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# The use of hospital discharge data to compare outcomes of different surgical techniques: the example of cholecystectomy.

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**The use of hospital discharge data to compare outcomes of different surgical techniques: the example of cholecystectomy.**


## Abstract

### Objective

There is an increasing interest in using routinely collected health data to support large-scale effectiveness evaluation of different treatment options. We evaluated short-term outcomes after laparoscopic cholecystectomy (LC) or open cholecystectomy (OC) in gallstones using hospital discharge data.

### Design

Population-based cohort study.

### Setting

Data were obtained from the Regional Hospital Discharge Registry Lazio Region in Central Italy (around 5 million inhabitants) in 2007-2008.

### Participants

All patients admitted to hospitals of Lazio with symptomatic gallstones (ICD9-CM = 574) who underwent LC (ICD9-CM 51.23) or OC (ICD9-CM 51.22).

### Outcome measures

1)"*30-day surgical-related complications*" defined as any complication of the biliary tract (including bile duct injury, bile leak, postoperative bleeding, wound infection, cholecystis injury); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events).

### Results

13,651 patients were included; 86.1% had LC, 13.9% OC. 2.0% experienced surgical-related complications (SRC), 2.1% systemic complications (SC). The Odds Ratio (OR) of complications after LC versus OC was 0.60 ($p<0.001$) for SRC and 0.52 ($p<0.001$) for SC. As regards SRC, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission (OR=0.94, p = 0.764). For SC, no significant advantage of LC was seen among very old people (OR=0.99, p=0.975) and among those with previous upper abdominal surgery (OR=0.86, p=0.905).

**Conclusions**

This large observational study confirms that LC is more effective than OC with respect to short-term complications. The advantage remains in sub-populations with higher preoperative risk, but it is different according to whether the complications affect the biliary tract or other organs or systems. Population-based linkage of administrative datasets can enlarge evidence of treatment benefits in clinical practice.

**Key words:** administrative data, cholecystectomy, complications, effectiveness, outcomes

## Article summary

### Article focus

-The advantage of laparoscopic cholecystectomy (LC) approach for the treatment of gallstone versus open surgery (OC) has been shown from RCTs but the evidence from observational studies is limited.

-The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments.

-We compared laparoscopic and open cholecystectomy in term of short-term outcomes using routinely collected databases in Lazio Region (Italy).

### Key messages

-This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting.

-As regards surgical-related complications, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission.

-For systemic complications, no significant advantage of LC was seen among very old people and among those with previous upper abdominal surgery.

### Strenghts and limitations

-Population-based design, large numbers and robustness of analytic procedures are the main strengths.

-It contributes to the debate on the complex methodology to estimated risk of adverse events after surgery using secondary databases to monitor quality of care.

-The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is a major limit.

**Introduction**

Comparative effectiveness research (CER) is becoming central to monitor real-life impact of treatments and support public health decisions (1, 2). Although the basic concept of comparing therapies is not new, over the last few years many initiatives have been implemented in many countries to provide large-scale evidence on benefits and harms of different treatments (3-5). The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments (6,7). They include hospital in-patients records, birth and death registrations, outpatient care records, dispensed pharmacy drugs. Despite the advantages due to the large numbers and the population-level coverage, the analytic methods to reduce bias in CER studies are complex and new approaches are continuously developed (8,9).

In the Lazio Region (around 5.000.000 inhabitants) the P.Re.Val.E. Project (*Regional Program for Assessing the Outcomes of Health-care Interventions*) was launched in 2005. Its aims are: to measure the quality of health care provided in the Lazio Region, to describe variability of care provision across institutions and populations and to compare effectiveness of treatments for different medical and surgical conditions (10, 11). Over 60 outcomes indicators are calculated based on data obtained from record-linkage procedures of different health systems. The results are periodically updated and publicly disseminated with discussion on critical methodological points.

Cholecystectomy is one of the most common abdominal surgical procedures in developed countries. Since its introduction in the late '80s, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) as the treatment of choice for symptomatic gallstones (12, 13). Although beneficial effects of LC have been widely demonstrated, there are relatively few studies showing the advantages from real-life settings using secondary databases (14-16). In the present study, we aimed at developing a methodology to measure short-term complications after LC or OC using large administrative databases on behalf of the P.Re.Val.E. Secondly, we tested the hypothesis that the advantages of LC versus OC could vary according to demographic and clinical patients' characteristics.

## Methods

Source of data

Data was derived from the Lazio Hospital Information System (HIS), which provides information on patients' demographic data (gender, age, place of birth, place of residence), admission and discharge dates, discharge diagnoses (up to 6) and medical procedures or surgical interventions ((up to 6) according to the International Classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM), status at discharge (alive, dead, transferred to another hospital), ward(s) of stay, date(s) of in-hospital transfer, and a regional code corresponding to the admitting facility for patients discharged from all public and private hospital of the Lazio Region (5.759.839 inhabitants).

Study population

All hospital admissions with a primary or secondary diagnosis of gallstones (International Classification of Diseases 9$^{th}$ Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases (age 18+ years). Information was retrieved from the HIS. In order to increase the case specificity, several exclusion criteria were applied including long-term hospitalizations, rehabilitations, day-hospitals, hospitalizations for delivery or trauma or cancer, hospitalizations with abdominal surgical procedures other than cholecystectomy. The final population consisted of 13,651 subjects (**Figure 1).** See the online **Supplementary Data** (Part 1) for details on the exclusion criteria and ICD9-CM codes.



Patient-level risk factors

The following characteristics were considered for each patient: Age (<70; 70-79; >=80 years old); Gender; Severity of gallstones: it was classified as *low* (not-complicated), *moderate* (presence of cholecystitis, cholangitis or biliary tract obstruction), and *high* (presence of both inflammation and obstruction of the biliary tract); Previous upper abdominal surgery (based on previous 2-year hospitalizations); Comorbidities (based on previous 2-year hospitalizations) following validated algorithms (17-19); Type of admission: either *elective* or *emergency*. See the online **Supplementary Data** (Part 2-4) for details on the ICD-9-CM codes. The choice of *cut off* for age category was based on previous studies to distinguish adult and old people (20-22).

Outcomes

We identified various complications within 30-days after the intervention and grouped them in two categories: 1) "*30-day surgical-related complications*" defined as any complication of the biliary tract (including bile duct injury, bile leak, postoperative bleeding, wound infection, cholecystis injury); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events). The complete list of complications with ICD-9-CM codes is reported in the online **Supplementary Data** (Part 5). Among the various complications we included some conditions reported in the list of Patient Safety Indicators recently developed by the Agency for Health Care Research and Quality (i.e. postoperative bleeding, wound infection), while other items were specifically created on the basis of scientific literature on digestive surgery (14-16,23,24). Depending on the type of complication, some ICD9-CM codes were searched in both the index admission and the following ones in the 30-day period after the surgery, others were searched only in later hospitalizations. For example, peritonitis or acute pancreatitis was not counted as complications when reported in the index admission. See the online **Supplementary Data** (Part 5) for details on the ICD9-CM codes. In the case of a subsequent hospitalization occurred out of the study area (for example, in a region other than Lazio), we obtained information through record linkage procedure between hospital information systems. Because of the short follow up time, this happened in a minimal proportion of cases (0.1%). The outcome variables were: "*30-day surgical-related complications*" and "*30-day systemic complications*"; they were coded "1" if at least one of the complications within the group was present and "0" if none was recorded.

Type of cholecystectomy

We defined the variable "*type of cholecystectomy*" (laparoscopic cholecystectomy, LC vs. open cholecystectomy, OC). Since a specific ICD-9-code for a case converted from LC to OC was not available, in the case of reported ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure.

Statistical analysis

Multiple logistic regression models were fitted to estimate the relative risk of 30-day complications (either "surgical-related" or "systemic") after LC versus OC, adjusting for demographical and clinical risk factors. The two outcome variables were analysed separately. Given the large amount of individual-level variables available, the risk factors were divided in two groups: 1) variables “a priori” chosen as confounders (age, gender, severity of gallstones, previous upper abdominal surgery, and type of admission); 2) variables empirically tested (comorbidities, which were selected using iterative stepwise statistical procedures) (9,25). Once the “best” predictive model was identified for each of the two outcome variables, the treatment variable “*type of cholecystectomy*” was included, and the adjusted odds ratio (OR) of LC versus open surgery was estimated, with corresponding 95% confidence interval (95% CI) and p-value.

In order to test the hypothesis of an effect modification by age, relative risk estimates for the age groups were derived by adding an interaction term between the age group and the treatment variable in the final multivariate logistic model. We obtained the OR of laparoscopic vs. open surgery within each age stratum by adding the corresponding interaction terms coefficients. Similarly, effect modification was tested with regard to severity of cholelithiasis, previous upper abdominal surgery and type of admission. The corresponding tests of heterogeneity of the stratum-specific risk estimates were computed but not reported for ease of presentation.

Sensitivity analyses were performed. First, in order to guarantee adequate control of confounding factors we identified and adjusted for all the individual factors associated with the treatment, within the propensity adjustment framework (26). This procedure is a two-step technique: 1. it estimates the a priori probability of exposure for each subject, based on clinical and demographic characteristics; 2. it standardizes for them in the association between treatment and the study outcome. The individual factors related to the exposure in the present study include age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, cardio-circulatory disease, cerebrovascular disease, COPD or respiratory failure, chronic nephropathy, chronic disease of the liver or pancreas. Second, to take into account the potential heterogeneous experience in laparoscopic surgery across different hospitals because of the patients' clustering within a single institution we perform a multilevel regression model with random intercepts for hospitals (27).

All the statistical analyses were performed using SAS Software version 8.0 (SAS Institute, Inc. SAS/STAT software).

**Results**

A description of the study population, overall and by cholecystectomy procedure, is presented in **Table 1**. Over 80% of the patients were younger than 70 years, and moderate to high severity of the gallstones was diagnosed for 61.7%. As compared with patients undergoing LC, those who underwent OC were more likely to be elderly, males, with a more sever baseline disease and more chronic conditions. Furthermore, they were operated in emergency in most of the cases (52.4%), whereas LC was performed in elective hospitalizations much more frequently (73.9%).

**Table 2** reports the relationship between demographic and clinical variables and the occurrence of complications. The adjusted risk of systemic complications increased with age and was much higher in patients with more severe baseline gallstones, whereas no clear age or severity-related differences in risk emerged with regard to surgical-related 30-day complications, once other co-factors were taken into account. Women were less likely to experience both types of complications. Having had a previous intervention on the upper digestive system seemed to enhance the risk of both surgical-related and systemic complications, though results are not statistically significant due to small power. Finally, the risk of both types of complications was more evident in emergency as opposed to scheduled interventions. Surgical-related complications were higher among subjects with obesity, blood disease, stroke or chronic nephropathy, whereas systemic complications were associated with blood diseases, ischemic heart disease, conduction disorders or dysrhythmias, COPD or respiratory failure, chronic nephropathy, and chronic diseases of the liver or pancreas.

**Table 3** shows the relationship between type of cholecystectomy and outcomes, adjusted for the risk factors identified in Table 2. We report rresults of the advantage of LC vs. OC (OR, 95% CI) in the cohort (first lines of the table) and in the each stratum of the variables tested in the models with interaction terms. The incidence of “30-day surgical-related complications” and “30-day systemic complications” was 2.0% and 2.1%, respectively. The incidence of “at least one 30-day complication” was 3%. The odds ratio of surgical related complications for patients who underwent LC as compared to patients with OC was 0.60 (p<0.001). The corresponding figure for systemic complications was 0.52 (p<0.001).

As regards 30-day surgical-related complications, the protective effect of LC vs. OC was consistent across the age category, severity of cholelithiasis and previous upper abdominal surgery, while among people with emergency admission there was no advantage (OR=0.94 p = 0.764). Similarly, for systemic complications, the superiority of LC vs. OC was consistent regardless level of cholelithiasis severity, and elective/emergency admission, but for those 80+ yrs aged people there was no advantage of LC vs. OC (OR 0.99, p = 0.975); also for patients with previous upper abdominal surgery there was a much weaker advantage (OR=0.86, p=0.905).

When the association between type of cholecystectomy and short-term complications was adjusted with the propensity adjustment method, results were consistent with those obtained with the risk-adjustment procedure (LC vs. OC OR= 0.61 and OR=0.52 respectively for the two outcomes). Finally, results were similar taking into account patients' clustering within different hospitals (*data not shown*).



**Discussion**

From this large observational study based on linked administrative health records - taking into account the disomogeneous distribution of factors related to the probability to be offered open surgery - people who end up having a LC have a better short-term prognosis than those that get an OC for the treatment of gallstones. The superiority of laparoscopic approach in term of short-term outcomes is consistent in both genders, different severity in disease presentation and past history of upper abdominal surgery.

This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting. It supports the usefulness of observational approaches. To our knowledge it is the first study in Italy to measure and compare outcomes of surgical treatments using data from secondary data sources. Despite RTCs are considered the optimal study design when comparing efficacy of treatments, observational studies provide a picture of treatment under usual circumstances of health-care practice and can answer to the question ''*Does it work in practice*?" (6, 3). RTCs often have small sample size and may under represent vulnerable patient groups, including elderly patients with multiple comorbidities, children, and young women, and operate in a highly controlled environment that is far from routine clinical practice. Our study supports that LC is a reliable approach safer than OC not only in old age group - confirming previous findings (20, 28) - but also in presence of severe disease presentation and in patients with past history of upper digestive system surgery. Beneficial effect of LC as regards systemic complications tends to be lower in 80+ yrs aged in comparison with younger ages, and in patients with emergency admission in comparison to elective admissions as regards 30-day surgical-related complications. These data add to the evidence on the complex relationship between age and outcomes after surgery (20-22, 28).

A number of potential biases are present. First of all, people in the two groups of patients analyzed are not homogenous with a higher frequency of elderly and more severe patients in the open group that in the laparoscopic one. When comparing the effect of the two techniques using two different populations, the so called "indication bias" may affect study validity (6, 29). To limit this problem we run the propensity adjustment analysis to take into account the different distribution of factors strongly associated with the probability to receive open surgery in the study population. This analytical approach confirmed the advantage of laparoscopic vs. open surgery obtained in the main logistic regression analysis. Another critical point is the potential different distribution of laparoscopic experience across surgeons; however a sensitivity analysis which took into account this point led to similar results. The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is another major limit. Discharge abstract data have little insight into clinical details and do not inform on the temporal relationship of the clinical conditions and processes, then defining complications is a difficult task (30). In this respect, we tried to improve the accuracy of our measures both 1) applying a specific coding algorithm with subsequent hospital admissions used to retrieve adverse events and 2) excluding in the "count" of complications specific items if reported in the index only (i.e. peritonitis) because of the difficulty to determine if it was already present at admission. Moreover, we cannot exclude an under-notification of complications but it is unlikely that is influenced by the type of surgery. Another major problem is the potential misclassification of exposure since we were not able to measure the occurrence of conversion of LC to OC. The number of people that were switched from LC to OP is low in comparison to figures documented in other studies and it may represent a severe source of bias in our study (28,31).

Beneficial effects of the laparoscopic approach versus traditional open surgery for the treatment of gallstones come from various randomized controlled trials (RCTs) (32). They found significant shorter hospital stay and quicker convalescence associated with LC but no differences in mortality, complications and operative time between the two procedures. A better trend with the laparoscopic approach, including morbidity and mortality, comes from some observational studies. From a surveillance system in eight Swiss hospitals, surgical site infections were less common in laparoscopic approach in comparison to traditional open surgery (0.5% in LC vs. 1.8% in OC) (33). Significantly lower incidence of venous thromboembolism and surgical site-infections in laparoscopic cases versus open cases was recently observed in a large administrative dataset–based study in USA (14, 15). In-hospital mortality after cholecystectomy over a ten-years period was studied in USA: LC was associated with a low mortality rate (mean value in the period: 0.52%) while OC with a significantly higher rate (corresponding value: 4.9%) (16). In the era of evidence-based health care, population-based linkage of administrative health data have been increasingly used also in the field of surgery. However the methodology is not standardized and estimated risk of adverse events vary widely according to the type of interventions and to the type of complications and their operative definition. As a recent example in Europe, the incidence of conversion to OC after LC in all hospitals in England from 2005 to 2006 has been examined using Hospital Episode Statistics and resulted 4.6% for elective procedures and 9.4% for emergency procedures) (34). In USA, a set of indicators (Patient Safety Indicators (PSIs) has been introduced, validated and continuously under revision as algorithms based on the International Classification of Diseases, Ninth Revision, Clinical Modification (17). Our study contributes to the experience in using population-based linked health data and ICD-9-CM coding algorithms to compare treatment outcomes.

Population-based linkage of routinely collected health data represents a precious tool to support large- scale and real-world practice evaluation by measuring specific outcomes and comparing them over time and across populations. Together with results from experimental research settings, the conclusions of research studies evaluating clinical outcomes through data linkage systems should be successfully incorporated into practice by clinicians/surgeons.

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**AUTHOR'S CONTRIBUTION**

All Authors participated in the study design, in defining the study protocol and methodology, in acquisition of data, in planning the analyses, in interpreting the results. M.S. performed the analyses. N.A and M.S. drafted the manuscript.

**COMPETING INTERESTS STATEMENT**

There is no competing interest.

**DATA SHARING STATEMENT**

We state that our work is an original research.

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**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelithiasis, previous upper abdominla surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September2008

| **Patient characteristics** | **Laparoscopic cholecystectomy** | | **Open cholecystectomy** | | **Total** | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | **No.** | **%** |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| Age (years) | | | | | | |
| *< 70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70 - 79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| Gender | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| Severity of cholelithiasis | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.473 | 55,1 | 1.210 | 63,7 | 7.683 | 56,3 |
| *High* | 512 | 4,4 | 219 | 11,5 | 731 | 5,4 |
| Previous upper abdominal surgery | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| Type of admission | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| Comorbidities (presence of the condition) | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorder or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

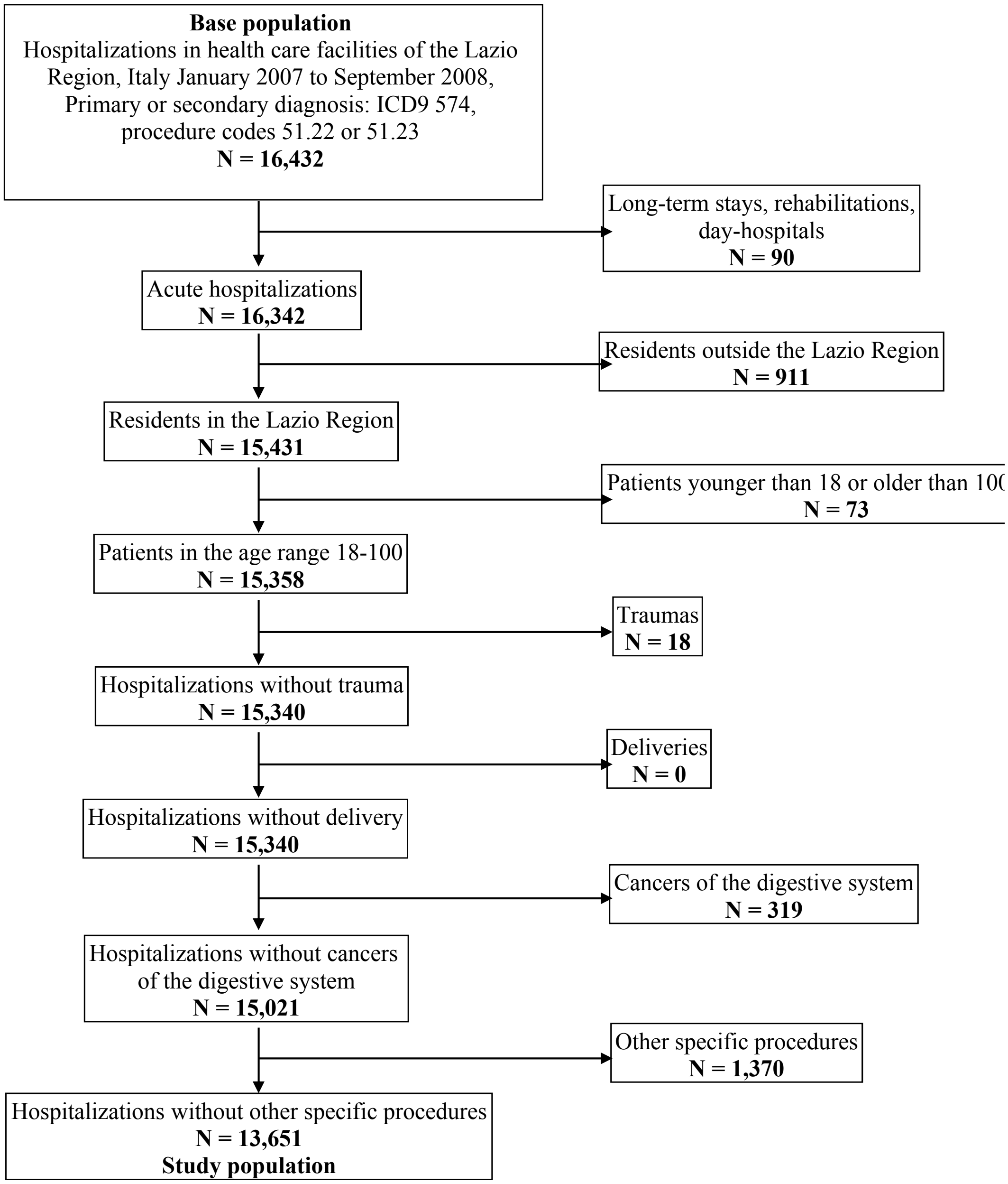
**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | 30-day systemic complications (N=280, 2.1%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | p | $OR_{adj}$ | p | % | $OR_{crude}$ | p | $OR_{adj}$ | p |
| Age (years) | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | 1,00 | - | 1,5 | 1,00 | - | 1,00 | - |
| *70 - 79* | 2,9 | 1,62 | 0,001 | 1,36 | 0,048 | 3,9 | 2,68 | 0,000 | 2,01 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 0,015 | 1,21 | 0,475 | 7,1 | 5,13 | 0,000 | 2,79 | 0,000 |
| Gender | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | 1,00 | - | 2,6 | 1,00 | - | 1,00 | - |
| *Women* | 1,7 | 0,69 | 0,002 | 0,75 | 0,022 | 1,7 | 0,66 | 0,001 | 0,80 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | 1,00 | - | 1,2 | 1,00 | - | 1,00 | - |
| *Moderate* | 2,0 | 1,08 | 0,538 | 0,96 | 0,733 | 2,2 | 1,84 | 0,000 | 1,55 | 0,004 |
| *High* | 3,7 | 2,03 | 0,001 | 1,43 | 0,122 | 6,2 | 5,30 | 0,000 | 3,40 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | 1,00 | - | 2,0 | 1,00 | - | 1,00 | - |
| *Yes* | 5,7 | 2,94 | 0,037 | 2,29 | 0,119 | 4,3 | 2,15 | 0,197 | 1,72 | 0,376 |
| Type of admission | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | 1,00 | - | 1,5 | 1,00 | - | 1,00 | - |
| *Emergency* | 3,0 | 1,85 | 0,000 | 1,66 | 0,000 | 3,4 | 2,34 | 0,000 | 1,64 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,476 | - | - | 3,6 | 1,81 | 0,059 | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,095 | - | - | 4,4 | 2,24 | 0,002 | - | - |
| *Obesity* | 5,0 | 2,57 | 0,016 | 2,35 | 0,034 | 4,3 | 2,16 | 0,067 | - | - |
| *Blood disease* | 5,8 | 3,03 | 0,000 | 2,09 | 0,022 | 7,7 | 4,16 | 0,000 | 1,96 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 0,050 | - | - | 4,0 | 2,20 | 0,000 | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,286 | - | - | 7,4 | 4,08 | 0,000 | 1,74 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,836 | - | - | 9,4 | 5,08 | 0,000 | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,875 | - | - | 4,6 | 2,29 | 0,107 | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,136 | - | - | 6,8 | 3,66 | 0,000 | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 0,008 | - | - | 7,0 | 3,81 | 0,000 | 1,73 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 0,000 | 1,98 | 0,025 | 7,7 | 4,19 | 0,000 | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,328 | - | - | 8,5 | 4,59 | 0,000 | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,534 | - | - | 7,7 | 4,22 | 0,000 | 2,02 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 0,000 | 3,24 | 0,001 | 10,5 | 5,82 | 0,000 | 2,27 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,087 | - | - | 4,8 | 2,51 | 0,001 | 1,97 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission - Lazio Region, Italy, January 2007 - September 2008

| | 30-day surgical-related complications (N=278, %=2.0) | | | | | 30-day systemic complications (N=280, %=2.1) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | p | $OR_{adj}$ | p | % | $OR_{crude}$ | p | $OR_{adj}$ | p |
| Open cholecystectomy | 3,9 | 1,00 | - | 1,00 | - | 5,2 | 1,00 | - | 1,00 | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,000 | 0,60 | 0,001 | 1,6 | 0,29 | 0,000 | 0,52 | 0,000 |
| *Stratified results by each category* | | | | | | | | | | |
| Age (years) | | | | | | | | | | |
| *< 70* | 1,8 | 0,49 | 0,000 | 0,62 | 0,012 | 1,5 | 0,34 | 0,000 | 0,47 | 0,000 |
| *70 - 79* | 2,9 | 0,45 | 0,003 | 0,57 | 0,043 | 3,9 | 0,35 | 0,000 | 0,47 | 0,002 |
| *≥ 80* | 3,3 | 0,41 | 0,082 | 0,51 | 0,184 | 7,1 | 0,71 | 0,309 | 0,99 | 0,975 |
| Severity of cholelithiasis | | | | | | | | | | |
| *Low* | 1,9 | 0,37 | 0,000 | 0,46 | 0,003 | 1,2 | 0,29 | 0,000 | 0,43 | 0,005 |
| *Moderate* | 2,0 | 0,58 | 0,005 | 0,78 | 0,224 | 2,2 | 0,34 | 0,000 | 0,55 | 0,001 |
| *High* | 3,7 | 0,24 | 0,000 | 0,30 | 0,004 | 6,2 | 0,38 | 0,002 | 0,56 | 0,071 |
| Previous upper abdominal surgery | | | | | | | | | | |
| *No* | 2,0 | 0,47 | 0,000 | 0,60 | 0,001 | 2,0 | 0,29 | 0,000 | 0,52 | 0,000 |
| *Yes* | 5,7 | 0,26 | 0,256 | 0,36 | 0,388 | 4,3 | 0,41 | 0,470 | 0,86 | 0,905 |
| Type of admission | | | | | | | | | | |
| *Elective* | 1,6 | 0,31 | 0,000 | 0,37 | 0,000 | 1,5 | 0,33 | 0,000 | 0,48 | 0,000 |
| *Emergency* | 3,0 | 0,76 | 0,178 | 0,94 | 0,764 | 3,4 | 0,35 | 0,000 | 0,56 | 0,002 |

**Figure 1.** Selection of the study population



) years

# SUPPLEMENTARY DATA

## DETAILED METHODS

### PART 1 - Cohort selection

Source of data: Hospital Information System (HIS)

*Inclusion criteria*

All hospital admissions with a primary or secondary contributing diagnosis of cholelithiasis (International Classification of Diseases 9th Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases. The final population, after sequential exclusions, consisted of 13,651 subjects.

*Exclusion criteria*

- long-term hospitalizations, rehabilitations and day-hospitals
- patients residents outside the Lazio Region
- subjects younger than 18 or older than 100 years old
- hospitalizations for delivery (MDC 14)
- hospitalizations for any type of trauma (ICD-9-CM codes ICD-9-CM 800-897)
- hospitalizations with diagnoses of cancer of the digestive system (IDC-9-CM codes150-159)
- hospitalizations with other abdominal surgical procedures, as follows:

**ICD-9-CM code Description**

Stomach

*43.5 Partial gastrectomy with anastomosis to esophagus*
*43.6 Partial gastrectomy with anastomosis to duodenum*
*43.7 Partial gastrectomy with anastomosis to jejunum*
*43.8 Other partial gastrectomy*
*43.9 Total gastrectomy*
*44.31 High gastric bypass*
*44.39 Other gastroenterostomy*
*44.40 Suture of peptic ulcer, not otherwise specified*
*44.41 Suture of gastric ulcer site*
*44.42 Suture of duodenal ulcer site*
*44.5 Revision of gastric anastomosis*
*44.61 Suture of laceration of stomach*
*44.63 Closure of other gastric fistula*
*44.64 Gastropexy*
*44.65 Esophagogastroplasty*
*44.69 Other*

Small intestine

*45.31 Other local excision of lesion of duodenum*
*45.32 Other destruction of lesion of duodenum*
*45.33 Local excision of lesion or tissue of small intestine, except duodenum*
*45.34 Other destruction of lesion of small intestine, except duodenum*
*45.50 Isolation of intestinal segment, not otherwise specified*
*45.51 Isolation of segment of small intestine*

*45.6 Other excision of small intestine*
*45.9 Intestinal anastomosis*
*45.91 Small-to-small intestinal anastomosis*
*45.92 Anastomosis of small intestine to rectal stump*
*45.93 Other small-to-large intestinal anastomosis*
*46.01 Exteriorization of small intestine*
*46.02 Resection of exteriorized segment of small intestine*
*46.60 Fixation of intestine, not otherwise specified*
*46.61 Fixation of small intestine to abdominal wall*
*46.62 Other fixation of small intestine*
*46.71 Suture of laceration of duodenum*
*46.72 Closure of fistula of duodenum*
*46.73 Suture of laceration of small intestine, except duodenum*
*46.74 Closure of fistula of small intestine, except duodenum*
*46.80 Intra-abdominal manipulation of intestine, not otherwise specified*
*46.81 Intra-abdominal manipulation of small intestine*
*46.93 Revision of anastomosis of small intestine*
*46.97 Transplant of intestine*

Liver
*50.2 Local excision or destruction of liver tissue or lesion*
*50.3 Lobectomy of liver*
*50.4 Total hepatectomy*
*50.5 Liver transplant*
*50.6 Repair of liver*

Pancreas
*52.22 Other excision or destruction of lesion or tissue of pancreas or pancreatic duct*
*52.3 Marsupialization of pancreatic cyst*
*52.4 Internal drainage of pancreatic cyst*
*52.5 Partial pancreatectomy*
*52.6 Total pancreatectomy*
*52.7 Radical pancreaticoduodenectomy*
*52.8 Transplant of pancreas*
*52.95 Other repair of pancreas*
*52.96 Anastomosis of pancreas*

Abdominal Hernia
*53.4 Repair of umbilical hernia*
*53.5 Repair of other hernia of anterior abdominal wall (without graft or prosthesis)*
*53.6 Repair of other hernia of anterior abdominal wall with graft or prosthesis*
*53.7 Repair of diaphragmatic hernia, abdominal approach*

Peritoneum
*54.4 Excision or destruction of peritoneal tissue*
*54.5 Lysis of peritoneal adhesions*
*54.6 Suture of abdominal wall and peritoneum*
*54.7 Other repair of abdominal wall and peritoneum*

Large intestine
*45.41 Excision of lesion or tissue of large intestine*

*45.49 Other destruction of lesion of large intestine*
*45.7 Open and other partial excision of large intestine*
*45.8 Total intra-abdominal colectomy*
*45.94 Large-to-large intestinal anastomosis*
*46.03 Exteriorization of large intestine*
*46.04 Resection of exteriorized segment of large intestine*
*46.63 Fixation of large intestine to abdominal wall*
*46.64 Other fixation of large intestine*
*46.75 Suture of laceration of large intestine*
*46.76 Closure of fistula of large intestine*
*46.79 Other repair of intestine*

Other surgery
*55.4 Partial nephrectomy*
*55.5 Complete nephrectomy*
*56.2 Ureterotomy*
*56.4 Ureterectomy*
*57.1 Cystotomy and cystostomy*
*57.6 Partial cystectomy*
*57.7 Total cystectomy*
*65.3 Unilateral oophorectomy*
*65.4 Unilateral salpingo-oophorectomy*
*65.5 Bilateral oophorectomy*
*65.6 Bilateral salpingo-oophorectomy*
*66.4 Total unilateral salpingectomy*
*66.5 Total bilateral salpingectomy*
*68.3 Subtotal abdominal hysterectomy*
*68.4 Total abdominal hysterectomy*
*68.6 Radical abdominal hysterectomy*
*68.8 Pelvic evisceration*

**PART 2 - Codes to describe severity of cholelithiasis**

**1 - Cholelithiasis of the biliary tract without complications**

*574.20 Calculus of gallbladder without mention of cholecystitis*
*574.50 Calculus of bile duct without mention of cholecystitis*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

**2. Cholelithiasis of the biliary tract with cholecystitis (without obstruction)**

*574.10 Calculus of gallbladder with other cholecystitis*
*574.40 Calculus of bile duct with other cholecystitis*
*574.70 Calculus of gallbladder and bile duct with other cholecystitis*

*575.1 Other cholecystitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

*574.00 Calculus of gallbladder with acute cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

*575.0 Acute cholecystitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*
*576.1 Cholangitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

**3. Cholelithiasis of the biliary tract with obstruction (without cholecystitis)**
*574.21 Calculus of gallbladder without mention of cholecystitis*
*574.51 Calculus of bile duct without mention of cholecystitis*
*574.91 Calculus of gallbladder and bile duct without cholecystitis*

*575.2 Obstruction of gallbladder AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

*576.2 Obstruction of bile duct AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*
*575.3 Hydrops of gallbladder*

**3. Cholelithiasis of the biliary tract with both obstruction and cholecystitis**

*574.01 Calculus of gallbladder with acute cholecystitis*
*574.11 Calculus of gallbladder with other cholecystitis*
*574.31 Calculus of bile duct with acute cholecystitis*
*574.41 Calculus of bile duct with other cholecystitis*
*574.61 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.71 Calculus of gallbladder and bile duct with other cholecystitis*
*574.81 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

*575.2 Obstruction of gallbladder AND*
*574.00 Calculus of gallbladder with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.70 Calculus of gallbladder and bile duct with other cholecystitis*

*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

*576.2 Obstruction of bile duct AND*

*574.00 Calculus of gallbladder with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.70 Calculus of gallbladder and bile duct with other cholecystitis*
*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

**PART 3 - Codes to describe previous upper abdominal surgery**

Codes in the index admission – post procedural states

stomach V44.1, V45.75, V55.1
intestine V44.2, V44.4, V45.3, V45.72, V53.5, V55.2, V55.4, V42.84
liver V42.7
pancreas 42.83

Codes in the previous 2-year- hospitalizations

Stomach
*43.5 Partial gastrectomy with anastomosis to esophagus*
*43.6 Partial gastrectomy with anastomosis to duodenum*
*43.7 Partial gastrectomy with anastomosis to jejunum*
*43.8 Other partial gastrectomy*
*43.9 Total gastrectomy*
*44.31 High gastric bypass*
*44.39 Other gastroenterostomy*
*44.40 Suture of peptic ulcer, not otherwise specified*
*44.41 Suture of gastric ulcer site*
*44.42 Suture of duodenal ulcer site*
*44.5 Revision of gastric anastomosis*
*44.61 Suture of laceration of stomach*
*44.63 Closure of other gastric fistula*
*44.64 Gastropexy*
*44.65 Esophagogastroplasty*
*44.69 Other*

Small intestine
*45.31 Other local excision of lesion of duodenum*
*45.32 Other destruction of lesion of duodenum*
*45.33 Local excision of lesion or tissue of small intestine, except duodenum*
*45.34 Other destruction of lesion of small intestine, except duodenum*

*45.50 Isolation of intestinal segment, not otherwise specified*
*45.51 Isolation of segment of small intestine*
*45.6 Other excision of small intestine*
*45.9 Intestinal anastomosis*
*45.91 Small-to-small intestinal anastomosis*
*45.92 Anastomosis of small intestine to rectal stump*
*45.93 Other small-to-large intestinal anastomosis*
*46.01 Exteriorization of small intestine*
*46.02 Resection of exteriorized segment of small intestine*
*46.60 Fixation of intestine, not otherwise specified*
*46.61 Fixation of small intestine to abdominal wall*
*46.62 Other fixation of small intestine*
*46.71 Suture of laceration of duodenum*
*46.72 Closure of fistula of duodenum*
*46.73 Suture of laceration of small intestine, except duodenum*
*46.74 Closure of fistula of small intestine, except duodenum*
*46.80 Intra-abdominal manipulation of intestine, not otherwise specified*
*46.81 Intra-abdominal manipulation of small intestine*
*46.93 Revision of anastomosis of small intestine*
*46.97 Transplant of intestine*

Liver
*50.2 Local excision or destruction of liver tissue or lesion*
*50.3 Lobectomy of liver*
*50.4 Total hepatectomy*
*50.5 Liver transplant*
*50.6 Repair of liver*

Pancreas
*52.22 Other excision or destruction of lesion or tissue of pancreas or pancreatic duct*
*52.3 Marsupialization of pancreatic cyst*
*52.4 Internal drainage of pancreatic cyst*
*52.5 Partial pancreatectomy*
*52.6 Total pancreatectomy*
*52.7 Radical pancreaticoduodenectomy*
*52.8 Transplant of pancreas*
*52.95 Other repair of pancreas*
*52.96 Anastomosis of pancreas*

Abdominal Hernia
*53.4 Repair of umbilical hernia*
*53.5 Repair of other hernia of anterior abdominal wall (without graft or prosthesis)*
*53.6 Repair of other hernia of anterior abdominal wall with graft or prosthesis*
*53.7 Repair of diaphragmatic hernia, abdominal approach*

Peritoneum
*54.4 Excision or destruction of peritoneal tissue*
*54.5 Lysis of peritoneal adhesions*
*54.6 Suture of abdominal wall and peritoneum*
*54.7 Other repair of abdominal wall and peritoneum*

Large intestine
*45.41 Excision of lesion or tissue of large intestine*
*45.49 Other destruction of lesion of large intestine*
*45.7 Open and other partial excision of large intestine*
*45.8 Total intra-abdominal colectomy*
*45.94 Large-to-large intestinal anastomosis*
*46.03 Exteriorization of large intestine*
*46.04 Resection of exteriorized segment of large intestine*
*46.63 Fixation of large intestine to abdominal wall*
*46.64 Other fixation of large intestine*
*46.75 Suture of laceration of large intestine*
*46.76 Closure of fistula of large intestine*
*46.79 Other repair of intestine*

Other surgery
*55.4 Partial nephrectomy*
*55.5 Complete nephrectomy*
*56.2 Ureterotomy*
*56.4 Ureterectomy*
*57.1 Cystotomy and cystostomy*
*57.6 Partial cystectomy*
*57.7 Total cystectomy*
*65.3 Unilateral oophorectomy*
*65.4 Unilateral salpingo-oophorectomy*
*65.5 Bilateral oophorectomy*
*65.6 Bilateral salpingo-oophorectomy*
*66.4 Total unilateral salpingectomy*
*66.5 Total bilateral salpingectomy*
*68.3 Subtotal abdominal hysterectomy*
*68.4 Total abdominal hysterectomy*
*68.6 Radical abdominal hysterectomy*
*68.8 Pelvic evisceration*

**PART 4 - Codes to describe coexisting conditions**
On the basis of previous 2-year hospitalizations (following a validated coding algorithm – enhanced Elixhauser AHRQ-Web-ICD-9-CM - see reference n. 17 cited in the text).

diabetes 250.xx; hypertension 401-405; obesity 280.0, ischemic disease 410-414, 429.7, previous revascularization V45.81, V45.82, procedures 36.0, 36.1, heart failure 428, other cardiac disease 093.2, 391, 393-398, 420-425, 429, 745, 746.3-646.6, V15.1, V42.2, V43.2, V43.3, V45.0 arrhythmia / conduction disorders 426-427, cerebrovascular disease 430-438, vascular disease 440-448, 557, hematologic disorders 280-285, 286, 287.1, 287.3-287.5, 288, 289, chronic respiratory disesase 490-496, 518.81, 518.82, chronic liver disease / pancreas 571, 572, 577.1, 577.9, chronic renal disease 582-583, 585-588, V42.0, V45.1m V56, cancer 140-208.9

**PART 5 - Codes to describe outcomes**

***A) Surgical-related complications (within 30 day after the surgery)***

<u>in the index or in the subsequent hospitalizations</u> (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*998.1 Hemorrhage or hematoma or seroma complicating a procedure*
*998.2 Accidental puncture or laceration during a procedure*
*998.3 Disruption of wound*
*998.4 Foreign body accidentally left during a procedure*
*998.5 Postoperative infection*
*998.6 Persistent postoperative fistula*
*998.7 Acute reaction to foreign substance accidentally left during a procedure*
*998.81 Emphysema (subcutaneous) (surgical) resulting from a procedure*
*998.83 Non-healing surgical wound*
*998.89 Other specified complications*
*997.4 Digestive system complications*
*998.9 Unspecified complication of procedure, not elsewhere classified*

<u>Only in the subsequent hospitalizations</u>

at least one of the following:
*567 Peritonitis and retroperitoneal infections*
*575.4 Perforation of gallbladder*
*575.5 Fistula of gallbladder*
*576.0 Postcholecystectomy syndrome*
*576.3 Perforation of bile duct*
*576.4 Fistula of bile duct*
*570 Acute and subacute necrosis of liver*
*789.0 Abdominal pain*

***B) Sistemic complications (within 30 day after the surgery)***

<u>in the index or in the subsequent hospitalizations</u> (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*997.0 Nervous system complications*
*997.1 Cardiac complications*
*997.3 Respiratory complications*
*998.0 Postoperative shock*
*410 Acute myocardial infarction*
*415.1 Pulmonary embolism and infarction*
*431 Intracerebral hemorrhage*
*433.x1 Occlusion and stenosis of precerebral arteries with infarction*
*434.x1 Occlusion of cerebral arteries with infarction*
*436 Acute, but ill-defined, cerebrovascular disease*
*480-486 Pneumonia*
*513.0 Abscess of lung*
*518.4 Acute edema of lung, unspecified*
*518.5 Pulmonary insufficiency following trauma and surgery*
*785.5 Shock without mention of trauma*

*788.2 Retention of urine*

Only in the subsequent hospitalizations
*038 Septicemia*

# Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.



| | |
|---|---|
| Journal: | *BMJ Open* |
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**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**

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# Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.


## Abstract

### Objective

The objective of the study is to evaluate short-term complications after laparoscopic (LC) or open cholecystectomy (OC) in patients with gallstones by using linked hospital discharge data.

### Design

Population-based cohort study.

### Setting

Data were obtained from the Regional Hospital Discharge Registry Lazio Region in Central Italy (around 5 million inhabitants) in 2007-2008.

### Participants

All patients admitted to hospitals of Lazio with symptomatic gallstones (ICD9-CM = 574) who underwent LC (ICD9-CM 51.23) or OC (ICD9-CM 51.22).

### Outcome measures

1)"*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events).

### Results

13,651 patients were included; 86.1% had LC, 13.9% OC. 2.0% experienced surgical-related complications (SRC), 2.1% systemic complications (SC). The Odds Ratio (OR) of complications after LC versus OC was 0.60 ($p<0.001$) for SRC and 0.52 ($p<0.001$) for SC. As regards SRC, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission (OR=0.94, p = 0.764). For SC, no significant advantage of LC was seen among very old people (OR=0.99, p=0.975) and among those with previous upper abdominal surgery (OR=0.86, p=0.905).

**Conclusions**

This large observational study confirms that LC is more effective than OC with respect to 30-day complications. Population-based linkage of administrative datasets can enlarge evidence of treatment benefits in clinical practice.

**Key words:** administrative data, cohort study, effectiveness, gallstones, hospital discharge data, laparoscopic cholecystectomy, open cholecystectomy, outcomes, population-based, post-operative complications.

## Article summary

### Article focus

-The advantage of laparoscopic cholecystectomy (LC) approach for the treatment of gallstone versus open surgery (OC) has been shown from RCTs and observational studies.

-The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments.

-We compared laparoscopic and open cholecystectomy in term of 30-day complications using routinely collected databases in Lazio Region (Italy).

### Key messages

-This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting.

-As regards surgical-related complications, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission.

-For systemic complications, no significant advantage of LC was seen among very old people and among those with previous upper abdominal surgery.

### Strengths and limitations

-Population-based design, 30-day outcomes, large numbers and robustness of analytic procedures are the main strengths.

-It contributes to the debate on the complex methodology to estimated risk of adverse events after surgery using secondary databases to monitor quality of care.

-The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is a major limit.

**Introduction**

Comparative effectiveness research is becoming central to monitor real-life impact of treatments and support public health decisions (1, 2). Although the basic concept of comparing therapies is not new, over the last few years many initiatives have been implemented in several countries to provide large-scale evidence on benefits and harms of different treatments (3-5). The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments. They include hospital in-patients records, birth and death registrations, outpatient care records, dispensed pharmacy drugs (6-9).

In the Lazio Region (around 5.000.000 inhabitants) the P.Re.Val.E. Project (*Regional Program for Assessing the Outcomes of Health-care Interventions*) was launched in 2005. Its aims are: to measure the quality of health care provided in the Lazio Region, to describe variability of care provision across institutions and populations and to compare effectiveness of treatments for different medical and surgical conditions (10,11). Over 60 outcomes indicators are calculated based on data obtained from record-linkage procedures of different health systems. The results are periodically updated and publicly disseminated with discussion on critical methodological points.

Cholecystectomy is one of the most common abdominal surgical procedures in developed countries. Since its introduction in the late '80s, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) as the treatment of choice for symptomatic gallstones (12, 13). Beneficial effects of LC have been demonstrated in studies showing the advantages from real-life settings using secondary databases (9,14-19). In the present study we aimed at developing a methodology to measure short-term complications after LC or OC using large administrative databases on behalf of the P.Re.Val.E. Secondly, we tested the hypothesis that

the advantages of LC versus OC could vary according to age and clinical patients' characteristics.

## Methods

Source of data

Data was derived from the Lazio Hospital Information System (HIS), which provides information on patients' demographic data (gender, age, place of birth, place of residence), admission and discharge dates, discharge diagnoses (up to 6) and medical procedures or surgical interventions ((up to 6) according to the International Classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM), status at discharge (alive, dead, transferred to another hospital), ward(s) of stay, date(s) of in-hospital transfer, and a regional code corresponding to the admitting facility for patients discharged from all public and private hospital of the Lazio Region (5.759.839 inhabitants).

Study population

All hospital admissions with a primary or secondary diagnosis of gallstones (International Classification of Diseases 9$^{th}$ Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases (age 18+ years). We a priori decided not to include codes for partial cholecystectomy (ICD-9-CM 51.21 and 51.24) to increase the specificity of our exposure. Information was retrieved from the HIS. In order to increase the case specificity, several exclusion criteria were applied including long-term hospitalizations, rehabilitations, day-hospitals, hospitalizations for delivery or trauma or cancer, hospitalizations with abdominal surgical procedures other than cholecystectomy. The final population consisted of 13,651 subjects (**Figure 1).** See the online **Supplementary Data** (Part 1) for details on the exclusion criteria and ICD9-CM codes.

Patient-level risk factors

The following characteristics were considered for each patient: Age (<70; 70-79; >=80 years old); Gender; Severity of gallstones: it was classified as *low* (not-complicated), *moderate* (presence of cholecystitis or biliary tract obstruction), and *high* (presence of both inflammation and obstruction of the biliary tract); Previous upper abdominal surgery (based on previous 2-year hospitalizations); Comorbidities (based on previous 2-year hospitalizations) following validated algorithms (20,21); Type of admission: either *elective* or *emergency*. See the online **Supplementary Data** (Part 2-4) for details on the ICD-9-CM codes. The choice of *cut off* for age category was based on previous studies to distinguish adult and old people (22-24).

Outcomes

We identified various complications within 30-days after the intervention and grouped them in two categories: 1) "*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound (); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events). The complete list of complications with ICD-9-CM codes is reported in the online **Supplementary Data** (Part 5). Among the various complications we included some conditions reported in the list of Patient Safety Indicators recently developed by the Agency for Health Care Research and Quality, while other items were specifically created on the basis of scientific literature on digestive surgery (14-19,25,26). Depending on the type of complication, some ICD9-CM codes were searched in both the index admission and the following ones in the 30-day period after the surgery, others were searched only in later hospitalizations. For example, peritonitis or acute pancreatitis was not counted as complications when reported in the index admission. See the online **Supplementary Data** (Part 5) for details on the ICD9-CM codes. In the case of a subsequent hospitalization occurred out of the study area (for example, in a region other than Lazio), we obtained information through record linkage procedure between hospital information systems. Because of the short follow up time, this happened in a minimal proportion of cases (0.1%). The outcome variables were: "*30-day surgical-related complications*" and "*30-day systemic complications*"; they were coded "1" if at least one of the complications within the group was present and "0" if none was recorded.



Type of cholecystectomy

As exposure variable we defined "*type of cholecystectomy*" (laparoscopic cholecystectomy, LC vs. open cholecystectomy, OC). In the case of ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure. We could not use the specific ICD-9-code for a case converted from LC to OC (ICD-9-CM code V 64.41) because it was highly under-reported in our Region in the study period.

Statistical analysis

Multiple logistic regression models were fitted to estimate the relative risk of 30-day complications (either "surgical-related" or "systemic") after LC versus OC, adjusting for demographical and clinical risk factors. The two outcome variables were analysed separately.

The predictive model was made of two sets of predictors: 1) variables "a priori" chosen as confounders (age, gender, severity of gallstones, previous upper abdominal surgery, and type of admission); 2) variables empirically tested (comorbidities) which were selected using iterative stepwise statistical procedures) (27). Once the "best" predictive model was identified for each of the two outcome, the variable "*type of cholecystectomy*" was included, and the adjusted odds ratio (OR) of LC versus open surgery was estimated, with corresponding 95% confidence interval (95% CI) and p-value.

In order to test the hypothesis of an effect modification by age, relative risk estimates for the age groups were derived by adding an interaction term between the age group and the treatment variable in the final multivariate logistic model. We obtained the OR of laparoscopic vs. open surgery within each age stratum by adding the corresponding interaction terms coefficients. This was accomplished by adding the coefficient from the reference category and that from the age stratum of interest, and by computing the corresponding standard error from the corresponding terms of the variance-covariance matrix. Similarly, effect modification was tested with regard to severity of cholelithiasis, previous upper abdominal surgery and type of admission. The corresponding tests of heterogeneity of the stratum-specific risk estimates were computed.

Sensitivity analyses were performed. First, in order to guarantee adequate control of confounding factors we identified and adjusted for all the individual factors associated with the treatment, within the propensity adjustment framework (28). This procedure is a two-step technique: 1. it estimates the a priori probability of exposure for each subject, based on clinical and demographic characteristics; 2. it standardizes for them in the association between treatment and the study outcome. The individual factors related to the exposure in the present study include age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, cardio-circulatory disease, cerebrovascular disease, COPD or respiratory failure, chronic nephropathy, chronic disease of the liver or pancreas. Second, to take into account the potential heterogeneous experience in laparoscopic surgery across different hospitals because of the patients' clustering within a single institution we perform a multilevel regression model with random intercepts for hospitals (29).

All the statistical analyses were performed using SAS Software version 8.0 (SAS Institute, Inc. SAS/STAT software).

**Results**

A description of the study population, overall and by cholecystectomy procedure, is presented in **Table 1**. Over 80% of the patients were younger than 70 years, and moderate to high severity of the gallstones was diagnosed for 61.7%. As compared with patients undergoing LC, those who underwent OC were more likely to be elderly, males, with a more sever baseline disease and more chronic conditions. Furthermore, they were operated in emergency in most of the cases (52.4%), whereas LC was performed in elective hospitalizations much more frequently (73.9%).

**Table 2** reports the relationship between demographic and clinical variables and the occurrence of complications. The adjusted risk of systemic complications increased with age and was much higher in patients with more severe baseline gallstones, whereas no clear age or severity-related differences in risk emerged with regard to surgical-related 30-day complications, once other co-factors were taken into account. Women were less likely to experience both types of complications. Having had a previous intervention on the upper digestive system seemed to enhance the risk of both surgical-related and systemic complications, though results are not statistically significant due to small power. Finally, the risk of both types of complications was more evident in emergency as opposed to scheduled interventions. Surgical-related complications were higher among subjects with obesity, blood disease, stroke or chronic nephropathy, whereas systemic complications were associated with blood diseases, ischemic heart disease, conduction disorders or dysrhythmias, COPD or respiratory failure, chronic nephropathy, and chronic diseases of the liver or pancreas.

**Table 3** shows the relationship between type of cholecystectomy and outcomes, adjusted for the risk factors identified in Table 2. We report results of the advantage of LC vs. OC (OR, 95% CI) in the cohort and in the each stratum of the variables tested in the models with interaction terms. The incidence of "30-day surgical-related complications" and "30-day systemic complications" was 2.0% and 2.1%, respectively. The odds ratio of surgical related complications for patients who underwent LC as compared to patients with OC was 0.60 (p<0.001). The corresponding figure for systemic complications was 0.52 (p<0.001).

As regards 30-day surgical-related complications, the protective effect of LC vs. OC was consistent across the age category, severity of cholelithiasis and previous upper abdominal surgery, while among people with emergency admission there was no advantage (OR=0.94 p = 0.764). Similarly, for systemic complications, the superiority of LC vs. OC was consistent regardless level of cholelithiasis severity, and elective/emergency admission, but for those 80+ yrs aged people there was no advantage of LC vs. OC (OR 0.99, p = 0.975); also for patients with previous upper abdominal surgery there was a much weaker advantage (OR=0.86, p=0.905).

When the association between type of cholecystectomy and 30-day complications was adjusted with the propensity adjustment method, results were consistent with those obtained with the risk-adjustment procedure (LC vs. OC OR= 0.61 and OR=0.52 respectively for the two outcomes). Finally, results were similar taking into account patients' clustering within different hospitals (*data not shown*).



**Discussion**

From this large observational study based on linked administrative health records - taking into account the disomogeneous distribution of factors related to the probability to be offered open surgery - people who end up having a LC have a better short-term prognosis than those that get an OC for the treatment of gallstones. The superiority of laparoscopic approach in term of 30-day complications is consistent in different age categories, different severity in disease presentation and past history of upper abdominal surgery.

This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting by providing an example from the Southern Europe area. It supports the usefulness of observational approaches. The 30-day outcomes linked to admission represent one strength of this study. Despite RTCs are considered the optimal study design when comparing efficacy of treatments, observational studies provide a picture of treatment under usual circumstances of health-care practice and can answer to the question ''*Does it work in practice*?" (3,8). RTCs often have small sample size and may under represent vulnerable patient groups, including elderly patients with multiple comorbidities, children, and young women, and operate in a highly controlled environment that is far from routine clinical practice. Our study supports that LC is a reliable approach safer than OC not only in old age group - confirming previous findings (22, 30) - but also in presence of severe disease presentation and in patients with past history of upper digestive system surgery. Beneficial effect of LC as regards systemic complications tends to be lower in 80+ yrs aged in comparison with younger ages, and in patients with emergency admission in comparison to elective admissions as regards 30-day surgical-related complications. These data add to the evidence on the complex relationship between age and outcomes after surgery (22-24,30).

A number of potential biases are present. First of all, people in the two groups of patients analyzed are not homogenous with a higher frequency of elderly and more severe patients in the open group that in the laparoscopic one. When comparing the effect of the two techniques using two different populations, the so called "indication bias" may affect study validity (8,31). To limit this problem we run the propensity adjustment analysis to take into account the different distribution of factors strongly associated with the probability to receive open surgery in the study population. This analytical approach confirmed the advantage of laparoscopic vs. open surgery obtained in the main logistic regression analysis. Another critical point is the potential different distribution of laparoscopic experience across surgeons; however a sensitivity analysis which took into account this point led to similar results. The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is another major limit. Discharge abstract data have little insight into clinical details and do not inform on the temporal relationship of the clinical conditions and processes, then defining complications is a difficult task (32). In this respect, we tried to improve the accuracy of our measures both 1) applying a specific coding algorithm with subsequent hospital admissions used to retrieve adverse events and 2) excluding in the "count" of complications specific items if reported in the index only (i.e. peritonitis) because of the difficulty to determine if it was already present at admission. Moreover, we cannot exclude an under-notification of complications – a major limit of our source of data - but it is unlikely that is influenced by the type of surgery. Another major problem is the potential misclassification of exposure since we were not able to measure the occurrence of conversion of LC to OC. The number of people that were switched from LC to OP is low in comparison to figures documented in other studies and it may represent a severe source of bias in our study (30,33).

Beneficial effects of the laparoscopic approach versus traditional open surgery for the treatment of gallstones come from various randomized controlled trials (RCTs) (34). They found significant shorter hospital stay and quicker convalescence associated with LC but no differences in mortality, complications and operative time between the two procedures. A better trend with the laparoscopic approach, including morbidity and mortality, comes from observational studies. From a surveillance system in eight Swiss hospitals, surgical site infections were less common in laparoscopic approach in comparison to traditional open surgery (0.5% in LC vs. 1.8% in OC) (35). Significantly lower incidence of venous thromboembolism and surgical site-infections in laparoscopic cases versus open cases was observed in a large administrative dataset–based study in USA (14, 15). National estimates for LC in USA showed an increase in LC from 52% in 1991 to 75% in 2000 with a constantly low mortality rate and a decrease in biliary reconstruction rate over time (16). On the basis of the 1997-2006 trend analysis by the same authors LC was associated with a low mortality rate (mean value in the period: 0.52%) while OC with a significantly higher rate (corresponding value: 4.9%) (9). In a retrospective study using Medicare beneficiaries common bile duct (CBD) injury during cholecystectomy was associated with a significant higher risk of death in comparison to cholecystectomy without CBD injury over a 9.2 year follow up period (17). From a Swiss 1995-2005 hospital database analysis the incidence rate of bile duct injury after LC was 0.3% and did not change over time (18). The incidence of conversion to OC after LC in all hospitals in England from 2005 to 2006 has been examined using Hospital Episode Statistics and resulted 4.6% for elective procedures and 9.4% for emergency procedures) (19).

Population-based linkage of routinely collected health data represents a precious tool to support large- scale and real-world practice evaluation by measuring specific outcomes and comparing them over time and across populations. Together with results from experimental research settings, the conclusions of research studies evaluating clinical outcomes through data linkage systems should be successfully incorporated into practice by clinicians/surgeons.

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**AUTHOR'S CONTRIBUTION**

All Authors participated in the study design, in defining the study protocol and methodology, in acquisition of data, in planning the analyses, in interpreting the results. M.S. performed the analyses. N.A and M.S. drafted the manuscript.

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**Figure 1.** Selection of the study population

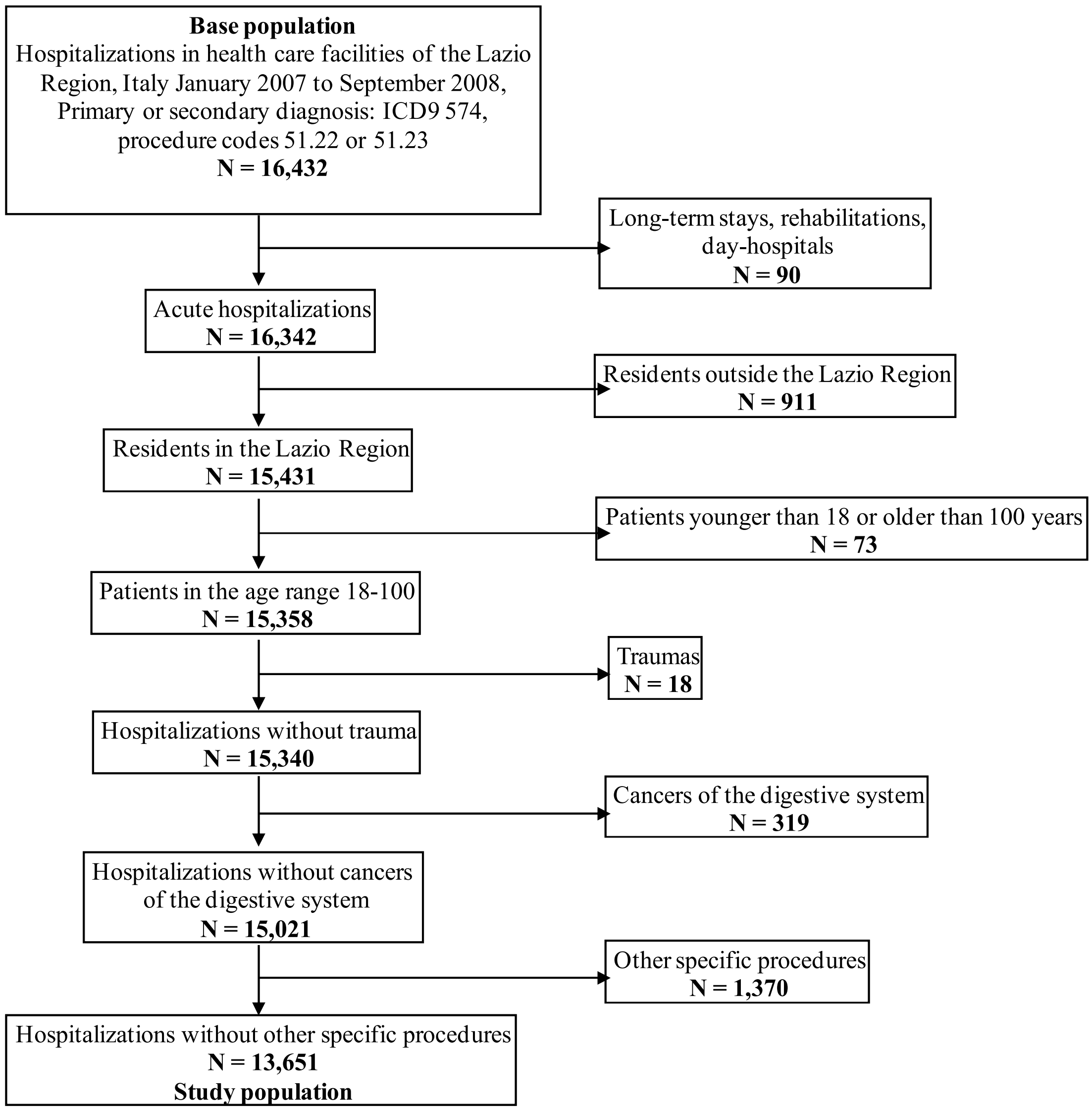

**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September 2008

| Patient characteristics | Laparoscopic cholecystectomy | | Open cholecystectomy | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| **Age (years)** | | | | | | |
| *<70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70-79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| | 11.752 | | | | | |
| **Gender** | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| **Severity of cholelitiasis** | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.456 | 54,9 | 1.200 | 63,2 | 7.656 | 56,1 |
| *High* | 529 | 4,5 | 229 | 12,1 | 758 | 5,6 |
| **Previous upper abdominal surgery** | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| **Tyoe od admission** | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| **Comorbidities** | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorders or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD* or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

*Chronic Obstructive Pulmonary Disease

**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | | | | | 30-day systemic complications (N=280, 2.1%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p |
| Age (years) | | | | | | | | | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *70 - 79* | 2,9 | 1,62 | 1,21 | 2,18 | 0,001 | 1,36 | 1,00 | 1,83 | 0,048 | 3,9 | 2,68 | 2,04 | 3,52 | 0,000 | 2,01 | 1,51 | 2,67 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 1,13 | 3,00 | 0,015 | 1,21 | 0,72 | 2,03 | 0,475 | 7,1 | 5,13 | 3,58 | 7,36 | 0,000 | 2,79 | 1,87 | 4,14 | 0,000 |
| Gender | | | | | | | | | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | - | - | 1,00 | - | - | - | 2,6 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Women* | 1,7 | 0,69 | 0,55 | 0,88 | 0,002 | 0,75 | 0,59 | 0,96 | 0,022 | 1,7 | 0,66 | 0,52 | 0,84 | 0,001 | 0,80 | 0,62 | 1,02 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | - | - | 1,00 | - | - | - | 1,2 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Moderate* | 2,0 | 1,08 | 0,84 | 1,40 | 0,538 | 0,96 | 0,74 | 1,24 | 0,733 | 2,2 | 1,84 | 1,38 | 2,46 | 0,000 | 1,55 | 1,15 | 2,08 | 0,004 |
| *High* | 3,7 | 2,03 | 1,32 | 3,14 | 0,001 | 1,43 | 0,91 | 2,24 | 0,122 | 6,2 | 5,30 | 3,59 | 7,83 | 0,000 | 3,40 | 2,26 | 5,11 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Yes* | 5,7 | 2,94 | 1,07 | 8,13 | 0,037 | 2,29 | 0,81 | 6,51 | 0,119 | 4,3 | 2,15 | 0,67 | 6,88 | 0,197 | 1,72 | 0,52 | 5,74 | 0,376 |
| Type of admission | | | | | | | | | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Emergency* | 3,0 | 1,85 | 1,45 | 2,35 | 0,000 | 1,66 | 1,29 | 2,13 | 0,000 | 3,4 | 2,34 | 1,85 | 2,97 | 0,000 | 1,64 | 1,27 | 2,11 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,64 | 2,64 | 0,476 | - | - | - | - | 3,6 | 1,81 | 0,98 | 3,34 | 0,059 | - | - | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,92 | 2,97 | 0,095 | - | - | - | - | 4,4 | 2,24 | 1,34 | 3,75 | 0,002 | - | - | - | - |
| *Obesity* | 5,0 | 2,57 | 1,19 | 5,55 | 0,016 | 2,35 | 1,29 | 2,13 | 0,034 | 4,3 | 2,16 | 0,95 | 4,94 | 0,067 | - | - | - | - |
| *Blood disease* | 5,8 | 3,03 | 1,67 | 5,50 | 0,000 | 2,09 | 1,11 | 3,93 | 0,022 | 7,7 | 4,16 | 2,46 | 7,03 | 0,000 | 1,96 | 1,09 | 3,51 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 1,00 | 2,13 | 0,050 | - | - | - | - | 4,0 | 2,20 | 1,58 | 3,05 | 0,000 | - | - | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,75 | 2,69 | 0,286 | - | - | - | - | 7,4 | 4,08 | 2,69 | 6,20 | 0,000 | 1,74 | 1,09 | 2,78 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,28 | 4,74 | 0,836 | - | - | - | - | 9,4 | 5,08 | 2,43 | 10,62 | 0,000 | - | - | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,27 | 4,57 | 0,875 | - | - | - | - | 4,6 | 2,29 | 0,83 | 6,29 | 0,107 | - | - | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,84 | 3,52 | 0,136 | - | - | - | - | 6,8 | 3,66 | 2,17 | 6,16 | 0,000 | - | - | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 1,21 | 3,62 | 0,008 | - | - | - | - | 7,0 | 3,81 | 2,47 | 5,88 | 0,000 | 1,73 | 1,07 | 2,79 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 1,76 | 5,54 | 0,000 | 1,98 | 1,09 | 3,60 | 0,025 | 7,7 | 4,19 | 2,52 | 6,98 | 0,000 | - | - | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,05 | 2,68 | 0,328 | - | - | - | - | 8,5 | 4,59 | 2,45 | 8,62 | 0,000 | - | - | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,60 | 2,72 | 0,534 | - | - | - | - | 7,7 | 4,22 | 2,66 | 6,70 | 0,000 | 2,02 | 1,23 | 3,31 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 2,82 | 10,00 | 0,000 | 3,24 | 1,65 | 6,36 | 0,001 | 10,5 | 5,82 | 3,16 | 10,72 | 0,000 | 2,27 | 1,15 | 4,46 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,92 | 3,33 | 0,087 | - | - | - | - | 4,8 | 2,51 | 1,45 | 4,35 | 0,001 | 1,97 | 1,11 | 3,48 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission; p value of heterogeneity of the strata-specific estimates - Lazio Region, Italy, January 2007 - September 2008

| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | $p_{het}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 30-day surgical-related complications: N=278, %=2.0 | | | | | | | | | | |
| Open cholecystectomy | 3,9 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,33 | 0,57 | 0,000 | 0,60 | 0,44 | 0,80 | 0,001 | - |
| Age (years) | | | | | | | | | | 0,917 |
| *< 70* | 1,8 | 0,49 | 0,35 | 0,71 | 0,000 | 0,62 | 0,43 | 0,90 | 0,012 | - |
| *70 - 79* | 2,9 | 0,45 | 0,26 | 0,76 | 0,003 | 0,57 | 0,33 | 0,98 | 0,043 | - |
| *≥ 80* | 3,3 | 0,41 | 0,15 | 1,12 | 0,082 | 0,51 | 0,18 | 1,38 | 0,184 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,053 |
| *Low* | 1,9 | 0,37 | 0,22 | 0,61 | 0,000 | 0,46 | 0,28 | 0,77 | 0,003 | - |
| *Moderate* | 2,0 | 0,58 | 0,40 | 0,85 | 0,005 | 0,78 | 0,53 | 1,16 | 0,224 | - |
| *High* | 3,7 | 0,24 | 0,11 | 0,53 | 0,000 | 0,30 | 0,13 | 0,68 | 0,004 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,654 |
| *No* | 2,0 | 0,45 | 0,34 | 0,59 | 0,000 | 0,60 | 0,44 | 0,81 | 0,001 | - |
| *Yes* | 5,7 | 0,26 | 0,03 | 2,64 | 0,256 | 0,36 | 0,03 | 3,69 | 0,388 | - |
| Type of admission | | | | | | | | | | 0,001 |
| *Elective* | 1,6 | 0,32 | 0,22 | 0,46 | 0,000 | 0,37 | 0,25 | 0,55 | 0,000 | - |
| *Emergency* | 3,0 | 0,76 | 0,51 | 1,13 | 0,178 | 0,94 | 0,62 | 1,42 | 0,764 | - |
| 30-day systemic complications: N=280, %=2.1 | | | | | | | | | | |
| Open cholecystectomy | 5,2 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,6 | 0,29 | 0,23 | 0,37 | 0,000 | 0,52 | 0,40 | 0,69 | 0,000 | - |
| Age (years) | | | | | | | | | | 0,136 |
| *< 70* | 1,5 | 0,34 | 0,24 | 0,49 | 0,000 | 0,47 | 0,32 | 0,68 | 0,000 | - |
| *70 - 79* | 3,9 | 0,35 | 0,22 | 0,55 | 0,000 | 0,47 | 0,29 | 0,75 | 0,002 | - |
| *≥ 80* | 7,1 | 0,71 | 0,37 | 1,37 | 0,309 | 0,99 | 0,50 | 1,94 | 0,975 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,755 |
| *Low* | 1,2 | 0,29 | 0,16 | 0,51 | 0,000 | 0,43 | 0,24 | 0,77 | 0,005 | - |
| *Moderate* | 2,2 | 0,34 | 0,25 | 0,47 | 0,000 | 0,55 | 0,39 | 0,77 | 0,001 | - |
| *High* | 6,2 | 0,38 | 0,21 | 0,70 | 0,002 | 0,56 | 0,30 | 1,05 | 0,071 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,702 |
| *No* | 2,0 | 0,29 | 0,22 | 0,37 | 0,000 | 0,52 | 0,39 | 0,69 | 0,000 | - |
| *Yes* | 4,3 | 0,41 | 0,04 | 4,69 | 0,470 | 0,86 | 0,07 | 10,40 | 0,905 | - |
| Type of admission | | | | | | | | | | 0,545 |
| *Elective* | 1,5 | 0,33 | 0,23 | 0,50 | 0,000 | 0,48 | 0,32 | 0,72 | 0,000 | - |
| *Emergency* | 3,4 | 0,35 | 0,25 | 0,49 | 0,000 | 0,56 | 0,39 | 0,81 | 0,002 | - |

[c] There are no 30-day complications in patients with moderately high severity and undergoing laparotomic cholecystectomy

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4/12/12

~~The use of hospital discharge data to compare outcomes of different surgical techniques: the example of cholecystectomy.~~

**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**

**Authors**

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Field Code Changed

**Short running head**: Effectiveness of cholecystectomy

**Word count for abstract**: ~~293~~264

**Word count for manuscript**: ~~2888~~ 2886

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Field Code Changed

~~**The use of hospital discharge data to compare outcomes of different surgical techniques: the example of cholecystectomy.**~~

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**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**

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**Abstract**

**Objective**

The objective of the study is to evaluate short-term complications after laparoscopic (LC) or open cholecystectomy (OC) in patients with gallstones by using linked hospital discharge data. There is an increasing interest in using routinely collected health data to support large-scale effectiveness evaluation of different treatment options. We evaluated short-term outcomes after laparoscopic cholecystectomy (LC) or open cholecystectomy (OC) in gallstones using hospital discharge data.

**Design**

Population-based cohort study.

**Setting**

Data were obtained from the Regional Hospital Discharge Registry Lazio Region in Central Italy (around 5 million inhabitants) in 2007-2008.

**Participants**

All patients admitted to hospitals of Lazio with symptomatic gallstones (ICD9-CM = 574) who underwent LC (ICD9-CM 51.23) or OC (ICD9-CM 51.22).

**Outcome measures**

1)"*30-day surgical-related complications*" defined as any complication of the biliary tract (including bile duct injury, bile leak, postoperative bleeding, wound infection, cholecystis injury post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound)); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events).

**Results**

13,651 patients were included; 86.1% had LC, 13.9% OC. 2.0% experienced surgical-related complications (SRC), 2.1% systemic complications (SC). The Odds Ratio (OR) of complications after LC versus OC was 0.60 (p<0.001) for SRC and 0.52 (p<0.001) for SC. As regards SRC, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission (OR=0.94, p = 0.764). For SC, no significant advantage of LC was seen among very old people (OR=0.99, p=0.975) and among those with previous upper abdominal surgery (OR=0.86, p=0.905).

**Conclusions**

This large observational study confirms that LC is more effective than OC with respect to 30-day short-term complications. The advantage remains in sub-populations with higher preoperative risk, but it is different according to whether the complications affect the biliary tract or other organs or systems. Population-based linkage of administrative datasets can enlarge evidence of treatment benefits in clinical practice.

**Key words:** administrative data, cholecystectomy, complications, effectiveness, outcomes administrative data, cohort study, effectiveness, gallstones, hospital discharge data, laparoscopic cholecystectomy, open cholecystectomy, outcomes, population-based, post-operative complications.

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**Article summary**

**Article focus**

-The advantage of laparoscopic cholecystectomy (LC) approach for the treatment of gallstone versus open surgery (OC) has been– shown from RCTs and observational studies. but the evidence from observational studies is limited.

-The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments.

-We compared laparoscopic and open cholecystectomy in term of 30-day complications short-term outcomes using routinely collected databases in Lazio Region (Italy).

**Key messages**

-This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting.

-As regards surgical-related complications, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission.

-For systemic complications, no significant advantage of LC was seen among very old people and among those with previous upper abdominal surgery.

**Strengthshts and limitations**

-Population-based design, 30-day outcomes, large numbers and robustness of analytic procedures are the main strengths.

-It contributes to the debate on the complex methodology to estimated risk of adverse events after surgery using secondary databases to monitor quality of care.

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-The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is a major limit.

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**Introduction**

Comparative effectiveness research (CER) is becoming central to monitor real-life impact of treatments and support public health decisions (1, 2). Although the basic concept of comparing therapies is not new, over the last few years many initiatives have been implemented in severalmany countries to provide large-scale evidence on benefits and harms of different treatments (3-5). The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments (6,7). They include hospital in-patients records, birth and death registrations, outpatient care records, dispensed pharmacy drugs (6-9).. Despite the advantages due to the large numbers and the population level coverage, the analytic methods to reduce bias in CER studies are complex and new approaches are continuously developed (8,9).

In the Lazio Region (around 5.000.000 inhabitants) the P.Re.Val.E. Project (*Regional Program for Assessing the Outcomes of Health-care Interventions*) was launched in 2005. Its aims are: to measure the quality of health care provided in the Lazio Region, to describe variability of care provision across institutions and populations and to compare effectiveness of treatments for different medical and surgical conditions (10,–11). Over 60 outcomes indicators are calculated based on data obtained from record-linkage procedures of different health systems. The results are periodically updated and publicly disseminated with discussion on critical methodological points.

Cholecystectomy is one of the most common abdominal surgical procedures in developed countries. Since its introduction in the late '80s, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) as the treatment of choice for symptomatic gallstones (12, 13). Although Bbeneficial effects of LC have been widely demonstrated in , there are relatively few studies showing the advantages from real-life settings using secondary databases (9,14-1914-16). In the present study, we aimed at developing a methodology to measure short-term complications after LC or OC using large administrative databases on behalf of the P.Re.Val.E. Secondly, we tested the hypothesis that the advantages of LC versus OC could vary according to age demographic and clinical patients' characteristics.

**Methods**

Source of data

Data was derived from the Lazio Hospital Information System (HIS), which provides information on patients' demographic data (gender, age, place of birth, place of residence), admission and discharge dates, discharge diagnoses (up to 6) and medical procedures or surgical interventions ((up to 6) according to the International Classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM), status at discharge (alive, dead, transferred to another hospital), ward(s) of stay, date(s) of in-hospital transfer, and a regional code corresponding to the admitting facility for patients discharged from all public and private hospital of the Lazio Region (5.759.839 inhabitants).

Study population

All hospital admissions with a primary or secondary diagnosis of gallstones (International Classification of Diseases 9$^{th}$ Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases (age 18+ years). We a priori decided not to include codes for partial

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cholecystectomy (ICD-9-CM 51.21 and 51.24) to increase the specificity of our exposure. Information was retrieved from the HIS. In order to increase the case specificity, several exclusion criteria were applied including long-term hospitalizations, rehabilitations, day-hospitals, hospitalizations for delivery or trauma or cancer, hospitalizations with abdominal surgical procedures other than cholecystectomy. The final population consisted of 13,651 subjects (**Figure 1).** See the online **Supplementary Data** (Part 1) for details on the exclusion criteria and ICD9-CM codes.

Patient-level risk factors

The following characteristics were considered for each patient: Age (<70; 70-79; >=80 years old); Gender; Severity of gallstones: it was classified as *low* (not-complicated), *moderate* (presence of cholecystitis or, cholangitis or biliary tract obstruction), and *high* (presence of both inflammation and obstruction of the biliary tract); Previous upper abdominal surgery (based on previous 2-year hospitalizations); Comorbidities (based on previous 2-year hospitalizations) following validated algorithms (20,2117-19); Type of admission: either *elective* or *emergency*. See the online **Supplementary Data** (Part 2-4) for details on the ICD-9-CM codes. The choice of *cut off* for age category was based on previous studies to distinguish adult and old people (22-2410-22).

Outcomes

We identified various complications within 30-days after the intervention and grouped them in two categories: 1) "*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound (including bile duct injury, bile leak, postoperative bleeding, wound infection,

~~cholecystis injury~~); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events). The complete list of complications with ICD-9-CM codes is reported in the online **Supplementary Data** (Part 5). Among the various complications we included some conditions reported in the list of Patient Safety Indicators recently developed by the Agency for Health Care Research and Quality~~ (i.e. postoperative bleeding, wound infection)~~, while other items were specifically created on the basis of scientific literature on digestive surgery (14-19~~6~~,25-26~~3,24~~). Depending on the type of complication, some ICD9-CM codes were searched in both the index admission and the following ones in the 30-day period after the surgery, others were searched only in later hospitalizations. For example, peritonitis or acute pancreatitis was not counted as complications when reported in the index admission. See the online **Supplementary Data** (Part 5) for details on the ICD9-CM codes. In the case of a subsequent hospitalization occurred out of the study area (for example, in a region other than Lazio), we obtained information through record linkage procedure between hospital information systems. Because of the short follow up time, this happened in a minimal proportion of cases (0.1%). The outcome variables were: "*30-day surgical-related complications*" and "*30-day systemic complications*"; they were coded "1" if at least one of the complications within the group was present and "0" if none was recorded.

Type of cholecystectomy

As exposure ~~We defined the~~ variable we defined "*type of cholecystectomy*" (laparoscopic cholecystectomy, LC vs. open cholecystectomy, OC). In the case of ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure.~~Since Unfortunately, thea~~ We could not use the ~~-~~specific ICD-9-code for a case converted from LC to OC (ICD-9-CM code V 64.41) because it was ~~was~~ highly under-reported in our Region in the study period.: no case in our study cohort. not available, in the case of reported ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure.

Statistical analysis

Multiple logistic regression models were fitted to estimate the relative risk of 30-day complications (either "surgical-related" or "systemic") after LC versus OC, adjusting for demographical and clinical risk factors. The two outcome variables were analysed separately. The predictive model was made of two sets of predictors: Given the large amount of individual-level variables available, the risk factors were divided in two groups: 1) variables "a priori" chosen as confounders (age, gender, severity of gallstones, previous upper abdominal surgery, and type of admission); 2) variables empirically tested (comorbidities), which were selected using iterative stepwise statistical procedures) (9,2775). Once the "best" predictive model was identified for each of the two outcome variables, the treatment variable "*type of cholecystectomy*" was included, and the adjusted odds ratio (OR) of LC versus open surgery was estimated, with corresponding 95% confidence interval (95% CI) and p-value.

In order to test the hypothesis of an effect modification by age, relative risk estimates for the age groups were derived by adding an interaction term between the age group and the treatment variable in the final multivariate logistic model. We obtained the OR of laparoscopic vs. open surgery within each age stratum by adding the corresponding interaction terms coefficients. This was accomplished by adding the coefficient from the reference category and that from the age stratum of interest, and by computing the corresponding standard error from the corresponding terms of the variance-covariance matrix. Similarly, effect modification was tested with regard to severity of cholelithiasis, previous upper abdominal surgery and type of admission. The corresponding tests of heterogeneity of the stratum-specific risk estimates were computed. ~~but not reported for ease of presentation.~~

Sensitivity analyses were performed. First, in order to guarantee adequate control of confounding factors we identified and adjusted for all the individual factors associated with the treatment, within the propensity adjustment framework (28~~6~~). This procedure is a two-step technique: 1. it estimates the a priori probability of exposure for each subject, based on clinical and demographic characteristics; 2. it standardizes for them in the association between treatment and the study outcome. The individual factors related to the exposure in the present study include age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, cardio-circulatory disease, cerebrovascular disease, COPD or respiratory failure, chronic nephropathy, chronic disease of the liver or pancreas. Second, to take into account the potential heterogeneous experience in laparoscopic surgery across different hospitals because of the patients' clustering within a single institution we perform a multilevel regression model with random intercepts for hospitals (29~~7~~).

All the statistical analyses were performed using SAS Software version 8.0 (SAS Institute, Inc. SAS/STAT software).

**Results**

A description of the study population, overall and by cholecystectomy procedure, is presented in **Table 1**. Over 80% of the patients were younger than 70 years, and moderate to high severity of the gallstones was diagnosed for 61.7%. As compared with patients undergoing LC, those who underwent OC were more likely to be elderly, males, with a more sever baseline disease and more chronic conditions. Furthermore, they were operated in emergency in most of the cases (52.4%), whereas LC was performed in elective hospitalizations much more frequently (73.9%).

**Table 2** reports the relationship between demographic and clinical variables and the occurrence of complications. The adjusted risk of systemic complications increased with age and was much higher in patients with more severe baseline gallstones, whereas no clear age or severity-related differences in risk emerged with regard to surgical-related 30-day complications, once other co-factors were taken into account. Women were less likely to experience both types of complications. Having had a previous intervention on the upper digestive system seemed to enhance the risk of both surgical-related and systemic complications, though results are not statistically significant due to small power. Finally, the risk of both types of complications was more evident in emergency as opposed to scheduled interventions. Surgical-related complications were higher among subjects with obesity, blood disease, stroke or chronic nephropathy, whereas systemic complications were associated with blood diseases, ischemic heart disease, conduction disorders or dysrhythmias, COPD or respiratory failure, chronic nephropathy, and chronic diseases of the liver or pancreas.

**Table 3** shows the relationship between type of cholecystectomy and outcomes, adjusted for the risk factors identified in Table 2. We report r~~r~~esults of the advantage of LC vs. OC (OR, 95% CI) in the cohort ~~(first lines of the table)~~ and in the each stratum of the variables tested in the models with interaction terms. The incidence of “30-day surgical-related complications” and “30-day systemic complications” was 2.0% and 2.1%, respectively. ~~The incidence of “at least one 30-day complication” was 3%.~~ The odds ratio of surgical related complications for patients who underwent LC as compared to patients with OC was 0.60 (p<0.001). The corresponding figure for systemic complications was 0.52 (p<0.001).

As regards 30-day surgical-related complications, the protective effect of LC vs. OC was consistent across the age category, severity of cholelithiasis and previous upper abdominal surgery, while among people with emergency admission there was no advantage (OR=0.94 p = 0.764). Similarly, for systemic complications, the superiority of LC vs. OC was consistent regardless level of cholelithiasis severity, and elective/emergency admission, but for those 80+ yrs aged people there was no advantage of LC vs. OC (OR 0.99, p = 0.975); also for patients with previous upper abdominal surgery there was a much weaker advantage (OR=0.86, p=0.905).

When the association between type of cholecystectomy and 30-day complications~~short-term complications~~ was adjusted with the propensity adjustment method, results were consistent with those obtained with the risk-adjustment procedure (LC vs. OC OR= 0.61 and OR=0.52 respectively for the two outcomes). Finally, results were similar taking into account patients' clustering within different hospitals (*data not shown*).

**Discussion**

From this large observational study based on linked administrative health records - taking into account the disomogeneous distribution of factors related to the probability to be offered open surgery - people who end up having a LC have a better short-term prognosis than those that get an OC for the treatment of gallstones. The superiority of laparoscopic approach in term of 30-day complications~~short-term outcomes~~ is consistent in different age categories, both genders, different severity in disease presentation and past history of upper abdominal surgery.

This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting by providing an example contribution from the Southern Europe area.. It supports the usefulness of observational approaches. The 30-day outcomes linked to admission represents one strength of this study. . To our knowledge it is the first study in Italy to measure and compare outcomes of surgical treatments using data from secondary data sources. Despite RTCs are considered the optimal study design when comparing efficacy of treatments, observational studies provide a picture of treatment under usual circumstances of health-care practice and can answer to the question ''*Does it work in practice*?'' (3,86, 3). RTCs often have small sample size and may under represent vulnerable patient groups, including elderly patients with multiple comorbidities, children, and young women, and operate in a highly controlled environment that is far from routine clinical practice. Our study supports that LC is a reliable approach safer than OC not only in old age group - confirming previous findings (220, 3028) - but also in presence of severe disease presentation and in patients with past history of upper digestive system surgery. Beneficial effect of LC as regards systemic complications tends to be lower in 80+ yrs aged in comparison with younger ages, and in patients with emergency admission in comparison to elective admissions as regards 30-day surgical-related complications. These data add to the evidence on the complex relationship between age and outcomes after surgery (22-24,300-22, 28).

A number of potential biases are present. First of all, people in the two groups of patients analyzed are not homogenous with a higher frequency of elderly and more severe patients in the open group that in the laparoscopic one. When comparing the effect of the two techniques using two different populations, the so called "indication bias" may affect study validity (8,316, 29). To limit this problem we run the propensity adjustment analysis to take into account the different distribution of factors strongly associated with the probability to receive open surgery in the study population. This analytical approach confirmed the advantage of laparoscopic vs. open surgery obtained in the main logistic regression analysis. Another critical point is the potential different distribution of laparoscopic experience across surgeons; however a sensitivity analysis which took into account this point led to similar results. The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is another major limit. Discharge abstract data have little insight into clinical details and do not inform on the temporal relationship of the clinical conditions and processes, then defining complications is a difficult task (320). In this respect, we tried to improve the accuracy of our measures both 1) applying a specific coding algorithm with subsequent hospital admissions used to retrieve adverse events and 2) excluding in the "count" of complications specific items if reported in the index only (i.e. peritonitis) because of the difficulty to determine if it was already present at admission. Moreover, we cannot exclude an under-notification of complications – aanother major limit of our source of data - but it is unlikely that is influenced by the type of surgery. Another major problem is the potential misclassification of exposure since we were not able to measure the occurrence of conversion of LC to OC. The number of people that were switched from LC to OP is low in comparison to figures documented in other studies and it may represent a severe source of bias in our study (30,3328,31).

Beneficial effects of the laparoscopic approach versus traditional open surgery for the treatment of gallstones come from various randomized controlled trials (RCTs) (342). They found significant shorter hospital stay and quicker convalescence associated with LC but no

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differences in mortality, complications and operative time between the two procedures. A better trend with the laparoscopic approach, including morbidity and mortality, comes from some observational studies. From a surveillance system in eight Swiss hospitals, surgical site infections were less common in laparoscopic approach in comparison to traditional open surgery (0.5% in LC vs. 1.8% in OC) (353). Significantly lower incidence of venous thromboembolism and surgical site-infections in laparoscopic cases versus open cases was recently observed in a large administrative dataset–based study in USA (14, 15). National estimates for LC in USA showed an increase in LC from 52% in 1991 to 75% in 2000 with a constantly low mortality rate (mean 0.45%) and a decrease in biliary reconstruction rate over time (from 0.25% in 1992 to 0.09% in 1999) (16). On the basis of the 1997-2006 trend analysis by the same authors In-hospital mortality after cholecystectomy over a ten-years period was studied in USA: LC was associated with a low mortality rate (mean value in the period: 0.52%) while OC with a significantly higher rate (corresponding value: 4.9%) (916). In a retrospective study using Medicare beneficiaries common bile duct (CBD) injury during cholecystectomy was associated with a significant higher risk of death in comparison to cholecystectomy without CBD injury over a 9.2 year follow up period (17). From a -Swiss 1995-2005 hospital database analysis the incidence rate of bile duct injury after LC was 0.3% and did not change over time (18). In the era of evidence-based health care, population-based linkage of administrative health data have been increasingly used also in the field of surgery. However the methodology is not standardized and estimated risk of adverse events vary widely according to the type of interventions and to the type of complications and their operative definition. As a recent example in Europe, Tthe incidence of conversion to OC after LC in all hospitals in England from 2005 to 2006 has been examined using Hospital Episode Statistics and resulted 4.6% for elective procedures and 9.4% for emergency procedures) (1934). In USA, a set of indicators (Patient Safety Indicators (PSIs) has been introduced,

~~validated and continuously under revision as algorithms based on the International Classification of Diseases, Ninth Revision, Clinical Modification (17). Our study contributes to the experience in using population-based linked health data and ICD-9-CM coding algorithms to compare treatment outcomes.~~

Population-based linkage of routinely collected health data represents a precious tool to support large- scale and real-world practice evaluation by measuring specific outcomes and comparing them over time and across populations. Together with results from experimental research settings, the conclusions of research studies evaluating clinical outcomes through data linkage systems should be successfully incorporated into practice by clinicians/surgeons.

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**AUTHOR'S CONTRIBUTION**

All Authors participated in the study design, in defining the study protocol and methodology, in acquisition of data, in planning the analyses, in interpreting the results. M.S. performed the analyses. N.A and M.S. drafted the manuscript.

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**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelithiasis, previous upper abdominla surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September2008

| Patient characteristics | Laparoscopic cholecystectomy | | Open cholecystectomy | | Total | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| Age (years) | | | | | | |
| *< 70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70 - 79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| Gender | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| Severity of cholelithiasis | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.473 | 55,1 | 1.210 | 63,7 | 7.683 | 56,3 |
| *High* | 512 | 4,4 | 219 | 11,5 | 731 | 5,4 |
| Previous upper abdominal surgery | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| Type of admission | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| Comorbidities (presence of the condition) | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorder or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | 30-day systemic complications (N=280, 2.1%) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | p | $OR_{adj}$ | p | % | $OR_{crude}$ | p | $OR_{adj}$ | p |
| Age (years) | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | 1,00 | - | 1,5 | 1,00 | - | 1,00 | - |
| *70 - 79* | 2,9 | 1,62 | 0,001 | 1,36 | 0,048 | 3,9 | 2,68 | 0,000 | 2,01 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 0,015 | 1,21 | 0,475 | 7,1 | 5,13 | 0,000 | 2,79 | 0,000 |
| Gender | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | 1,00 | - | 2,6 | 1,00 | - | 1,00 | - |
| *Women* | 1,7 | 0,69 | 0,002 | 0,75 | 0,022 | 1,7 | 0,66 | 0,001 | 0,80 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | 1,00 | - | 1,2 | 1,00 | - | 1,00 | - |
| *Moderate* | 2,0 | 1,08 | 0,538 | 0,96 | 0,733 | 2,2 | 1,84 | 0,000 | 1,55 | 0,004 |
| *High* | 3,7 | 2,03 | 0,001 | 1,43 | 0,122 | 6,2 | 5,30 | 0,000 | 3,40 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | 1,00 | - | 2,0 | 1,00 | - | 1,00 | - |
| *Yes* | 5,7 | 2,94 | 0,037 | 2,29 | 0,119 | 4,3 | 2,15 | 0,197 | 1,72 | 0,376 |
| Type of admission | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | 1,00 | - | 1,5 | 1,00 | - | 1,00 | - |
| *Emergency* | 3,0 | 1,85 | 0,000 | 1,66 | 0,000 | 3,4 | 2,34 | 0,000 | 1,64 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,476 | - | - | 3,6 | 1,81 | 0,059 | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,095 | - | - | 4,4 | 2,24 | 0,002 | - | - |
| *Obesity* | 5,0 | 2,57 | 0,016 | 2,35 | 0,034 | 4,3 | 2,16 | 0,067 | - | - |
| *Blood disease* | 5,8 | 3,03 | 0,000 | 2,09 | 0,022 | 7,7 | 4,16 | 0,000 | 1,96 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 0,050 | - | - | 4,0 | 2,20 | 0,000 | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,286 | - | - | 7,4 | 4,08 | 0,000 | 1,74 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,836 | - | - | 9,4 | 5,08 | 0,000 | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,875 | - | - | 4,6 | 2,29 | 0,107 | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,136 | - | - | 6,8 | 3,66 | 0,000 | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 0,008 | - | - | 7,0 | 3,81 | 0,000 | 1,73 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 0,000 | 1,98 | 0,025 | 7,7 | 4,19 | 0,000 | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,328 | - | - | 8,5 | 4,59 | 0,000 | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,534 | - | - | 7,7 | 4,22 | 0,000 | 2,02 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 0,000 | 3,24 | 0,001 | 10,5 | 5,82 | 0,000 | 2,27 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,087 | - | - | 4,8 | 2,51 | 0,001 | 1,97 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission - Lazio Region, Italy, January 2007 - September 2008

| | 30-day surgical-related complications (N=278, %=2.0) | | | | | 30-day systemic complications (N=280, %=2.1) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | p | $OR_{adj}$ | p | % | $OR_{crude}$ | p | $OR_{adj}$ | p |
| Open cholecystectomy | 3,9 | 1,00 | - | 1,00 | - | 5,2 | 1,00 | - | 1,00 | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,000 | 0,60 | 0,001 | 1,6 | 0,29 | 0,000 | 0,52 | 0,000 |
| *Stratified results by each category* | | | | | | | | | | |
| Age (years) | | | | | | | | | | |
| *< 70* | 1,8 | 0,49 | 0,000 | 0,62 | 0,012 | 1,5 | 0,34 | 0,000 | 0,47 | 0,000 |
| *70 - 79* | 2,9 | 0,45 | 0,003 | 0,57 | 0,043 | 3,9 | 0,35 | 0,000 | 0,47 | 0,002 |
| *≥ 80* | 3,3 | 0,41 | 0,082 | 0,51 | 0,184 | 7,1 | 0,71 | 0,309 | 0,99 | 0,975 |
| Severity of cholelithiasis | | | | | | | | | | |
| *Low* | 1,9 | 0,37 | 0,000 | 0,46 | 0,003 | 1,2 | 0,29 | 0,000 | 0,43 | 0,005 |
| *Moderate* | 2,0 | 0,58 | 0,005 | 0,78 | 0,224 | 2,2 | 0,34 | 0,000 | 0,55 | 0,001 |
| *High* | 3,7 | 0,24 | 0,000 | 0,30 | 0,004 | 6,2 | 0,38 | 0,002 | 0,56 | 0,071 |
| Previous upper abdominal surgery | | | | | | | | | | |
| *No* | 2,0 | 0,47 | 0,000 | 0,60 | 0,001 | 2,0 | 0,29 | 0,000 | 0,52 | 0,000 |
| *Yes* | 5,7 | 0,26 | 0,256 | 0,36 | 0,388 | 4,3 | 0,41 | 0,470 | 0,86 | 0,905 |
| Type of admission | | | | | | | | | | |
| *Elective* | 1,6 | 0,31 | 0,000 | 0,37 | 0,000 | 1,5 | 0,33 | 0,000 | 0,48 | 0,000 |
| *Emergency* | 3,0 | 0,76 | 0,178 | 0,94 | 0,764 | 3,4 | 0,35 | 0,000 | 0,56 | 0,002 |

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**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September 2008

| Patient characteristics | Laparoscopic cholecystectomy | | Open cholecystectomy | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| **Age (years)** | | | | | | |
| *<70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70-79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| | 11.752 | | | | | |
| **Gender** | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| **Severity of cholelitiasis** | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.456 | 54,9 | 1.200 | 63,2 | 7.656 | 56,1 |
| *High* | 529 | 4,5 | 229 | 12,1 | 758 | 5,6 |
| **Previous upper abdominal surgery** | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| **Tyoe od admission** | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| **Comorbidities** | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorders or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD* or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

*Chronic Obstructive Pulmonary Disease

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**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | | | | | 30-day systemic complications (N=280, 2.1%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p |
| Age (years) | | | | | | | | | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *70 - 79* | 2,9 | 1,62 | 1,21 | 2,18 | 0,001 | 1,36 | 1,00 | 1,83 | 0,048 | 3,9 | 2,68 | 2,04 | 3,52 | 0,000 | 2,01 | 1,51 | 2,67 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 1,13 | 3,00 | 0,015 | 1,21 | 0,72 | 2,03 | 0,475 | 7,1 | 5,13 | 3,58 | 7,36 | 0,000 | 2,79 | 1,87 | 4,14 | 0,000 |
| Gender | | | | | | | | | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | - | - | 1,00 | - | - | - | 2,6 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Women* | 1,7 | 0,69 | 0,55 | 0,88 | 0,002 | 0,75 | 0,59 | 0,96 | 0,022 | 1,7 | 0,66 | 0,52 | 0,84 | 0,001 | 0,80 | 0,62 | 1,02 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | - | - | 1,00 | - | - | - | 1,2 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Moderate* | 2,0 | 1,08 | 0,84 | 1,40 | 0,538 | 0,96 | 0,74 | 1,24 | 0,733 | 2,2 | 1,84 | 1,38 | 2,46 | 0,000 | 1,55 | 1,15 | 2,08 | 0,004 |
| *High* | 3,7 | 2,03 | 1,32 | 3,14 | 0,001 | 1,43 | 0,91 | 2,24 | 0,122 | 6,2 | 5,30 | 3,59 | 7,83 | 0,000 | 3,40 | 2,26 | 5,11 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Yes* | 5,7 | 2,94 | 1,07 | 8,13 | 0,037 | 2,29 | 0,81 | 6,51 | 0,119 | 4,3 | 2,15 | 0,67 | 6,88 | 0,197 | 1,72 | 0,52 | 5,74 | 0,376 |
| Type of admission | | | | | | | | | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Emergency* | 3,0 | 1,85 | 1,45 | 2,35 | 0,000 | 1,66 | 1,29 | 2,13 | 0,000 | 3,4 | 2,34 | 1,85 | 2,97 | 0,000 | 1,64 | 1,27 | 2,11 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,64 | 2,64 | 0,476 | - | - | - | - | 3,6 | 1,81 | 0,98 | 3,34 | 0,059 | - | - | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,92 | 2,97 | 0,095 | - | - | - | - | 4,4 | 2,24 | 1,34 | 3,75 | 0,002 | - | - | - | - |
| *Obesity* | 5,0 | 2,57 | 1,19 | 5,55 | 0,016 | 2,35 | 1,29 | 2,13 | 0,034 | 4,3 | 2,16 | 0,95 | 4,94 | 0,067 | - | - | - | - |
| *Blood disease* | 5,8 | 3,03 | 1,67 | 5,50 | 0,000 | 2,09 | 1,11 | 3,93 | 0,022 | 7,7 | 4,16 | 2,46 | 7,03 | 0,000 | 1,96 | 1,09 | 3,51 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 1,00 | 2,13 | 0,050 | - | - | - | - | 4,0 | 2,20 | 1,58 | 3,05 | 0,000 | - | - | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,75 | 2,69 | 0,286 | - | - | - | - | 7,4 | 4,08 | 2,69 | 6,20 | 0,000 | 1,74 | 1,09 | 2,78 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,28 | 4,74 | 0,836 | - | - | - | - | 9,4 | 5,08 | 2,43 | 10,62 | 0,000 | - | - | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,27 | 4,57 | 0,875 | - | - | - | - | 4,6 | 2,29 | 0,83 | 6,29 | 0,107 | - | - | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,84 | 3,52 | 0,136 | - | - | - | - | 6,8 | 3,66 | 2,17 | 6,16 | 0,000 | - | - | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 1,21 | 3,62 | 0,008 | - | - | - | - | 7,0 | 3,81 | 2,47 | 5,88 | 0,000 | 1,73 | 1,07 | 2,79 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 1,76 | 5,54 | 0,000 | 1,98 | 1,09 | 3,60 | 0,025 | 7,7 | 4,19 | 2,52 | 6,98 | 0,000 | - | - | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,05 | 2,68 | 0,328 | - | - | - | - | 8,5 | 4,59 | 2,45 | 8,62 | 0,000 | - | - | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,60 | 2,72 | 0,534 | - | - | - | - | 7,7 | 4,22 | 2,66 | 6,70 | 0,000 | 2,02 | 1,23 | 3,31 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 2,82 | 10,00 | 0,000 | 3,24 | 1,65 | 6,36 | 0,001 | 10,5 | 5,82 | 3,16 | 10,72 | 0,000 | 2,27 | 1,15 | 4,46 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,92 | 3,33 | 0,087 | - | - | - | - | 4,8 | 2,51 | 1,45 | 4,35 | 0,001 | 1,97 | 1,11 | 3,48 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission; p value of heterogeneity of the strata-specific estimates - Lazio Region, Italy, January 2007 - September 2008

| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | $p_{het}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 30-day surgical-related complications: N=278, %=2.0 | | | | | | | | | | |
| Open cholecystectomy | 3,9 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,33 | 0,57 | 0,000 | 0,60 | 0,44 | 0,80 | 0,001 | - |
| Age (years) | | | | | | | | | | 0,917 |
| *< 70* | 1,8 | 0,49 | 0,35 | 0,71 | 0,000 | 0,62 | 0,43 | 0,90 | 0,012 | - |
| *70 - 79* | 2,9 | 0,45 | 0,26 | 0,76 | 0,003 | 0,57 | 0,33 | 0,98 | 0,043 | - |
| *≥ 80* | 3,3 | 0,41 | 0,15 | 1,12 | 0,082 | 0,51 | 0,18 | 1,38 | 0,184 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,053 |
| *Low* | 1,9 | 0,37 | 0,22 | 0,61 | 0,000 | 0,46 | 0,28 | 0,77 | 0,003 | - |
| *Moderate* | 2,0 | 0,58 | 0,40 | 0,85 | 0,005 | 0,78 | 0,53 | 1,16 | 0,224 | - |
| *High* | 3,7 | 0,24 | 0,11 | 0,53 | 0,000 | 0,30 | 0,13 | 0,68 | 0,004 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,654 |
| *No* | 2,0 | 0,45 | 0,34 | 0,59 | 0,000 | 0,60 | 0,44 | 0,81 | 0,001 | - |
| *Yes* | 5,7 | 0,26 | 0,03 | 2,64 | 0,256 | 0,36 | 0,03 | 3,69 | 0,388 | - |
| Type of admission | | | | | | | | | | 0,001 |
| *Elective* | 1,6 | 0,32 | 0,22 | 0,46 | 0,000 | 0,37 | 0,25 | 0,55 | 0,000 | - |
| *Emergency* | 3,0 | 0,76 | 0,51 | 1,13 | 0,178 | 0,94 | 0,62 | 1,42 | 0,764 | - |
| 30-day systemic complications: N=280, %=2.1 | | | | | | | | | | |
| Open cholecystectomy | 5,2 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,6 | 0,29 | 0,23 | 0,37 | 0,000 | 0,52 | 0,40 | 0,69 | 0,000 | - |
| Age (years) | | | | | | | | | | 0,136 |
| *< 70* | 1,5 | 0,34 | 0,24 | 0,49 | 0,000 | 0,47 | 0,32 | 0,68 | 0,000 | - |
| *70 - 79* | 3,9 | 0,35 | 0,22 | 0,55 | 0,000 | 0,47 | 0,29 | 0,75 | 0,002 | - |
| *≥ 80* | 7,1 | 0,71 | 0,37 | 1,37 | 0,309 | 0,99 | 0,50 | 1,94 | 0,975 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,755 |
| *Low* | 1,2 | 0,29 | 0,16 | 0,51 | 0,000 | 0,43 | 0,24 | 0,77 | 0,005 | - |
| *Moderate* | 2,2 | 0,34 | 0,25 | 0,47 | 0,000 | 0,55 | 0,39 | 0,77 | 0,001 | - |
| *High* | 6,2 | 0,38 | 0,21 | 0,70 | 0,002 | 0,56 | 0,30 | 1,05 | 0,071 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,702 |
| *No* | 2,0 | 0,29 | 0,22 | 0,37 | 0,000 | 0,52 | 0,39 | 0,69 | 0,000 | - |
| *Yes* | 4,3 | 0,41 | 0,04 | 4,69 | 0,470 | 0,86 | 0,07 | 10,40 | 0,905 | - |
| Type of admission | | | | | | | | | | 0,545 |
| *Elective* | 1,5 | 0,33 | 0,23 | 0,50 | 0,000 | 0,48 | 0,32 | 0,72 | 0,000 | - |
| *Emergency* | 3,4 | 0,35 | 0,25 | 0,49 | 0,000 | 0,56 | 0,39 | 0,81 | 0,002 | - |

[c] There are no 30-day complications in patients with moderately high severity and undergoing laparotomic cholecystectomy

# SUPPLEMENTARY DATA

## DETAILED METHODS

**PART 1 - Cohort selection**

Source of data: Hospital Information System (HIS)

*Inclusion criteria*
All hospital admissions with a primary or secondary contributing diagnosis of *cholelithiasis* (International Classification of Diseases 9th Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of *cholecystectomy* (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases. The final population, after sequential exclusions, consisted of 13,651 subjects.

*Exclusion criteria*
- long-term hospitalizations, rehabilitations and day-hospitals
- patients residents outside the Lazio Region
- subjects younger than 18 or older than 100 years old
- hospitalizations for delivery (MDC 14)
- hospitalizations for any type of trauma (ICD-9-CM codes ICD-9-CM 800-897)
- hospitalizations with diagnoses of cancer of the digestive system (IDC-9-CM codes150-159)
- hospitalizations with other abdominal surgical procedures (selected ICD-9-CM codes)

**PART 2 - Codes to describe severity of cholelithiasis**

**1 - Cholelithiasis of the biliary tract without complications**

*574.20; 574.50; 574.90*

**2. Cholelithiasis of the biliary tract with cholecystitis (without obstruction)**

*574.10;574.40; 574.70; 575.1 AND 574.20 or574.50 or574.90; 574.00; 574.30; 574.60; 574.80; 575.0 AND 574.20 or 574.50 or 574.90*

**3. Cholelithiasis of the biliary tract with obstruction (without cholecystitis)**
*574.21; 574.51; 574.01; 574.91; 575.2 AND 574.20 or574.50 or574.90; 576.2 AND 574.20 or 574.50 or 574.90; 575.3*

**4. Cholelithiasis of the biliary tract with both obstruction and cholecystitis**
*574.01; 574.11; 574.31; 574.41; 574.61; 574.71; 574.81; 575.2 AND 574.00; 575.0 AND 574.20 575.1 AND 574.20 574.30; 575.0 AND 574.50; 575.1 AND 574.50; 574.60; 574.70; 574.80; 576.1; 576.2 AND 574.00; 575.0 AND 574.20; 575.1 AND 574.20; 574.30; 575.0 AND 574.50; 575.1 AND 574.50; 574.60; 574.70; 574.80*

**PART 3 - Codes to describe previous upper abdominal surgery**

Codes in the index admission – post procedural states
*stomach V44.1, V45.75, V55.1; intestine V44.2, V44.4, V45.3, V45.72, V53.5, V55.2, V55.4, V42.84; liver V42.7; pancreas 42.83*

Codes in the previous 2-year- hospitalizations

Stomach
*43.5,43.6,43.7,,43.8,43.9,44.31,44.39,44.40,44.41,44.42,44.5,44.61,44.63,44.64,44.65,44.69*
Small intestine
*45.31,45.32,45.33,45.34,45.50,45.51,45.6,45.9,45.91,45.92,45.93,46.01,46.02,46.60,46.61, 46.62,46.71,46.72,46.73,46.74,46.80,46.81,46.93,46.97*
Liver
*50.2,50.3, 50.4,50.5,50.6*
Pancreas
*52.22,52.3,52.4,52.5,52.6,52.7,52.8,52.95,52.96*
Abdominal Hernia
*53.4,53.5,53.6,53.7*
Peritoneum
*54.4,54.5,54.6,54.7*
Large intestine
*45.41,45.49,45.7,45.8,45.94,46.03,46.04,46.63,46.64,46.75,46.76,46.79*
Other surgery
*55.4,55.5,56.2,56.4,57.1,57.6,57.7,65.3,65.4,65.5,65.6,66.4,66.5,68.3,68.4,68.6,68.8*

**PART 4 - Codes to describe coexisting conditions**
On the basis of previous 2-year hospitalizations (following a validated coding algorithm – enhanced Elixhauser AHRQ-Web-ICD-9-CM - see reference n. 17 cited in the text).

*diabetes 250.xx; hypertension 401-405; obesity 280.0, ischemic disease 410-414, 429.7, previous revascularization V45.81, V45.82, procedures 36.0, 36.1, heart failure 428, other cardiac disease 093.2, 391, 393-398, 420-425, 429, 745, 746.3-646.6, V15.1, V42.2, V43.2, V43.3, V45.0 arrhythmia / conduction disorders 426-427, cerebrovascular disease 430-438, vascular disease 440-448, 557, hematologic disorders 280-285, 286, 287.1, 287.3-287.5, 288, 289, chronic respiratory disesase 490-496, 518.81, 518.82, chronic liver disease / pancreas 571, 572, 577.1, 577.9, chronic renal disease 582-583, 585-588, V42.0, V45.1m V56, cancer 140-208.9*

**PART 5 - Codes to describe outcomes**

***A) Surgical-related complications (within 30 day after the surgery)***
in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*998.1 Hemorrhage or hematoma or seroma complicating a procedure; 998.2 Accidental puncture or laceration during a procedure; 998.3 Disruption of wound; 998.4 Foreign body accidentally left during a procedure; 998.5 Postoperative infection; 998.6 Persistent postoperative fistula; 998.7 Acute reaction to foreign substance accidentally left during a procedure; 998.81 Emphysema (subcutaneous) (surgical) resulting from a procedure; 998.83 Non-healing surgical wound; 998.89 Other specified complications; 997.4 Digestive system complications; 998.9 Unspecified complication of procedure, not elsewhere classified*

Only in the subsequent hospitalizations

at least one of the following:
*567 Peritonitis and retroperitoneal infections; 575.4 Perforation of gallbladder; 575.5 Fistula of gallbladder; 576.0 Postcholecystectomy syndrome; 576.3 Perforation of bile duct; 576.4 Fistula of bile duct; 570 Acute and subacute necrosis of liver; 789.0 Abdominal pain*

***B) Sistemic complications (within 30 day after the surgery)***

in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*997.0 Nervous system complications; 997.1 Cardiac complications; 997.3 Respiratory complications; 998.0 Postoperative shock; 410 Acute myocardial infarction; 415.1 Pulmonary embolism and infarction; 431 Intracerebral haemorrhage; 433.x1 Occlusion and stenosis of precerebral arteries with infarction; 434.x1 Occlusion of cerebral arteries with infarction; 436 Acute, but ill-defined, cerebrovascular disease; 480-486 Pneumonia; 513.0 Abscess of lung 518.4 Acute edema of lung, unspecified; 518.5 Pulmonary insufficiency following trauma and surgery; 785.5 Shock without mention of trauma; 788.2 Retention of urine*

Only in the subsequent hospitalizations
*038 Septicemia*

SUPPLEMENTARY DATA

DETAILED METHODS

**PART 1 - Cohort selection**

Source of data: Hospital Information System (HIS)

*Inclusion criteria*
All hospital admissions with a primary or secondary contributing diagnosis of cholelithiasis (International Classification of Diseases 9th Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases. The final population, after sequential exclusions, consisted of 13,651 subjects.

*Exclusion criteria*
- long-term hospitalizations, rehabilitations and day-hospitals
- patients residents outside the Lazio Region
- subjects younger than 18 or older than 100 years old
- hospitalizations for delivery (MDC 14)
- hospitalizations for any type of trauma (ICD-9-CM codes ICD-9-CM 800-897)
- hospitalizations with diagnoses of cancer of the digestive system (IDC-9-CM codes150-159)
- hospitalizations with other abdominal surgical procedures (selected ICD-9-CMcodes, as follows:

**ICD-9-CM code Description**

Stomach
*43.5 Partial gastrectomy with anastomosis to esophagus*
*43.6 Partial gastrectomy with anastomosis to duodenum*
*43.7 Partial gastrectomy with anastomosis to jejunum*
*43.8 Other partial gastrectomy*
*43.9 Total gastrectomy*
*44.31 High gastric bypass*
*44.39 Other gastroenterostomy*
*44.40 Suture of peptic ulcer, not otherwise specified*
*44.41 Suture of gastric ulcer site*
*44.42 Suture of duodenal ulcer site*
*44.5 Revision of gastric anastomosis*
*44.61 Suture of laceration of stomach*
*44.63 Closure of other gastric fistula*
*44.64 Gastropexy*
*44.65 Esophagogastroplasty*
*44.69 Other*

Small intestine
*45.31 Other local excision of lesion of duodenum*
*45.32 Other destruction of lesion of duodenum*
*45.33 Local excision of lesion or tissue of small intestine, except duodenum*
*45.34 Other destruction of lesion of small intestine, except duodenum*
*45.50 Isolation of intestinal segment, not otherwise specified*

*45.51 Isolation of segment of small intestine*
*45.6 Other excision of small intestine*
*45.9 Intestinal anastomosis*
*45.91 Small-to-small intestinal anastomosis*
*45.92 Anastomosis of small intestine to rectal stump*
*45.93 Other small-to-large intestinal anastomosis*
*46.01 Exteriorization of small intestine*
*46.02 Resection of exteriorized segment of small intestine*
*46.60 Fixation of intestine, not otherwise specified*
*46.61 Fixation of small intestine to abdominal wall*
*46.62 Other fixation of small intestine*
*46.71 Suture of laceration of duodenum*
*46.72 Closure of fistula of duodenum*
*46.73 Suture of laceration of small intestine, except duodenum*
*46.74 Closure of fistula of small intestine, except duodenum*
*46.80 Intra-abdominal manipulation of intestine, not otherwise specified*
*46.81 Intra-abdominal manipulation of small intestine*
*46.93 Revision of anastomosis of small intestine*
*46.97 Transplant of intestine*

Liver
*50.2 Local excision or destruction of liver tissue or lesion*
*50.3 Lobectomy of liver*
*50.4 Total hepatectomy*
*50.5 Liver transplant*
*50.6 Repair of liver*

Pancreas
*52.22 Other excision or destruction of lesion or tissue of pancreas or pancreatic duct*
*52.3 Marsupialization of pancreatic cyst*
*52.4 Internal drainage of pancreatic cyst*
*52.5 Partial pancreatectomy*
*52.6 Total pancreatectomy*
*52.7 Radical pancreaticoduodenectomy*
*52.8 Transplant of pancreas*
*52.95 Other repair of pancreas*
*52.96 Anastomosis of pancreas*

Abdominal Hernia
*53.4 Repair of umbilical hernia*
*53.5 Repair of other hernia of anterior abdominal wall (without graft or prosthesis)*
*53.6 Repair of other hernia of anterior abdominal wall with graft or prosthesis*
*53.7 Repair of diaphragmatic hernia, abdominal approach*

Peritoneum
*54.4 Excision or destruction of peritoneal tissue*
*54.5 Lysis of peritoneal adhesions*
*54.6 Suture of abdominal wall and peritoneum*
*54.7 Other repair of abdominal wall and peritoneum*

Large intestine

2

*45.41 Excision of lesion or tissue of large intestine*
*45.49 Other destruction of lesion of large intestine*
*45.7 Open and other partial excision of large intestine*
*45.8 Total intra-abdominal colectomy*
*45.94 Large-to-large intestinal anastomosis*
*46.03 Exteriorization of large intestine*
*46.04 Resection of exteriorized segment of large intestine*
*46.63 Fixation of large intestine to abdominal wall*
*46.64 Other fixation of large intestine*
*46.75 Suture of laceration of large intestine*
*46.76 Closure of fistula of large intestine*
*46.79 Other repair of intestine*

Other surgery
*55.4 Partial nephrectomy*
*55.5 Complete nephrectomy*
*56.2 Ureterotomy*
*56.4 Ureterectomy*
*57.1 Cystotomy and cystostomy*
*57.6 Partial cystectomy*
*57.7 Total cystectomy*
*65.3 Unilateral oophorectomy*
*65.4 Unilateral salpingo-oophorectomy*
*65.5 Bilateral oophorectomy*
*65.6 Bilateral salpingo-oophorectomy*
*66.4 Total unilateral salpingectomy*
*66.5 Total bilateral salpingectomy*
*68.3 Subtotal abdominal hysterectomy*
*68.4 Total abdominal hysterectomy*
*68.6 Radical abdominal hysterectomy*
*68.8 Pelvic evisceration*

**PART 2 - Codes to describe severity of cholelithiasis**

**1 - Cholelithiasis of the biliary tract without complications**

*574.20, Calculus of gallbladder without mention of cholecystitis*
*574.50 Calculus of bile duct without mention of cholecystitis*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

**2. Cholelithiasis of the biliary tract with cholecystitis (without obstruction)**

*574.10 Calculus of gallbladder with other cholecystitis*
*574.40 Calculus of bile duct with other cholecystitis*
*574.70 Calculus of gallbladder and bile duct with other cholecystitis*

*575.1 Other cholecystitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis oror*
*574.50 Calculus of bile duct without mention of cholecystitis oror*

*574.90 Calculus of gallbladder and bile duct without cholecystitis*
*574.00 Calculus of gallbladder with acute cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

*575.0 Acute cholecystitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis oror*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*
*576.1 Cholangitis AND*
*574.20 Calculus of gallbladder without mention of cholecystitis oror*
*574.50 Calculus of bile duct without mention of cholecystitis oror*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

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**3. Cholelithiasis of the biliary tract with obstruction (without cholecystitis)**

*574.21 Calculus of gallbladder without mention of cholecystitis*
*574.51 Calculus of bile duct without mention of cholecystitis*
*574.91 Calculus of gallbladder and bile duct without cholecystitis*

*575.2 Obstruction of gallbladder AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*

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*576.2 Obstruction of bile duct AND*
*574.20 Calculus of gallbladder without mention of cholecystitis or*
*574.50 Calculus of bile duct without mention of cholecystitis or*
*574.90 Calculus of gallbladder and bile duct without cholecystitis*
*575.3 Hydrops of gallbladder*

**4. Cholelithiasis of the biliary tract with both obstruction and cholecystitis**

*574.01 Calculus of gallbladder with acute cholecystitis*
*574.11 Calculus of gallbladder with other cholecystitis*
*574.31 Calculus of bile duct with acute cholecystitis*
*574.41 Calculus of bile duct with other cholecystitis*
*574.61 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.71 Calculus of gallbladder and bile duct with other cholecystitis*
*574.81 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

*575.2 Obstruction of gallbladder AND*
*574.00 Calculus of gallbladder with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*

*574.70 Calculus of gallbladder and bile duct with other cholecystitis*
*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

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*576.1 cholangitis*

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*576.2 Obstruction of bile duct AND*
*574.00 Calculus of gallbladder with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.20 Calculus of gallbladder without mention of cholecystitis*
*574.30 Calculus of bile duct with acute cholecystitis*
*575.0 Acute cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*575.1 Other cholecystitis AND 574.50 Calculus of bile duct without mention of cholecystitis*
*574.60 Calculus of gallbladder and bile duct with acute cholecystitis*
*574.70 Calculus of gallbladder and bile duct with other cholecystitis*
*574.80 Calculus of gallbladder and bile duct with acute and chronic cholecystitis*

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**PART 3 - Codes to describe previous upper abdominal surgery**

Codes in the index admission – post procedural states
stomach V44.1, V45.75, V55.1;
intestine V44.2, V44.4, V45.3, V45.72, V53.5, V55.2, V55.4, V42.84;
liver V42.7;
ppancreas 42.83

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Codes in the previous 2-year- hospitalizations

Stomach
*43.5 Partial gastrectomy with anastomosis to esophagus*
*43.6 Partial gastrectomy with anastomosis to duodenum*
*43.7 Partial gastrectomy with anastomosis to jejunum*
*43.8 Other partial gastrectomy*
*43.9 Total gastrectomy*
*44.31 High gastric bypass*
*44.39 Other gastroenterostomy*
*44.40 Suture of peptic ulcer, not otherwise specified*
*44.41 Suture of gastric ulcer site*
*44.42 Suture of duodenal ulcer site*
*44.5 Revision of gastric anastomosis*
*44.61 Suture of laceration of stomach*
*44.63 Closure of other gastric fistula*
*44.64 Gastropexy*
*44.65 Esophagogastroplasty*
*44.69 Other*

Small intestine
*45.31 Other local excision of lesion of duodenum*

45.32 ~~Other destruction of lesion of duodenum~~
45.33 ~~Local excision of lesion or tissue of small intestine, except duodenum~~
45.34 ~~Other destruction of lesion of small intestine, except duodenum~~
45.50 ~~Isolation of intestinal segment, not otherwise specified~~
45.51 ~~Isolation of segment of small intestine~~
45.6 ~~Other excision of small intestine~~
45.9 ~~Intestinal anastomosis~~
45.91 ~~Small-to-small intestinal anastomosis~~
45.92 ~~Anastomosis of small intestine to rectal stump~~
45.93 ~~Other small-to-large intestinal anastomosis~~
46.01 ~~Exteriorization of small intestine~~
46.02 ~~Resection of exteriorized segment of small intestine~~
46.60 ~~Fixation of intestine, not otherwise specified~~
46.61 ~~Fixation of small intestine to abdominal wall~~
46.62 ~~Other fixation of small intestine~~
46.71 ~~Suture of laceration of duodenum~~
46.72 ~~Closure of fistula of duodenum~~
46.73 ~~Suture of laceration of small intestine, except duodenum~~
46.74 ~~Closure of fistula of small intestine, except duodenum~~
46.80 ~~Intra-abdominal manipulation of intestine, not otherwise specified~~
46.81 ~~Intra-abdominal manipulation of small intestine~~
46.93 ~~Revision of anastomosis of small intestine~~
46.97 ~~Transplant of intestine~~

Liver
50.2 ~~Local excision or destruction of liver tissue or lesion~~
50.3 ~~Lobectomy of liver~~
50.4 ~~Total hepatectomy~~
50.5 ~~Liver transplant~~
50.6 ~~Repair of liver~~

Pancreas
52.22 ~~Other excision or destruction of lesion or tissue of pancreas or pancreatic duct~~
52.3 ~~Marsupialization of pancreatic cyst~~
52.4 ~~Internal drainage of pancreatic cyst~~
52.5 ~~Partial pancreatectomy~~
52.6 ~~Total pancreatectomy~~
52.7 ~~Radical pancreaticoduodenectomy~~
52.8 ~~Transplant of pancreas~~
52.95 ~~Other repair of pancreas~~
52.96 ~~Anastomosis of pancreas~~

Abdominal Hernia
53.4 ~~Repair of umbilical hernia~~
53.5 ~~Repair of other hernia of anterior abdominal wall (without graft or prosthesis)~~
53.6 ~~Repair of other hernia of anterior abdominal wall with graft or prosthesis~~
53.7 ~~Repair of diaphragmatic hernia, abdominal approach~~

Peritoneum
54.4 ~~Excision or destruction of peritoneal tissue~~
54.5 ~~Lysis of peritoneal adhesions~~

6

*54.6 Suture of abdominal wall and peritoneum*
*54.7 Other repair of abdominal wall and peritoneum*

Large intestine
*45.41 Excision of lesion or tissue of large intestine*
*45.49 Other destruction of lesion of large intestine*
*45.7 Open and other partial excision of large intestine*
*45.8 Total intra-abdominal colectomy*
*45.94 Large-to-large intestinal anastomosis*
*46.03 Exteriorization of large intestine*
*46.04 Resection of exteriorized segment of large intestine*
*46.63 Fixation of large intestine to abdominal wall*
*46.64 Other fixation of large intestine*
*46.75 Suture of laceration of large intestine*
*46.76 Closure of fistula of large intestine*
*46.79 Other repair of intestine*

Other surgery
*55.4 Partial nephrectomy*
*55.5 Complete nephrectomy*
*56.2 Ureterotomy*
*56.4 Ureterectomy*
*57.1 Cystotomy and cystostomy*
*57.6 Partial cystectomy*
*57.7 Total cystectomy*
*65.3 Unilateral oophorectomy*
*65.4 Unilateral salpingo-oophorectomy*
*65.5 Bilateral oophorectomy*
*65.6 Bilateral salpingo-oophorectomy*
*66.4 Total unilateral salpingectomy*
*66.5 Total bilateral salpingectomy*
*68.3 Subtotal abdominal hysterectomy*
*68.4 Total abdominal hysterectomy*
*68.6 Radical abdominal hysterectomy*
*68.8 Pelvic evisceration*

**PART 4 - Codes to describe coexisting conditions**
On the basis of previous 2-year hospitalizations (following a validated coding algorithm – enhanced Elixhauser AHRQ-Web-ICD-9-CM - see reference n. 17 cited in the text).

diabetes 250.xx; hypertension 401-405; obesity 280.0, ischemic disease 410-414, 429.7, previous revascularization V45.81, V45.82, procedures 36.0, 36.1, heart failure 428, other cardiac disease 093.2, 391, 393-398, 420-425, 429, 745, 746.3-646.6, V15.1, V42.2, V43.2, V43.3, V45.0 arrhythmia / conduction disorders 426-427, cerebrovascular disease 430-438, vascular disease 440-448, 557, hematologic disorders 280-285, 286, 287.1, 287.3-287.5, 288, 289, chronic respiratory disease 490-496, 518.81, 518.82, chronic liver disease / pancreas 571, 572, 577.1, 577.9, chronic renal disease 582-583, 585-588, V42.0, V45.1m V56, cancer 140-208.9

**PART 5 - Codes to describe outcomes**

***A) Surgical-related complications (within 30 day after the surgery)***

in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:

*998.1 Hemorrhage or hematoma or seroma complicating a procedure*
*998.2 Accidental puncture or laceration during a procedure*
*998.3 Disruption of wound*
*998.4 Foreign body accidentally left during a procedure*
*998.5 Postoperative infection*
*998.6 Persistent postoperative fistula*
*998.7 Acute reaction to foreign substance accidentally left during a procedure*
*998.81 Emphysema (subcutaneous) (surgical) resulting from a procedure*
*998.83 Non-healing surgical wound*
*998.89 Other specified complications*
*997.4 Digestive system complications*
*998.9 Unspecified complication of procedure, not elsewhere classified*

Only in the subsequent hospitalizations

at least one of the following:

*567 Peritonitis and retroperitoneal infections*
*575.4 Perforation of gallbladder*
*575.5 Fistula of gallbladder*
*576.0 Postcholecystectomy syndrome*
*576.3 Perforation of bile duct*
*576.4 Fistula of bile duct*
*570 Acute and subacute necrosis of liver*
*789.0 Abdominal pain*

***B) Sistemic complications (within 30 day after the surgery)***

in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:

*997.0 Nervous system complications*
*997.1 Cardiac complications*
*997.3 Respiratory complications*
*998.0 Postoperative shock*
*410 Acute myocardial infarction*
*415.1 Pulmonary embolism and infarction*
*431 Intracerebral hemorrhage*
*433.x1 Occlusion and stenosis of precerebral arteries with infarction*
*434.x1 Occlusion of cerebral arteries with infarction*
*436 Acute, but ill-defined, cerebrovascular disease*
*480-486 Pneumonia*
*513.0 Abscess of lung*

*518.4 Acute edema of lung, unspecified*
*518.5 Pulmonary insufficiency following trauma and surgery*
*785.5 Shock without mention of trauma*
*788.2 Retention of urine*

Only in the subsequent hospitalizations
*038 Septicemia*

# Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.

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| | |

**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**

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# Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.

## Abstract

### Objective

The objective of the study is to evaluate short-term complications after laparoscopic (LC) or open cholecystectomy (OC) in patients with gallstones by using linked hospital discharge data.

### Design

Population-based cohort study.

### Setting

Data were obtained from the Regional Hospital Discharge Registry Lazio Region in Central Italy (around 5 million inhabitants) in 2007-2008.

### Participants

All patients admitted to hospitals of Lazio with symptomatic gallstones (ICD9-CM = 574) who underwent LC (ICD9-CM 51.23) or OC (ICD9-CM 51.22).

### Outcome measures

1)“*30-day surgical-related complications*” defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound); 2) “*30-day systemic complications*” defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events).

### Results

13,651 patients were included; 86.1% had LC, 13.9% OC. 2.0% experienced surgical-related complications (SRC), 2.1% systemic complications (SC). The Odds Ratio (OR) of complications after LC versus OC was 0.60 ($p<0.001$) for SRC and 0.52 ($p<0.001$) for SC. As regards SRC, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission (OR=0.94, p = 0.764). For SC, no significant advantage of LC was seen among very old people (OR=0.99, p=0.975) and among those with previous upper abdominal surgery (OR=0.86, p=0.905).

**Conclusions**

This large observational study confirms that LC is more effective than OC with respect to 30-day complications. Population-based linkage of administrative datasets can enlarge evidence of treatment benefits in clinical practice.

**Key words:** administrative data, cohort study, effectiveness, gallstones, hospital discharge data, laparoscopic cholecystectomy, open cholecystectomy, outcomes, population-based, post-operative complications.

## Article summary

### Article focus

-The advantage of laparoscopic cholecystectomy (LC) approach for the treatment of gallstone versus open surgery (OC) has been shown from RCTs and observational studies.

-The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments.

-We compared laparoscopic and open cholecystectomy in term of 30-day complications using routinely collected databases in Lazio Region (Italy).

### Key messages

-This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting.

-As regards surgical-related complications, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission.

-For systemic complications, no significant advantage of LC was seen among very old people and among those with previous upper abdominal surgery.

### Strengths and limitations

-Population-based design, 30-day outcomes, large numbers and robustness of analytic procedures are the main strengths.

-It contributes to the debate on the complex methodology to estimated risk of adverse events after surgery using secondary databases to monitor quality of care.

-The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is a major limit.

## Introduction

Comparative effectiveness research is becoming central to monitor real-life impact of treatments and support public health decisions (1, 2). Although the basic concept of comparing therapies is not new, over the last few years many initiatives have been implemented in several countries to provide large-scale evidence on benefits and harms of different treatments (3-5). The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments. They include hospital in-patients records, birth and death registrations, outpatient care records, dispensed pharmacy drugs (6-9).

In the Lazio Region (around 5.000.000 inhabitants) the P.Re.Val.E. Project (*Regional Program for Assessing the Outcomes of Health-care Interventions*) was launched in 2005. Its aims are: to measure the quality of health care provided in the Lazio Region, to describe variability of care provision across institutions and populations and to compare effectiveness of treatments for different medical and surgical conditions (10,11). Over 60 outcomes indicators are calculated based on data obtained from record-linkage procedures of different health systems. The results are periodically updated and publicly disseminated with discussion on critical methodological points.

Cholecystectomy is one of the most common abdominal surgical procedures in developed countries. Since its introduction in the late ‘80s, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) as the treatment of choice for symptomatic gallstones (12, 13). Beneficial effects of LC have been demonstrated in studies showing the advantages from real-life settings using secondary databases (9,14-19). In the present study we aimed at developing a methodology to measure short-term complications after LC or OC using large administrative databases on behalf of the P.Re.Val.E. Secondly, we tested the hypothesis that

the advantages of LC versus OC could vary according to age and clinical patients' characteristics.

## Methods

Source of data

Data was derived from the Lazio Hospital Information System (HIS), which provides information on patients' demographic data (gender, age, place of birth, place of residence), admission and discharge dates, discharge diagnoses (up to 6) and medical procedures or surgical interventions ((up to 6) according to the International Classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM), status at discharge (alive, dead, transferred to another hospital), ward(s) of stay, date(s) of in-hospital transfer, and a regional code corresponding to the admitting facility for patients discharged from all public and private hospital of the Lazio Region (5.759.839 inhabitants).

Study population

All hospital admissions with a primary or secondary diagnosis of gallstones (International Classification of Diseases 9th Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases (age 18+ years). We a priori decided not to include codes for partial cholecystectomy (ICD-9-CM 51.21 and 51.24) to increase the specificity of our exposure. Information was retrieved from the HIS. In order to increase the case specificity, several exclusion criteria were applied including long-term hospitalizations, rehabilitations, day-hospitals, hospitalizations for delivery or trauma or cancer, hospitalizations with abdominal surgical procedures other than cholecystectomy. The final population consisted of 13,651 subjects (**Figure 1).** See the online **Supplementary Data** (Part 1) for details on the exclusion criteria and ICD9-CM codes. According to the Regional Law, the present study, which was based on anonymous computer records from health information systems, did not require for ethical approval.

Patient-level risk factors

The following characteristics were considered for each patient: Age (<70; 70-79; >=80 years old); Gender; Severity of gallstones: it was classified as *low* (not-complicated), *moderate* (presence of cholecystitis or biliary tract obstruction), and *high* (presence of both inflammation and obstruction of the biliary tract); Previous upper abdominal surgery (based on previous 2-year hospitalizations); Comorbidities (based on previous 2-year hospitalizations) following validated algorithms (20,21); Type of admission: either *elective* or *emergency*. See the online **Supplementary Data** (Part 2-4) for details on the ICD-9-CM codes. The choice of *cut off* for age category was based on previous studies to distinguish adult and old people (22-24).

Outcomes

We identified various complications within 30-days after the intervention and grouped them in two categories: 1) "*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound (); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events). The complete list of complications with ICD-9-CM codes is reported in the online **Supplementary Data** (Part 5). Among the various complications we included some conditions reported in the list of Patient Safety Indicators recently developed by the Agency for Health Care Research and Quality, while other items were specifically created on the basis of scientific literature on digestive surgery (14-19,25,26). Depending on the type of complication, some ICD9-CM codes were searched in both the index admission and the following ones in the 30-day period after the surgery, others were searched only in later hospitalizations. For example, peritonitis or acute pancreatitis was not counted as complications when reported in the index admission. See the online **Supplementary Data** (Part 5) for details on the ICD9-CM codes. In the case of a subsequent hospitalization occurred out of the study area (for example, in a region other than Lazio), we obtained information through record linkage procedure between hospital information systems. Because of the short follow up time, this happened in a minimal proportion of cases (0.1%). The outcome variables were: "*30-day surgical-related complications*" and "*30-day systemic complications*"; they were coded "1" if at least one of the complications within the group was present and "0" if none was recorded.

Type of cholecystectomy

As exposure variable we defined "*type of cholecystectomy*" (laparoscopic cholecystectomy, LC vs. open cholecystectomy, OC). In the case of ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure. We could not use the specific ICD-9-code for a case converted from LC to OC (ICD-9-CM code V 64.41) because it was highly under-reported in our Region in the study period.

Statistical analysis

Multiple logistic regression models were fitted to estimate the relative risk of 30-day complications (either "surgical-related" or "systemic") after LC versus OC, adjusting for demographical and clinical risk factors. The two outcome variables were analysed separately. The predictive model was made of two sets of predictors: 1) variables "a priori" chosen as confounders (age, gender, severity of gallstones, previous upper abdominal surgery, and type of admission); 2) variables empirically tested (comorbidities) which were selected using iterative stepwise statistical procedures) (27). Once the "best" predictive model was identified for each of the two outcome, the variable "*type of cholecystectomy*" was included, and the adjusted odds ratio (OR) of LC versus open surgery was estimated, with corresponding 95% confidence interval (95% CI) and p-value.

In order to test the hypothesis of an effect modification by age, relative risk estimates for the age groups were derived by adding an interaction term between the age group and the treatment variable in the final multivariate logistic model. We obtained the OR of laparoscopic vs. open surgery within each age stratum by adding the corresponding interaction terms coefficients. This was accomplished by adding the coefficient from the reference category and that from the age stratum of interest, and by computing the corresponding standard error from the corresponding terms of the variance-covariance matrix. Similarly, effect modification was tested with regard to severity of cholelithiasis, previous upper abdominal surgery and type of admission. The corresponding tests of heterogeneity of the stratum-specific risk estimates were computed.

Sensitivity analyses were performed. First, in order to guarantee adequate control of confounding factors we identified and adjusted for all the individual factors associated with the treatment, within the propensity adjustment framework (28). This procedure is a two-step technique: 1. it estimates the a priori probability of exposure for each subject, based on clinical and demographic characteristics; 2. it standardizes for them in the association between treatment and the study outcome. The individual factors related to the exposure in the present study include age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, cardio-circulatory disease, cerebrovascular disease, COPD or respiratory failure, chronic nephropathy, chronic disease of the liver or pancreas. Second, to take into account the potential heterogeneous experience in laparoscopic surgery across different hospitals because of the patients' clustering within a single institution we perform a multilevel regression model with random intercepts for hospitals (29).

All the statistical analyses were performed using SAS Software version 8.0 (SAS Institute, Inc. SAS/STAT software).

**Results**

A description of the study population, overall and by cholecystectomy procedure, is presented in **Table 1**. Over 80% of the patients were younger than 70 years, and moderate to high severity of the gallstones was diagnosed for 61.7%. As compared with patients undergoing LC, those who underwent OC were more likely to be elderly, males, with a more sever baseline disease and more chronic conditions. Furthermore, they were operated in emergency in most of the cases (52.4%), whereas LC was performed in elective hospitalizations much more frequently (73.9%).

**Table 2** reports the relationship between demographic and clinical variables and the occurrence of complications. The adjusted risk of systemic complications increased with age and was much higher in patients with more severe baseline gallstones, whereas no clear age or severity-related differences in risk emerged with regard to surgical-related 30-day complications, once other co-factors were taken into account. Women were less likely to experience both types of complications. Having had a previous intervention on the upper digestive system seemed to enhance the risk of both surgical-related and systemic complications, though results are not statistically significant due to small power. Finally, the risk of both types of complications was more evident in emergency as opposed to scheduled interventions. Surgical-related complications were higher among subjects with obesity, blood disease, stroke or chronic nephropathy, whereas systemic complications were associated with blood diseases, ischemic heart disease, conduction disorders or dysrhythmias, COPD or respiratory failure, chronic nephropathy, and chronic diseases of the liver or pancreas.

**Table 3** shows the relationship between type of cholecystectomy and outcomes, adjusted for the risk factors identified in Table 2. We report results of the advantage of LC vs. OC (OR, 95% CI) in the cohort and in the each stratum of the variables tested in the models with interaction terms. The incidence of “30-day surgical-related complications” and “30-day systemic complications” was 2.0% and 2.1%, respectively. The odds ratio of surgical related complications for patients who underwent LC as compared to patients with OC was 0.60 ($p<0.001$). The corresponding figure for systemic complications was 0.52 ($p<0.001$).

As regards 30-day surgical-related complications, the protective effect of LC vs. OC was consistent across the age category, severity of cholelithiasis and previous upper abdominal surgery, while among people with emergency admission there was no advantage (OR=0.94 p = 0.764). Similarly, for systemic complications, the superiority of LC vs. OC was consistent regardless level of cholelithiasis severity, and elective/emergency admission, but for those 80+ yrs aged people there was no advantage of LC vs. OC (OR 0.99, p = 0.975); also for patients with previous upper abdominal surgery there was a much weaker advantage (OR=0.86, p=0.905).

When the association between type of cholecystectomy and 30-day complications was adjusted with the propensity adjustment method, results were consistent with those obtained with the risk-adjustment procedure (LC vs. OC OR= 0.61 and OR=0.52 respectively for the two outcomes). Finally, results were similar taking into account patients' clustering within different hospitals (*data not shown*).

**Discussion**

From this large observational study based on linked administrative health records - taking into account the disomogeneous distribution of factors related to the probability to be offered open surgery - people who end up having a LC have a better short-term prognosis than those that get an OC for the treatment of gallstones. The superiority of laparoscopic approach in term of 30-day complications is consistent in different age categories, different severity in disease presentation and past history of upper abdominal surgery.

This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting by providing an example from the Southern Europe area. It supports the usefulness of observational approaches. The 30-day outcomes linked to admission represent one strength of this study. Despite RTCs are considered the optimal study design when comparing efficacy of treatments, observational studies provide a picture of treatment under usual circumstances of health-care practice and can answer to the question ''*Does it work in practice*?" (3,8). RTCs often have small sample size and may under represent vulnerable patient groups, including elderly patients with multiple comorbidities, children, and young women, and operate in a highly controlled environment that is far from routine clinical practice. Our study supports that LC is a reliable approach safer than OC not only in old age group - confirming previous findings (22, 30) - but also in presence of severe disease presentation and in patients with past history of upper digestive system surgery. Beneficial effect of LC as regards systemic complications tends to be lower in 80+ yrs aged in comparison with younger ages, and in patients with emergency admission in comparison to elective admissions as regards 30-day surgical-related complications. These data add to the evidence on the complex relationship between age and outcomes after surgery (22-24,30).

A number of potential biases are present. First of all, people in the two groups of patients analyzed are not homogenous in term of anesthesia risk due to higher frequency of elderly and more comorbidities in the open group than in the laparoscopic one. When comparing the effect of the two techniques using two different populations, the so called "indication bias" may affect study validity (8,31). To limit this problem we run the propensity adjustment analysis to take into account the different distribution of factors strongly associated with the probability to receive open surgery in the study population. This analytical approach confirmed the advantage of laparoscopic vs. open surgery obtained in the main logistic regression analysis. Another critical point is the potential different distribution of laparoscopic experience across surgeons; however a sensitivity analysis which took into account this point led to similar results. The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is another major limit. Discharge abstract data have little insight into clinical details and do not inform on the temporal relationship of the clinical conditions and processes, then defining complications is a difficult task (32). In this respect, we tried to improve the accuracy of our measures both 1) applying a specific coding algorithm with subsequent hospital admissions used to retrieve adverse events and 2) excluding in the "count" of complications specific items if reported in the index only (i.e. peritonitis) because of the difficulty to determine if it was already present at admission. Moreover, we cannot exclude an under-notification of complications – a major limit of our source of data - but it is unlikely that is influenced by the type of surgery. Another major problem is the potential misclassification of exposure since we were not able to measure the occurrence of conversion of LC to OC. The number of people that were switched from LC to OP is low in comparison to figures documented in other studies and it may represent a severe source of bias in our study (30,33).

Beneficial effects of the laparoscopic approach versus traditional open surgery for the treatment of gallstones come from various randomized controlled trials (RCTs) (34). They found significant shorter hospital stay and quicker convalescence associated with LC but no differences in mortality, complications and operative time between the two procedures. A better trend with the laparoscopic approach, including morbidity and mortality, comes from observational studies. From a surveillance system in eight Swiss hospitals, surgical site infections were less common in laparoscopic approach in comparison to traditional open surgery (0.5% in LC vs. 1.8% in OC) (35). Significantly lower incidence of venous thromboembolism and surgical site-infections in laparoscopic cases versus open cases was observed in a large administrative dataset–based study in USA (14, 15). National estimates for LC in USA showed an increase in LC from 52% in 1991 to 75% in 2000 with a constantly low mortality rate and a decrease in biliary reconstruction rate over time (16). On the basis of the 1997-2006 trend analysis by the same authors LC was associated with a low mortality rate (mean value in the period: 0.52%) while OC with a significantly higher rate (corresponding value: 4.9%) (9). In a retrospective study using Medicare beneficiaries common bile duct (CBD) injury during cholecystectomy was associated with a significant higher risk of death in comparison to cholecystectomy without CBD injury over a 9.2 year follow up period (17). From a Swiss 1995-2005 hospital database analysis the incidence rate of bile duct injury after LC was 0.3% and did not change over time (18). The incidence of conversion to OC after LC in all hospitals in England from 2005 to 2006 has been examined using Hospital Episode Statistics and resulted 4.6% for elective procedures and 9.4% for emergency procedures) (19).

Population-based linkage of routinely collected health data represents a precious tool to support large- scale and real-world practice evaluation by measuring specific outcomes and comparing them over time and across populations. Together with results from experimental research settings, the conclusions of research studies evaluating clinical outcomes through data linkage systems should be successfully incorporated into practice by clinicians/surgeons.

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**AUTHOR'S CONTRIBUTION**

All Authors participated in the study design, in defining the study protocol and methodology, in acquisition of data, in planning the analyses, in interpreting the results. M.S. performed the analyses. N.A and M.S. drafted the manuscript.

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**Figure 1.** Selection of the study population

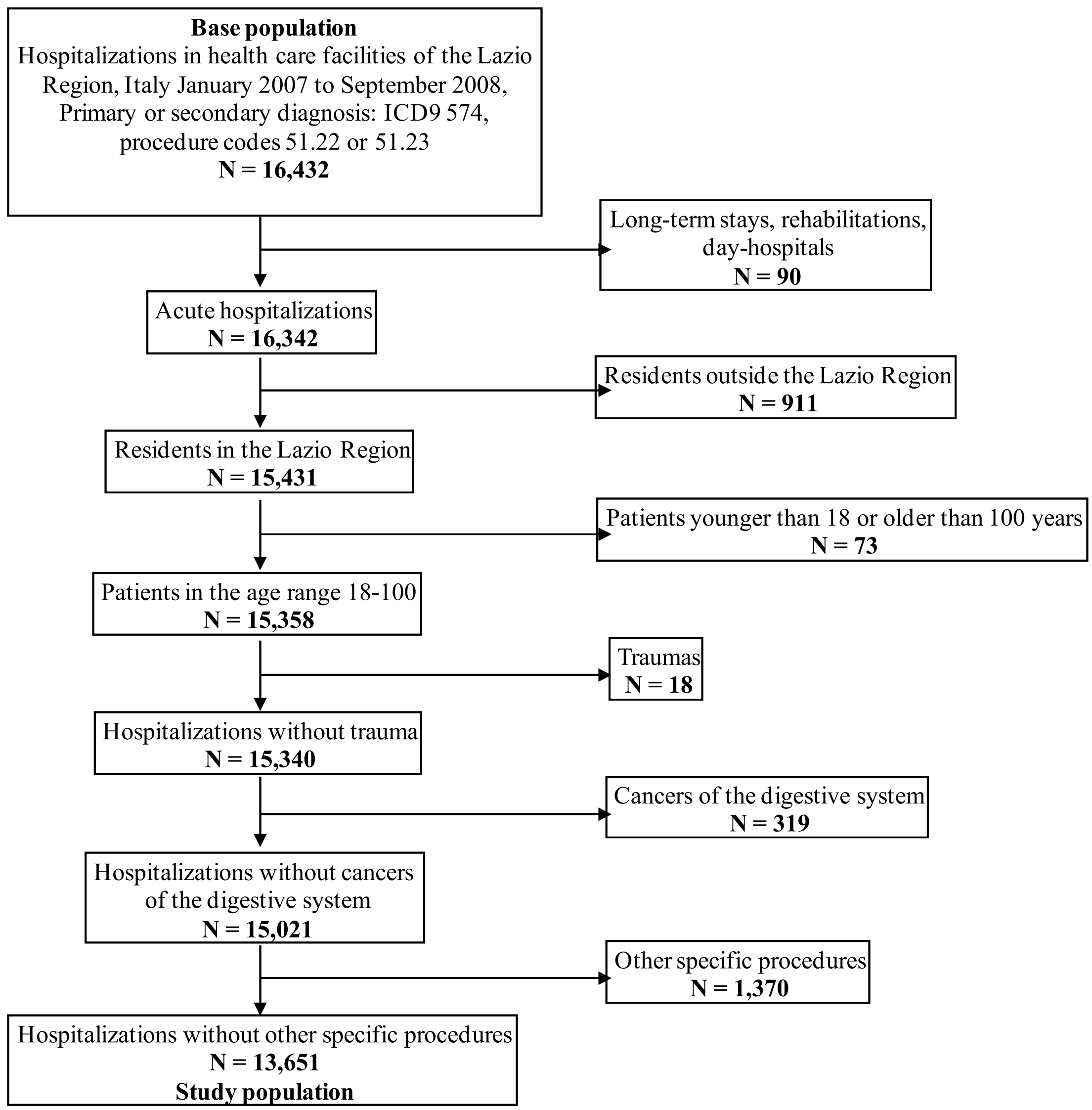

**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September 2008

| Patient characteristics | Laparoscopic cholecystectomy | | Open cholecystectomy | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| **Age (years)** | | | | | | |
| *<70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70-79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| | 11.752 | | | | | |
| **Gender** | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| **Severity of cholelitiasis** | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.456 | 54,9 | 1.200 | 63,2 | 7.656 | 56,1 |
| *High* | 529 | 4,5 | 229 | 12,1 | 758 | 5,6 |
| **Previous upper abdominal surgery** | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| **Tyoe od admission** | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| **Comorbidities** | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorders or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD* or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

*Chronic Obstructive Pulmonary Disease

**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | | | | | 30-day systemic complications (N=280, 2.1%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p |
| Age (years) | | | | | | | | | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *70 - 79* | 2,9 | 1,62 | 1,21 | 2,18 | 0,001 | 1,36 | 1,00 | 1,83 | 0,048 | 3,9 | 2,68 | 2,04 | 3,52 | 0,000 | 2,01 | 1,51 | 2,67 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 1,13 | 3,00 | 0,015 | 1,21 | 0,72 | 2,03 | 0,475 | 7,1 | 5,13 | 3,58 | 7,36 | 0,000 | 2,79 | 1,87 | 4,14 | 0,000 |
| Gender | | | | | | | | | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | - | - | 1,00 | - | - | - | 2,6 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Women* | 1,7 | 0,69 | 0,55 | 0,88 | 0,002 | 0,75 | 0,59 | 0,96 | 0,022 | 1,7 | 0,66 | 0,52 | 0,84 | 0,001 | 0,80 | 0,62 | 1,02 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | - | - | 1,00 | - | - | - | 1,2 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Moderate* | 2,0 | 1,08 | 0,84 | 1,40 | 0,538 | 0,96 | 0,74 | 1,24 | 0,733 | 2,2 | 1,84 | 1,38 | 2,46 | 0,000 | 1,55 | 1,15 | 2,08 | 0,004 |
| *High* | 3,7 | 2,03 | 1,32 | 3,14 | 0,001 | 1,43 | 0,91 | 2,24 | 0,122 | 6,2 | 5,30 | 3,59 | 7,83 | 0,000 | 3,40 | 2,26 | 5,11 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Yes* | 5,7 | 2,94 | 1,07 | 8,13 | 0,037 | 2,29 | 0,81 | 6,51 | 0,119 | 4,3 | 2,15 | 0,67 | 6,88 | 0,197 | 1,72 | 0,52 | 5,74 | 0,376 |
| Type of admission | | | | | | | | | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Emergency* | 3,0 | 1,85 | 1,45 | 2,35 | 0,000 | 1,66 | 1,29 | 2,13 | 0,000 | 3,4 | 2,34 | 1,85 | 2,97 | 0,000 | 1,64 | 1,27 | 2,11 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,64 | 2,64 | 0,476 | - | - | - | - | 3,6 | 1,81 | 0,98 | 3,34 | 0,059 | - | - | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,92 | 2,97 | 0,095 | - | - | - | - | 4,4 | 2,24 | 1,34 | 3,75 | 0,002 | - | - | - | - |
| *Obesity* | 5,0 | 2,57 | 1,19 | 5,55 | 0,016 | 2,35 | 1,29 | 2,13 | 0,034 | 4,3 | 2,16 | 0,95 | 4,94 | 0,067 | - | - | - | - |
| *Blood disease* | 5,8 | 3,03 | 1,67 | 5,50 | 0,000 | 2,09 | 1,11 | 3,93 | 0,022 | 7,7 | 4,16 | 2,46 | 7,03 | 0,000 | 1,96 | 1,09 | 3,51 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 1,00 | 2,13 | 0,050 | - | - | - | - | 4,0 | 2,20 | 1,58 | 3,05 | 0,000 | - | - | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,75 | 2,69 | 0,286 | - | - | - | - | 7,4 | 4,08 | 2,69 | 6,20 | 0,000 | 1,74 | 1,09 | 2,78 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,28 | 4,74 | 0,836 | - | - | - | - | 9,4 | 5,08 | 2,43 | 10,62 | 0,000 | - | - | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,27 | 4,57 | 0,875 | - | - | - | - | 4,6 | 2,29 | 0,83 | 6,29 | 0,107 | - | - | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,84 | 3,52 | 0,136 | - | - | - | - | 6,8 | 3,66 | 2,17 | 6,16 | 0,000 | - | - | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 1,21 | 3,62 | 0,008 | - | - | - | - | 7,0 | 3,81 | 2,47 | 5,88 | 0,000 | 1,73 | 1,07 | 2,79 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 1,76 | 5,54 | 0,000 | 1,98 | 1,09 | 3,60 | 0,025 | 7,7 | 4,19 | 2,52 | 6,98 | 0,000 | - | - | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,05 | 2,68 | 0,328 | - | - | - | - | 8,5 | 4,59 | 2,45 | 8,62 | 0,000 | - | - | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,60 | 2,72 | 0,534 | - | - | - | - | 7,7 | 4,22 | 2,66 | 6,70 | 0,000 | 2,02 | 1,23 | 3,31 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 2,82 | 10,00 | 0,000 | 3,24 | 1,65 | 6,36 | 0,001 | 10,5 | 5,82 | 3,16 | 10,72 | 0,000 | 2,27 | 1,15 | 4,46 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,92 | 3,33 | 0,087 | - | - | - | - | 4,8 | 2,51 | 1,45 | 4,35 | 0,001 | 1,97 | 1,11 | 3,48 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission; p value of heterogeneity of the strata-specific estimates - Lazio Region, Italy, January 2007 - September 2008

| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | $p_{het}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 30-day surgical-related complications: N=278, %=2.0 | | | | | | | | | | |
| Open cholecystectomy | 3,9 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,33 | 0,57 | 0,000 | 0,60 | 0,44 | 0,80 | 0,001 | - |
| Age (years) | | | | | | | | | | 0,917 |
| *< 70* | 1,8 | 0,49 | 0,35 | 0,71 | 0,000 | 0,62 | 0,43 | 0,90 | 0,012 | - |
| *70 - 79* | 2,9 | 0,45 | 0,26 | 0,76 | 0,003 | 0,57 | 0,33 | 0,98 | 0,043 | - |
| *≥ 80* | 3,3 | 0,41 | 0,15 | 1,12 | 0,082 | 0,51 | 0,18 | 1,38 | 0,184 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,053 |
| *Low* | 1,9 | 0,37 | 0,22 | 0,61 | 0,000 | 0,46 | 0,28 | 0,77 | 0,003 | - |
| *Moderate* | 2,0 | 0,58 | 0,40 | 0,85 | 0,005 | 0,78 | 0,53 | 1,16 | 0,224 | - |
| *High* | 3,7 | 0,24 | 0,11 | 0,53 | 0,000 | 0,30 | 0,13 | 0,68 | 0,004 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,654 |
| *No* | 2,0 | 0,45 | 0,34 | 0,59 | 0,000 | 0,60 | 0,44 | 0,81 | 0,001 | - |
| *Yes* | 5,7 | 0,26 | 0,03 | 2,64 | 0,256 | 0,36 | 0,03 | 3,69 | 0,388 | - |
| Type of admission | | | | | | | | | | 0,001 |
| *Elective* | 1,6 | 0,32 | 0,22 | 0,46 | 0,000 | 0,37 | 0,25 | 0,55 | 0,000 | - |
| *Emergency* | 3,0 | 0,76 | 0,51 | 1,13 | 0,178 | 0,94 | 0,62 | 1,42 | 0,764 | - |
| 30-day systemic complications: N=280, %=2.1 | | | | | | | | | | |
| Open cholecystectomy | 5,2 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,6 | 0,29 | 0,23 | 0,37 | 0,000 | 0,52 | 0,40 | 0,69 | 0,000 | - |
| Age (years) | | | | | | | | | | 0,136 |
| *< 70* | 1,5 | 0,34 | 0,24 | 0,49 | 0,000 | 0,47 | 0,32 | 0,68 | 0,000 | - |
| *70 - 79* | 3,9 | 0,35 | 0,22 | 0,55 | 0,000 | 0,47 | 0,29 | 0,75 | 0,002 | - |
| *≥ 80* | 7,1 | 0,71 | 0,37 | 1,37 | 0,309 | 0,99 | 0,50 | 1,94 | 0,975 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,755 |
| *Low* | 1,2 | 0,29 | 0,16 | 0,51 | 0,000 | 0,43 | 0,24 | 0,77 | 0,005 | - |
| *Moderate* | 2,2 | 0,34 | 0,25 | 0,47 | 0,000 | 0,55 | 0,39 | 0,77 | 0,001 | - |
| *High* | 6,2 | 0,38 | 0,21 | 0,70 | 0,002 | 0,56 | 0,30 | 1,05 | 0,071 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,702 |
| *No* | 2,0 | 0,29 | 0,22 | 0,37 | 0,000 | 0,52 | 0,39 | 0,69 | 0,000 | - |
| *Yes* | 4,3 | 0,41 | 0,04 | 4,69 | 0,470 | 0,86 | 0,07 | 10,40 | 0,905 | - |
| Type of admission | | | | | | | | | | 0,545 |
| *Elective* | 1,5 | 0,33 | 0,23 | 0,50 | 0,000 | 0,48 | 0,32 | 0,72 | 0,000 | - |
| *Emergency* | 3,4 | 0,35 | 0,25 | 0,49 | 0,000 | 0,56 | 0,39 | 0,81 | 0,002 | - |

[c] There are no 30-day complications in patients with moderately high severity and undergoing laparotomic cholecystectomy

1

**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**

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Field Code Changed

**Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy.**


**Abstract**

**Objective**

The objective of the study is to evaluate short-term complications after laparoscopic (LC) or open cholecystectomy (OC) in patients with gallstones by using linked hospital discharge data.

**Design**

Population-based cohort study.

**Setting**

Data were obtained from the Regional Hospital Discharge Registry Lazio Region in Central Italy (around 5 million inhabitants) in 2007-2008.

**Participants**

All patients admitted to hospitals of Lazio with symptomatic gallstones (ICD9-CM = 574) who underwent LC (ICD9-CM 51.23) or OC (ICD9-CM 51.22).

**Outcome measures**

1)"*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events).

**Results**

13,651 patients were included; 86.1% had LC, 13.9% OC. 2.0% experienced surgical-related complications (SRC), 2.1% systemic complications (SC). The Odds Ratio (OR) of complications after LC versus OC was 0.60 (p<0.001) for SRC and 0.52 (p<0.001) for SC. As regards SRC, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission (OR=0.94, p = 0.764). For SC, no significant advantage of LC was seen among very old people (OR=0.99, p=0.975) and among those with previous upper abdominal surgery (OR=0.86, p=0.905).

**Conclusions**

This large observational study confirms that LC is more effective than OC with respect to 30-day complications. Population-based linkage of administrative datasets can enlarge evidence of treatment benefits in clinical practice.

**Key words:** administrative data, cohort study, effectiveness, gallstones, hospital discharge data, laparoscopic cholecystectomy, open cholecystectomy, outcomes, population-based, post-operative complications.

## Article summary

### Article focus

-The advantage of laparoscopic cholecystectomy (LC) approach for the treatment of gallstone versus open surgery (OC) has been shown from RCTs and observational studies.

-The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments.

-We compared laparoscopic and open cholecystectomy in term of 30-day complications using routinely collected databases in Lazio Region (Italy).

### Key messages

-This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting.

-As regards surgical-related complications, the advantage of LC was consistent across age categories, severity of gallstones and previous upper abdominal surgery, while there was no advantage among people with emergency admission.

-For systemic complications, no significant advantage of LC was seen among very old people and among those with previous upper abdominal surgery.

### Strengths and limitations

-Population-based design, 30-day outcomes, large numbers and robustness of analytic procedures are the main strengths.

-It contributes to the debate on the complex methodology to estimated risk of adverse events after surgery using secondary databases to monitor quality of care.

-The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is a major limit.

**Introduction**

Comparative effectiveness research is becoming central to monitor real-life impact of treatments and support public health decisions (1, 2). Although the basic concept of comparing therapies is not new, over the last few years many initiatives have been implemented in several countries to provide large-scale evidence on benefits and harms of different treatments (3-5). The use of linked administrative health records has become one of the most powerful tools in observational studies aimed at comparing treatments. They include hospital in-patients records, birth and death registrations, outpatient care records, dispensed pharmacy drugs (6-9).

In the Lazio Region (around 5.000.000 inhabitants) the P.Re.Val.E. Project (*Regional Program for Assessing the Outcomes of Health-care Interventions*) was launched in 2005. Its aims are: to measure the quality of health care provided in the Lazio Region, to describe variability of care provision across institutions and populations and to compare effectiveness of treatments for different medical and surgical conditions (10,11). Over 60 outcomes indicators are calculated based on data obtained from record-linkage procedures of different health systems. The results are periodically updated and publicly disseminated with discussion on critical methodological points.

Cholecystectomy is one of the most common abdominal surgical procedures in developed countries. Since its introduction in the late '80s, laparoscopic cholecystectomy (LC) has replaced open cholecystectomy (OC) as the treatment of choice for symptomatic gallstones (12, 13). Beneficial effects of LC have been demonstrated in studies showing the advantages from real-life settings using secondary databases (9,14-19). In the present study we aimed at developing a methodology to measure short-term complications after LC or OC using large administrative databases on behalf of the P.Re.Val.E. Secondly, we tested the hypothesis that

the advantages of LC versus OC could vary according to age and clinical patients' characteristics.

**Methods**

Source of data

Data was derived from the Lazio Hospital Information System (HIS), which provides information on patients' demographic data (gender, age, place of birth, place of residence), admission and discharge dates, discharge diagnoses (up to 6) and medical procedures or surgical interventions ((up to 6) according to the International Classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM), status at discharge (alive, dead, transferred to another hospital), ward(s) of stay, date(s) of in-hospital transfer, and a regional code corresponding to the admitting facility for patients discharged from all public and private hospital of the Lazio Region (5.759.839 inhabitants).

Study population

All hospital admissions with a primary or secondary diagnosis of gallstones (International Classification of Diseases 9$^{th}$ Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of cholecystectomy (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases (age 18+ years). We a priori decided not to include codes for partial cholecystectomy (ICD-9-CM 51.21 and 51.24) to increase the specificity of our exposure. Information was retrieved from the HIS. In order to increase the case specificity, several exclusion criteria were applied including long-term hospitalizations, rehabilitations, day-hospitals, hospitalizations for delivery or trauma or cancer, hospitalizations with abdominal surgical procedures other than cholecystectomy. The final population consisted of 13,651 subjects (**Figure 1).** See the online **Supplementary Data** (Part 1) for details on the exclusion criteria and ICD9-CM codes. According to the Regional Law, the present study, which was based on anonymous computer records from health information systems, did not require for ethical approval.

Patient-level risk factors

The following characteristics were considered for each patient: Age (<70; 70-79; >=80 years old); Gender; Severity of gallstones: it was classified as *low* (not-complicated), *moderate* (presence of cholecystitis or biliary tract obstruction), and *high* (presence of both inflammation and obstruction of the biliary tract); Previous upper abdominal surgery (based on previous 2-year hospitalizations); Comorbidities (based on previous 2-year hospitalizations) following validated algorithms (20,21); Type of admission: either *elective* or *emergency*. See the online **Supplementary Data** (Part 2-4) for details on the ICD-9-CM codes. The choice of *cut off* for age category was based on previous studies to distinguish adult and old people (22-24).

Outcomes

We identified various complications within 30-days after the intervention and grouped them in two categories: 1) "*30-day surgical-related complications*" defined as any complication of the biliary tract (including post-operative infection, hemorrhage or hematoma or seroma complicating a procedure, persistent postoperative fistula, perforation of bile duct, disruption of wound (); 2) "*30-day systemic complications*" defined as any complications of other organs (including sepsis, infections from other organs, major cardiovascular events and selected adverse events). The complete list of complications with ICD-9-CM codes is reported in the online **Supplementary Data** (Part 5). Among the various complications we included some conditions reported in the list of Patient Safety Indicators recently developed by the Agency for Health Care Research and Quality, while other items were specifically created on the basis of scientific literature on digestive surgery (14-19,25,26). Depending on the type of complication, some ICD9-CM codes were searched in both the index admission and the following ones in the 30-day period after the surgery, others were searched only in later hospitalizations. For example, peritonitis or acute pancreatitis was not counted as complications when reported in the index admission. See the online **Supplementary Data** (Part 5) for details on the ICD9-CM codes. In the case of a subsequent hospitalization occurred out of the study area (for example, in a region other than Lazio), we obtained information through record linkage procedure between hospital information systems. Because of the short follow up time, this happened in a minimal proportion of cases (0.1%). The outcome variables were: "*30-day surgical-related complications*" and "*30-day systemic complications*"; they were coded "1" if at least one of the complications within the group was present and "0" if none was recorded.

Type of cholecystectomy

As exposure variable we defined "*type of cholecystectomy*" (laparoscopic cholecystectomy, LC vs. open cholecystectomy, OC). In the case of ICD-9-CM codes for both LC and OC (5%), the patient was considered exposed to the open surgical procedure. We could not use the specific ICD-9-code for a case converted from LC to OC (ICD-9-CM code V 64.41) because it was highly under-reported in our Region in the study period.

Statistical analysis

Multiple logistic regression models were fitted to estimate the relative risk of 30-day complications (either "surgical-related" or "systemic") after LC versus OC, adjusting for demographical and clinical risk factors. The two outcome variables were analysed separately. The predictive model was made of two sets of predictors: 1) variables "a priori" chosen as confounders (age, gender, severity of gallstones, previous upper abdominal surgery, and type of admission); 2) variables empirically tested (comorbidities) which were selected using iterative stepwise statistical procedures) (27). Once the "best" predictive model was identified for each of the two outcome, the variable "*type of cholecystectomy*" was included, and the adjusted odds ratio (OR) of LC versus open surgery was estimated, with corresponding 95% confidence interval (95% CI) and p-value.

In order to test the hypothesis of an effect modification by age, relative risk estimates for the age groups were derived by adding an interaction term between the age group and the treatment variable in the final multivariate logistic model. We obtained the OR of laparoscopic vs. open surgery within each age stratum by adding the corresponding interaction terms coefficients. This was accomplished by adding the coefficient from the reference category and that from the age stratum of interest, and by computing the corresponding standard error from the corresponding terms of the variance-covariance matrix. Similarly, effect modification was tested with regard to severity of cholelithiasis, previous upper abdominal surgery and type of admission. The corresponding tests of heterogeneity of the stratum-specific risk estimates were computed.

Sensitivity analyses were performed. First, in order to guarantee adequate control of confounding factors we identified and adjusted for all the individual factors associated with the treatment, within the propensity adjustment framework (28). This procedure is a two-step technique: 1. it estimates the a priori probability of exposure for each subject, based on clinical and demographic characteristics; 2. it standardizes for them in the association between treatment and the study outcome. The individual factors related to the exposure in the present study include age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, cardio-circulatory disease, cerebrovascular disease, COPD or respiratory failure, chronic nephropathy, chronic disease of the liver or pancreas. Second, to take into account the potential heterogeneous experience in laparoscopic surgery across different hospitals because of the patients' clustering within a single institution we perform a multilevel regression model with random intercepts for hospitals (29).

All the statistical analyses were performed using SAS Software version 8.0 (SAS Institute, Inc. SAS/STAT software).

**Results**

A description of the study population, overall and by cholecystectomy procedure, is presented in **Table 1**. Over 80% of the patients were younger than 70 years, and moderate to high severity of the gallstones was diagnosed for 61.7%. As compared with patients undergoing LC, those who underwent OC were more likely to be elderly, males, with a more sever baseline disease and more chronic conditions. Furthermore, they were operated in emergency in most of the cases (52.4%), whereas LC was performed in elective hospitalizations much more frequently (73.9%).

**Table 2** reports the relationship between demographic and clinical variables and the occurrence of complications. The adjusted risk of systemic complications increased with age and was much higher in patients with more severe baseline gallstones, whereas no clear age or severity-related differences in risk emerged with regard to surgical-related 30-day complications, once other co-factors were taken into account. Women were less likely to experience both types of complications. Having had a previous intervention on the upper digestive system seemed to enhance the risk of both surgical-related and systemic complications, though results are not statistically significant due to small power. Finally, the risk of both types of complications was more evident in emergency as opposed to scheduled interventions. Surgical-related complications were higher among subjects with obesity, blood disease, stroke or chronic nephropathy, whereas systemic complications were associated with blood diseases, ischemic heart disease, conduction disorders or dysrhythmias, COPD or respiratory failure, chronic nephropathy, and chronic diseases of the liver or pancreas.

**Table 3** shows the relationship between type of cholecystectomy and outcomes, adjusted for the risk factors identified in Table 2. We report results of the advantage of LC vs. OC (OR, 95% CI) in the cohort and in the each stratum of the variables tested in the models with interaction terms. The incidence of "30-day surgical-related complications" and "30-day systemic complications" was 2.0% and 2.1%, respectively. The odds ratio of surgical related complications for patients who underwent LC as compared to patients with OC was 0.60 ($p<0.001$). The corresponding figure for systemic complications was 0.52 ($p<0.001$).

As regards 30-day surgical-related complications, the protective effect of LC vs. OC was consistent across the age category, severity of cholelithiasis and previous upper abdominal surgery, while among people with emergency admission there was no advantage (OR=0.94 p = 0.764). Similarly, for systemic complications, the superiority of LC vs. OC was consistent regardless level of cholelithiasis severity, and elective/emergency admission, but for those 80+ yrs aged people there was no advantage of LC vs. OC (OR 0.99, p = 0.975); also for patients with previous upper abdominal surgery there was a much weaker advantage (OR=0.86, p=0.905).

When the association between type of cholecystectomy and 30-day complications was adjusted with the propensity adjustment method, results were consistent with those obtained with the risk-adjustment procedure (LC vs. OC OR= 0.61 and OR=0.52 respectively for the two outcomes). Finally, results were similar taking into account patients' clustering within different hospitals (*data not shown*).

**Discussion**

From this large observational study based on linked administrative health records - taking into account the disomogeneous distribution of factors related to the probability to be offered open surgery - people who end up having a LC have a better short-term prognosis than those that get an OC for the treatment of gallstones. The superiority of laparoscopic approach in term of 30-day complications is consistent in different age categories, different severity in disease presentation and past history of upper abdominal surgery.

This population-based study contributes to enlarge the evidence on effectiveness of LC in a real-life setting by providing an example from the Southern Europe area. It supports the usefulness of observational approaches. The 30-day outcomes linked to admission represent one strength of this study. Despite RTCs are considered the optimal study design when comparing efficacy of treatments, observational studies provide a picture of treatment under usual circumstances of health-care practice and can answer to the question ''*Does it work in practice*?" (3,8). RTCs often have small sample size and may under represent vulnerable patient groups, including elderly patients with multiple comorbidities, children, and young women, and operate in a highly controlled environment that is far from routine clinical practice. Our study supports that LC is a reliable approach safer than OC not only in old age group - confirming previous findings (22, 30) - but also in presence of severe disease presentation and in patients with past history of upper digestive system surgery. Beneficial effect of LC as regards systemic complications tends to be lower in 80+ yrs aged in comparison with younger ages, and in patients with emergency admission in comparison to elective admissions as regards 30-day surgical-related complications. These data add to the evidence on the complex relationship between age and outcomes after surgery (22-24,30).

A number of potential biases are present. First of all, people in the two groups of patients analyzed are not homogenous in term of ~~with a higher~~ anesthesia risk due to higher frequency of elderly and more comorbidities ~~severe patients~~ in the open group ~~in the open group~~ than~~t~~ in the laparoscopic one. When comparing the effect of the two techniques using two different populations, the so called "indication bias" may affect study validity (8,31). To limit this problem we run the propensity adjustment analysis to take into account the different distribution of factors strongly associated with the probability to receive open surgery in the study population. This analytical approach confirmed the advantage of laparoscopic vs. open surgery obtained in the main logistic regression analysis. Another critical point is the potential different distribution of laparoscopic experience across surgeons; however a sensitivity analysis which took into account this point led to similar results. The use of ICD-9-CM codes in the definition of severity of disease presentation and of complications is another major limit. Discharge abstract data have little insight into clinical details and do not inform on the temporal relationship of the clinical conditions and processes, then defining complications is a difficult task (32). In this respect, we tried to improve the accuracy of our measures both 1) applying a specific coding algorithm with subsequent hospital admissions used to retrieve adverse events and 2) excluding in the "count" of complications specific items if reported in the index only (i.e. peritonitis) because of the difficulty to determine if it was already present at admission. Moreover, we cannot exclude an under-notification of complications – a major limit of our source of data - but it is unlikely that is influenced by the type of surgery. Another major problem is the potential misclassification of exposure since we were not able to measure the occurrence of conversion of LC to OC. The number of people that were switched from LC to OP is low in comparison to figures documented in other studies and it may represent a severe source of bias in our study (30,33).

Beneficial effects of the laparoscopic approach versus traditional open surgery for the treatment of gallstones come from various randomized controlled trials (RCTs) (34). They found significant shorter hospital stay and quicker convalescence associated with LC but no differences in mortality, complications and operative time between the two procedures. A better trend with the laparoscopic approach, including morbidity and mortality, comes from observational studies. From a surveillance system in eight Swiss hospitals, surgical site infections were less common in laparoscopic approach in comparison to traditional open surgery (0.5% in LC vs. 1.8% in OC) (35). Significantly lower incidence of venous thromboembolism and surgical site-infections in laparoscopic cases versus open cases was observed in a large administrative dataset–based study in USA (14, 15). National estimates for LC in USA showed an increase in LC from 52% in 1991 to 75% in 2000 with a constantly low mortality rate and a decrease in biliary reconstruction rate over time (16). On the basis of the 1997-2006 trend analysis by the same authors LC was associated with a low mortality rate (mean value in the period: 0.52%) while OC with a significantly higher rate (corresponding value: 4.9%) (9). In a retrospective study using Medicare beneficiaries common bile duct (CBD) injury during cholecystectomy was associated with a significant higher risk of death in comparison to cholecystectomy without CBD injury over a 9.2 year follow up period (17). From a Swiss 1995-2005 hospital database analysis the incidence rate of bile duct injury after LC was 0.3% and did not change over time (18). The incidence of conversion to OC after LC in all hospitals in England from 2005 to 2006 has been examined using Hospital Episode Statistics and resulted 4.6% for elective procedures and 9.4% for emergency procedures) (19).

Population-based linkage of routinely collected health data represents a precious tool to support large- scale and real-world practice evaluation by measuring specific outcomes and comparing them over time and across populations. Together with results from experimental research settings, the conclusions of research studies evaluating clinical outcomes through data linkage systems should be successfully incorporated into practice by clinicians/surgeons.

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**AUTHOR'S CONTRIBUTION**

All Authors participated in the study design, in defining the study protocol and methodology, in acquisition of data, in planning the analyses, in interpreting the results. M.S. performed the analyses. N.A and M.S. drafted the manuscript.

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**Figure 1.** Selection of the study population

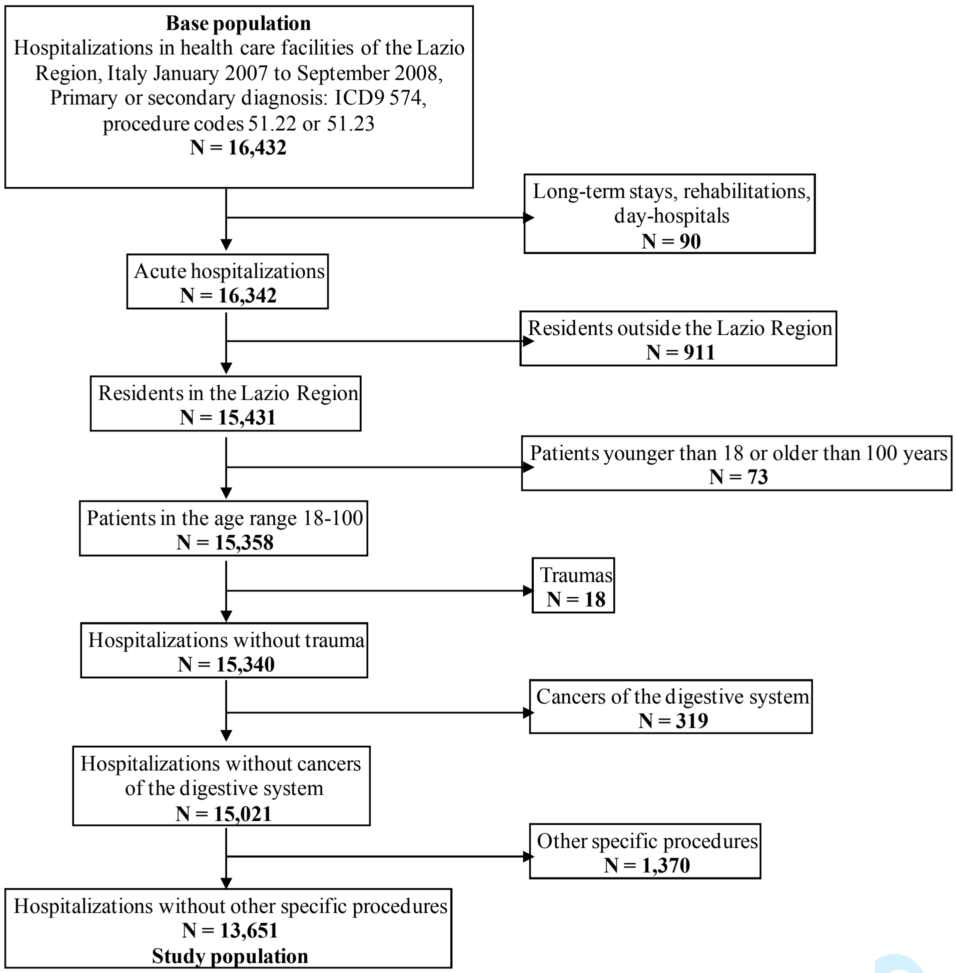


**Table 1.** Study population, overall and by cholecystectomy procedure: distribution by age, gender, severity of cholelitiasis, previous upper abdominal surgery, type of admission, comorbidities - Lazio Region, Italy, January 2007-September 2008

| Patient characteristics | Laparoscopic cholecystectomy | | Open cholecystectomy | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| **Total** | **11.752** | **86,1** | **1.899** | **13,9** | **13.651** | **100,0** |
| **Age (years)** | | | | | | |
| *<70* | 9.913 | 84,4 | 1.162 | 61,2 | 11.075 | 81,1 |
| *70-79* | 1.543 | 13,1 | 485 | 25,5 | 2.028 | 14,9 |
| *≥ 80* | 296 | 2,5 | 252 | 13,3 | 548 | 4,0 |
| | 11.752 | | | | | |
| **Gender** | | | | | | |
| *Men* | 4.349 | 37,0 | 979 | 51,6 | 5.328 | 39,0 |
| *Women* | 7.403 | 63,0 | 920 | 48,4 | 8.323 | 61,0 |
| **Severity of cholelitiasis** | | | | | | |
| *Low* | 4.767 | 40,6 | 470 | 24,7 | 5.237 | 38,4 |
| *Moderate* | 6.456 | 54,9 | 1.200 | 63,2 | 7.656 | 56,1 |
| *High* | 529 | 4,5 | 229 | 12,1 | 758 | 5,6 |
| **Previous upper abdominal surgery** | | | | | | |
| *No* | 11.714 | 99,7 | 1.867 | 98,3 | 13.581 | 99,5 |
| *Yes* | 38 | 0,3 | 32 | 1,7 | 70 | 0,5 |
| **Tyoe od admission** | | | | | | |
| *Elective* | 8.690 | 73,9 | 903 | 47,6 | 9.593 | 70,3 |
| *Emergency* | 3.062 | 26,1 | 996 | 52,4 | 4.058 | 29,7 |
| **Comorbidities** | | | | | | |
| *Cancer* | 232 | 2,0 | 75 | 3,9 | 307 | 2,2 |
| *Diabetes* | 268 | 2,3 | 100 | 5,3 | 368 | 2,7 |
| *Obesity* | 115 | 1,0 | 25 | 1,3 | 140 | 1,0 |
| *Blood disease* | 146 | 1,2 | 62 | 3,3 | 208 | 1,5 |
| *Hypertension* | 842 | 7,2 | 247 | 13,0 | 1.089 | 8,0 |
| *Ischemic heart disease* | 246 | 2,1 | 107 | 5,6 | 353 | 2,6 |
| *Past coronary revascularization* | 63 | 0,5 | 22 | 1,2 | 85 | 0,6 |
| *Heart failure* | 47 | 0,4 | 41 | 2,2 | 88 | 0,6 |
| *Other heart disease* | 158 | 1,3 | 76 | 4,0 | 234 | 1,7 |
| *Conduction disorders or dysrhythmia* | 250 | 2,1 | 95 | 5,0 | 345 | 2,5 |
| *Cerebrovascular disease* | 146 | 1,2 | 74 | 3,9 | 220 | 1,6 |
| *Vascular disease* | 91 | 0,8 | 38 | 2,0 | 129 | 0,9 |
| *COPD* or respiratory failure* | 189 | 1,6 | 84 | 4,4 | 273 | 2,0 |
| *Chronic nephropathy* | 68 | 0,6 | 46 | 2,4 | 114 | 0,8 |
| *Chronic disease of the liver or pancreas* | 219 | 1,9 | 70 | 3,7 | 289 | 2,1 |

*Chronic Obstructive Pulmonary Disease

**Table 2. Factors related to the incidence of 30-day complications after cholecystectomy. OR crude and adjusted, p-values - Lazio Region, Italy, January 2007-September2008 (N = 13,651)**

| Patient characteristics | 30-day surgical-related complications (N=278, 2.0%) | | | | | | | | | 30-day systemic complications (N=280, 2.1%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p |
| Age (years) | | | | | | | | | | | | | | | | | | |
| *< 70* | 1,8 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *70 - 79* | 2,9 | 1,62 | 1,21 | 2,18 | 0,001 | 1,36 | 1,00 | 1,83 | 0,048 | 3,9 | 2,68 | 2,04 | 3,52 | 0,000 | 2,01 | 1,51 | 2,67 | 0,000 |
| *≥ 80* | 3,3 | 1,84 | 1,13 | 3,00 | 0,015 | 1,21 | 0,72 | 2,03 | 0,475 | 7,1 | 5,13 | 3,58 | 7,36 | 0,000 | 2,79 | 1,87 | 4,14 | 0,000 |
| Gender | | | | | | | | | | | | | | | | | | |
| *Men* | 2,5 | 1,00 | - | - | - | 1,00 | - | - | - | 2,6 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Women* | 1,7 | 0,69 | 0,55 | 0,88 | 0,002 | 0,75 | 0,59 | 0,96 | 0,022 | 1,7 | 0,66 | 0,52 | 0,84 | 0,001 | 0,80 | 0,62 | 1,02 | 0,070 |
| Severity of cholelithiasis | | | | | | | | | | | | | | | | | | |
| *Low* | 1,9 | 1,00 | - | - | - | 1,00 | - | - | - | 1,2 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Moderate* | 2,0 | 1,08 | 0,84 | 1,40 | 0,538 | 0,96 | 0,74 | 1,24 | 0,733 | 2,2 | 1,84 | 1,38 | 2,46 | 0,000 | 1,55 | 1,15 | 2,08 | 0,004 |
| *High* | 3,7 | 2,03 | 1,32 | 3,14 | 0,001 | 1,43 | 0,91 | 2,24 | 0,122 | 6,2 | 5,30 | 3,59 | 7,83 | 0,000 | 3,40 | 2,26 | 5,11 | 0,000 |
| Previous upper abdominal surgery | | | | | | | | | | | | | | | | | | |
| *No* | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - | 2,0 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Yes* | 5,7 | 2,94 | 1,07 | 8,13 | 0,037 | 2,29 | 0,81 | 6,51 | 0,119 | 4,3 | 2,15 | 0,67 | 6,88 | 0,197 | 1,72 | 0,52 | 5,74 | 0,376 |
| Type of admission | | | | | | | | | | | | | | | | | | |
| *Elective* | 1,6 | 1,00 | - | - | - | 1,00 | - | - | - | 1,5 | 1,00 | - | - | - | 1,00 | - | - | - |
| *Emergency* | 3,0 | 1,85 | 1,45 | 2,35 | 0,000 | 1,66 | 1,29 | 2,13 | 0,000 | 3,4 | 2,34 | 1,85 | 2,97 | 0,000 | 1,64 | 1,27 | 2,11 | 0,000 |
| Comorbidities (presence of the condition) | | | | | | | | | | | | | | | | | | |
| *Cancer* | 2,6 | 1,30 | 0,64 | 2,64 | 0,476 | - | - | - | - | 3,6 | 1,81 | 0,98 | 3,34 | 0,059 | - | - | - | - |
| *Diabetes* | 3,3 | 1,65 | 0,92 | 2,97 | 0,095 | - | - | - | - | 4,4 | 2,24 | 1,34 | 3,75 | 0,002 | - | - | - | - |
| *Obesity* | 5,0 | 2,57 | 1,19 | 5,55 | 0,016 | 2,35 | 1,29 | 2,13 | 0,034 | 4,3 | 2,16 | 0,95 | 4,94 | 0,067 | - | - | - | - |
| *Blood disease* | 5,8 | 3,03 | 1,67 | 5,50 | 0,000 | 2,09 | 1,11 | 3,93 | 0,022 | 7,7 | 4,16 | 2,46 | 7,03 | 0,000 | 1,96 | 1,09 | 3,51 | 0,024 |
| *Hypertension* | 2,9 | 1,46 | 1,00 | 2,13 | 0,050 | - | - | - | - | 4,0 | 2,20 | 1,58 | 3,05 | 0,000 | - | - | - | - |
| *Ischemic heart disease* | 2,8 | 1,42 | 0,75 | 2,69 | 0,286 | - | - | - | - | 7,4 | 4,08 | 2,69 | 6,20 | 0,000 | 1,74 | 1,09 | 2,78 | 0,020 |
| *Past coronary revascularization* | 2,4 | 1,16 | 0,28 | 4,74 | 0,836 | - | - | - | - | 9,4 | 5,08 | 2,43 | 10,62 | 0,000 | - | - | - | - |
| *Heart failure* | 2,3 | 1,12 | 0,27 | 4,57 | 0,875 | - | - | - | - | 4,6 | 2,29 | 0,83 | 6,29 | 0,107 | - | - | - | - |
| *Other heart disease* | 3,4 | 1,72 | 0,84 | 3,52 | 0,136 | - | - | - | - | 6,8 | 3,66 | 2,17 | 6,16 | 0,000 | - | - | - | - |
| *Conduction disorder or dysrhythmia* | 4,1 | 2,09 | 1,21 | 3,62 | 0,008 | - | - | - | - | 7,0 | 3,81 | 2,47 | 5,88 | 0,000 | 1,73 | 1,07 | 2,79 | 0,025 |
| *Cerebrovascular disease* | 5,9 | 3,12 | 1,76 | 5,54 | 0,000 | 1,98 | 1,09 | 3,60 | 0,025 | 7,7 | 4,19 | 2,52 | 6,98 | 0,000 | - | - | - | - |
| *Vascular disease* | 0,8 | 0,37 | 0,05 | 2,68 | 0,328 | - | - | - | - | 8,5 | 4,59 | 2,45 | 8,62 | 0,000 | - | - | - | - |
| *COPD or respiratory failure* | 2,6 | 1,27 | 0,60 | 2,72 | 0,534 | - | - | - | - | 7,7 | 4,22 | 2,66 | 6,70 | 0,000 | 2,02 | 1,23 | 3,31 | 0,006 |
| *Chronic nephropathy* | 9,7 | 5,31 | 2,82 | 10,00 | 0,000 | 3,24 | 1,65 | 6,36 | 0,001 | 10,5 | 5,82 | 3,16 | 10,72 | 0,000 | 2,27 | 1,15 | 4,46 | 0,018 |
| *Chronic disease of the liver or pancreas* | 3,5 | 1,75 | 0,92 | 3,33 | 0,087 | - | - | - | - | 4,8 | 2,51 | 1,45 | 4,35 | 0,001 | 1,97 | 1,11 | 3,48 | 0,020 |

**Table 3.** Association between type of cholecystectomy and 30-day complications: OR and p-values from crude model, risk-adjusted model, and models with interaction with age group, severity of cholelithiasis, previous upper abdominal surgery and type of admission; p value of heterogeneity of the strata-specific estimates - Lazio Region, Italy, January 2007 - September 2008

| | % | $OR_{crude}$ | 95% CI | | p | $OR_{adj}$ | 95% CI | | p | $p_{het}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 30-day surgical-related complications: N=278, %=2.0 | | | | | | | | | | |
| Open cholecystectomy | 3,9 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,7 | 0,44 | 0,33 | 0,57 | 0,000 | 0,60 | 0,44 | 0,80 | 0,001 | - |
| Age (years) | | | | | | | | | | 0,917 |
| *< 70* | 1,8 | 0,49 | 0,35 | 0,71 | 0,000 | 0,62 | 0,43 | 0,90 | 0,012 | - |
| *70 - 79* | 2,9 | 0,45 | 0,26 | 0,76 | 0,003 | 0,57 | 0,33 | 0,98 | 0,043 | - |
| *≥ 80* | 3,3 | 0,41 | 0,15 | 1,12 | 0,082 | 0,51 | 0,18 | 1,38 | 0,184 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,053 |
| *Low* | 1,9 | 0,37 | 0,22 | 0,61 | 0,000 | 0,46 | 0,28 | 0,77 | 0,003 | - |
| *Moderate* | 2,0 | 0,58 | 0,40 | 0,85 | 0,005 | 0,78 | 0,53 | 1,16 | 0,224 | - |
| *High* | 3,7 | 0,24 | 0,11 | 0,53 | 0,000 | 0,30 | 0,13 | 0,68 | 0,004 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,654 |
| *No* | 2,0 | 0,45 | 0,34 | 0,59 | 0,000 | 0,60 | 0,44 | 0,81 | 0,001 | - |
| *Yes* | 5,7 | 0,26 | 0,03 | 2,64 | 0,256 | 0,36 | 0,03 | 3,69 | 0,388 | - |
| Type of admission | | | | | | | | | | 0,001 |
| *Elective* | 1,6 | 0,32 | 0,22 | 0,46 | 0,000 | 0,37 | 0,25 | 0,55 | 0,000 | - |
| *Emergency* | 3,0 | 0,76 | 0,51 | 1,13 | 0,178 | 0,94 | 0,62 | 1,42 | 0,764 | - |
| 30-day systemic complications: N=280, %=2.1 | | | | | | | | | | |
| Open cholecystectomy | 5,2 | 1,00 | - | - | - | 1,00 | - | - | - | - |
| Laparoscopic cholecystectomy | 1,6 | 0,29 | 0,23 | 0,37 | 0,000 | 0,52 | 0,40 | 0,69 | 0,000 | - |
| Age (years) | | | | | | | | | | 0,136 |
| *< 70* | 1,5 | 0,34 | 0,24 | 0,49 | 0,000 | 0,47 | 0,32 | 0,68 | 0,000 | - |
| *70 - 79* | 3,9 | 0,35 | 0,22 | 0,55 | 0,000 | 0,47 | 0,29 | 0,75 | 0,002 | - |
| *≥ 80* | 7,1 | 0,71 | 0,37 | 1,37 | 0,309 | 0,99 | 0,50 | 1,94 | 0,975 | - |
| Severity of cholelithiasis | | | | | | | | | | 0,755 |
| *Low* | 1,2 | 0,29 | 0,16 | 0,51 | 0,000 | 0,43 | 0,24 | 0,77 | 0,005 | - |
| *Moderate* | 2,2 | 0,34 | 0,25 | 0,47 | 0,000 | 0,55 | 0,39 | 0,77 | 0,001 | - |
| *High* | 6,2 | 0,38 | 0,21 | 0,70 | 0,002 | 0,56 | 0,30 | 1,05 | 0,071 | - |
| Previous upper abdominal surgery | | | | | | | | | | 0,702 |
| *No* | 2,0 | 0,29 | 0,22 | 0,37 | 0,000 | 0,52 | 0,39 | 0,69 | 0,000 | - |
| *Yes* | 4,3 | 0,41 | 0,04 | 4,69 | 0,470 | 0,86 | 0,07 | 10,40 | 0,905 | - |
| Type of admission | | | | | | | | | | 0,545 |
| *Elective* | 1,5 | 0,33 | 0,23 | 0,50 | 0,000 | 0,48 | 0,32 | 0,72 | 0,000 | - |
| *Emergency* | 3,4 | 0,35 | 0,25 | 0,49 | 0,000 | 0,56 | 0,39 | 0,81 | 0,002 | - |

[c] There are no 30-day complications in patients with moderately high severity and undergoing laparotomic cholecystectomy

# SUPPLEMENTARY DATA

## DETAILED METHODS

### PART 1 - Cohort selection

Source of data: Hospital Information System (HIS)

*Inclusion criteria*
All hospital admissions with a primary or secondary contributing diagnosis of *cholelithiasis* (International Classification of Diseases 9th Revision, Clinical Modification - ICD9-CM = 574) and a procedure code of *cholecystectomy* (ICD9-CM 51.22, 51.23), occurred in private and public hospitals of the Lazio Region between January 2007 and September 2008 were included, for a total of 16,432 cases. The final population, after sequential exclusions, consisted of 13,651 subjects.

*Exclusion criteria*
- long-term hospitalizations, rehabilitations and day-hospitals
- patients residents outside the Lazio Region
- subjects younger than 18 or older than 100 years old
- hospitalizations for delivery (MDC 14)
- hospitalizations for any type of trauma (ICD-9-CM codes ICD-9-CM 800-897)
- hospitalizations with diagnoses of cancer of the digestive system (IDC-9-CM codes150-159)
- hospitalizations with other abdominal surgical procedures (selected ICD-9-CM codes)

### PART 2 - Codes to describe severity of cholelithiasis

**1 - Cholelithiasis of the biliary tract without complications**

*574.20; 574.50; 574.90*

**2. Cholelithiasis of the biliary tract with cholecystitis (without obstruction)**

*574.10;574.40; 574.70; 575.1 AND 574.20 or574.50 or574.90; 574.00; 574.30; 574.60; 574.80; 575.0 AND 574.20 or 574.50 or 574.90*

**3. Cholelithiasis of the biliary tract with obstruction (without cholecystitis)**
*574.21; 574.51; 574.01; 574.91; 575.2 AND 574.20 or574.50 or574.90; 576.2 AND 574.20 or 574.50 or 574.90; 575.3*

**4. Cholelithiasis of the biliary tract with both obstruction and cholecystitis**
*574.01; 574.11; 574.31; 574.41; 574.61; 574.71; 574.81; 575.2 AND 574.00; 575.0 AND 574.20 575.1 AND 574.20 574.30; 575.0 AND 574.50; 575.1 AND 574.50; 574.60; 574.70; 574.80; 576.1; 576.2 AND 574.00; 575.0 AND 574.20; 575.1 AND 574.20; 574.30; 575.0 AND 574.50; 575.1 AND 574.50; 574.60; 574.70; 574.80*

### PART 3 - Codes to describe previous upper abdominal surgery

Codes in the index admission – post procedural states
*stomach V44.1, V45.75, V55.1; intestine V44.2, V44.4, V45.3, V45.72, V53.5, V55.2, V55.4, V42.84; liver V42.7; pancreas 42.83*

Codes in the previous 2-year- hospitalizations

Stomach
*43.5,43.6,43.7,,43.8,43.9,44.31,44.39,44.40,44.41,44.42,44.5,44.61,44.63,44.64,44.65,44.69*
Small intestine
*45.31,45.32,45.33,45.34,45.50,45.51,45.6,45.9,45.91,45.92,45.93,46.01,46.02,46.60,46.61, 46.62,46.71,46.72,46.73,46.74,46.80,46.81,46.93,46.97*
Liver
*50.2,50.3, 50.4,50.5,50.6*
Pancreas
*52.22,52.3,52.4,52.5,52.6,52.7,52.8,52.95,52.96*
Abdominal Hernia
*53.4,53.5,53.6,53.7*
Peritoneum
*54.4,54.5,54.6,54.7*
Large intestine
*45.41,45.49,45.7,45.8,45.94,46.03,46.04,46.63,46.64,46.75,46.76,46.79*
Other surgery
*55.4,55.5,56.2,56.4,57.1,57.6,57.7,65.3,65.4,65.5,65.6,66.4,66.5,68.3,68.4,68.6,68.8*

**PART 4 - Codes to describe coexisting conditions**
On the basis of previous 2-year hospitalizations (following a validated coding algorithm – enhanced Elixhauser AHRQ-Web-ICD-9-CM - see reference n. 17 cited in the text).

*diabetes 250.xx; hypertension 401-405; obesity 280.0, ischemic disease 410-414, 429.7, previous revascularization V45.81, V45.82, procedures 36.0, 36.1, heart failure 428, other cardiac disease 093.2, 391, 393-398, 420-425, 429, 745, 746.3-646.6, V15.1, V42.2, V43.2, V43.3, V45.0 arrhythmia / conduction disorders 426-427, cerebrovascular disease 430-438, vascular disease 440-448, 557, hematologic disorders 280-285, 286, 287.1, 287.3-287.5, 288, 289, chronic respiratory disesase 490-496, 518.81, 518.82, chronic liver disease / pancreas 571, 572, 577.1, 577.9, chronic renal disease 582-583, 585-588, V42.0, V45.1m V56, cancer 140-208.9*

**PART 5 - Codes to describe outcomes**

***A) Surgical-related complications (within 30 day after the surgery)***
in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*998.1 Hemorrhage or hematoma or seroma complicating a procedure; 998.2 Accidental puncture or laceration during a procedure; 998.3 Disruption of wound; 998.4 Foreign body accidentally left during a procedure; 998.5 Postoperative infection; 998.6 Persistent postoperative fistula; 998.7 Acute reaction to foreign substance accidentally left during a procedure; 998.81 Emphysema (subcutaneous) (surgical) resulting from a procedure; 998.83 Non-healing surgical wound; 998.89 Other specified complications; 997.4 Digestive system complications; 998.9 Unspecified complication of procedure, not elsewhere classified*

Only in the subsequent hospitalizations

at least one of the following:
*567 Peritonitis and retroperitoneal infections; 575.4 Perforation of gallbladder; 575.5 Fistula of gallbladder; 576.0 Postcholecystectomy syndrome; 576.3 Perforation of bile duct; 576.4 Fistula of bile duct; 570 Acute and subacute necrosis of liver; 789.0 Abdominal pain*

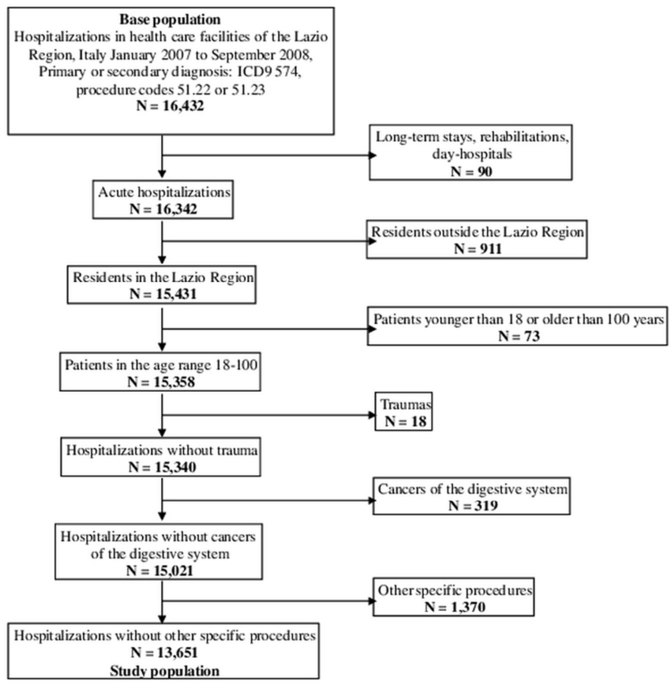
***B) Sistemic complications (within 30 day after the surgery)***

in the index or in the subsequent hospitalizations (excluding hospitalizations for trauma ICD-9-CM 800-897) and delivery (MDC 14)

at least one of the following:
*997.0 Nervous system complications; 997.1 Cardiac complications; 997.3 Respiratory complications; 998.0 Postoperative shock; 410 Acute myocardial infarction; 415.1 Pulmonary embolism and infarction; 431 Intracerebral haemorrhage; 433.x1 Occlusion and stenosis of precerebral arteries with infarction; 434.x1 Occlusion of cerebral arteries with infarction; 436 Acute, but ill-defined, cerebrovascular disease; 480-486 Pneumonia; 513.0 Abscess of lung 518.4 Acute edema of lung, unspecified; 518.5 Pulmonary insufficiency following trauma and surgery; 785.5 Shock without mention of trauma; 788.2 Retention of urine*

Only in the subsequent hospitalizations
*038 Septicemia*

**Figure 1.** Selection of the study population

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