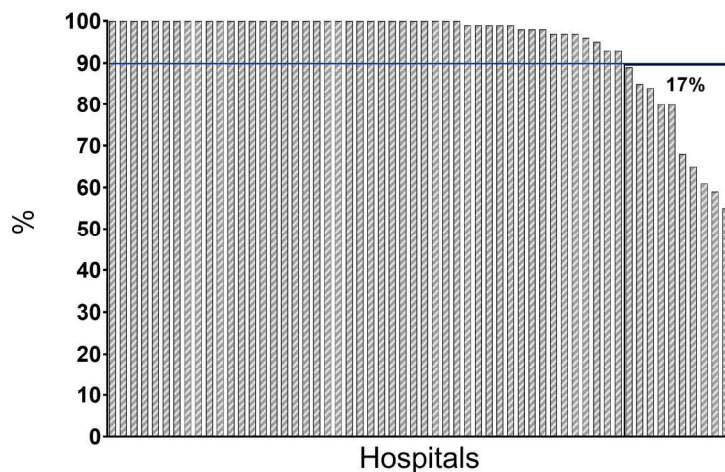
254x338mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Complete 30-day follow-up cholecystectomies



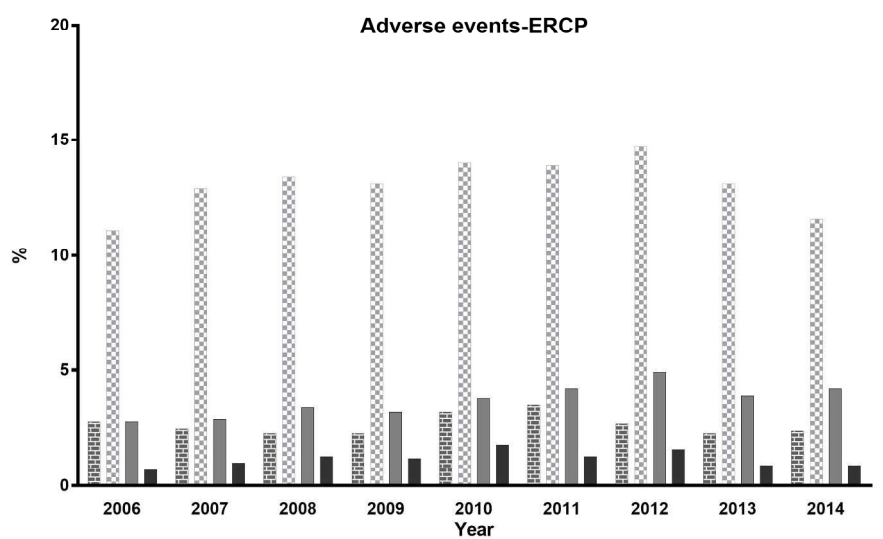
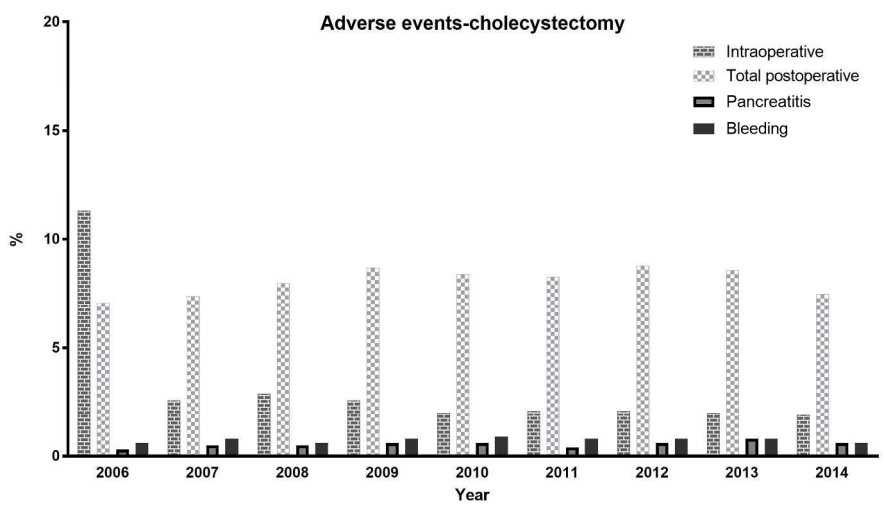
Complete 30-day follow-up ERCP



Complete 30-day follow-up frequencies following cholecystectomies and ERCP. The hospitals are ordered on the x-axis by level of completeness.

167x256mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Adverse event rates after cholecystectomies and ERCP.

198x247mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 2	Population-based register study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Pages 4-5	
Objectives	3	State specific objectives, including any prespecified hypotheses	Abstract and page 5	
Methods				
Study design	4	Present key elements of study design early in the paper	Page 4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Pages 5-6	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	Pages 5-6	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 6-7	
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 5-7	
Bias	9	Describe any efforts to address potential sources of bias	Pages 10-11	
Study size	10	Explain how the study size was arrived at	Pages 5-6	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 7
		(b) Describe any methods used to examine subgroups and interactions	Page 7
		(c) Explain how missing data were addressed	Partly described on page 7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	The article is about this subject
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Described in results.
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	That is what this article is all about
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Tables 2-3
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2-3
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	In Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.