Surgical Outcomes in Gynaecological Oncology

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Thesis Submitted For the Degree of Doctor of Medicine (Research)

At

University College London

2015

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DECLARATION

I, Rema Iyer, declare that this thesis has been composed and the work described in it has been performed by me. It has not been submitted for another degree either at this or another university. All sources of information have been acknowledged.

This was a multicentred study with input from many individuals. I would particularly like to acknowledge Mr. Robert Liston, software architect, who built the database, and Dr. Matthew Burnell who performed all the statistical analysis including development of the risk prediction model for this study.

ABSTRACT

Presently there are no reliable statistics available on complication rates associated with surgery in gynaecological cancer in the UK, apart from data from small studies involving individual centres and clinical trials. This thesis describes the *United Kingdom Gynaecological Oncology Surgical Outcomes and Complications study* (UKGOSOC) that was set up to prospectively capture data from ten UK gynaecological cancer centres on surgical procedures and complications in a uniform manner using agreed definitions so that data could be analysed and compared. A web-based database was set up to capture surgery and complications contemporaneously from the hospitals, and, consented women were sent a follow-up letter eight weeks postoperatively. Intraoperative and postoperative complications were recorded using a pre-determined list. Postoperative complications were graded (I-V) in increasing severity using the Clavien-Dindo system. Grade I complications were excluded from analysis. Univariable and multivariable regression analyses were performed to determine the predictors for intraoperative and postoperative complications. The Lasso method of penalised regression was used to create a risk-prediction model for comparing outcomes between the centres.

Data on 2948 eligible major surgical procedures were analysed and 1462 follow-up letters were received. The overall intraoperative complication rate was 4.7% (95% CI 4.0-5.6). The hospital-reported postoperative complication rate was 14.4% (95% CI 13.2-15.7) which increased to 25.9% (95% CI 23.7-28.2) when both hospital and patient- reported postoperative complications were included. The predictors for intraoperative and postoperative complications were different apart from diabetes which was common to both. Risk-adjustment had a modest effect on the complication rates for individual centres but allowed for a fairer comparison. There was no

concordance between the ranking order of the centres for intraoperative and postoperative complication rates.

The overall intraoperative (≈5%) and postoperative (≈26%) complication rates and funnel graphs derived from this study could be used to benchmark performance of gynaecological oncology centres and even individual surgeons if a larger dataset becomes available nationally.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my principal supervisor Professor Usha Menon for her advice, guidance and unstinting support. Without her encouragement and belief in me, I would not have been able to complete this thesis on time. I am also very grateful to Mr. Tim Mould, my secondary supervisor for always being positive and encouraging.

I am thankful to the all the women who participated in this study, especially to those who took time to reply to the follow-up letters.

I am indebted to Mr. Andy Nordin for involving me in this study right from its inception when the database was being trialled in his department, and also for introducing me to Professor Menon and the brilliant team at UCL. I am especially grateful to Andy for his constant encouragement, guidance, constructive criticism and comments on the myriad drafts of the papers that were written from this study.

At UCL, I am grateful to Dr. Aleksandra Gentry-Maharaj for her continuous support and for her hard work in obtaining ethics approval for this study; Dr. Matthew Burnell for all the statistical analysis, especially for building the risk prediction model; Mr. Robert Liston for building a fantastic database and accommodating all my requests for changes and additions; Mr. Ranjit Manchanda for his friendship, support, constant encouragement and help with analysis; Mr. Rakshit Desai and Miss. Alice Beardmore-Gray for helping me with data entry; Ms. Saz Chamberlain and Miss. Katharine Bailey for their help with the follow-up letters, their friendship and support; and, Mr. Andy Ryan for his help with the Access Database.

I am very grateful to Eve Appeal for funding this study.

I am also thankful to all the clinical leads and other staff from the participating centres for recruiting the women and helping with data entry locally. I would like to thank Miss. Karina Reynolds, Miss. Adeola Olaitan, Mr. James Nevin, Mr. Tito Lopes, Mr. Nagindra Das, Mr. Rob Gornall, Miss. Kathryn Hillaby, Mr. Anders Linder, Mr. Simon Leeson, Mr. Nick Wood and Miss. Smruta Shanbhag.

I am also grateful to Dr. David Meechan and Ms. Aleksandra Thackeray from Public Health England for their support and help with hosting of the database on the Trent Cancer Registry server.

With my busy work schedule, finding time for writing up was a huge challenge. Therefore I am especially grateful to Mr. Geoff Lane my current supervisor for being considerate and giving me much needed time off from clinical work.

I am indebted to my dear husband Murali for his patience, for never saying no to my infinite requests for cups of tea and food even at odd hours. Without his support and encouragement, this would not have been possible. I am also grateful to my parents for believing in me and for supporting me all the way through. I dedicate this work to them.

ABBREVIATIONS

ACE-27	Adult Comorbidity Evaluation-27
AF	Atrial fibrillation
ASA	American Society of Anesthesiologists
AUC	Area under the curve
BMI	Body Mass Index
CC	Coordinating centre
CCAD	Central Cardiac Audit Database
CIRS	Cumulative Illness Rating Scale
CR	Complication rate
CTCAE	Common terminology (toxicity) criteria for adverse events
CV	Cross validation
DVT	Deep vein thrombosis
EPV	Events per variable
FIGO	International Federation of Gynecology and Obstetrics
FUL	Follow-up letter
HANA	Head and Neck Cancer Audit
ICD	International Classification of Diseases
IQR	Inter Quartile Range
KFI	Kaplan Feinstein Index
LASSO	Least absolute shrinkage and selection operator
LOO	Leave one out
ML	Maximum likelihood
MSE	Mean square error
MV	Multivariable
NBOCAP	National Bowel Cancer Audit Project

NCIN	National Cancer Intelligence Network
NHS	National Health Service
NJR	National Joint Registry
NSQIP	National Surgical Quality Improvement Programme
O/E ratio	Observed to expected ratio
OPCS	Office of the Population Censuses and Surveys
PAS	Patient administrative system
PE	Pulmonary embolism
POSSUM	Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity
PROM	Patient reported outcome measure
ROC	Receiver operating curve
SAS	Surgical Apgar Score
SCRN	Surgical Clinical Nurse Reviewer
SCTS	Society for Cardiothoracic Surgery
UV	Univariable
VAMC	Veterans Affairs Medical Center
VLAD	Variable Life-adjusted Display

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1 Introduction

1.1 Overall purpose of the study

Presently there are no reliable statistics available on complication rates associated with surgery in gynaecological cancer apart from data sourced from individual centres (case series) and clinical trials. Data from individual centers cannot be easily compared as they have been collected in different formats using different definitions. The United Kingdom Gynaecological Oncology Surgical Outcomes and Complications audit (UKGOSOC) was set up to prospectively capture data from various gynaecological cancer centres on a large number of surgical procedures and complications in a uniform manner using agreed definitions, so that data from various centres could be compared and analysed.

On the National Health Service (NHS), outcomes of surgery are evaluated using surrogate markers such as length of stay, re-admission rates, and post-operative mortality. This data from NHS hospitals in England is available through the Hospital Episode Statistics (HES). [(1)]

HES, is one aspect of the NHS information centre which contains details on all hospital admissions in England from 1989 onwards. Each episode of care has a unique record in HES containing information on diagnosis, interventions e.g. surgery and other aspects of care such as the NHS trust where the care was provided, waiting time, length of stay, readmissions etc. The International classification of diseases (ICD) [(2)] codes are used to code for diseases and the OPCS (Office of Population, Census and Surveys: Classification of Interventions and Procedures)[(3)] codes are used to code for interventions and surgical procedures.

The OPCS codes for the surgical procedures are entered by coding officers who obtain the information required from the surgical notes which are hand written in most hospitals. The information thus entered into HES may be prone to errors as the coders who do not have a clinical background, have to rely on hand written operation notes by the surgeon to enter the codes. There is a lack of clinical engagement in this data entry as the data entered is not checked for accuracy or completeness by the surgeons.

It is important that the data available on HES is reliable and from a trusted source as it has wide implications. This data is used to rate the quality of care by a particular NHS trust / consultant team and will be used in future for revalidation of individual doctors in the UK. [4] This data is increasingly being used for payment by results and for health care commissioning. The data is also available to the public through HES online and through websites such as the Dr. Foster Health Guide [5] which provides information on the performance of all NHS hospitals in England. The public can, in turn, use this information to compare the performance of their local hospital with other hospitals in the same region or elsewhere and make an informed choice regarding their health care provider.

Accuracy of surgery data can be improved if the codes were derived from electronically entered notes rather than hand written notes and would be even better if the codes were entered by surgeons themselves. Information thus entered by the surgeons would also be more acceptable to the surgical community.

The aim of UKGOSOC was to prospectively gather information on gynaecological cancer surgery using OPCS codes and on complications arising from surgery in a uniform format so that data from various centres was comparable and could be

analysed. Collecting data on complications is only one aspect of measurement of quality and therefore should not be taken on its own. Therefore in addition to the crude rates of complications, the risk adjusted complication rates were also calculated taking into account pre-operative and surgical risk factors such as comorbidity, surgical complexity etc.

It is envisaged that the UKGOSOC database will be integrated with the Patient Administrative System (PAS) in individual hospitals and eventually pave the way towards the formation of a national gynaecological oncology surgery database.

1.2 Thesis chapter plan

Chapter 1 is the introduction and contains a brief background and the rationale behind this study. Chapter 2 includes a literature review. Chapter 3 covers the methods. Chapter 4 describes the baseline characteristics and surgery details. Chapter 5 details intraoperative and postoperative complications reported by the hospitals. Chapter 6 describes patient reported postoperative complications using two formats of follow-up letters. Chapter 7 describes the predictors of intraoperative and postoperative complications using both univariable and multivariable regression. Chapter 8 describes the development of a risk prediction model and the calculation of observed and expected complication rates for individual centres/hospitals. Chapter 9 contains the discussion and conclusion.

2 Literature review

This study describes the development of a database, collection of surgery and complications data, and, the development of a risk-adjusted model for the purpose of benchmarking gynaecological oncology centres in the UK. Surgical outcomes data available for gynaecological oncology surgery is sparse. A literature review was undertaken prior to developing the database for this study. The review examined the definition of a surgical complication, indices used to measure comorbidity, methods for grading surgical complexity, databases available in other surgical specialties and risk prediction algorithms developed in some of these databases.

2.1 Definition of a surgical complication

Since this study was about collating data on surgical complications, it was important to define what was meant by a 'complication'. The dictionary defines a medical complication as 'a secondary disease or condition aggravating an already existing one'. A surgical complication may be described as an *'undesirable result'* of an operation [6, 7]. However not all 'undesirable results' are necessarily complications of surgery. An example quoted by Dindo et al is a surgical scar [8] which even though undesirable, is an expected result/sequela of an operation and not a complication per se. One of the definitions by Sokol et al states that 'a complication is an *undesirable, unexpected and unintended'* result of an operation affecting the patient that occurs as a direct result of the operation' [6]. However not all unexpected and undesirable events occur as a direct result of the surgery itself. Surgery can exacerbate/worsen pre-existing medical conditions such as atrial fibrillation, chronic kidney disease, hypertension, chronic obstructive airway disease etc., which may require additional supportive measures in the postoperative period and delay recovery. The National Cancer Institute which developed the Common Toxicity

Criteria to record adverse events following cancer therapy also recognised that not all adverse events are a direct result of treatment and by using the term ‘toxicity’ all the blame is assigned to therapy. As a result, the word ‘toxicity’ was replaced with ‘terminology’ in the newer versions, to read Common Terminology Criteria for Adverse Events (CTCAE) .[9]

Although complications are not ‘routine’ in all operations, they are not truly ‘*unexpected*’ either and for this very reason surgeons counsel patients regarding their possibility prior to surgery and take precautions to prevent them. However, surgeons are likely to agree that complications are *‘unintended’* results of an operation. A revised definition by Sokol et al states that ‘*a surgical complication is any undesirable, unintended, and direct result of an operation affecting the patient, which would not have occurred had the operation gone as well as could reasonably be hoped’*. The success rate of an operation however, is variable and this definition suggests that if a procedure with a high failure rate fails, then this would not necessarily be considered a complication of that surgery, but an ‘expected’ adverse outcome.

In this study (UKGOSOC) a modified version of the definition suggested by Sokol et al was used which stated that a surgical complication was ‘*an undesirable and unintended result of an operation affecting the patient that occurs as a direct result of the operation*’.

2.2 Classification of complications

Surgical complications can be classified as intraoperative and postoperative depending upon when they occur and be further classified according to the various organ systems (e.g. cardiac, respiratory etc.) or the types of complications (infection, bowel obstruction etc.). In some studies they have been simply classified as minor and major complications. [10]

In order for complications to be comparable across different centres or from the same centre over a period of time, they need to be uniformly captured using clear definitions. For example, a wound infection can vary from something requiring regular dressing to debridement under general anaesthesia. Although in both instances the complication is a wound infection, this apparent difference cannot be captured unless the severity of the 'wound infection' is also accounted for. Grading of complications helps capture this apparent difference as it stratifies complications according to their severity and intervention required. There are various systems for complication grading and some of them are detailed below.

The T92 [11] or the Toronto system of grading was developed by Dindo et al and was first used to grade postoperative complications after cholecystectomy. There were four grades (I-IV) with two subsets in grade II (IIa and IIb). Grade I included those complications which either resolved spontaneously or required simple bedside intervention requiring minimal or no analgesia. Drugs required included anti-emetics, antipyretics, analgesics and anti-diarrhoeals and those required for urinary retention and low urinary tract infection. Grade II were those complications which were potentially life threatening and therefore required specific intervention. Grade IIa included those requiring drug therapy, total parenteral nutrition (TPN) and blood transfusion for postoperative haemorrhage. Grade IIb included invasive procedures and operative procedures for iatrogenic injuries. Grade III included complications that caused lasting disability (e.g. myocardial infarction, cerebrovascular accident with disability). Grade IV was death as a result of any complication. (Table 1)

The T92 was further modified by Dindo et al [8] who classified the complications into five grades with two subsets in Grade III and IV. Modifications focused on the reporting of life threatening and permanently disabling complications. Grade II complications were

restricted to those requiring specific drug therapy, and blood transfusion and TPN were included. Grade IIIa were those complications requiring intervention under local anaesthesia and IIIb were those requiring general anaesthesia. Grade IVa included those complications resulting in single organ failure and Grade IVb those resulting in multi-organ failure. Grade V was death due to a complication.

The Accordion Severity Grading System of Surgical Complications [12] was a further modification of the T92 and the Dindo classification for use in studies of different sizes and complexity. This system has two versions- contracted and expanded. In the contracted version, complications are graded into four groups as mild, moderate, severe and death and in the expanded version there are three subgroups in the severe category (IIIa, IIIb and IV sub-group of the Dindo classification). The authors of the accordion system found that in studies that used the Dindo system, there were very few complications graded as IVb (multi-organ failure) and therefore this was combined with IVa (single organ failure/requiring intensive care management) to form a sub-group of the 'severe' category. (Table 1)

Table 1 Grading of complications

T92	Clavien and Dindo	Accordion system	
		Contracted version	**Expanded version**
Grade 1. Complications carrying minor risks. At most requires bedside procedure. Allowed therapeutic regimens are: antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. Hospital stay required for treatment of complication does not exceed twice the median length of stay for the procedure.	**Grade 1**. Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at bedside.	1. **Mild complication**- Requires only invasive procedures that can be done at the bedside such as insertion of intravenous lines, urinary catheters and nasogastric tubes, drainage of wound and infections. Physiotherapy and the following drugs are allowed- antiemeteics, antipyretics, analgesics, diuretics, electrolytes, and, physiotherapy.	1. **Mild complication**-Requires only invasive procedures that can be done at the bedside such as insertion of intravenous lines, urinary catheters and nasogastric tubes, drainage of wound and infections. Physiotherapy and the following drugs are allowed- antiemeteics, antipyretics, analgesics, diuretics, electrolytes, and, physiotherapy.
Grade 2. Potentially life threatening **Grade 2A**- Requiring pharmacological treatment with drugs other than such allowed for grade 1 complications. Blood transfusions and total parenteral nutrition are also included. Any patient with a complication exceeding twice the median length of stay for the procedure and not falling into a higher category.	**Grade 2.** Requiring pharmacological treatment with drugs other than such allowed for grade 1 complications. Blood transfusions and parenteral nutrition are also included.	**2. Moderate complication**- requires pharmacologic treatment with drugs other than such allowed for minor complications, for instance antibiotics. Blood transfusions and total parenteral nutrition are also included.	**2. Moderate complication-** requires pharmacologic treatment with drugs other than such allowed for minor complications, for instance antibiotics. Blood transfusions and total parenteral nutrition are also included.
Grade2b. Requiring invasive procedures: surgical, endoscopic or radiological (invasive) intervention	**Grade 3**. Requiring surgical, endoscopic or radiological intervention **Grade 3A**. Intervention not under general anaesthesia **Grade 3b**. Intervention under general anaesthesia	**3. Severe complication-** All complications requiring endoscopic or interventional radiologic procedures or re-operation as well as complications resulting in failure of one or more organ systems	**3. Severe**: invasive procedure without general anaesthesia-Requires management by an endoscopic, interventional procedure or re-operation* without general anaesthesia. 4.**Severe:**operation under general anaesthesia
Grade 3. Complications with residual or lasting disability *	**Grade 4** Life-threatening complication (including Central Nervous Systems complications)		
(e.g. stroke, organ/limb loss)	requiring IC/ICU management		
	Grade 4a. Single organ dysfunction (including dialysis)		5. Severe: organ system failure
	Grade 4b. Multi-organ dysfunction		
Grade 4. Death of a patient	**Grade 5** Death of a patient	**4. Death**- Postoperative death	**6. Death**- Postoperative death

2.2.1 Common terminology (toxicity) criteria for adverse events (CTCAE)

The CTCAE was developed to capture adverse events following chemotherapy and radiotherapy for cancer, primarily for use in clinical research and trials. The third version of the CTCAE however includes provision to capture surgical complications as well.[13] The CTCAE is broadly classified into category (broad classification based on anatomy/pathophysiology), adverse event terms (list of adverse events) within each category, and short name of the adverse event followed by grades. (Table 2) There are five grades according to severity: mild, moderate, severe, life threatening or disabling and death related to adverse event. The advantage of the CTCAE is that it can be used to record both intraoperative and postoperative complications. However since it was primarily developed for capturing complications from chemotherapy and radiotherapy, the lists are long and exhaustive and would need to be condensed to be more user friendly in a surgical database.

Table 2 Example for CTCAE classification and grading of a complication

Gastrointestinal						
Adverse event	**Short Name**	**Grade**				
		1	**2**	**3**	**4**	**5**
Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation)	Ileus	Asymptomatic Radiographic findings only	Symptomatic Altered GI function e.g. altered dietary habits; iv fluids indicated <24hours	Symptomatic and severely altered GI function; IV fluids, tube feeding, or TPN indicated ≥24 hrs	Life-threatening consequences	Death
REMARK: Ileus, GI is to be used for altered upper or lower GI function (e.g., delayed gastric or colonic emptying).						

In this study (UKGOSOC) the Clavien and Dindo method of complication grading was adopted as the list was concise, easy to comprehend and user friendly. (Table 1) Also,

this system had been tested in a cohort of 6336 patients undergoing elective surgery and was found to be reliable and reproducible.[8]

2.3 Patient reported complications

Traditionally complications data are collected from hospital records which are captured by the clinicians. The drawback of this method is that only those complications occurring in hospital and important to clinicians get recorded and others that occur outside of hospital are missed. There are a small number of studies which have looked at concordance between surgeon and patient reporting of complications following joint replacement surgery. These studies found that patients accurately report clearly defined complications such as pulmonary embolism and deep vein thrombosis and less accurately when the complication is ill defined, for example, 'major bleeding'.[14, 15]

2.3.1 Patient reported outcome measures (PROMs)

PROMs are another source of obtaining information on outcomes after surgery. As they are reported by patients themselves, they may be able to give a better insight into the effects of surgery on patients. They are not primarily designed to collect data on complications per se, but are useful in assessing symptoms and quality of life after an intervention such as surgery. PROMs collect data on health related quality of life (HRQOL), functional status, symptom status, overall well-being, satisfaction with care and adherence to treatment.[16] The aim of collecting PROMs is to help improve delivery of care, and in the UK, they are routinely collected after hip and knee replacements, varicose vein surgery and groin hernia repair.[17] A PROM designed for a particular intervention should include a generic health questionnaire and a disease specific questionnaire. For e.g. a PROM for gynaecological oncology would have three components- a generic health questionnaire such as the EQ-5D, a generic cancer questionnaire such as the EORTC QLQ C-30 and a cancer specific questionnaire, for

e.g. the EORTC QLQ EN-24 for endometrial cancer.[18] Andikyan et al evaluated the feasibility of using web-based PROMs for assessing patient recovery after gynaecologic cancer surgery.[19] The questionnaire was a combination of an adaptation the CTCAE 3.0 to capture surgical complications and the EORTC QLQ C-30 to measure quality of life. They concluded that this was a feasible approach which was also highly acceptable to patients.

Outcomes data mainly in the form of morbidity and mortality rates are being used to benchmark performance of hospitals and individual surgeons. However Varagunam et al explored the use of PROMs after elective surgery in the UK and concluded that PROMs were a more sensitive method for comparing outcomes between consultants.[20] At present, a PROM specifically for gynaecological cancers has not been developed and validated. However in future when routine collection of PROMS become mandatory for all cancers, including gynaecological oncology, they may prove to be a useful alternative to or complimentary to complications data for benchmarking of centres and individual consultants.

In this study (UKGOSOC), a patient follow-up letter was designed and sent to patients eight weeks following surgery to gather information on postoperative complications that may have developed in the community and subsequently treated in primary care or in a hospital different to where the initial surgery had been performed.

2.4 Comorbidity

Comorbidity refers to coexistent illnesses present in the individual other than the index disease or the disease of interest. It was important to account for comorbidity as pre-existing diseases in an individual can affect surgical outcome. There are different methods for assessing co-morbidity. The easiest is to list the various medical conditions [21] or have a list of specific conditions [22] and simply count the total number. Although this is easy to perform, this method is prone to error as the criteria

to consider a condition as a comorbidity can vary and the definitions of the disease conditions can also vary. To overcome this problem, researchers commonly use ICD codes [2] to define the various conditions. [21] In addition to listing the various comorbid conditions, it would be more informative to assess their severity. For e.g. diabetes can vary in severity. A mild form of the disease which is managed by controlling diet alone is less likely to have long term sequelae where as a more severe form of the disease is more likely it is to cause end organ damage such as nephropathy and neuropathy. Instead of merely listing diabetes as comorbidity, it might be more informative and useful to account for its severity as well. Various co-morbidity indices have been developed over the years to assess the risk of overall morbidity / mortality. Some of the indices assign a score either for individual co-morbidities or particular medical conditions for e.g. the Charlson index [23] and some others classify the comorbidities according to their respective organ systems and grade them according to severity, for e.g. The Cumulative Illness Rating Scale. (CIRS) [24] Some of the indices also assign an overall score for an individual that gives a snapshot assessment of the general health of the patient, for e.g. the American Society for Anaesthesiologists' (ASA) Grade. [25] Quantifying co-morbidity in this way is useful in clinical situations where a decision has to be made regarding the appropriate treatment for the patient. An overall comorbidity score is also useful in statistical analysis as it helps to mathematically describe the confounding effects or the relationship between the co-morbidity and the outcome being studied.

de Groot et al systematically reviewed the different methods to assess co-morbidity [26] and concluded that the Charlson Index, the CIRS, the ICED (Index of co-existent disease) and the Kaplan index were valid and reliable methods to measure co-morbidity in clinical research. Some of these indices are discussed below.

2.4.1 Cumulative Illness Rating Scale (CIRS)

This scale was developed by Linn and colleagues in 1968. [24] Their aim was to develop a *'comprehensive and reliable instrument for assessing physical impairment'* for use in research. In this scale 13 independent organ systems or domains are evaluated on a severity scale ranging from 0 to 4 where 0= no impairment, 1= mild, 2=moderate, 3=severe, 4=extremely severe (life threatening) impairment. Every subject would also have a final score which is a sum total of the individual score for each organ system. This scale was validated in two studies on elderly patients and the authors concluded that the CIRS performed better than chronological age in estimating the life span of an individual [27] [28]. Miller et al modified the CIRS for use in psychogeriatric patients, added a suffix G for geriatric and named it CIRS-G [29]. The CIRS has mostly been used to assess morbidity in elderly patients [30, 31]. More recently, Groome et al [32] used the CIRS-G to assess the comorbidity in prostate cancer patients. They found that respiratory and cardiac diseases followed by vascular and renal diseases and diabetes were the most common comorbidities in this cohort.

2.4.2 Charlson Index

This was developed by Mary Charlson and her colleagues in a cohort of 559 medical inpatients who were followed up for a year. A weighted index was developed which took into account the type of comorbid illness and the severity. The aim of the study was to assess the ability of the index to predict one year survival among these patients. Relative risk of mortality was calculated for each condition and those with a relative risk (RR) of 1.2 or less were dropped. Conditions with a relative risk of >1.2 and <1.5 were assigned a weight of 1, conditions with a RR of >1.5 and <2.5 were given a weight of 2, those with a RR of >2.5 and <3.5 were given a weight of 3, and two conditions with a RR of >6 were given a weight of 6. The index was then further validated in a 10 year follow up of 685 patients previously treated for breast cancer

(population with a low incidence of comorbidity), to assess the ability of this index to predict mortality over a ten year period. In the second study, age was also found to be a strong predictor along with comorbidity. The relative risk of mortality with each increasing level of comorbidity was 2.3 and with each decade of age, 2.4. With each decade of age, the risk of dying from a comorbid disease was equivalent to an increase of 1 to the overall comorbidity score. The authors thus recommended taking age into account in studies with long periods of follow-up, i.e. 5 years or more.

The Charlson index has been widely used to assess comorbidity in patients with various types of malignancies [33, 34] including gynaecological cancers. A randomised controlled trial comparing open with laparoscopic approach for early stage endometrial cancer found that higher Charlson index scores was one of the significant risk factors associated with an increased incidence of adverse events. [35]

2.4.3 Kaplan Feinstein Index

Kaplan and Feinstein developed this index in 1974 to assess the effects of comorbidity on maturity onset diabetes mellitus. [36] The study aimed to demonstrate that comorbidity is an important confounding variable when assessing the risk of mortality from chronic diseases such as diabetes. This study was a retrospective analysis of medical records of 188 male patients treated at a Veteran's Affairs Hospital. They were newly diagnosed diabetics (diagnosed within six months- between 1959 and 1962) and were followed up for five years. The comorbidities were classified into two groups- vascular and non-vascular and were graded using a categorical severity scale- 1, 2 and 3 where grade 1 was mild, 2 moderate and 3 severe. Vascular conditions included hypertension and its sequelae; cardiac disorders excluding cor pulmonale; peripheral vascular disease; retinopathy and cerebrovascular disease. All other disease conditions were classified as non-vascular and included diseases of the lungs, liver, bones etc. They concluded that the 5 year mortality rate in patients with

diabetes was influenced by the type of comorbidity and more importantly, the severity of the comorbidity. Since the publications of the original index, it has been used to assess comorbidity in diseases other than diabetes including cancers such as prostate cancer [37], multiple myeloma [38] and head and neck cancer [39].

2.4.4 Adult Comorbidity Evaluation-27 (ACE-27)

The ACE-27 was a modified version of the KFI (the Modified Medical Comorbidity Index) developed by Picorillo et al, to prospectively study the incidence and burden of comorbidity in a cohort of 3378 patients suffering from different types of cancers including head and neck cancer, colorectal, lung, breast and prostate.[40] In the modified version, diabetes, AIDS and dementia were added to the disease categories. This study concluded that comorbidity was a significant prognostic factor in cancers of the head and neck, lung, breast and prostate even after controlling for other factors such as age and cancer stage. This study led to the development of the Adult Comorbidity Evaluation – 27 (ACE-27) in its present form; an index specifically for assessment of comorbidity from chart review, in cancer patients.[41] (Table 3) In this system, comorbidity is captured according to the various organ systems like cardiovascular, respiratory etc. and the severity is graded as 1 (mild decompensation), 2 (moderate decompensation) and 3 (severe decompensation). The overall score is determined by the highest grade in any organ system/ailment. However if the patient scores grade 2 in two or more different organ systems, then the overall grade is calculated as 3.

Table 3 ACE- 27

Adult Comorbidity Evaluation-27

Identify the important medical comorbidities and grade severity using the index. Overall comorbidity score is defined according to the highest ranked single ailment, except in the case where two or more Grade 2 ailments occur in different organ systems. In this situation the overall comorbidity score should be designated Grade 3.			
Cogent Comorbid Ailment	**Grade 3** **Severe Decompensation**	**Grade 2** **Moderate Decompensation**	**Grade 1** **Mild decompensation**
Cardiovascular system			
Myocardial Infarct	□ MI ≤ 6 months	□ MI > 6 months ago	□ MI by ECG only, age undetermined
Congestive Heart Failure (CHF)	□ Hospitalized for CHF within past 6 months □ Ejection fraction < 20%	□ Hospitalized for CHF >6 months prior □ CHF with dyspnoea which limits activities	□ CHF with dyspnoea which has responded to treatment □ Exertional dyspnoea □ Paroxysmal Nocturnal Dyspnoea (PND)
Arrhythmias	□ Ventricular arrhythmia ≤ 6 months	□ Ventricular arrhythmia > 6 months □ Chronic atrial fibrillation or flutter □ Pacemaker	□ Sick Sinus Syndrome □Supraventricular tachycardia
Hypertension	□ DBP>130 mm Hg □ Severe malignant papilledema or other eye changes □ Encephalopathy	□ DBP 115-129 mm Hg □ DBP 90-114 mm Hg while taking antihypertensive medications □ Secondary cardiovascular symptoms: vertigo, epistaxis, headaches	□ DBP 90-114 mm Hg while not taking antihypertensive medications □ DBP <90 mm Hg while taking antihypertensive medications □ Hypertension, not otherwise specified
Venous Disease	□ Recent PE (≤R6 mos.) □ Use of venous filter for PE's	□ DVT controlled with Coumadin or heparin □ Old PE > 6 months	□ Old DVT no longer treated with Coumadin or Heparin
Peripheral Arterial Disease	□ Bypass or amputation for gangrene or arterial insufficiency < 6 months ago □ Untreated thoracic or abdominal aneurysm (>6 cm)	□ Bypass or amputation for gangrene or arterial insufficiency > 6 months ago □ Chronic insufficiency	□ Intermittent claudication □ Untreated thoracic or abdominal aneurysm (< 6 cm) □ s/p abdominal or thoracic aortic aneurysm repair
Respiratory System			
	□ Marked pulmonary insufficiency □ Restrictive Lung Disease or COPD with dyspnoea at rest despite treatment □ Chronic supplemental O2 □ CO2 retention (pCO2 > 50 torr) □ Baseline pO2 < 50 torr □ FEV1 (< 50%)	□ Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnoea which limits activities □ FEV1 (51%-65%)	□ Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnoea which has responded to treatment □ FEV1 (66%-80%)
Gastrointestinal System			
Hepatic	□ Portal hypertension and/or oesophageal bleeding ≤l6 mos. (Encephalopathy, Ascites, Jaundice with Total Bilirubin > 2)	□ Chronic hepatitis, cirrhosis, portal hypertension with moderate symptoms "compensated hepatic failure"	□ Chronic hepatitis or cirrhosis without portal hypertension □ Acute hepatitis without cirrhosis □ Chronic liver disease manifested on biopsy or persistently elevated bilirubin (>3 mg/dl)

ACE 27 continued….

Stomach/Intestine	□ Recent ulcers(≤R6 months ago) requiring blood transfusion	□ Ulcers requiring surgery or transfusion > 6 months ago	□ Diagnosis of ulcers treated with meds □ Chronic malabsorption syndrome □ Inflammatory bowel disease (IBD) on meds or h/o with complications and/or surgery
Pancreas	□ Acute or chronic pancreatitis with major complications (phlegmon, abscess, or pseudocyst)	□ Uncomplicated acute pancreatitis □ Chronic pancreatitis with minor complications (malabsorption, impaired glucose tolerance, or GI bleeding)	□ Chronic pancreatitis w/o complications
Renal System			
End-stage renal disease	□ Creatinine > 3 mg% with multi-organ failure, shock, or sepsis □ Acute dialysis	□ Chronic Renal Insufficiency with creatinine >3 mg% □ Chronic dialysis	□ Chronic Renal Insufficiency with creatinine 2-3 mg%.
Endocrine System (Code the comorbid ailments with the (*) in both the Endocrine system and other organ systems if applicable)			
Diabetes Mellitus	□ Hospitalization ≤H6 months for DKA □ Diabetes causing end-organ failure □ retinopathy □ neuropathy □ nephropathy* □ coronary disease* □ peripheral arterial disease*	□ IDDM without complications □ Poorly controlled AODM with oral agents	□ AODM controlled by oral agents only
Neurological System			
Stroke	□ Acute stroke with significant neurologic deficit	□ Old stroke with neurologic residual	□ Stroke with no residual □ Past or recent TIA
Dementia	□ Severe dementia requiring full support for activities of daily living	□ Moderate dementia (not completely self-sufficient, needs supervising)	□ Mild dementia (can take care of self)
Paralysis	□ Paraplegia or hemiplegia requiring full support for activities of daily living	□ Paraplegia or hemiplegia requiring wheelchair, able to do some self-care	□ Paraplegia or hemiplegia, ambulatory and providing most of self-care
Neuromuscular	□ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder and requiring full support for activities of daily living	□ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder, but able to do some self-care	□ MS, Parkinson's, Myasthenia Gravis, or other chronic neuromuscular disorder, but ambulatory and providing most of self-care
Psychiatric			
	□ Recent suicidal attempt □ Active schizophrenia	□ Depression or bipolar disorder uncontrolled □ Schizophrenia controlled w/ meds	□ Depression or bipolar disorder controlled w/ medication
Rheumatologic (Incl. Rheumatoid Arthritis, Systemic Lupus, Mixed Connective Tissue Disorder, Polymyositis, Rheumatic Polymyositis)			
	□ Connective Tissue Disorder with secondary end-organ failure (renal, cardiac, CNS)	□ Connective Tissue Disorder on steroids or immunosuppressant medications	□ Connective Tissue Disorder on NSAIDS or no treatment

ACE 27 continued…

Immunological System (AIDS should not be considered a comorbidity for Kaposi's Sarcoma or Non-Hodgkin's Lymphoma)			
AIDS	□ Fulminant AIDS w/KS, MAI, PCP (AIDS defining illness)	□ HIV+ with h/o defining illness. CD4+ < 200/ μ L	□ Asymptomatic HIV+ patient. □ HIV+ w/o h/o AIDS defining illness. CD4+ > 200/ μ L
Malignancy (Excluding Cutaneous Basal Cell Ca., Cutaneous SCCA, Carcinoma in-situ, and Intraepithelial Neoplasm)			
Solid Tumour including melanoma	□ Uncontrolled cancer □ Newly diagnosed but not yet treated □ Metastatic solid tumour	□ Any controlled solid tumour without documented metastases, but initially diagnosed and treated within the last 5 years	□ Any controlled solid tumour without documented metastases, but initially diagnosed and treated > 5 years ago
Leukaemia and Myeloma	□ Relapse □ Disease out of control	□ 1st remission or new dx <1yr □ Chronic suppressive therapy	□ H/o leukaemia or myeloma with last Rx > 1 yr prior
Lymphoma	□ Relapse	□ 1st remission or new dx <1yr □ Chronic suppressive therapy	□ H/o lymphoma w/ last Rx >1 yr prior
Substance Abuse (Must be accompanied by social, behavioural, or medical complications)			
Alcohol	□ Delirium tremens	□ Active alcohol abuse with social, behavioural, or medical complications	□ H/o alcohol abuse but not presently drinking
Illicit Drugs	□ Acute Withdrawal Syndrome	□ Active substance abuse with social, behavioural, or medical complications	□ H/o substance abuse but not presently using
Body Weight			
Obesity		□ Morbid (i.e., BMI ≥M38)	
Overall Comorbidity Score (Circle one)	**0-None**	**1-Mild**	**2- Moderate** **3- Severe** **9-Unknown**
Revised November 2003	**Washington University School of Medicine**		**Clinical Outcomes Research Office**

2.4.5 American Society of Anaesthesiologists' (ASA) physical status classification system

The ASA grading system was first described by Saklad in 1941.[42] The original grading had six classes, ASA 1-6 with one being a healthy person to 4 being someone with extreme systemic disorders that is already an imminent threat to life. Class 5 included emergencies that would otherwise be graded in class 1 or 2 and class 6 included emergencies that would otherwise be in class 3 and 4. The aim of the scale was to address the pre-operative state of the person. In 1963, the scale was modified to have 5 grades in which 1 was a healthy person, 2 person with mild systemic disease, 3 with severe systemic disease, 4 severe systemic disease which is a constant threat to life, 5 a moribund person who is not expected to survive without the operation. The suffix E was added to the grade if the surgery was being performed as

an emergency. [25] Later on a sixth category was added which was a brain dead person whose organs were being removed for donor purposes.

ASA grade is widely used to assess the general fitness of an individual in nearly all specialties and can be easily obtained from the anaesthetic charts. Since it is a dynamic assessment of the patient's fitness at the time of surgery, it is not a fixed score and can change from time to time for the same patient depending on their current state of health. In gynaecological oncology, Aletti et al found that ASA grade was an independent predictor of adverse events in ovarian cancer surgery [43] and Kondalsamy-Chennakesavan et al also found that it was a significant predictor of morbidity for all gynaecological cancer surgeries. [35]

2.4.6 Comorbidity data in gynaecological oncology surgery

In the studies that looked at surgical morbidity in gynaecological oncology, ASA grade was captured in both the studies, as mentioned above. In addition, Aletti et al captured albumin and creatinine levels when comparing outcomes between three centres for ovarian cancer surgery. No other comorbidity index was used. [44] In the second study by Kondalsamy-Chennakesavan et al, which looked at overall morbidity in gynaecological oncology surgery, comorbidity was captured according to various organ systems and in addition, laboratory parameters such as levels of liver enzymes (including albumin level) and electrolyte levels were also included. [45] Other than ASA grade, this study also did not use any other index to capture comorbidity.

In this study (UKGOSOC), comorbidity was captured according to the various organ systems as there was limited evidence for the use of any particular comorbidity index, other than ASA grade. In addition to ASA grade ACE-27 was also incorporated into the database as the latter had been recommended by the National Cancer Intelligence Network (NCIN) for use in all cancers at the time when this study was being designed.

2.5 Morbidity data in gynaecological oncology surgery

Data in gynaecological oncology is limited to single centre studies and a three centre study from the US. The POSSUM (Physiological and Operative Severity Score for the enumeration of mortality and morbidity) index [46] originally developed to predict morbidity and mortality in general surgery was validated in gynaecological oncology by Das et al. The P-POSSUM (Portsmouth modification of the Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) index was used to predict mortality in gynaecological oncology surgery.[47] This was a prospective single centre study from a UK tertiary gynaecological centre over a 12 month period which found that the POSSUM index over estimated mortality. The authors concluded that the P-POSSUM could not be used in its current form for gynaecological oncology surgery and would require modifications if it were to be used.

Kondalsamy-Chennakesavan et al prospectively analysed all surgery for suspected gynaecological cancer in a tertiary centre in Australia over a 20 month period and developed a risk scoring system to predict adverse events. [45] In this study, surgical complexity, elevated serum glutamic oxaloacetic transaminase (SGOT), higher American Society for Anaesthesiologists' (ASA) scores and overweight were independently associated with adverse events.

Aletti et al analysed the relationship between surgical complexity, morbidity and overall survival in ovarian cancer.[43] This was a single centre US study over a four year period which found that even though complex surgery had an increased risk of complications, it had a positive impact on overall survival. In a different study, Aletti et al also developed a risk-adjusted model to compare the outcomes for ovarian cancer surgery between three tertiary gynaecological oncology centres in the US and found that the outcomes were comparable in the three participating centres.[44] Their model was based on the National Surgical Quality improvement programme (NSQIP). [48]

They concluded that the use of a risk prediction model derived from multivariable regression and the use of observed:expected complications ratios was a feasible method to compare outcomes between centres.

2.6 Databases in other surgical specialties

Various general surgical specialties have their own databases to collect data on morbidity and mortality. A brief description of some of the databases is given below.

2.6.1 National Surgical Quality Improvement Programme (NSQIP)

The National Surgical Quality Improvement Programme (NSQIP) in the US is one of the most successful programmes established in 1994 to provide risk-adjusted morbidity and mortality rates for major surgery in the participating Veterans Affairs Medical Centres (VAMCs). [48] Data was collected on pre-surgical patient risk factors, surgical factors, complications and 30 day mortality. Trained surgical clinical nurse reviewers (SCNRs) under the guidance of the chief of surgery of each VAMC were responsible for the collection and transmission of data to the coordinating centre. The data was transmitted electronically onto a national database. Patients were also sent a follow-up letter from the coordinating centre 30 days after the procedure. Logistic regression was used to develop a risk prediction model for morbidity and 30-day mortality for various surgical specialties. For each VAMC, the expected morbidity and mortality rates were calculated using this risk-prediction model and observed to expected ratios were calculated. This programme has helped in the considerable reduction of morbidity and mortality rates after surgery over the years. [49] Success of the programme has been down to the dedicated nurse reviewers, a common electronic database for collection and transmission of data, a set of agreed list of complications, and a coordinating centre responsible for the smooth running of the study, for all the

analyses and for generating outcome reports. Since its inception, the NSQIP now also includes non-veteran hospitals including those in the private sector.

2.6.2 The adult cardiac surgery register

The Society for Cardiothoracic Surgery (SCTS) of Great Britain and Ireland established the adult cardiac surgery register in 1994. [50] This is clinically led and data is fed into the Central Cardiac Audit Database (CCAD) which is now a part of the NHS information centre. Encrypted data on patient demographics and pre-operative risk factors, surgery details and in-hospital postoperative outcomes are entered. Risk-adjusted mortality data for individual hospitals are available, and, since 2004, outcomes for individual surgeons have also been made available, which is accessible to the public. The problem of incomplete data with clinician led databases has not been an issue with the cardiac register. The missing data for important fields for risk stratification has been <5% and for postoperative complications around 15%. [50] This register has demonstrated that with the dedication of the participating clinicians, it is possible to have a database that consistently generates high quality morbidity and mortality data.

2.6.3 National Bowel Cancer Audit Project (NBOCAP)

The first bowel cancer audit was published in 2000. The audit captures outcomes of colorectal cancer in the UK. Data capture has increased from 30% of the NHS trusts at its inception in 2000 to 98% in 2010. [51] Unlike the cardiac surgery register which captures real time data, the NBOCAP has relied on information on a minimum dataset and collects information on patient demographics, stage of cancer, surgery and adjuvant treatment. Main outcome measures are 30-day mortality and length of stay. In future the audit aims to collect more details on postoperative complications.

2.6.4 The National Joint registry (NJR)

Established in 2002 in the UK, the NJR collects information on all joint replacement surgery including shoulder, elbow, hip and knee and ankle replacements to monitor their performance and to assess the effectiveness of different types of surgery.[52] Main outcomes data include 90 day mortality and revision rates. Patient reported outcome measures (PROMs) are also available for hip and knee replacement surgeries. The NJR has recently started publishing data for individual surgeons as well.

2.6.5 Head and neck cancer audit (HANA)

The UK national head and neck cancer audit publishes outcomes on treatment for head and neck cancers.[53] Perioperative mortality and 90 day postoperative mortality rates for individual hospitals are published in addition to details of surgery and adjuvant therapy. Risk adjusted mortality rates after accounting for patient comorbidity; performance status and stage of the disease are also published.

2.7 Surgical Complexity

Surgery for gynaecological cancers often includes procedures for staging and tumour debulking. In addition to a hysterectomy and salpingo-oophorectomy, procedures commonly performed include lymphadenectomy, omentectomy, appendicectomy, bowel resections and ureterolysis. Radical debulking surgery includes additional procedures like diaphragm stripping, splenectomy, liver resection etc. Therefore it is important to adjust for surgical complexity whilst determining the morbidity from surgery. In general surgery the POSSUM index was developed to predict morbidity and mortality.[46] In this system surgery was graded as minor, moderate, major and major+ depending on the complexity of the procedure. (Table 3) However this classification was only for general surgical procedures and did not include any gynaecological procedures. When Das et al adapted the Portsmouth modification of

the POSSUM index (P-POSSUM) for predicting mortality in gynaecological oncology [47] they classified surgery into three groups- minor, major and complex major. Minor included laparoscopy and biopsy. Major included hysterectomy ± bilateral salpingo-oophorectomy, pelvic lymphadenectomy, para-aortic lymphadenectomy, simple vulvectomy, omentectomy, appendicetomy, bowel resection ± anastomosis, ureteric re-anastamosis. Complex major included radical hysterectomy ± pelvic node dissection, radical trachelectomy, radical vulvectomy ± inguinofemoral lymphadenectomy, anovulvectomy, radical debulking surgery (ovary/primary peritoneal), exenteration, vascular graft insertion and ileal conduit.

Kondalsamy-Chennakesavan et al classified gynaecological cancer surgery into three groups- categories 0, 1 and 2 for inclusion in a risk prediction model. [45] Complex procedures in category 1 included radical hysterectomy, pelvic lymphadenectomy, para-aortic lymphadenectomy, omentectomy, adhesiolysis and ureterolysis. Complex procedures in category 2 included anterior rectal resection, colonic resection, small bowel resection, exenteration, urinary conduit, splenectomy, (sub) total peritonectomy and resection of the diaphragm.

The difficulty with classifying surgery as per the above methods is that it is not feasible to account for additional procedures that may sometimes be required to perform with an otherwise straight forward procedure. For example, a hysterectomy for extensive endometriosis or in a patient with intra-abdominal adhesions as a result of previous surgery/infection, may require ureterolysis or adhesiolysis making it a more complex procedure when compared to a hysterectomy in a patient with no pelvic pathology. In such situations it would be important to account for the additional procedures, and this is not possible with the above systems of classifications. Aletti et al adopted a different approach to accounting for surgical complexity. [43] In this system, every individual component of the overall surgery was given a score. For example, if the surgery

included a total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), omentectomy and pelvic lymphadenectomy, the overall score for the procedure was a sum of the scores for the individual procedures- TAH+BSO+Omentectomy+pelvic lymphadenectomy. Depending on the overall score the surgery was then classified as low (≤3), intermediate (4-7) and high (≥8) complexity. Since this method accounts for every procedure performed as part of the whole surgery, it helps to distinguish between easy and difficult procedures as well. In this system, the score for a simple hysterectomy would be different to that for a difficult one e.g. for severe endometriosis requiring adhesiolysis, ureterolysis etc. An additional point would be allocated to the additional procedures such as adhesiolysis and ureterolysis thus increasing the total score from 1 for a TAH and BSO to 3 for a TAH, BSO with ureterolysis and adhesiolysis. A modified version of the Aletti scoring system to include procedures for all gynaecological cancers was used in UKGOSOC and this has been detailed in the next chapter.

2.8 Risk prediction models

Risk prediction models have been developed in various specialties to predict morbidity and mortality. The aim of such models is to be able to predict the outcome as accurately as possible whilst accounting for confounding patient and surgical factors. The ratio between observed and predicted morbidity/mortality (observed/expected ratio) derived from risk prediction models have been used to assess performance of a surgical unit or individual surgeon. They have also been used to monitor performance of the same unit or surgeon over a period of time. The Observed/Expected (O/E) ratio is a better alternative to crude rates when comparing the morbidity and mortality across different specialties as well, since the rates for each specialty can vary with some specialties in general having high mortality rates, some others high morbidity rates and some others with low morbidity and mortality rates. Generally, an O/E ratio

equal to 1 indicates that the performance is as expected, >1 worse than expected and <1 better than expected. Some of the risk prediction models developed in different surgical specialties are detailed below.

2.8.1 The POSSUM surgical scoring system

Copeland et al developed the POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) index to predict morbidity and mortality for all general surgical procedures, excluding cardiac surgery. [46] This is a two part scoring system consisting of a physiological part with 12 variables and a surgical part with six variables to account for operative severity. (Table 4) Each variable is also divided into four grades (one, two, four and eight) of increasing severity and complications are recorded according to a pre-determined list. The POSSUM score was tested prospectively on 1372 patients admitted for surgery at a single institution, using the physiological score pre-operatively and the surgical score at discharge. [46] A good correlation was observed between O/E rates for morbidity and mortality. (p <0.001) Further studies also found good correlation between O/E rates for various surgical specialties and for surgical units in different countries with varying case-mix. [54] Since its initial development, the POSSUM score has been modified for use in different surgical specialties to improve its predictive ability, for example the CR-POSSUM (CR-colorectal) for colorectal surgery. A study comparing POSSUM with CR-POSSUM found that CR-POSSUM was better at predicting mortality rates for individual surgeons for colorectal cancer surgery. [55] However as mentioned previously, the POSSUM was found to over predict mortality in gynaecological oncology surgery. [47]

Table 4 POSSUM Score

POSSUM Physiological Score				
	Score			
	1	**2**	**4**	**8**
Age	≤60	61-70	≥71	
Cardiac signs	No failure	Diuretic, digoxin, antianginal or hypertensive therapy	peripheral oedema, warfarin therapy	Raised jugular venous pressure
Chest radiograph			Borderline cardiomegaly	Cardiomegaly
Respiratory history	No dyspnoea	Dyspnoea on exertion	Limiting dyspnoea (one flight)	Dyspnoea at rest (rate ≥30/min)
Chest Radiograph		Mild COAD	Moderate COAD	Fibrosis or consolidation
Blood pressure (systolic) (mmHg)	110-130	131-170	>171	
		100-109	90-99	≤89
Pulse (beats/min)	50-80	81-100	101-120	≥121
		40-49		≤39
Glasgow Coma Score	15	12-14	9-11	≤8
Haemoglobin (g/100ml)	13-16	11.5-12.9	10.0-11.4	≤9.9
		16.1 - 17.0	17.1-18.0	≥18.1
White cell count (x10^{12} /l)	4-10	10.1-20.0	≥20.1	
		3.1-4.0	≤3.0	
Urea (mmol/l)	≤7.5	7.6-10.0	10.1-15.0	≥15.1
Sodium (mmol/l)	≥136	131-135	126-130	≤125
Potassium (mmol/l)	3.5-5.0	3.2-3.4	2.9-3.1	≤2.8
		5.1-5.3	5.4-5.9	≥6.0
Electrocardiogram	Normal		Atrial fibrillation (rate 60-90)	Any other abnormal rhythm or > 5 ectopics/min Q waves or ST/T wave changes
Operative severity score				
	Score			
	1	**2**	**4**	**8**
Operative severity*	Minor	Moderate	Major	Major+
Multiple procedures	1		2	>2
Total blodd loss (ml)	<100	101-500	501-999	>1000
Peritoneal soiling	None	Minor (serous fluid)	Local Pus	Free bowel content, pus or blood)
Presence of malignancy	None	Primary only	Nodal metastases	Distant metastases
Mode of surgery	Elective		Emergency resuscitation of >2h possible** Operation <24hrs after admission	Emergency (immediate surgery <2h needed)

Surgery of moderate severity includes appendicectomy, cholecystectomy, mastectomy, transurethral resection of prostate; major surgery includes any laparotomy, bowel resection, cholecytectomy, peripheral vascular procedure or major amputation; major + surgery includes any aortic procedure, abdomino perineal resection, pancreatic or liver resection, oesophagogastrectomy;

** indicates that resuscitation is possible even if this period is not actually utilised

2.8.2 The National Surgical Quality Improvement Programme (NSQIP)

The NSQIP has been described previously (section 2.3.1). Logistic regression was used to predict the risk of surgical morbidity and mortality. [48] A predetermined list of twenty complications was used to define morbidity and mortality was defined as death within thirty days after surgery. Maximum likelihood methods were used to determine the intercept term and beta coefficients attached to the independent variables in the

model. The most important patient risk factor was first entered into the model followed by the second most important factor until all important predictor variables were in the model at the α =0.05 level of significance. The model thus developed was used to predict the morbidity/mortality for each individual patient, taking into account their preoperative risk factors. These probabilities were then summed up to predict the number of patients with complications or deaths for each surgical specialty or hospital. O/E ratios were then calculated for each surgical specialty and hospital. The very first analysis in the NSQIP found that without risk adjustment 25 out of 39 hospitals would have been wrongly incriminated as outliers. [48] Various studies looking at trends over a period of time have shown that the risk adjusted outcomes data generated by the NSQIP have helped to reduce morbidity and mortality in individual hospitals. [49]

2.8.3 Variable Life-adjusted Display (VLAD)

Developed initially for cardiac surgery, the VLAD is a graphical display of surgical performance over time. The display charts the difference between expected and actual outcomes (i.e. mortality/morbidity) over a time period for individual surgeons or specialty or surgical units.[56] The formula or algorithm to derive values for expected outcomes varies from one specialty to the other. Although initially developed to monitor mortality trends in cardiac surgery, it has been used to assess trends in the incidence of surgical site infections (SSI), [57] mortality trends in oesophageal cancer surgery, [58] neonatal deaths in low resource settings etc. [59] The advantage of a visual display is that it helps in easy interpretation of the trends by hospital staff and clinicians.

2.8.4 Surgical Apgar Score (SAS)

This score was developed to easily and accurately grade a patient's condition soon after surgery and predict the chances of major postoperative complications or death

(within 30 days of surgery) after general or vascular surgery. [60] A ten point score was developed based on estimated blood loss, lowest heart rate and lowest mean arterial pressure. It was developed by analysing 99 intraoperative and postoperative variables in patients undergoing colectomy and was then validated in general surgery and vascular surgery patients. The aim of the score was to have an easy method of identifying patients who were at low and high risk of developing complications after surgery to optimise their postoperative care. It was not designed for comparing outcomes between hospitals or to monitor outcomes of individual surgeons. Lower scores indicated poorer outcomes. The SAS has been validated in prospective studies in elective general [61] and spinal surgery [62] and found to be a significant predictor of postoperative complications. In a different study following emergency general surgery [63] lower SAS scores were also found to be associated with an increased readmission rate.

2.8.5 Risk scoring systems in gynaecological oncology

Kondalsamy-Chennakesavan et al developed a clinical risk score to predict adverse events in patients undergoing surgery for suspected or proven gynaecological cancers. [45] Patient comorbidity, clinical characteristics, pre-operative lab results, surgical complexity, duration of surgery, surgical approach, surgeon's experience, intraoperative and postoperative complications and duration of stay were prospectively collected from a single tertiary cancer centre. Postoperative complications were graded according to the Clavien and Dindo system. Univariable logistic regression analysis was first performed to identify the significant predictors of adverse events which were then included into multivariable regression model. To develop the risk scoring system coefficients from the multivariable regression model were scaled using a factor of 2 and rounded off to the nearest integer. Risk points for each variable were determined by these rounded integers. The sum of all the risk points formed the

overall risk score. Risk (%) for an adverse event was calculated using the formula, 100/(1+e(3.697−(risk score / 2))). This model has not yet been validated by external datasets.

Aletti et al developed a risk-adjusted model to compare the outcomes of ovarian cancer surgery between three tertiary cancer centres in the US. [44] Patient with FIGO Stage IIIC and IV ovarian cancer were included in the study. Patient characteristics including age, ASA grade, pre-operative serum albumin and creatinine levels were recorded. Surgical parameters included surgical stage and grade, complexity of procedure, presence and volume of ascites. Outcomes included length of hospital stay, major postoperative morbidity (defined using a pre-determined list), three month mortality and inability to receive chemotherapy. Univariate analysis followed by multivariable regression was performed to develop a risk prediction model. Observed to expected ratios were then calculated for each of the centres for the different outcomes. The study found that serum albumin, ASA grade, age and complexity of surgery were significant predictors of the outcomes. The O/E ratios for the dependent outcome variables were found to be similar for the three centres.

2.9 Conclusion

Various surgical specialties have developed databases for ongoing collection and publication of outcomes data. Some of them like the cardiac surgery database are entirely clinician led and some others like the head and neck cancer database collect information both from Hospital Episode Statistics and clinicians. Most databases use only hospital reported data and patient reported complications are not used. However, studies that have looked at patient-reporting suggest that patients accurately report complications, if they are clearly defined. Various indices are available for assessing comorbidity and ICD codes are usually used to collect information on various comorbid illnesses. The comorbidity indices not only record information about a particular illness

but also account for its severity. Some studies have also collected information on laboratory results such as liver enzymes, electrolyte levels etc. and incorporated these into the risk prediction algorithms. Of the various indices, ACE-27 was specifically developed to capture comorbidity in cancer patients from chart review. Complications are traditionally recorded according to a pre-determined list. However, grading of complications (especially postoperative), helps to account for the severity of a complication, which can have implications on extent of surgical morbidity. Surgical complexity has been shown to have a significant impact on morbidity. This has been accounted for by either grouping the procedures into categories according to their complexity or by using a scoring system to account for each individual procedure performed as part of the whole surgery.

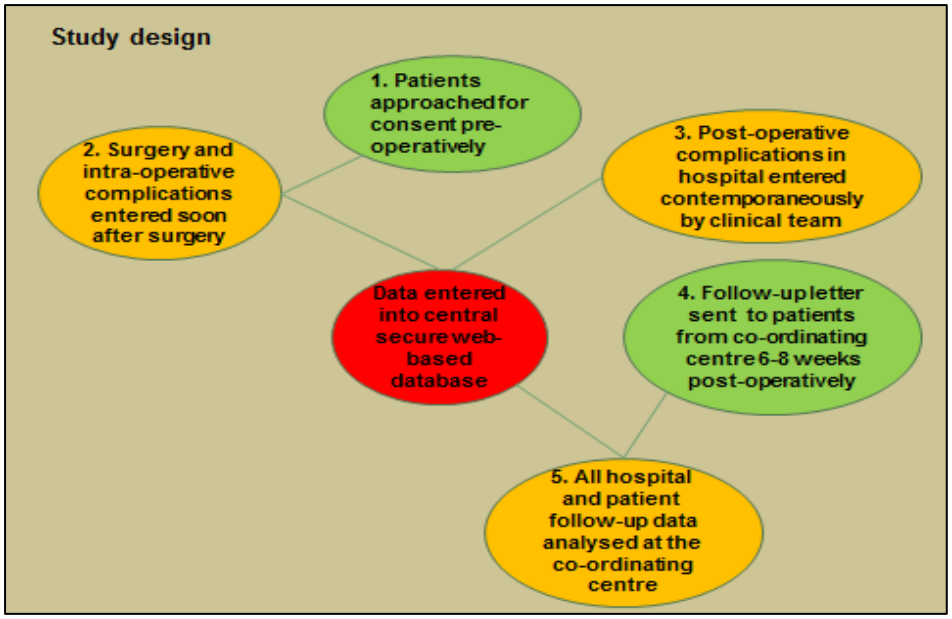
There is limited multi-centred data on surgical morbidity in gynaecological oncology and currently a national database does not exist. However the information gathered from other surgical databases can be used to develop one for gynaecological oncology.

3 Methods

3.1 Study design

The study was set out to capture data on all consecutive surgeries on consented patients, on a gynaecological oncologist's theatre list. It was designed in such a way that data could be entered contemporaneously from the operating theatre and hospital wards onto a web-based database. Details of surgery, intra-operative complications were entered by the surgeons in the operating theatre. The discharge date and post-operative complications were entered on the ward by junior doctors. The diagnosis was then entered once the pathology results were available. In order to capture complications patients may have suffered after being discharged from hospital, patients were sent a follow-up letter (FUL) from the coordinating centre (CC). All the analysis was carried out centrally at the CC at University College London. (Figure 1)

Figure 1 Study design



3.2 Participants and subjects

In the UK, surgery for gynaecological cancers in centralised in cancer centres where surgery is performed by accredited gynaecological oncologists. This study was therefore open for participation to all gynaecological cancer centres in the UK National Health Service (NHS). Participation was voluntary and in order to recruit the centres, the study proposal was announced at various network and society meetings of gynaecological oncologists.

Women who were being operated upon by gynaecological oncologists were approached for consent (Appendix 1) to participate in the study to include their identifiers and surgery data in the study. Consent was also obtained for a follow-up letter to capture complications post discharge from hospital. However, if women preferred not to receive the follow-up letter, they had the option of providing anonymised data. Surgery details of those women who declined consent were not included in the study.

3.3 Database

A web-based custom built database was designed in Microsoft SQL server to contemporaneously capture data from the participating centres. It was hosted on a secure server at the Trent Cancer Registry and the website was accessible only through N3 which is a secure private network service used by NHS hospitals in England, Wales and Scotland. The database was accessible to users who were each given a unique username and password. The users included administrative staff who entered details of consecutive patients on a surgeon's theatre list onto the database and clinicians who entered surgery, complications and diagnosis data. To ease the process of data entry and analysis, most of the fields had drop down lists which also minimised the use of free text. (Appendix 2, 3, 4, & 5) The database was designed in

such a way that data once entered and saved could not be altered unless the local clinical teams contacted the CC.

3.3.1 Training

Training in the use of the web-based programme was provided by one of the CC team members either in person by visiting the centre, or, remotely via web conferencing.

3.4 Ethical approval

Ethics approval was sought from the Joint UCL/UCLH Committees on the Ethics of Human Research in June 2008, which advised that the project was considered to be an audit, not requiring formal ethical review. However since patients were sent a follow-up letter (FUL) from the CC at University College London, informed consent was obtained to include their personal identifiers. Patients also had the option to provide anonymised data if they so preferred.

3.4.1 Inclusion criteria

All major surgical procedures performed in a gynaecological oncology theatre list were eligible for inclusion in the study. In addition to cancer surgery, the procedures also included surgery for benign conditions where there was a high pre-operative suspicion of cancer, cases with a complex surgical history that had been referred to the gynaecological oncology team and risk reducing/prophylactic surgery.

3.4.2 Exclusion criteria

Minor diagnostic procedures such as hysteroscopy, examination under anaesthesia loop excision of cervix and diagnostic laparoscopy; surgery for complications arising as a result of the primary surgery, and, those major procedures where patients had refused consent, were excluded.

3.5 Data collection

Patient identifiers included name, date of birth, address, hospital number and NHS number a unique identification number given to every patient treated on the NHS.

Pre-operative information on patients included age, comorbidity, American Society of anaesthesiologists (ASA) grade [25], Body Mass Index (BMI) and details of any previous abdominal surgery (with the exclusion of diagnostic laparoscopy).

3.5.1 Co-morbidity:

Comorbidity was captured under specific categories which included autoimmune, cardiac, integumentary/dermatology, gastrointestinal, genitourinary, musculoskeletal, metabolic/endocrine (excluding diabetes), neurology/psychiatric, respiratory, vascular, infections, hypertension, diabetes, low albumin, smoking and other neoplasms. ACE-27 comorbidity index was built into the database to capture the severity of the comorbidities. The severity was graded as 1(mild), 2(moderate), 3 (severe) and 9 (unknown). (Table 3) However during the course of the study, capturing of ACE-27 score had to be discontinued due to licensing issues for individual centres. In addition, ASA Grade was also recorded which takes into account the patient's comorbidities and their severity, and, overall performance status at the time of surgery.

3.5.2 Diagnosis

The diagnosis was recorded using International Classification of Diseases (ICD)10 codes.[2] The International Federation of Gynecology and Obstetrics (FIGO) system was used for staging the cancers.[64, 65]

For the analysis, the final diagnosis was classified into five groups - 'Ovarian' included primary ovarian, fallopian tube, peritoneal, synchronous cancers (where one of the primary sites was ovary) and cancers of unknown primary (assumed to have been ovarian cancer prior to surgery); 'Uterine' included cancers of endometrial origin,

carcinosarcomas and uterine sarcomas; ‘Cervical’ included primary cervical cancers; ‘vulval’ included primary vulval and vaginal cancers, and ‘benign’ included all the benign pathology.

3.5.3 Surgical procedures

Procedures were captured using the relevant Office of the Population Censuses and Surveys (OPCS) codes version 4.5 and 4.6.[66], which are alphanumeric codes used by clinical coders to code for interventions and surgical procedures in the NHS.

3.5.4 Surgical complexity

In addition to a hysterectomy and salpingo-oophorectomy, surgery for gynaecological cancers often involves lymphadenectomy, omentectomy, bowel resection (if there is bowel involvement) and upper abdominal procedures like stripping of the diaphragm, splenectomy etc, for staging and tumour debulking. In order to account for all the procedures performed, a scoring system was developed based on the system developed by Aletti et al for ovarian cancer surgery.[43] The modified version also included procedures used for uterine, cervical and vulval cancers in addition to those for ovarian cancer. (Table 5)

In this system each individual procedure is given a score and the total score for the surgery is the sum of the individual scores. For example, if omentectomy and pelvic lymphadenectomy were performed along with a total abdominal hysterectomy (TAH), according to this system, there would be a score of 1 for TAH, 1 for omentectomy and 2 for pelvic lymphadenectomy giving a total score of 4. Based on the overall score, Aletti et al classified the surgery as low (<3), intermediate (4-7) or high complexity (>8). In UKGOSOC, the surgeries were categorised into five groups (total complexity score of 1& 2= group 1; 3&4=group 2; 5&6=group 3; 7&8 = group 4; >8=group 5) as

surgical complexity was found to be a significant predictor of intraoperative complications during preliminary analysis.

In addition to the surgical procedure, the grade of operating surgeon (consultant, sub-specialty trainee, general obstetrics and gynaecology trainee), duration of surgery (in minutes), surgical approach (open/laparoscopic/vaginal) and estimated blood loss (<500mls, 500-1500mls, >1500-2500mls, >2500mls) were also recorded.

Table 5 Surgical complexity scoring

Procedure	Points
Laparoscopic approach	1
Total hysterectomy +/- Bilateral Salpingo-oophorectomy	1
Bilateral Salpingo-oophorectomy	1
Radical hysterectomy +/- Bilateral Salpingo-oophorectomy	4
Radical trachelectomy	3
Simple trachelectomy	1
Cervical stumpectomy	2
Ureterolysis (mobilisation of ureter from tumour / adhesions)	1
Re-implantation of ureter	2
Omental Biopsy / Staging Infracolic Omentectomy	1
Supracolic + Infracolic Omentectomy	2
Adhesiolysis (any code for adhesiolysis)	1
Pelvic Lymphadenectomy	2
Para aortic Lymphadenectomy	2
Peritoneum resection / stripping	1
Large bowel resection with primary anastomosis	3
Large bowel resection with stoma	2
Small bowel resection with anastomosis	2
Small bowel resection with end small bowel stoma	1
Appendicectomy	1
Diaphragm stripping / resection	2
Splenectomy	2
Liver resection (s)	2
Wide local excision of vulva	1
Simple vulvectomy	1
Radical vulvectomy	2
Sentinel node biopsy	1
Inguinofemoral Lymphadenectomy	2
Posterior Exenteration	5
Anterior exenteration +/- urinary conduit	7
Total exenteration	7
Surgical Complexity Score	
Complexity Score Group	**Points**
1	**<3**
2	**3-4**
3	**5-6**
4	**7-8**
5	**>8**

3.5.5 Complications

To capture intraoperative and postoperative complications, a pre-determined list of complications was compiled by reviewing the literature and following several group discussions involving the participating surgeons.

3.5.5.1 Intraoperative complications

Intraoperative complications captured included injury to various organs such as bladder, bowel, ureters and major blood vessels such as the iliac vessels, aorta, inferior venacava and renal vessels. If the estimated blood loss was more than 2.5 litres, then this was considered as an Intraoperative complication. In cases of injury to bladder and bowel, a full thickness injury was considered to be a complication. (Table 6)

Table 6 Intraoperative complications

Intra-operative complications	
Anaesthetic complications	
Cardiac	e.g. Cardiac arrythmias, Intra-operative cardic arrest
Respiratory	e.g. Aspiration, pneumothorax, pulmonary oedema
Allergic reactions	Allergic reactions including anaphylaxis
Injury to viscera	
Uterine perforation	Perforation of uterus during instrumentation
Vascular injury	Injury to major blood vessel e.g. superior and inferior mesenteric, renal, aorta, Inferior vena cava, iliacs, femorals,
GI tract injury – Stomach	Accidental injury involving complete penetration Into the lumen: Stomach
GI tract injury – Small bowel	Accidental injury involving complete penetration Into the lumen:Small bowel
GI tract injury – Large bowel	Accidental injury involving complete penetration Into the lumen: Large bowel
Bladder injury	Accidental bladder injury (full thickness)
Ureteric injury	Ligation / Transection / Diathermy burn
Intra-operative Haemorrhage	Estimated blood loss >2.5l
Other intra-operative complications (give details)	Other intraoperative complications not included in the list

3.5.5.2 Postoperative complications

Postoperative complications were captured as per the pre-determined list (Table 7).

Table 7 Postoperative complications

Post-operative complications	
Abscess/Haematoma	Pelvic or abdominal abscess / haematoma
Anastomotic leak	Anastomotic leak: Small bowel
	Anastomotic leak: Large bowel
Ileus	Post op Ileus requiring NG tube / Total parental nutrition
Bowel obstruction	Bowel Obstruction – small bowel
	Bowel Obstruction – large bowel
Bowel perforation	Small / large bowel
Bowel - other	Constipation / Diarrhoea / faecal incontinence/urgency
Bladder	Urinary retention requiring catheterisation
	Urinary obstruction
	Incontinence- stress / urge
Cardiac	Atrial fibrillation, Myocardial infarction, Cardiac failure & other cardiac problems
DVT	Confirmed DVT on imaging / Doppler
PE	Confirmed PE on imaging
Fistula	Enterocutaneous
	Enterovaginal
	Vesicovaginal
	Ureterovaginal
	Other types of fistula
Hernia	Hernia as a result of surgery
Infection	Pyrexia (>38.5°C on 2 separate occasions) after 48 hours post op requiring antibiotics or infection confirmed by culture
	MRSA/ C. difficile
Lymphocyst/Lymphoedema	Lymphoedema
	Lymphocyst
Neurological	Neuropathic pain/ paraesthesia / nerve palsy
Psychiatric	unexpected psychiatric problems postoperatively e.g. Delirium, Psychosis, Depression and other
Primary haemorrhage	Haemorrhage within 24 hours of surgery
Secondary haemorrhage	Haemorrhage after 24hours of surgery
Respiratory	Pulmonary oedema, Pneumothorax, Atelectasis, Pleural effusion and other respiratory problems excluding pneumonia (to be included in infections)
Ureteric Obstruction	Ureteric obstruction postoperative
Wound breakdown	Wound breakdown: Superficial - skin & subcutaneous tissue
	Wound breakdown: Deep - involving fascia / muscle
	Burst abdomen requiring repair under anaesthesia
Other	Other postoperative complications not included in the list

Complications were graded based on their severity and intervention required using the Clavien and Dindo system.[8] In this system, complications were graded from I to V (with two subsets each in Grade III and IV) according to severity and intervention required. Grade 1 included 'any deviation from the normal post-operative course, not requiring any pharmacological/surgical/radiological intervention', such as pain and nausea. Grade II complications included those requiring specific pharmacological intervention (e.g. infections requiring antibiotic therapy). Grade III were those complications requiring intervention (IIIa not requiring general anaesthesia and Grade IIIb requiring general anaesthesia), Grade IV were life threatening complications requiring intensive care management (IVa - single organ failure, IVb - multi-organ failure) and Grade V was death. For the final analysis, Grade 1 complications being the least severe and more likely to be subject to individual variation were excluded from the analysis.

3.5.6 Follow-up letters

The women who had given consent, were sent a FUL from the CC to capture any complications they may have suffered since leaving the hospital. They were requested to provide their contact phone numbers for any clarification. Initially a free text questionnaire (Appendix 7) was sent and the participants were asked to choose one of the two statements – 'No, I did not have a complication following my gynaecological surgery' or 'yes; I had a complication following my gynaecological surgery'. If the answer was yes, then they were asked to provide details. During the latter half of the study, a structured follow-up questionnaire (Appendix 8) was developed containing a list of complications and specific questions regarding the management of the complication to aid in easier grading of the complications according to the Clavien and Dindo system (detailed in chapter 6).

In cases where the women had mentioned complications with sequelae such as readmission, re-operation and admission to intensive care, confirmation was sought from the hospitals. All the replies were analysed by an independent clinician (RI) at the CC and graded according to the Clavien and Dindo system as mentioned previously. All Grade II-V complications were included in the analysis.

3.6 Data Analysis:

Descriptive statistics were used to characterise the cohort. Surgery was used as the denominator for all the analyses as there were women who had undergone two separate procedures as part of their treatment (repeat surgeries for complications were excluded). In addition it was possible that age, comorbidity and ASA grade could change over time in an individual woman.

The crude or unadjusted intraoperative and postoperative complications rates (CRs) were calculated. Two types of postoperative CRs were calculated: Hospital-reported and hospital- and-patient reported. All eligible surgeries were included to calculate the crude intraoperative and hospital-reported postoperative CRs. To calculate the hospital-and-patient reported postoperative CR, only those surgeries with a reply to the follow-up letter were included.

Statistical analysis was performed using STATA version 12.1 (StataCorp 2012). Multivariable regression was used to determine significant predictors of Intraoperative and Postoperative complications. This is detailed in chapter 7.

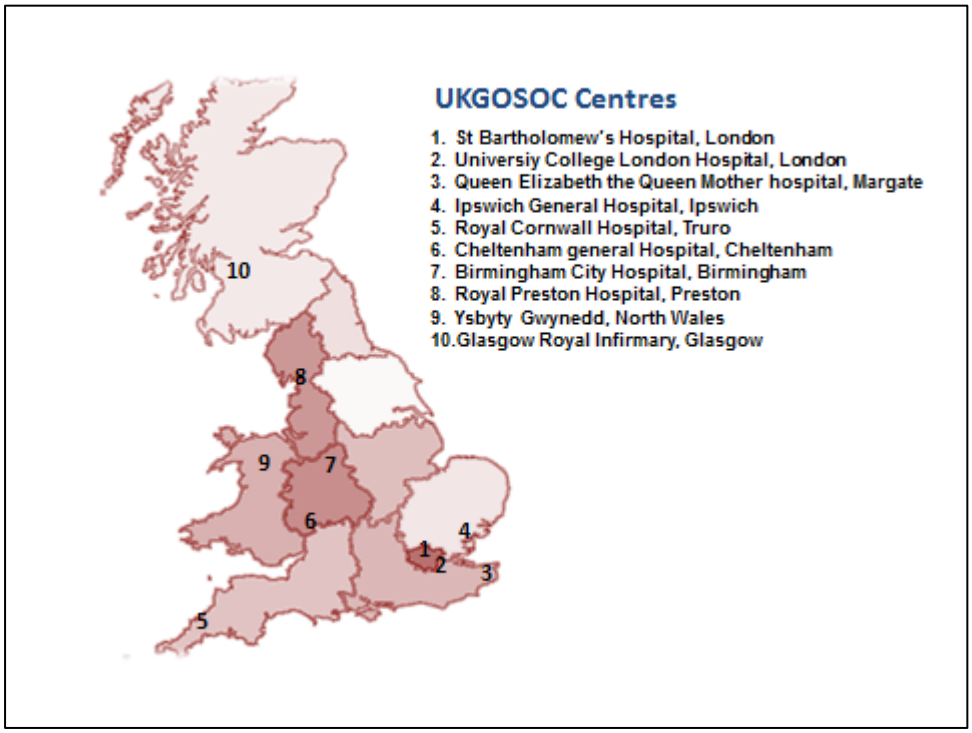
The penalised (Lasso) method of regression was used to develop risk prediction models. Observed and risk-adjusted expected CRs for individual centres (hospitals) were calculated to benchmark the performance of individual centres against the overall CR. The observed/expected complication rate ratio for individual centres was also calculated. A ratio of >1 suggested that the complication rates in that centre were

higher and a ratio of <1 suggested that they were lower than expected. The Lasso regression methodology and the calculation of observed/expected ratio are detailed in chapter 8. [67]

4 Baseline characteristics and Surgery details

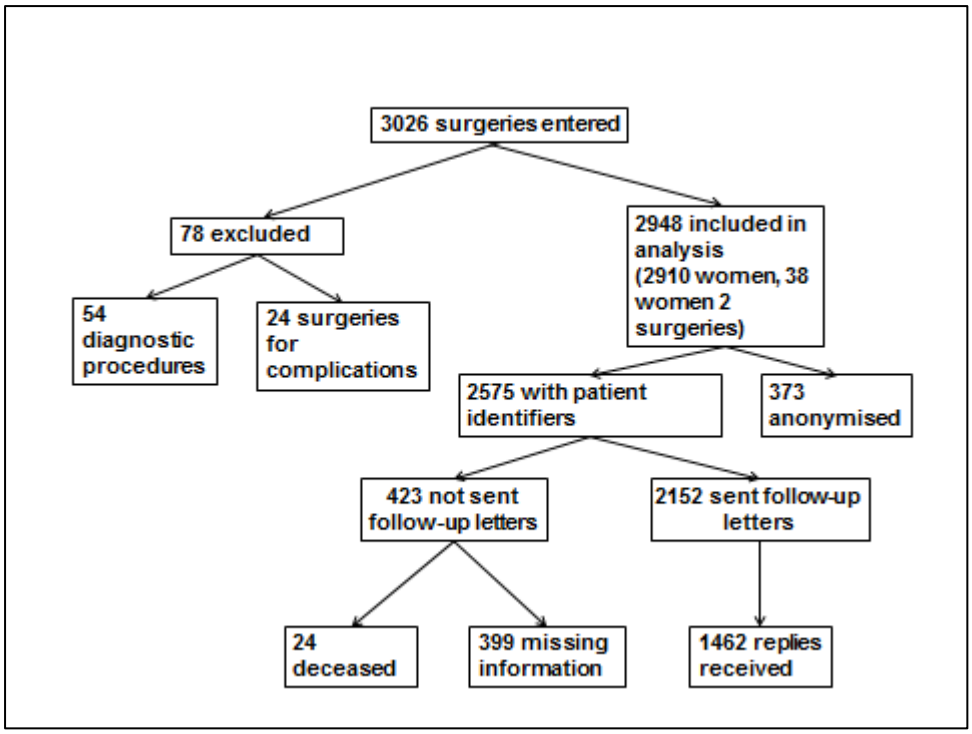
Ten accredited gynaecological oncology centres participated in the study. Eight centres were from England, one each from North Wales and Scotland. (Figure 2) During the pilot phase between 1st April 2010 and 31st January 2011, four centres participated. Six additional centres joined the main phase of the study which lasted for a thirteen month period from 1st February 2011 to 29th February 2012.

Figure 2 UKGOSOC centres



Including the pilot and the main phase, a total of 3026 operations were captured. 78 operations were excluded - 54 diagnostic procedures and 24 surgeries for complications. The remaining 2948 operations were analysed which included 373 anonymised and 2575 surgeries with patient identifiers. (Figure 3) These 2948 surgeries were performed on 2910 women with 38 women having had two surgeries each.

Figure 3 Number of surgeries

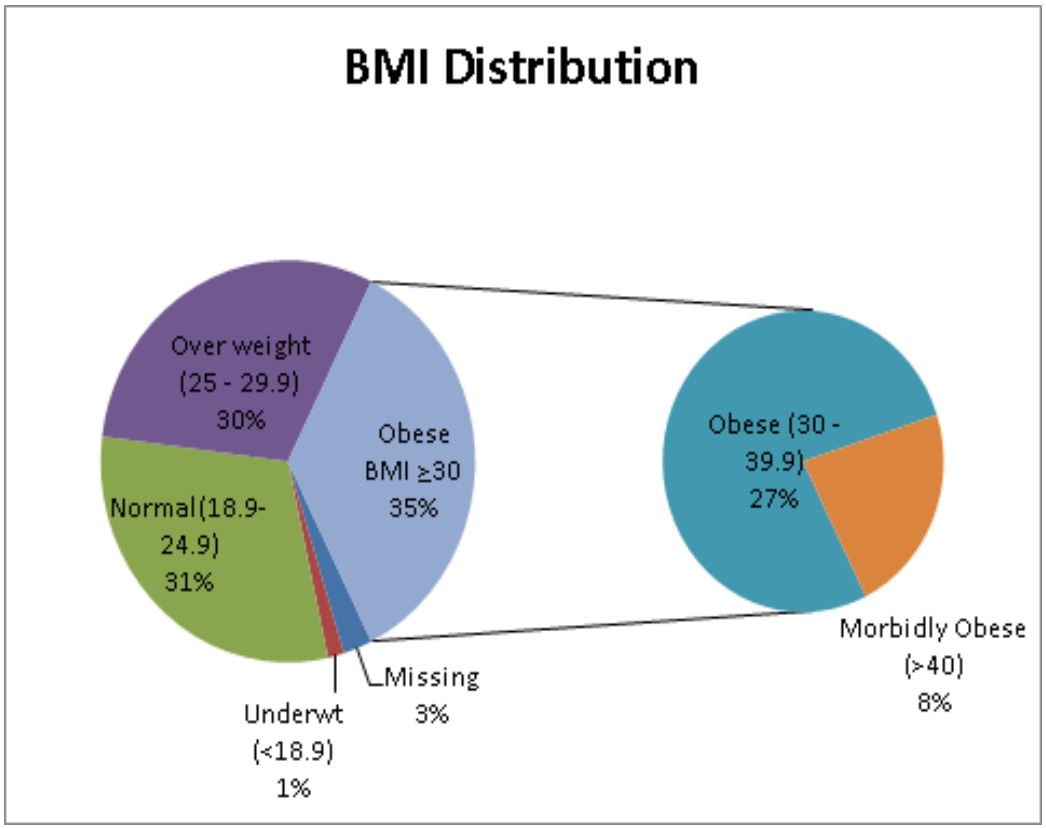


Follow-up letters: Out of the 2575 surgeries where women had given consent to receive an FUL, 2152 were sent and 1462 replies were received (68%). (Figure 3)

4.1 Baseline characteristics:

The baseline characteristics are detailed in Table 8. Surgery was used as the denominator for all calculations as there were 38 women who had undergone two surgeries as part of their treatment. The median age was 62 years (Inter quartile range [IQR] - 50-71). The median BMI was 27 (IQR- 23.8-32.4) and was $\geq$30 in 35% of the surgeries. (Figure 4) Comorbidities were present in 62.5% of the surgeries and hypertension was the commonest comorbidity (33%). The ASA grade was $\leq$ 2 in 79.4% and $\geq$3 in 20.4% of cases.

Figure 4 BMI distribution



4.2 Surgery

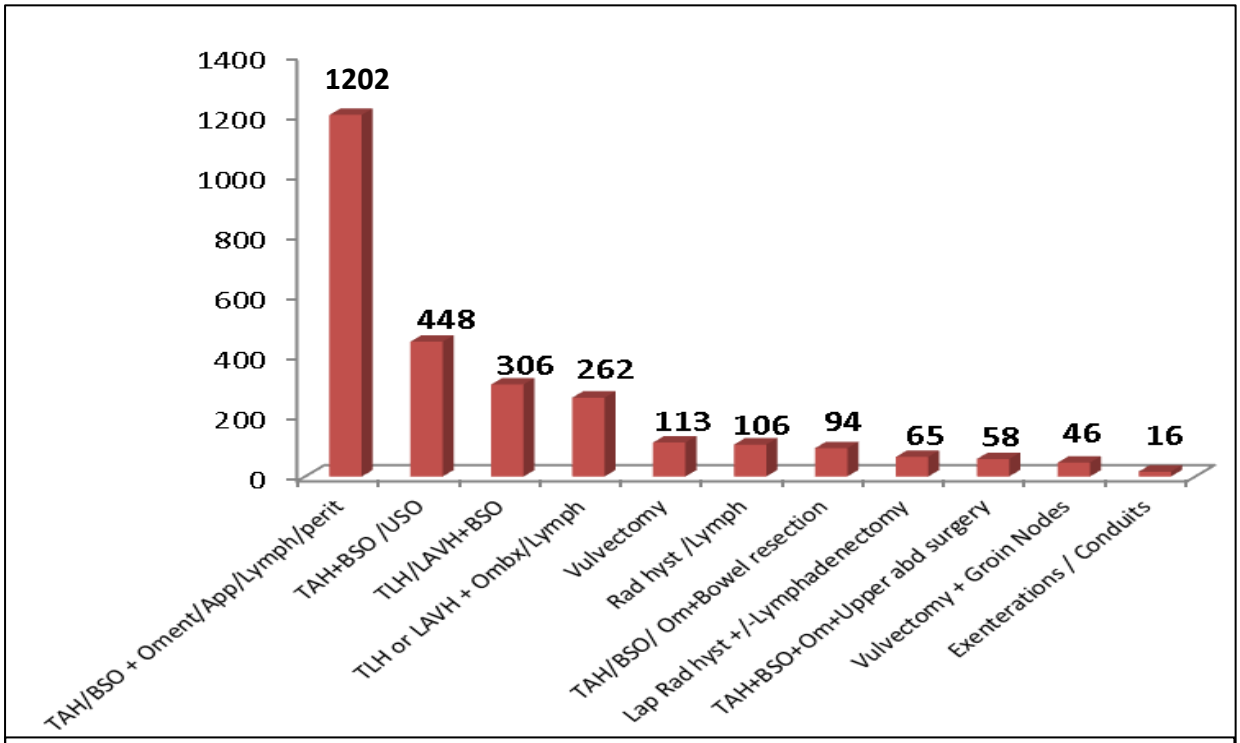
Majority of the operations were performed by consultants (n=2191, 74.3%) followed by trainees specialising in Gynaecological Oncology (n=573, 19.4%). (Table 9) 70% of procedures (n=2069) were performed through the open approach, 23% laparoscopically (n=681) and 7% were vulval / vaginal procedures (n=198). 1.6% of the laparoscopic procedures (n=11) required an emergency laparotomy. The mean duration of surgery in minutes was 120 (IQR- 90-167) for open procedures, 120 (IQR 85-170) for laparoscopic procedures and 87 (IQR 50-148) for vulval/vaginal procedures.

Table 8 Baseline characteristics

Total no. of eligible surgery	2948
Age (in years, Median, IQR)	62 (50-71)
BMI	
BMI (median, IQR)	27.4 (23.8-32.4)
BMI Category	**n (%)**
Underweight (<18.5)	41 (1.4)
Normal (18.5-24.9)	897 (30.4)
Overweight (25-29.9)	895 (30.4)
Obese (30-39.9)	805 (27.3)
Morbidly obese (≥ 40)	236 (8)
Missing	74 (2.5)
ASA Grade	**n (%)**
1&2	2341 (79.4)
≥3	600 (20.4)
Missing	7 (0.2)
Co-morbidity	**n (%)**
0	1105 (37.5)
1 - 3	1716 (58.2)
>3	127 (4.3%)
Type of co-morbidity	**n (%)**
Hypertension	973 (33)
Cardiac	308 (10)
Diabetes	298 (10)
Respiratory	287 (10)
Musculoskeletal	261 (9)
Neurology/Psychiatric	208 (7)
Other Neoplasms	148 (5)
Coagulation/Thrombosis	116 (4)
Gastrointestinal	104 (4)
Smoking	95 (3)
Vascular	86 (3)
Genitourinary	52 (2)
Autoimmune	37 (1)
Integumentary/Dermatology	30 (1)
Infections	13 (0.4)
Low Albumin	11 (0.4)
Previous abdominal surgery	1025 (34.7)

The median length of stay in days was 4 (IQR 3-6) for open procedures, 2 (IQR 1-2) for laparoscopic procedures and 4 (IQR 2-7) for vulval/vaginal procedures.

Figure 5 Key procedures performed



TAH- Total abdominal hysterectomy; BSO- Bilateral salpingo-oophorectomy; Oment- omentectomy; App- Appendicectomy; Lymph- Lymphadenectomy; perit- peritonectomy; USO- Unilateral Salpingo-oophorectomy; TLH- Total Laparoscopic Hysterectomy; LAVH- Laparoscopically Assisted Vaginal Hysterectomy; OmBx-Omental Biopsy; Rad hyst- Radical hysterectomy; Om-Omentectomy; Lap Rad Hyst- Laparoscopic Radical Hysterectomy; abd- abdominal

Staging procedure including bilateral salpingo-oophorectomy+/-total abdominal hysterectomy and pelvic/para-aortic lymphadenectomy+/- omentectomy+/-appendicectomy+/-peritonectomy was the commonest procedure performed followed by a simple open hysterectomy and bilateral salpingo-oophorectomy. Total laparosopic/laparoscopically assisted vaginal hysterectomy was the third commonest procedure performed. (Figure 5)

Table 9 Surgery details

Grade of operating surgeon	**n (%)**
Consultant	2191 (74.3)
Sub-specialty trainee	573 (19.4)
General Obstetrics & Gynaecology Trainee	108 (3.7)
Missing	76 (2.6)
Diagnosis	
Ovarian*	989 (33.5)
Uterine**	820 (27.8)
Cervical	207 (7.0)
Vulval***	176 (6.0)
Benign	756 (25.7)
Surgical approach	**n (%)**
Open	2001 (67.9)
Laparoscopic elective proceed to laparotomy	68 (2.3)
Laparoscopic emergency proceed to laparotomy	11 (0.3)
Laparoscopic****	670 (22.7)
Vulval/Vaginal procedures	198 (6.7)
Duration of surgery (minutes)	**Median, IQR**
Open procedures	120 (90- 167)
Laparoscopic procedures	120 (85- 170)
Vulval/Vaginal procedures	87 (50 -148)
Surgical Complexity	**n (%)**
Group 1 (Complexity score 1&2)	1398 (47)
Group 2 (Complexity score 3&4)	982 (33)
Group 3 (Complexity score 5&6)	430 (15)
Group 4 (Complexity score 7&8)	93 (3)
Group 5 (Complexity score >8)	45 (2)
Surgical procedures	**n (%)**
TAH+/-BSO+Omentectomy /Appendicectomy/Lymphadenectomy/peritonectomy	1202 (40.8)
TAH+/-BSO /USO	448 (15.2)
Radical hysterectomy+/- BSO+/- Lymphadenectomy	106 (3.6)
TAH/BSO/ Omentectomy+Bowel resection	94 (3.2)
TAH+BSO+Omentectomy+Upper abdominal surgery	58 (2.0)
Exenterations +/- Conduits	16 (0.5)
Open Lymphadenectomy	14 (0.5)
Exploratory/Abandoned procedure	29 (1.0)
Other open procedures	105 (3.6)
TLH/ LAVH+BSO	306 (10.4)
TLH or LAVH +/- Omental biopsy+ Lymphadenectomy	262 (8.9)
Laparoscopic Radical hysterectomy +/-Lymphadenectomy	65 (2.2)
Laparoscopic Lymphadenectomy	30 (1.0)

Table 9 Surgery details continued…..

Other Laparoscopic procedures	18 (0.6)
Vulvectomy (Radical/simple)	113 (3.8)
Vulvectomy + Inguinofemoral lymphadenectomy	46 (1.6)
Inguinofemoral lymphadenectomy	18 (0.6)
Vaginectomy	12 (0.4)
Other vulval/vaginal procedures	6 (0.2)
Length of Stay	**Days, Median (IQR)**
Open procedures	4 (3-6)
Laparoscopic	2 (1-2)
Vulval/Vaginal procedures	4 (2-7)

*Includes primary ovarian, fallopian tube, primary peritoneal, synchronous, non-gynae primary cancers
**Includes primary endometrial cancer, carcinosarcoma & sarcoma of the uterus
***Includes primary vulval and vaginal cancers
****Includes total laparoscopic and laparoscopic and vaginal procedures
TAH- Total abdominal hysterectomy
BSO- Bilateral salpingo-oophorectomy
USO- Unilateral salpingo-oophorectomy
TLH- Total laparoscopic hysterectomy
LAVH- Laparoscopic assisted vaginal hysterectomy

989 operations (33.5%) were performed for ovarian and related cancers. This group included primary ovarian, fallopian tube and primary peritoneal cancers and those cases where the suspected primary had been ovarian prior to surgery (unknown primary, non-gynae primary and synchronous cancers, n=70). 733 (74.1%) were debulking procedures that comprised of hysterectomy with bilateral salpingo-ooporectomy with omentectomy / lymphadenectomy / appendicectomy /peritonectomy, 81 (8.2%) were debulking procedures requiring bowel resection with anastomosis / stoma and 57 (5.8%) were procedures requiring upper abdominal debulking involving the diaphragm, spleen, liver etc.

820 operations were for ‘uterine’ cancers (27.8%) and this included primary endometrial adenocarcinomas, carcinosarcomas and uterine sarcomas. Total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO) with lymphadenectomy (n=284, 34.6%) was the commonest procedure followed by

laparoscopic hysterectomy (n=211, 25.7%), TAH with BSO (n=168, 20.5%), and laparoscopic hysterectomy with lymphadenectomy (n= 97, 11.8%).

207 operations were for primary cervical cancer (7%). Open radical hysterectomy (and lymphadenectomy) was the commonest procedure (n=69, 33.3%) followed by laparoscopic radical hysterectomy (and lymphadenectomy) (n= 59, 28.5%).

There were 176 surgeries for 'vulval' cancer (6%) which included primary vulval and vaginal cancers. Vulvectomy (radical/simple) was the commonest procedure (n=95, 54%) followed by vulvectomy with inguinofemoral lymphadenectomy (n=46, 26.1%).

There were 756 operations for benign pathology (25.6%). TAH, BSO with omentectomy/lymphadenectomy/appendicectomy (n=318, 42.1%) was the commonest procedure followed by TAH with BSO (n=178, 23.5%) and laparoscopic hysterectomy with BSO (n= 117, 15.5%).

4.3 Discussion:

Majority of the patients were in the older age group with the average age being 62 years. A third of the patients were obese and more than half of the patients had one or more comorbidities. Even though uterine cancers are commoner than ovarian cancers in the general population, in this study, there were more ovarian than uterine cancers. This could have been due to the early stage low grade (Stage 1A, Grade1) endometrial cancers being operated upon in the local hospitals (cancer units) rather than at the cancer centres that participated in the study. Overall there were 919 operations performed for primary ovarian/tubal/primary peritoneal cancers. In addition, operations performed for synchronous cancers (where one of the primary sites was ovary), cancers of unknown primary and non-gynaecological primary cancers were included in the 'ovarian cancer' category (n=70) as pre-operatively the primary had been assumed to be ovary in these cases and also, the surgery performed was very

similar to that for ovarian cancer. This further increased the number of surgeries performed for ‘ovarian cancer’ to 989. It was very much a consultant led service with the consultant being the primary surgeon in three out of four (74%) cases. Only four of the ten centres had trainees specialising in gynaecological oncology and therefore they were the primary surgeons in just 19% of the operations.

5 Intraoperative and hospital-reported postoperative complications

This chapter summarises hospital-reported complications which include intraoperative and those postoperative complications reported/entered by the clinicians.

5.1 Method

Intraoperative complications were entered by the surgeons soon after the surgery, preferably in the operating theatre and the postoperative complications were recorded by the clinical teams as when they occurred on the ward using a predetermined list. (Table 6 & 7) The Clavien and Dindo system was used to grade the postoperative complications according to their severity and intervention required. (Table 10) [8] Only Grade II-V complications were included in the analysis. Grade 1 complications were excluded as they were by definition 'any deviation from the normal post-operative course not requiring any pharmacological/surgical/radiological intervention'. They were therefore likely to be subject to individual variation and to have minimal impact on the post-operative course.

Table 10 Clavien and Dindo's Classification of complications

Grade 1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions
	Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and TPN are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anaesthesia
IIIb	Intervention under general anaesthesia
Grade IV	Life-threatening complication (including CNS complications- excludes TIA)* requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
Grade V	Death of a patient

5.1.1 Complication rate

Intraoperative complication rate (CR) was calculated by dividing the number of surgeries with intraoperative complications by the total number of eligible surgeries.

Hospital reported postoperative CR was calculated by dividing the number of surgeries with Grade II-V postoperative complications by the total number of eligible surgeries.

5.2 Results

5.2.1 Intraoperative complications

There were 143 intraoperative complications in 139 surgeries (two complications each in two surgeries). Therefore the overall Intraoperative complication rate (CR) in 2948 surgeries was 4.7% (139/2948; 95% CI 4.0 - 5.6). Intraoperative haemorrhage (1.4%) followed by bladder and small bowel injury (0.7%) were the most frequently occurring intraoperative complications. (Table 11)

For those operations resulting in a cancer diagnosis, there were 121 complications in 118 out of 2192 operations giving an Intra Op CR of 5.4% (95% CI 4.5 – 6.4) for cancer surgery.

5.2.1.1 Intraoperative complications by diagnostic category

Ovarian cancer: The highest Intraoperative CR was seen for ovarian cancer surgery (78/989; 7.9%, 95% CI – 6.4 - 9.7). (Table 11)Two out of the three exenterations had an Intra-op complication (66.8%). The Intra-op CR was 19.8% (16/81) for procedures with bowel resection and 14% (8/57) for procedures involving upper abdominal surgery.

Cervical cancer: The second highest Intra-op CR (10/207, 4.8%; 95% CI 2.6-8.7) was seen for cervical cancer surgery. (Table 11) The Intra-op CR for the subset of open radical hysterectomies was 5.5% (3/55) and was almost double (10%, 5/50) for

laparoscopic radical hysterectomies. Emergency laparotomy was required for only one (2%; 1/50) of the laparoscopic radical hysterectomies.

Uterine cancer: 28 out of 820 surgeries for uterine cancer had Intraoperative complications (3.4%, 95% CI 2.4 - 4.9). (Table 11) Intraoperative haemorrhage was again the commonest complication (n=8, 1%) followed by vaginal tear during laparoscopic hysterectomy (n=5, 0.6%) and small bowel injury (n=4, 0.5%). (Table 12)

Open vs laparoscopic hysterectomy: Since hysterectomy or hysterectomy with pelvic lymphadenectomy is the main surgical procedure for most uterine cancers, comparisons were made between the open and laparoscopic approach. Out of a total 738 hysterectomies, 431 were open (58.4%) and 307 laparoscopic (41.6%). The intraoperative complication rate was 2.6% for open (n=11) and 3.6% for the laparoscopic approach (n=11). Emergency laparotomy was required in five out of 307 (1.6%) laparoscopic hysterectomies. Pelvic lymphadenectomy was performed with 166 (38.5%) of open and 82 (38.9%) of laparoscopic hysterectomies. For the subset of hysterectomies with lymphadenectomy, the intraoperative complication rate was 1.8% for open (n=3) and 7.3% (n=6) for the laparoscopic approach.

Intraoperative haemorrhage was the most common complication for ovarian, uterine and cervical cancer surgery. (Table 12)

Vulval cancer: There were only two surgeries with an intraoperative complication for vulval cancer (2/176, 1.1%) and both were bladder injuries. (Table 12)

Table 11 Intraoperative complication rate for each diagnostic category

Primary site (diagnosis)	No. of surgery with complications/Total no. of surgery	Rate (%)
Ovary	78/989	7.9
Uterine	28/820	3.4
Cervix	10/207	4.8
Vulva	2/176	1.1
Benign	21/756	2.8

Table 12 Types of intraoperative complications

Intraoperative Complications (No. of surgery = 2948)						
Complication category	**Total No. (%)**	**Primary cancer site**				**Benign**
		Ovary[1]	**Uterine[2]**	**Cervix**	**Vulva[3]**	
Intra-operative Haemorrhage	**41 (1.4)**	27	8	3		3
Bladder injury	**22 (0.7)**	11	3	2	2	4
GI tract injury- Small bowel	**22 (0.7)**	16	4			2
GI tract injury- Large bowel	**11 (0.4)**	4	2	1		4
Vascular Injury	**13 (0.4)**	7	2	1		3
Vaginal tear	**7 (0.2)**		5			2
Cardiac	**6 (0.2)**	2		1		3
Diaphragmatic injury	**5 (0.2)**	5				
Ureteric Injury	**5 (0.2)**	1	2	1		1
Splenic injury	**3 (0.1)**	3				
Gall bladder injury	**1 (0.03)**		1			
Liver laceration	**1 (0.03)**	1				
Nerve injury	**1 (0.03)**			1		
Respiratory	**1 (0.03)**	1				
Uterine perforation	**1 (0.03)**		1			
Anaphylaxis	**1 (0.03)**		1			
Other	**2 (0.07)**	1	1			
Total intraoperative complications	**143**	**79**	**30**	**10**	**2**	**22**
Total no. of Surgery	**2948**	**989**	**820**	**207**	**176**	**756**

1- Includes primary ovarian, fallopian tube, primary peritoneal, synchronous, non-gynae primary and unknown primary cancers
2- Includes primary endometrial cancer, carcinosarcoma & sarcoma of the uterus
3- Includes primary vulval and vaginal cancers

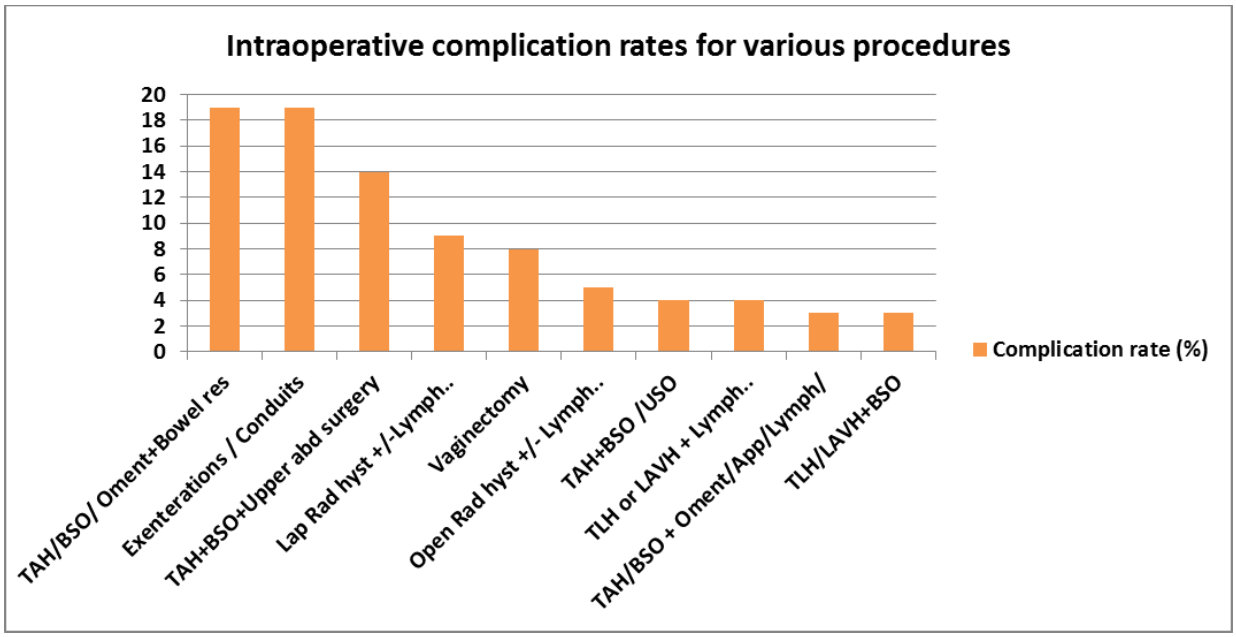
Benign diagnosis: Of the 756 operations for benign conditions, there were 21 surgeries with Intraoperative complications (2.8%). (Table 11) Bladder and large bowel injury were the most commonly occurring complications (n=4, 0.5%), followed by

Intraoperative haemorrhage, vascular injury and cardiac complications (n=3, 0.4% each). (Table 12)

Overall, intraoperative haemorrhage was the most frequently occurring complication (n=41, 1.4%) followed by bladder and small bowel injury (n=22, 0.7%) (Table 12)

The intraoperative CR increased with increasing surgical complexity with rates of 2.9% (41/1398) for a surgical score of <3, 4.4% (43/982) for a score of 3-4, 7.9% (34/430) for a score of 5-6, 12.9% (12/93) for a score of 7-8 and 20% (9/45) for a score of >8. Overall, procedures with bowel resection had the highest intraoperative complication rate (18 out of 94, 19.1%) followed by exenterations (3 out of 16, 18.8%), debulking surgery requiring upper abdominal resections (8 out of 58, 13.8%) and laparoscopic radical hysterectomy (6 out of 65, 9.2%). (Figure 6)

Figure 6 Intraoperative complications for individual surgical procedures



TAH- Total abdominal hysterectomy; BSO- Bilateral salpingo-oophorectomy; abd- abdominal, lap- laparoscopic, Lap Rad Hyst- Laparoscopic Radical Hysterectomy; Lymph- Lymphadenectomy; USO- unilateral salpingo-oophorectomy; Omen bx- omental biopsy; App- Appendicectomy; perit- peritonectomy; TLH- Total Laparoscopic Hysterectomy; LAVH- Laparoscopically Assisted Vaginal Hysterectomy

5.2.2 Hospital reported postoperative complications

Hospitals reported 481 Grade II-V postoperative complications in 424 out of the total 2948 surgeries resulting in a postoperative CR of 14.4% (95% CI 13.2-15.7). The highest postoperative CR was noted for Vulval cancer surgery (51/176, 29% 95% CI – 22.7 – 36.0). (Table 13)

For those operations resulting in a cancer diagnosis, 398 Grade II-V complications were recorded in 349 out of 2192 operations giving a postoperative Op CR of 15.9% (95% CI 14.4 – 17.5).

Table 13 Hospital-reported postoperative complication rate for each diagnostic category

Primary site (diagnosis)	No. of surgery with complications/Total no. of surgery	Rate (%)
Ovary	167/989	16.9
Uterine	87/820	10.6
Cervix	44/207	21.3
Vulva	51/176	29.0
Benign	75/756	9.9

Infections (131/2948, 4.4%) and wound breakdown (114/2948, 3.87%) were the most common complications. (Table 14)

5.2.3 Grade of hospital-reported postoperative complications

Out of the total 481 complications, 380 (79%) were Grade II, i.e. requiring medical intervention only. Remaining 101 (21%) were Grade III or worse, i.e. requiring some radiological/surgical intervention/ management in intensive care (15 Grade IIIa, 60 Grade IIIb, 21 Grade IVa and five Grade V). (Table 15)

Table 14 Hospital-reported postoperative complications

Hospital-reported Grade II-V postoperative complications (No. of surgery = 2948)						
Complication category	**Total (% of total surgery)**	**Primary cancer site**				**Benign**
		Ovary	**Uterine**	**Cervix**	**Vulva**	
Infection	**131 (4.4)**	47	30	20	12	22
Wound breakdown	**114 (3.9)**	34	27	3	29	21
Abscess/Haematoma	**25 (0.8)**	9	5	3	1	7
Bladder	**22 (0.7)**	4	6	4	1	7
Lymphocyst/Lymphoedema	**20 (0.7)**	3	3	3	11	
PE	**10 (0.3)**	8	2			
DVT	**2 (0.1)**	2				
Primary haemorrhage	**9 (0.3)**	4	2	1		2
Secondary haemorrhage	**14 (0.5)**	7	3	1		3
Ileus	**21 (0.7)**	14	3			4
Bowel obstruction	**10 (0.3)**	6	2	1		1
Bowel perforation	**6 (0.2%)**	3	1		1	1
Bowel - other	**11 (0.4)**	7	1			3
Fistula	**10 (0.3)**	6	1	3		
Anastomotic leak	**5 (0.2%)**	4		1		
Respiratory	**13 (0.4)**	7	4	1		1
Cardiac	**11 (0.4)**	6	3		1	1
Neurological	**7 (0.2)**	1	1	2	2	1
Psychiatric	**7 (0.2)**	4			1	2
Hernia	**1 (0.03)**					1
Hydronephrosis	**1 (0.03)**	1				
Other	**31 (1.1)**	17	5	2	1	6
Total	**481**	**194**	**99**	**45**	**60**	**83**
Total no. of surgery	**2948**	**989**	**820**	**207**	**176**	**756**

Re-operation/return to theatre was required following 63 operations (60 Grade IIIb and three Grade IVa; 2.1%), admission to intensive care following 21 (0.7%) and readmission following 56 operations (1.9%).

There were five (0.2%) peri-operative deaths, i.e. deaths within thirty days of surgery reported by the hospitals. Two deaths were from septicaemia, one each from chest

infection, adult respiratory distress syndrome and acute renal failure leading to multi-organ failure.

Table 15 Grade of hospital-reported postoperative complications

Grade of hospital reported complications (No. of surgery = 2948)						
Complication category	**Complication Grade II-V**					
	II	**IIIa**	**IIIb**	**IV**	**V**	**Total**
Infection	123	1		4	3	**131**
Wound breakdown	97		16	1		**114**
Abscess/Haematoma	15	5	5			**25**
Bladder	21		1			**22**
Lymphocyst/Lymphoedema	20					**20**
PE	8	1		1		**10**
DVT	2					**2**
Primary haemorrhage			9			**9**
Secondary haemorrhage	11	1	1	1		**14**
Ileus	21					**21**
Bowel obstruction	5		5			**10**
Bowel perforation			5	1		**6**
Bowel - other	8	1	2			**11**
Fistula	1	1	8			**10**
Anastomotic leak			4	1		**5**
Respiratory	6	1		5	1	**13**
Cardiac	10			1		**11**
Neurological	7					**7**
Psychiatric	7					**7**
Hernia	1					**1**
Hydronephrosis		1				**1**
Other	17	3	4	6	1	**31**
Total	**380**	**15**	**60**	**21**	**5**	**481**

5.3 Discussion

The overall intraoperative complication rate was 4.7% (95% CI 4.0 - 5.6) and 5.4% (95% CI 4.5 – 6.4) when limited to confirmed malignancies.

The overall intraoperative complication rate of 4.7% was lower than the 8% reported from a tertiary gynaecological oncology centre in Australia (Kondalsamy Chennakesavan et al, 2009), which was probably influenced by the small sample size

of 381 women in their study compared to nearly 3,000 in UKGOSOC. [45] Rates for gynaecological malignancy alone were lower than intraoperative complication rates in women undergoing pelvic surgery for rectal cancer (12%).[68] Lower complication rates in surgeries for gynaecological compared to colorectal cancer are likely to be related to the lower rates of bowel resection and possible anastomosis and resultant lower incidence of anastomotic leaks, peritonitis or other bowel complications. In UKGOSOC only 4.2% (91/2192) of the cancer surgeries required a bowel resection.

The lower incidence of intraoperative complications was paralleled by the lower (1.6%) laparoscopic to emergency laparotomy conversion rates compared to the Australian study (2.4%) and the rectal cancer surgery multi-centre trial (16%).[68] Although only 25% of all the abdominal procedures were performed using the laparoscopic approach, for endometrial cancer, this approach was used in 41.8% of the hysterectomies. The intra-operative complication rates in the open and laparoscopic groups were similar but there was a higher postoperative complication rate for open compared to laparoscopic procedures. These findings were similar to that reported in two randomised controlled trials comparing laparoscopic and open approaches for hysterectomy+/- lymphadenectomy for endometrial cancer [69] [70]. For laparoscopic radical hysterectomies, the conversion to laparotomy rate was 2%, similar to the 1.7% reported in a Korean study comparing open vs laparoscopic approaches for early stage cervical cancer. [71]

The hospital reported postoperative CR was 14.4% (95% CI 13.2-15.7) for the entire cohort and 15.9% when limited to confirmed malignancies (95% CI 14.4 – 17.5). These rates were slightly lower than the 21% quoted in the Australian study. The rate of 3.3% for Grade III & IV complications was however was similar to that in the Australian study (3.5%). [45]

Vulval cancer surgery had the highest postoperative CR (29%) with a 17% wound infection/breakdown rate and a 7% lymphoedema rate. The wound infection rate was comparable to the 17 - 39% reported in a review of complications of vulval cancer surgery but the lymphoedema rate was much lower compared to the 14 - 49% reported in the same review.[72] This discrepancy is likely due to these complications occurring following discharge from hospital and therefore not recorded by the centre/hospital where the initial surgery was performed.

Surgery for cervical cancer had the second highest postoperative complication rate of 21%. All the three fistulae and three out of the four bladder complications had occurred following laparoscopic radical hysterectomies. The fistula rate of 1.5% was comparable to the 1.7% for laparoscopic radical hysterectomies in the Korean study.[71] For uterine cancers, the overall hospital reported wound infection rate was 3.3% and all of them were as a result of open surgery. This rate was comparable to the 4% wound infection rate seen in a randomised controlled trial comparing open and laparoscopic approaches for endometrial cancer surgery. [70]

6 Patient follow-up and postoperative complications

Surgical complications data are conventionally collected from review of hospital case notes or from administrative data such as Hospital Episode Statistics (HES). The former is time consuming and resource intensive and the latter can lead to errors from miscoding of complications by administrative staff. [73] Also, complications that occur following discharge can be missed as patients tend to consult their general practitioner or their local hospital for their treatment. This is more likely after cancer surgery which is centralised in accredited centres in the UK. Therefore in UKGOSOC, patients were sent a follow-up letter (FUL) six to eight weeks postoperatively with the aim of specifically capturing these complications.

There is limited literature on the additional value of patient-reported complications following surgery. Three studies [14, 15, 74] examining concordance of clinical and patient-reported complications, in elective hip and knee replacement surgery were found. These suggested variable rates of correct reporting for different complications with good concordance for clearly defined complications such as deep vein thrombosis (DVT) and pulmonary embolism (PE) and poor concordance for those less clearly defined such as ‘major bleeding’.

In UKGOSOC two types of FUL letters were used to capture complications data- a free-text format and a questionnaire format. Concordance between hospital and patient reporting and the difference in the estimates of overall postoperative morbidity according to data source were calculated.

6.1 Method

Patient consent was obtained to send FUL postoperatively. Initially a free text format of FUL was sent to patients. The women were asked an open ended question- ‘*Have you*

had a complication following your gynaecological surgery? If so, please give details' (Appendix 7). They were also requested to provide their telephone numbers so that they could be contacted for any clarifications.

Interim analysis of the FUL was undertaken in July 2011 to elucidate the common postoperative complications experienced by women following which a closed format questionnaire was developed to capture data in a uniform fashion that could be easily interpreted and analysed. A list of 11 common postoperative complications was derived which included wound breakdown, infections, pelvic/abdominal abscess/haematoma, heavy vaginal bleeding, lymphoedema, lymphocyst, constipation, other bowel problems, bladder problems (including incontinence, urinary retention), DVT and PE. Every complication was briefly described and the questions included a sub-set on management (whether readmission or reoperation had been necessary). Space was provided after each question for the patient to add any additional details if they so wished. Women were also asked questions about the main language spoken in their home, whether the questionnaire was in a language that they could easily understand, and their educational status. The responses were kept to simple 'yes/no' answers, with a view to minimising free text. (Appendix 8)

Initially two formats of the questionnaire were designed. These were then circulated among eight non-medical female colleagues and two lay volunteers. They were asked to comment on the questions and the format of the questionnaire. In the first format, women were asked if they had suffered a particular complication from surgery. Following the main question, space was provided to enter details regarding the management. In the second format, the main question was followed by a subset of specific questions regarding management with yes/no answers. Seven out of the ten women who had been asked to evaluate the questionnaire preferred the second

format as the questionnaire though longer than the first was easier to complete with minimum writing required. Hence this latter format was adopted (Appendix 8).

All replies were entered on the central audit database. The data was cleaned and analysed by a single clinician (RI), who also contacted the women for clarification of equivocal replies. The postoperative complications were once again classified according to the Clavien and Dindo system from Grade I to V (with two subsets each in Grade III and IV), based on their severity and the intervention required [8] (Table 9). Grade I complications being the least severe (not requiring any specific pharmacological / surgical / radiological intervention) were excluded from future analysis as it was felt these could be subject to individual variation. Clinical teams were contacted for individual confirmation of all Grade II-V Postoperative complications not previously reported by the hospital. Patient-reported readmissions, reoperations, and admissions to intensive care were forwarded as soon as the replies were received and all other patient-reported complications were forwarded at quarterly intervals.

The postoperative complication rate (CR) was calculated as the proportion of eligible surgeries with a Grade II-V postoperative complication. Concordance was calculated as proportion of Grade II-V patient-reported complications that were verified by the hospital clinician.

Those complications that could not be graded but were included in the analysis were grouped with Grade II complications when calculating Postoperative complication rates, concordance and sensitivity according to complication Grade.

6.2 Results

A total of 2575 FULs were sent to consented women (423 not sent- 399 missing or incomplete address, 24 deceased) and 1462 (68%) replies were received. (Figure 3)

The final diagnosis in the 1462 surgeries included ovarian cancer in 481, uterine cancer in 427, cervical cancer in 80, vulval cancer in 79 and benign pathology in 395.

In 256 of 265 (97%) questionnaire format replies, women reported that English was the main language spoken at home. Of the remaining nine (3%) only two women reported having difficulty understanding English and requiring help to complete the questionnaire. 30% of the women had left school before 15 years of age and 15% had completed a bachelor's degree (Table 16).

Table 16 Details of women who replied to questionnaire format of follow-up letter

	Number	**%**
Main Language spoken at home* (n=265)		
English	256	**97**
Other**	9	**3**
Questionnaire in a language that could be understood* (n=265)		
Yes	263	**99**
No	2	**1**
Help required to complete questionnaire* (n=265)		
Yes	2	**1**
No	263	**99**
Educational status* (n=265)		
Finished school at or before 15 years of age	79	**30**
Completed GCSEs, O levels or equivalent	67	**25**
Completed A levels or equivalent	21	**8**
Completed further education but not a degree	45	**17**
Completed a bachelor's degree/master's degree/PhD	41	**15**
Other (Please specify)	5	**2**
Missing	7	**3**
Total	**265**	

**5 Welsh, 2 Polish, 1 Greek, 1 French

6.2.1 Hospital reported complications

In 172 of these 1462 surgeries, hospitals reported 200 Grade II-V Postoperative complications. The commonest complications reported were infections (51, 26%),

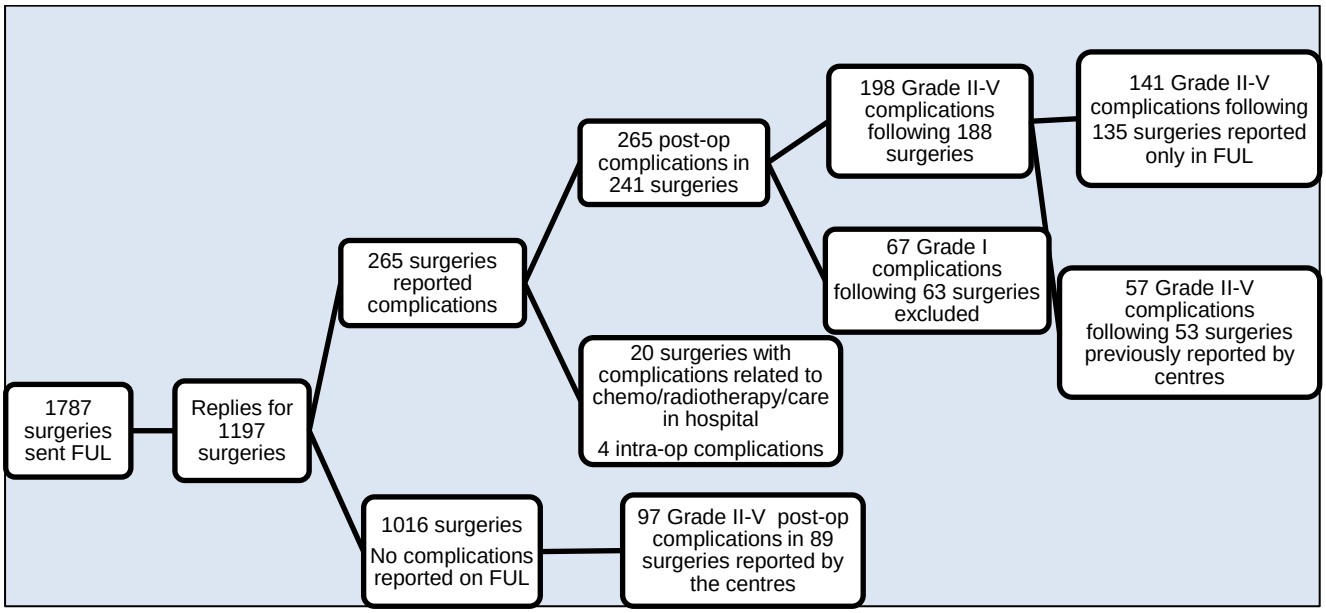
wound breakdown (48, 24%), ileus (13, 7%) and bladder related complications such as urinary retention (13, 7%).

6.2.2 Patient-reported complications

6.2.2.1 Free-text format FUL

In 1787 of the 2152 surgeries (1st Nov 2010 to 31st December 2011), FUL was sent using the free-text format (Figure 7). Replies were received for 1197 (67%). There were 289 patient-reported complications in 265 surgeries. 91 were excluded as they were Grade I Postoperative complications (67), intra-operative (four) or related to chemo/radiotherapy or care in hospital (20).

Figure 7 Follow-up letters that used free text format



Patient-reported Grade II-V complications: There were 198 complications related to 188 surgeries which included 26 re-admissions, 22 reoperations, four complications requiring management in intensive care and two perioperative deaths. The commonest patient-reported complications were wound breakdown, infections (mostly

urinary tract and chest infections) and lymphocysts/lymphoedema (Table 17). 57 (53 surgeries) of the 198 patient-reported complications had already been reported by the hospitals.

Patient-only-reported complications: The remaining 141 complications (135 surgeries) were reported solely on FUL. They included 125 Grade II, two Grade IIIa, nine Grade IIIb, three Grade IVa complications.(Table 17) In reply to the FUL, the family members of two patients informed the CC of their relatives' perioperative deaths (Grade V), one due to cardiac failure and the other due to bowel perforation. In this subgroup of patient-only-reported complications, the commonest complications were wound breakdown, infections and lymphocysts/lymphedema. (Table 17)

Hospital-only-reported complications: For this cohort, there were an additional 113 Grade II-V complications in 104 surgeries reported by hospitals but not reported by patients on FUL, with the commonest being infections followed by wound breakdown and lymphocysts / lymphoedema. This included 10 readmissions, 3 re-operations and 3 admissions to intensive care. (Table 17)

Patient comments: Women were able to add comments on the follow-up letters. Three of 1787 women commented that they were unsure of what was meant by a 'complication'. One woman also felt that the question had been 'too poorly defined to answer'.

Table 17 Grade II-V postoperative complications from free-text format follow-up letters

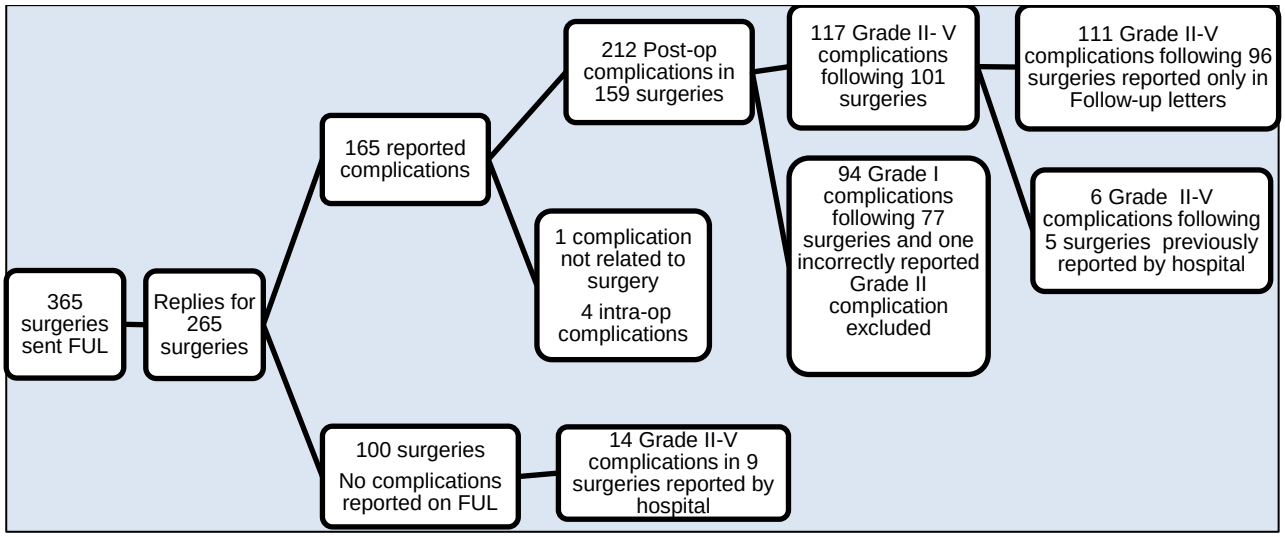
Complication category	Patient reported complications- All (Only reported by patient)						Only reported by hospital	Overall Total
	Total	Grade II	Grade IIIa	Grade IIIb	Grade IVa	Grade V		
Wound breakdown	73 (54)	63 (47)		9 (6)	1(1)		22	**95**
Infection	42 (32)	42 (32)					35	**77**
Lymphocyst/Lymphoedema	19(18)	19(18)					8	**27**
Abscess/Haematoma	8 (4)	5 (3)	2 (1)	1			4	**12**
Bladder problems	5 (4)	5 (4)					6	**11**
Ileus	5 (2)	5 (2)					6	**11**
Bowel obstruction	2 (1)	1		1 (1)			3	**5**
Bowel perforation	1(1)					1(1)	0	**1**
Bowel - other	4 (2)	4 (2)					2	**6**
Fistula	4 (1)			4 (1)			2	**6**
Primary haemorrhage	4 (1)			3	1 (1)		1	**5**
Secondary haemorrhage	2	2					4	**6**
Deep Vein Thrombosis	2 (2)	2 (2)					1	**3**
Pulmonary Embolism	2 (2)	2 (2)					2	**4**
Cardiac	3 (1)	2				1 (1)	4	**7**
Respiratory	2 (2)		1 (1)		1(1)		4	**6**
Neurological	3 (2)	3 (2)					1	**4**
Hernia	3(3)	3(3)					0	**3**
Anastomotic leak	2			2			0	**2**
Psychiatric	1 (1)	1 (1)					1	**2**
Other complications	11 (8)	8 (7)		2 (1)	1		7	**18**
Total	**198 (141)**	**167 (125)**	**3 (2)**	**22 (9)**	**4 (3)**	**2 (2)**	**113**	**311**

Complications reported by both hospital and patients = All patient reported – those only reported by patient

6.2.2.2 Questionnaire format FUL

Following 365 surgeries between January and February 2012, FUL were sent using the closed questionnaire format (Figure 8). 265 (72%) replies were received. 217 complications were reported in 165 surgeries. 99 complications were excluded as they were Grade I (94), intraoperative complications (4) and not related to surgery (1). The latter was one where the family had reported death of the patient due to progression of cancer, as a postoperative complication.

Figure 8 Follow-up letters that used questionnaire format



Patient-reported Grade II-V complications: The remaining 117 Grade II-V postoperative complications (101 surgeries) included nine readmissions, two reoperations and two requiring intensive care management (Table 18). The commonest patient-reported complications were infection, wound breakdown and lymphocyst/lymphoedema. Six of the complications had already been reported by the hospitals.

Patient-only-reported complications: The 111 complications (96 surgeries) reported only on FUL included 108 Grade II, one Grade IIIa, one Grade IIIb, one Grade IVa. In

this sub-group, once again the commonest complications were infection, wound breakdown and lymphocyst/lymphoedema (Table 18).

Hospital-only-reported complications: For this cohort, there were an additional 24 complications in 21 surgeries that were reported by the hospitals but not by patients with the commonest being infections, bladder problems and wound breakdown. This included three readmissions, three re-operations and one admission to intensive care. (Table 18)

Patient comments: Women were asked to for their views on how the questionnaire could be improved. Two women felt inclusion of “Gynaecological Cancer Research Centre” in the return address (printed at the back of the envelope), breached confidentiality about their diagnosis. The other comments included the question on educational status being inappropriate, request for larger print size and for the questionnaire to be sent soon after surgery to avoid surgical complications being confused with those related to chemo/radiotherapy.

Table 18 Grade II-V postoperative complications from follow-up letters which used questionnaire format

Complication category	Patient reported complications - All (Only reported by patient)					Only reported by hospital	Overall Total
	Total	Grade II	Grade IIIa	Grade IIIb	Grade IVa		
Infection	**44 (43)**	43 (43)			1	5	**49**
Wound breakdown	**41 (38)**	40 (37)		1 (1)		4	**45**
Lymphocyst/Lymphoedema	**12 (12)**	12 (12)				0	**12**
Bladder problems	**1**	1				5	**6**
Ileus	**1 (1)**	1 (1)				4	**5**
Bowel obstruction	**1 (1)**	1 (1)				1	**2**
Bowel perforation						1	**1**
Bowel - other	**3 (3)**	3 (3)				2	**5**
Fistula	**1 (1)**	1 (1)				0	**1**
Secondary haemorrhage	**4 (3)**	3 (3)		1		0	**4**
Abscess/Haematoma	**2 (2)**	2 (2)				0	**2**
Deep Vein Thrombosis	**2 (2)**	2 (2)				0	**2**
Pulmonary Embolism	**1 (1)**	1 (1)				0	**1**
Hernia	**1 (1)**	1(1)				0	**1**
Ureteric Obstruction	**1 (1)**		1(1)			0	**1**
Other complications	**2 (2)**	1(1)			1(1)	2	**4**
Total	**117 (111)**	**112 (108)**	**1 (1)**	**2 (1)**	**2 (1)**	**24**	**141**

6.2.3 Concordance of complications

Grade III-V complications: There were 36 patient-reported complications with significant sequelae such as reoperations, admissions to intensive care and perioperative deaths of which 17 had been previously reported by the hospitals. The Grade of the remaining patient-only reported 19 complications was confirmed by the clinicians resulting in 100% concordance for complication Grade. The details of one of these 19 patient-only reported complications were found to be incorrect. This was a case of patient-reported vault dehiscence requiring re-suturing in theatre when in fact the vault was intact and only an examination under anaesthesia had been performed. This resulted in 97.2% (35/36) concordance for complication Type for Grade III-V patient-reported complications.

Grade II complications:

There were 280 patient-reported Grade II complications of which 46 had been previously reported by the hospitals. The remaining 234 patient-only reported complications were forwarded to the respective centres for the clinicians to verify from hospital records. Case notes for 221 (94.4%) of these complications were checked and the complication grade and type was confirmed for 113. These included 34 infections (25 urinary tract infections, five pyrexia of unknown origin, one each of chest infection, cellulitis, gastroenteritis and clostridium difficile diarrhoea), 33 wound breakdowns, nine lymphoedema, six lymphocysts, five haematomas, four DVTs, four PEs, three secondary haemorrhages, three readmissions to hospital with vomiting and abdominal pains (no obvious cause found), two cases of ileus, two cases of severe constipation, two hernias, one case each of dural tap, colovaginal fistula, urinary retention, pressure sore, haematemesis (secondary to stress ulcer) and allergic reaction to antibiotics. One case of PE had been wrongly reported by the patient as a

postoperative complication when in fact it had occurred prior to surgery and therefore was excluded. The concordance for complication Grade for patient-reported Grade II complications was 56.4% (46+112=158/280). Excluding the incorrectly reported PE, 279 patient-reported Grade II complications were included in further analysis.

In the case of allergic reaction, the patient had reported allergy to antibiotics when in fact the allergy was transfusion-related to pooled platelets. There was also a case of readmission for diarrhoea which was confirmed by the clinician. Although the complication type was correctly reported, the causative agent was not Clostridium difficile as reported by the patient. This resulted in 55.7% (156/280) concordance for complication Type for patient-reported Grade II complications.

The centres were unable to confirm the remaining 108 Grade II complications which included 43 wound breakdowns, 39 infections (25 urinary tract infections, eight chest and six pyrexia of unknown origin), nine lymphoedema (five treated with compression stocking and four treated with physiotherapy), five lymphocysts (drained in the outpatients department), four bowel related complications (two cases of severe constipation requiring readmission and enemas, one case of ileus requiring nasogastric tube insertion, one case of bowel obstruction requiring readmission and steroids), three bladder related complications (two cases of urinary retention requiring re-catheterisation and one case of extreme urge incontinence requiring treatment by urologists), two hernias, one case each of neuropathic pain, depression and pressure sores.

6.2.4 Postoperative complication rate

6.2.4.1 Postoperative complication rate for all surgery

A postoperative Grade II-V complication was reported in 379 of the 1462 surgeries. This included a total of 452 (402 Grade II which includes four hernias, 50 Grade III-V)

complications. Of the 379 surgeries with a reported postoperative Grade II-V complication, 172 had at least one hospital-reported complication - 231 had at least one patient-reported complication of which 124 were verified and 107 were not (Table 19).

On hospital-reporting, the proportion of surgeries with a postoperative complication was 11.8% (172/1462; 95% CI 11–14) and on patient-only-reporting it was 15.8% (231/1462; 95% CI 14 –17.8). Using hospital and hospital verified FUL data, this rate increased to 19.4% (283/1462; 95% CI 17.4- 21.4). Using hospital and all FUL data, the rate was 25.9% (379/1462; 95% CI 24-28).

Excluding Grade II complications, the hospital reported Grade III-V postoperative CR was 2.0% (29/1462; 95% CI 1.4-2.8). Using hospital and hospital verified FUL data, this rate increased to 3.3% (48/1462; 95% CI 2.5-4.3). Since all the Grade III-V patient-only reported complications had been confirmed and found to be correct, this rate was the same when all FUL data was included.

Table 19 Proportion of surgeries with a Grade II-V postoperative complication

Post-operative complications						
Highest grade of complication	**Hospital-reported**	**Patient- reported**			**Hospital and patient verified**	**All hospital and patient reported**
		Verified on hospital notes review	**Not verified on hospital notes review**	**Total**		
II	143	105	107	212	235	331
III-V	29	19	0	19	48	48
Total surgery	**172**	**124**	**107**	**231**	**283**	**379**

6.2.4.2 Post-op complication rate for cancer surgery

The hospital reported Grade II-V postoperative CR for gynaecological cancer surgery (1067) after excluding surgery for benign disease (395) was 14% (146/1067; 95% CI 12-17). Using hospital and hospital verified FUL data, this rate increased to 21.5% (229/1067; 95% CI 19-24). Using hospital and all FUL data, the rate was 27% (289/1067; 95% CI 25-30).

Excluding Grade II complications, the hospital reported Grade III-V postoperative CR for gynaecological cancer surgery (1067) was 2.3% (24/1067; 95% CI 1.5-3.3). Using hospital and hospital verified FUL data, this rate increased to 3.5% (37/1067; 95% CI 2.5-4.7). Since all the Grade III-V patient-only reported complications had been confirmed and found to be correct, this rate was the same when all FUL data was included.

6.2.5 Sensitivity for detection of postoperative complications

The sensitivity of hospital reporting for detection of all 379 surgeries with Grade II-V postoperative complications was 44% (200/452; 95% CI 40-49) and that of patient reporting was 70% (252/1462; 95% CI 65-74) . When the free-text format was used for FUL, sensitivity for hospital reporting was 55% (95% CI 49-60) and 64% (95% CI 58-69) for patient reporting. With the questionnaire format, sensitivity of hospital reporting of complications was 21% (95% CI 15-29) and with patient reporting 83% (95% CI 76-88). (Table 20)

Excluding the 121 (108 Grade II and 13 notes not checked) complications not confirmed by the hospital, the sensitivity for patient reporting was 59% (194/331; 95% CI 53-64) using both questionnaire formats and 60% (200/331; 95%CI 55-66) for hospital reporting. (Table 20)

Table 20 Sensitivity of patient and hospital reporting for Grade II-V postoperative complications

Data source	No. of Grade II-V complications	Sensitivity (95%CI)	
		Patient reporting	Hospital reporting
All Grade II-V complications			
Patient reporting using free-text format			
Patient-reported alone	141		
Patient & Hospital reported	57	**64%**	**55%**
Hospital reported alone	113	**(58-69)**	**(49-60)**
Total	311		
Patient reporting using questionnaire format			
Patient-reported alone	111		
Patient & Hospital reported	6	**83%**	**21%**
Hospital reported alone	24	**(76-88)**	**(15-29)**
Total	141		
Patient reporting using both formats			
Patient-reported alone	252		
Patient & Hospital reported	63	**70%**	**44%**
Hospital reported alone	137	**(65-74)**	**(40-49)**
Total	452		
Patient reporting using both formats excluding complications not confirmed by the hospital (n=121*)			
Patient reported alone	131		
Patient & Hospital reported	63	**59%**	**60%**
Hospital reported alone	137	**(53-64)**	**(55-66)**
Total	331		
Grade III-V Complications only			
Patient reporting using both formats			
Patient-reported alone	19		
Patient & Hospital reported	17	**72%**	**62%**
Hospital reported alone	14	**(58-83)**	**(48-74)**
Total	50		

*108 Grade II, 13 notes not checked

Grade II complications accounted for 402 (89%) (275 Grade II and 4 hernias patient-reported, 123 hospital-only reported) out of the total 452 complications. Excluding these, the overall sensitivity of hospital reporting for detection of Grade III-V postoperative complications was 62% (31/50; 95% CI 48 -74) and patient reporting was 72% (36/50; 95% CI 58 - 83) (Table 20).

6.2.6 Types of complications reported by hospital and patients

Hospital reporting appeared to be better for cardiac complications, ileus, bladder complications, bowel obstruction, and respiratory complications. (Table 21)

Table 21 Types of complications reported by hospital and patients

Complication category	Total	Reported by hospital		Reported by patients	
		No.	%	No.	%
Wound breakdown	140	48	34	114	81
Infection	126	51	40	86	68
Lymphocyst/Lymphoedema	39	9	23	31	79
Bladder	17	13	76	6	35
Ileus	16	13	81	6	38
Abscess/Haematoma	14	8	57	10	71
Bowel – other	11	6	55	7	64
Secondary haemorrhage	10	7	70	6	60
Cardiac	7	6	86	3	43
Bowel obstruction	7	5	71	3	43
Fistula	7	5	71	5	71
Respiratory	6	4	67	2	33
Primary haemorrhage	5	4	80	4	80
Pulmonary Embolism	5	2	40	3	60
Deep Vein Thrombosis	5	1	20	4	80
Neurological	4	2	50	3	75
Hernia	4	0	0	4	100
Anastomotic leak	2	2	100	2	100
Psychiatric	2	1	50	1	50
Bowel perforation	2	1	50	1	50
Ureteric obstruction	1	0	0	1	100
Other	22	12	55	13	59
Total	**452**	**200**	**44**	**315**	**70**

Patients were better at reporting hernia, wound breakdown, DVT, lymphocysts/lymphoedema, neurological complications, pelvic/abdominal abscess / haematoma. Both hospital and patients had similar reporting rates for anastomotic leak, fistula, primary haemorrhage, bowel perforation and psychiatric complications. (Table 21) The numbers were too small for any formal statistical comparisons.

6.3 Discussion:

This is the first study to use both hospital and patient-reported information to estimate overall postoperative morbidity in gynaecological oncology surgery. Concordance of patient-reported complications with hospital case note review was 100% for Grade III-V and 56.4% for Grade II postoperative complications. The hospital reported postoperative Grade II-V complication rate for major surgery undertaken in gynaecological oncology centres of 11.8% increased to 19.4% if hospital verified patient-reported complications were also included and 25.9% on inclusion of all patient-reported complications. The hospital and patient verified Grade III-V postoperative CR was 3.3%. Overall, sensitivity for patient-reporting was 70% and hospital-reporting was 44%. During the study a closed format questionnaire was developed that enabled more accurate capture of complication rates. The questionnaire and the process set up in UKGOSOC could therefore better inform future data capture of complications in gynaecological oncology surgery.

Patients reported a higher proportion of the overall 452 Grade II-V complications when compared to hospitals (55.8% vs 44.2%). A survey of patients following radical prostatectomy also noted that patients reported more complications in comparison to previous hospital/clinician reported rates. [75] However, the sensitivity of patient and hospital reporting was similar (59% versus 60%) when the 121 Grade II complications not confirmed on hospital case note review, were excluded. Patients were better at

reporting complications that had occurred following discharge such as wound breakdown, pelvic abscess/haematoma, DVT, lymphocysts / lymphoedema and hernias while hospitals seemed better at reporting complications that had occurred during the hospital stay such as ileus, bowel obstruction, bladder (e.g. urinary retention), cardiac (e.g. atrial fibrillation) and respiratory complications (e.g. pulmonary oedema).

Hospital notes of 94.8% (240/253) of those with patient-reported complications previously undocumented by the clinical staff were reviewed. The clinical team confirmed all Grade III-V patient-reported complications. This probably reflects the fact that these were complications with significant sequelae requiring secondary care management. Grade II complications such as infections treated with antibiotics and lymphoedema treated with compression stockings and physiotherapy were less likely (concordance 56.4%) to be confirmed. While it is unlikely that patients incorrectly reported use of antibiotics or compression stockings, the possibility cannot be entirely ruled out. However the more likely explanation is that the surgical teams did not manage these complications. A significant proportion was probably managed in primary care. The wording of patient consent meant that the coordinating centre team was unable to request review of primary care records. In addition some of the readmissions are likely to have involved local hospitals, different from where the initial surgery had been performed. Both these issues were noted in the elective hip and knee replacement studies in which about half the surgical complications were managed outside the institution where the initial surgery was undertaken [14, 15] and would have been missed if only clinician reported data was used. Logistic issues may also have contributed to clinicians not entering some of the post discharge Grade II-V complications that they were aware of. As it is medical treatment that defines a

complication as Grade II, the issue of variation in threshold for prescription of antibiotics for postoperative infections also needs to be considered.

The open free-text format for collecting patient data proved time consuming to analyse, requiring a clinician's input to decipher and enter the complications into the database. A minority of women did not understand what was meant by a complication and some women mentioned complications related to non-surgical treatments or detailed problems related to their care in hospital. The structured questionnaire (closed) format for patient reporting developed in the course of the study allowed easier interpretation and grading of the complications. It comprised of specific questions pertaining to the management of 11 common postoperative complications that were highlighted on analysis of the free-text format of follow-up letters. Every question included a brief description of the complication with management options clearly specified. Simple Yes/No answers also probably made completion easier for women. The closed format also decreased the number of replies with complications not related to surgery. The proportion of replies reporting a complication was higher with this format (63% vs 22%) when compared to the free-text format. However, a large proportion (44% vs 25%) were Grade I complications, with the commonest being constipation requiring diet changes / laxatives and urinary incontinence not requiring any medication. This was probably related to the inclusion of specific questions regarding bowel and bladder problems. At present there is no nationally agreed list of complications that could be used to audit surgical outcomes in gynaecological oncology. It might be feasible to shorten the list of complications in the closed format from eleven to five or six core complications for use in future local and or national audits. The reliability of this approach would however have to be tested in a further prospective study.

In this study, the overall response rate was 68% with a similar rate (72% vs 68%) associated with use of a closed versus free-text format for postal follow-up. Studies investigating patient-reported postoperative complications following elective surgery have reported response rates ranging from 80% (hip and knee replacement surgery), 73% for hernia repair and 65% for varicose vein surgery [15, 74, 76]. These studies also used a questionnaire format containing questions regarding specific postoperative complications and simple yes/no answers. It is likely that response rates could have been improved by sending reminders to non-responders.

Strengths of this study include the size, multicentre design and prospective online data collection by clinical teams, 68% patient response rate, the same clinician undertaking all patient interviews where data was equivocal, hospital case note review of patient only reported complications and central independent data analysis. The main limitation was that the CC could not contact the primary care teams to verify complications that were not managed by the surgical team. Only those women who had provided telephone numbers could be contacted directly for clarification. In the absence of a validated questionnaire on postoperative complications in gynaecological oncology, a new one was designed to capture more accurate and precise information regarding complications. Although it was piloted and women provided feedback on its content, it requires further validation in future studies. In common with all questionnaire studies, one could speculate that women were more likely to respond to the questionnaire if they had experienced a complication.

Finally though the intention was to send the FULs eight weeks postoperatively this was not always possible due to delays in receiving updates from the hospitals regarding any patients who might have died or were terminally ill. The latter step was essential to avoid causing unnecessary distress to family members. Despite this, four (0.2%) FUL

were sent to deceased patients and one of the families complained prompting a written apology. Delays in sending the follow-up letter probably contributed to recall bias causing some women to confuse surgical complications with side effects from chemo/radiotherapy (commenced usually within six weeks of surgery).

There is growing interest in using Patient Reported Outcome Measures (PROMs) to assess outcomes of cancer treatment [77]. PROMs are designed to assess the quality of life and long term disability from treatment and not surgical complications in particular. A recent study [19] in gynaecological cancer looked at the feasibility of capturing patient-reported symptoms electronically in the immediate six week postoperative period following major surgery. The authors concluded that this method was highly acceptable to the women and provided useful information regarding problems experienced by patients which could be helpful to the clinicians in providing timely and appropriate interventions where required. The Royal College of Obstetricians and Gynaecologists (RCOG) also have published a scientific impact paper evaluating the use of PROMs in gynaecology and gynaecological oncology [18]. It is envisaged that in future PROMs will routinely be collected in the UK for all gynaecological cancer patients. Linking or combining our follow-up questionnaire to PROMs would be a cost effective method of collecting data on postoperative complications.

7 Predictors of surgical complications

This chapter describes the identification of significant predictors of Intraoperative and Postoperative complications using univariable and multivariable logistic regression.

7.1 Method for regression analysis

Statistical analysis was performed using STATA version 12.1 (StataCorp 2012). To identify predictors for intraoperative complications, all eligible surgeries (n=2948) were included and for postoperative complications only those surgeries with both hospital and patient follow-up data (n=1462) were included as these surgeries were more likely to have complete information on the postoperative course.

7.1.1 Univariable logistic regression

To assess how each potential predictor affected the complication rate (CR) individually, univariable (UV) logistic regressions were performed separately for all predictors.

For intraoperative complication as the outcome (yes/no), the independent variables included age (continuous variable), number of comorbidities (continuous variable), type of comorbidities (binary variable- yes/no), BMI (continuous variable and categorical - underweight, normal, overweight, obese and morbidly obese), ASA grade (categorical- 1-4), previous abdominal surgery (binary variable-yes/no), grade of operating surgeon (categorical – consultant, sub-specialty trainee, general obstetrics and gynaecology trainee), approach for surgery (categorical - laparotomy/ laparoscopy), surgical complexity (categorical – 1-5; Complexity score 1&2=group 1, 3&4=group 2, 5&6=group 3, 7&8=group 4, >8=group 5) and final diagnosis (categorical- ovarian, uterine, cervix, vulva and benign).

For postoperative complication as the outcome (yes/no), the independent variables included all the above and, duration of surgery (continuous, in minutes) and estimated blood loss (categorical, <500mls, 500-1000mls, >1000-2500mls, >2500mls).

7.1.2 Multivariable regression

For both intraoperative and postoperative complication analyses the same procedure was applied. To create a risk prediction model for both the intraoperative CR and postoperative CR, useful predictors were identified in a multivariable (MV) logistic regression model by running a stepwise regression with backward elimination, with p (removal) = 0.05. Categorical predictors with more than 2 categories were retained complete rather than drop any insignificant categories. Goodness of fit was assessed using the Hosmer-Lemeshow test (with the data split into 10 groups based on estimated probabilities). Formally, the data should be considered longitudinal because 38 women had repeated outcomes, so a random effects logistic regression model was also fitted using the identified predictors to check that the standard errors did not change substantially i.e. that the predictors were still significant when the correlated structure was accounted for.

In the absence of a suitable external validation set it was necessary to test the risk prediction model using cross-validation (CV) methods. Specifically, a leave-one-out (LOO) CV method was employed where, for each subject, the predicted probability of complication was estimated based on a prediction model that excluded that subject in the parameter estimation. These LOO predicted probabilities could be used to estimate the sensitivity and specificity of the risk prediction model at various cut-offs. A receiver operating characteristic (ROC) curve plotted all possible cut-offs of the predicted probabilities.

7.2 Results

7.2.1 Predictors of intraoperative complications

7.2.1.1 Univariable analysis

For intraoperative complication as the outcome, diabetes (Odds Ratio [OR] 1.63, 95% CI 1.006 - 2.630), other metabolic/endocrine disorders (OR 0.383, 95% CI 0.168 - 0.876) and previous abdominal surgery (OR 1.74, 95% CI 1.239- 2.455) were found to be statistically significant. Among the categorical predictors, surgical complexity and final diagnosis were found to be statistically significant. (Table 22)

Table 22 Predictors of intraoperative complications in univariable analysis

Variable	Odds ratio	95% Confidence Interval	p value
Surgical complexity group 1 to 5			
Group 1	1		
Group 2	1.516	0.980 – 2.344	0.061
Group 3	2.841	1.779 – 4.539	0.000
Group 4	4.903	2.481 – 9.690	0.000
Group 5	8.274	3.741 – 18.301	0.000
Joint significance for all the categories			**0.000**
Final Diagnosis			
Ovary	1		
Uterine	0.413	0.265 – 0.643	0.000
Benign	0.334	0.204 – 0.546	0.000
Vulva	0.134	0.033 – 0.551	0.005
Cervix	0.593	0.302 – 1.166	0.130
Joint significance for all the categories			**0.000**
Previous abdominal surgery	1.74	1.239-2.455	**0.001**
Comorbidity			
Diabetes	1.627	1.006 – 2.630	**0.047**
Metabolic / Endocrine	0.383	0.168 – 0.876	**0.023**
Other neoplasms	1.857	1.003 – 3.440	0.050
Low Albumin	4.542	0.972 – 21.222	0.054
Autoimmune	2.418	0.846 – 6.913	0.099
Hypertension	1.265	0.891 – 1.798	0.189
Cardiac	1.381	0.838 – 2.274	0.205
Respiratory	0.709	0.368 – 1.364	0.303
Coagulation / Thrombosis	1.313	0.599 – 2.877	0.495
Vascular	0.724	0.226 – 2.321	0.588

Table 22 Predictors of intraoperative complications in univariable analysis continued…

Variable	Odds ratio	95% Confidence Interval	p value
Gastrointestinal	1.248	0.537 - 2.898	0.606
Integumentary / Dermatology	1.449	0.342 - 6.149	0.614
Infections	1.689	0.218 - 13.082	0.616
Genitourinary	0.806	0.194 - 3.345	0.766
Neurology / Psychiatric	0.908	0.455 - 1.811	0.784
Smoking	0.885	0.320 - 2.445	0.814
Musculoskeletal	0.971	0.529 - 1.781	0.925
Age	1.003	0.991 - 1.014	0.661
Body Mass Index (categorical variable)			
Normal (19.9 - 24.9)	1		
Underweight (<19.9)	0.509	0.683 - 3.792	0.510
Overweight (25 - 29.9)	0.927	0.594 - 1.449	0.741
Obese (30 - 39.9)	1.149	0.743 - 1.777	0.533
Morbidly obese (>40)	0.714	0.331 - 1.543	0.392
Body Mass Index (Continuous variable)	0.993	0.968 - 1.019	0.608
ASA Grade			
ASA Grade 1	1		
ASA Grade 2	1.467	0.934 - 2.304	0.097
ASA Grade $\geq$3	1.682	0.998 - 2.836	0.051
Surgeon grade			
General O & G Trainee	1		
Sub-specialty trainee	0.877	0.248 - 3.103	0.838
Consultant	2.064	0.646 - 6.597	0.222
Approach for surgery			
Open	1		
Laparoscopic	0.833	0.545 - 1.272	0.397

For surgical complexity, groups- 3 (OR 2.841, 95% CI 1.779 - 4.539), 4 (OR 4.903, 95% CI 2.481- 9.690) and 5 (OR 8.274, 95% CI 3.741 - 18.301) were significant whereas group 2 (OR 1.516, 95% CI 0.980 - 2.344) was not found to be significant when compared to the reference category- group 1. For the final diagnosis category - uterine (OR 0.413, 95% CI 0.265 - 0.643), vulva (OR 0.134, 95% CI 0.033 - 0.551) and benign (OR 0.334, 95% CI 0.204 - 0.546) diagnoses were significant whereas cervix

was not statistically significant (OR 0.593, 95% CI 0.302 - 1.166) when compared to the reference category- ovary. (Table 22)

7.2.1.2 Multivariable regression:

In multivariable regression analysis, the same factors were found to be statistically significant predictors of an intraoperative complication. (Table 23) Diabetes (2.015, 95% CI 1.223 - 3.324) and previous abdominal surgery (OR 1.561, 95% CI 1.099-2.219) were found to increase the risk of a complication whereas metabolic/endocrine disorders (excluding diabetes) (OR 0.351, 95% CI 0.152 - 0.809) were found to be protective.

Table 23 Significant predictors of intraoperative complications in multivariable regression

Variable	Odds ratio	95% Confidence Interval	Standard Error	p value
Diabetes	2.015	1.223 - 3.324	0.514	0.006
Metabolic/Endocrine disorders (excluding diabetes)	0.351	0.152 - 0.809	0.150	0.014
Previous abdominal surgery	1.561	1.099 - 2.219	0.280	0.013
Surgical complexity group				
1	1			
2	1.302	0.834 - 2.033	0.296	0.246
3	2.311	1.396 - 3.826	0.594	0.001
4	3.397	1.660 - 6.951	1.241	0.001
5	5.399	2.335 - 12.48	2.309	0.000
Final diagnosis				
Ovary	1			
Uterine	0.555	0.348 - 0.887	0.133	0.014
Cervix	0.599	0.296 - 1.212	0.215	0.154
Vulva	0.193	0.046 - 0.805	0.141	0.024
Benign	0.468	0.278 - 0.787	0.124	0.004

Surgical complexity groups 3 (OR 2.311, 95% CI1.396 - 3.826), 4 (OR 3.397, 1.660 - 6.951) and 5 (OR 5.399, 95% CI 2.335 - 12.48) were statistically significant when compared to group 1 (reference category). Even though group 2 was not statistically significant (OR 1.302, 95% CI 0.834 - 2.033), it was retained as it was part of the same

categorical variable. In the categorical variable final diagnosis, when compared to the reference group ovary, other diagnostic categories namely uterine (OR 0.555, 95% CI 0.348 - 0.887), vulva (OR 0.193, 95% CI 0.046 - 0.805) and benign (OR 0.468, 95% CI 0.278 - 0.787) were found to be protective and statistically significant. Cervix (OR 0.599, 95% CI 0.296 - 1.212), although not statistically significant, was retained. (Table 23)

7.2.2 Predictors of postoperative complications

7.2.2.1 Univariable analysis

In univariable analysis, age (OR 1.013, 95% CI 1.002-1.026), comorbidity status (OR 1.477, 95%CI 1.049 - 2.077), comorbidity categories namely coagulation/thrombosis (OR 2.228, 95% CI 1.174 - 4.229) and diabetes (OR 1.916, 95% CI 1.233 - 2.977), and, duration of surgery (OR 1.486, 95% CI 1.320-1.672) were found to be significant predictors of postoperative complications. (Table 24)

Among the categorical variables, laparoscopic (OR 0.506, 95% CI 0.326 - 0.787), when compared to the open approach, was protective. ASA grade 2 (OR 1.623, 95% CI 1.042 - 2.527) and ASA grade $\geq$3 (OR 2.178, 95% CI 1.315 - 3.608) when compared to the reference group ASA 1, were statistically significant predictors. For surgical complexity, group 2 (OR 1.719, 95% CI 1.196 - 2.469), group 3 (OR 1.896, 95% CI 1.198 - 3.002), group 4 (OR 2.652, 95% CI 1.218 - 5.774) and group 5 (OR 6.562, 95% CI 2.454 - 17.543) were statistically significant when compared to the reference group 1.

For estimated blood loss, categories, 500-1000mls (OR 2.554, 95% CI 1.7367 - 3.756) and >1000-2500mls (OR 2.443, 95% CI 1.381 - 4.319), >2500mls (OR 4.049, 95% CI- 1.383-11.852) were statistically significant when compared to the reference

Table 24 Predictors of postoperative complications in univariable analysis

Variable	Odds ratio	95% Confidence Interval	p value
Age	1.014	1.002 - 1.026	**0.027**
Body Mass Index (Categorical variable)			
Underweight (<19.9)	1		
Normal (19.9 - 24.9)	0.709	0.156 - 3.231	0.657
Overweight (25 - 29.9)	0.888	0.196 - 4.017	0.877
Obese (30 - 39.9)	1.359	0.302 - 6.120	0.689
Morbidly obese (>40)	0.948	0.193 - 4.652	0.947
Joint significance for all the categories			**0.037**
Body Mass Index (Continuous variable)	1.023	1.001 - 1.045	**0.039**
ASA Grade (1 to 3)			
ASA Grade 1	1		
ASA Grade 2	1.623	1.0422 - 2.527	0.032
ASA Grade ≥3	2.178	1.315 - 3.608	0.002
Joint significance for all the categories			**0.008**
Comorbidity			
Comorbidity status (yes/no)	1.477	1.049 - 2.077	**0.025**
Diabetes	1.916	1.233 - 2.977	**0.004**
Coagulation / Thrombosis	2.228	1.174 - 4.229	0.014
Neurology / Psychiatric	0.41	0.164 - 1.025	0.057
Respiratory	1.444	0.888 - 2.348	0.138
Cardiac	1.365	0.856 - 2.177	0.191
Metabolic / Endocrine	1.323	0.823 - 2.125	0.248
Integumentary/Dermatology	2.142	0.584 - 7.858	0.251
Musculoskeletal	1.2889	0.803 - 2.069	0.294
Hypertension	1.176	0.854 - 1.618	0.321
Gastrointestinal	0.621	0.221 - 1.747	0.366
Smoking	1.382	0.569 - 3.361	0.475
Other neoplasms	1.142	0.608 - 2.144	0.680
Genitourinary	1.184	0.406 - 3.451	0.758
Infections	1.181	0.141 - 9.862	0.878
Autoimmune	0.943	0.214 - 4.158	0.938
Vascular	1.011	0.391 - 2.616	0.981
Previous abdominal surgery	1.465	1.068 – 2.011	**0.018**
Grade of operating surgeon			
General O & G Trainee	1		
Sub-specialty trainee	0.92	0.402 - 2.106	0.844
Consultant	1.251	0.588 - 2.664	0.560
Approach for surgery			
Open	1		
Laparoscopic	0.506	0.326 - 0.787	**0.002**

Table 24 Predictors of postoperative complications in univariable analysis continued…

Variable	Odds ratio	95% Confidence Interval	p value
Surgical complexity group 1 to 5			
Group 1	1		
Group 2	1.719	1.196 - 2.469	0.003
Group 3	1.896	1.198 - 3.003	0.006
Group 4	2.652	1.218 - 5.774	0.014
Group 5	6.562	2.454 - 17.543	0.000
Joint significance for all the categories			**0.000**
Estimated Blood Loss			
<500 mls	1		
500 - 1000mls	2.554	1.737 - 3.756	0.000
>1000 - 2500 mls	2.443	1.381 - 4.319	0.002
>2500 mls	0.797	0.102 - 6.226	0.829
Joint significance for all the categories			**0.000**
Duration of surgery	1.496	1.324 - 1.690	**0.000**
Final Diagnosis			
Ovary	1		
Uterine	0.609	0.407 - 0.914	0.016
Cervix	1.623	0.908 - 2.901	0.102
Vulva	2.024	1.158 - 3.535	0.013
Benign	0.41	0.258 - 0.652	0.000
Joint significance for all the categories			**0.000**

category <500mls. For the final diagnosis variable, when compared to the reference category ovary, uterine (OR 0.61, 95% CI 0.407 - 0.914) and benign (OR 0.41, 95% CI 0.258 - 0.652) diagnoses were protective, vulva (OR 2.024, 95% CI 1.158 - 3.535) was found to increase postoperative complication risk and cervix (OR 1.623, 95% CI 0.908 - 2.901) was not statistically significant.

7.2.2.2 Multivariable regression

Comorbidity status i.e. presence/absence of comorbidity (OR 1.338, 95% CI 1.012 - 1.769), diabetes (OR 1.642, 95% CI 1.113 - 2.421), age (OR 0.989, 95% CI 0.979 - 1.000) and duration of surgery (OR 1.285, 95% CI 1.149 - 1.439) were statistically significant predictors. Laparoscopic (OR 0.653, 95% CI 0.469 - 0.909), when

compared to the open approach, was protective. Among the categorical variables only final diagnosis was a significant predictor in multivariable regression. When compared to the reference group ovary, vulva was statistically significant (OR 2.398, 95% CI 1.438 - 3.999). Although uterine (OR 0.998, 95% CI 0.716 - 1.392), cervix (OR 1.664, 95% CI 0.958 - 2.891) and benign (OR 1.046 95% CI 0.738 - 1.481) diagnoses were not statistically significant, they were retained as part of the final diagnoses categorical variable. (Table 25)

Table 25 Significant predictors of postoperative complications in multivariable regression

Variable	Odds ratio	95% Confidence Interval	Standard Error	p value
Comorbidity status (Yes/No)	1.338	1.012 - 1.769	0.191	0.041
Diabetes	1.642	1.113 - 2.421	0.325	0.012
Age	0.989	0.979 - 1.000	0.005	0.052
Laparoscopic approach	0.653	0.469 - 0.909	0.110	0.012
Duration of surgery	1.285	1.149 - 1.439	0.074	0.000
Final diagnosis				
Ovary	1			
Uterine	0.998	0.716 - 1.392	0.169	0.992
Cervix	1.664	0.958 - 2.891	0.469	0.071
Vulva	2.398	1.438 - 3.999	0.626	0.001
Benign	1.046	0.738 - 1.481	0.186	0.802

7.3 Discussion:

Previous abdominal surgery, diabetes, surgical complexity and final diagnosis were significant predictors of increased intraoperative complication risk. The only common predictors of both intraoperative and postoperative complications were diabetes and final diagnosis. Other significant associations with postoperative complications were age, presence of comorbidity, surgical approach and duration of surgery.

In 10% of surgeries, patients had Metabolic/Endocrine disorders other than diabetes. This mainly included hypercholesterolaemia and thyroid dysfunction and was a

predictor of reduced intraoperative complication rate. The reason for this is not clear, and, as previous studies have not looked at this separately, there is no data for comparison. Some pre-operative biochemical markers such as serum albumin and liver enzymes which have been reported to be predictors of surgical complications [44, 45, 48, 54] could not be included as they are not routinely assayed in all patient undergoing gynaecological oncology surgery in UK.

Previous abdominal surgery was a significant predictor of intraoperative complications probably due to intra-abdominal adhesions following previous surgery. This is in keeping with results of a prospective multi-centre centre Finnish study (FINHYST) of over 5000 hysterectomies for benign indications [78] which found that prior laparotomy (OR=1.1) but not caesarean section or laparoscopy increased the risk of major complications. In the latter study, adhesiolysis during surgery was the strongest single risk factor (OR=2.4). In bowel surgery, previous three or more laparotomies have been found to increase risk of enterotomy by tenfold (OR=10.4) [79]. The other comorbidity that significantly increased intraoperative complication risk was diabetes (OR=2). While several studies have demonstrated the association of diabetes with increased postoperative morbidity [80-82], this is the first study to demonstrate its effect specifically on intraoperative complications.

Intraoperative complication rates increased with surgical complexity with highest rates for those procedures with an overall surgical complexity score of >8. In Aletti's study on ovarian cancer surgery as well as in the Australian study [45], surgical complexity was found to be a significant predictor of overall morbidity. In order to capture complexity accurately in UKGOSOC, the surgical complexity scoring system for ovarian cancer developed by Aletti et al [43, 44] was modified to include procedures for all gynaecological cancers and stratified into five rather than the three originally

described (low, intermediate and high) groups as preliminary analysis had demonstrated it to be a key predictor.

Similar to studies comparing open versus laparoscopic approaches for endometrial and cervical cancer surgery [70, 71] , the latter reduced the likelihood of a postoperative complication in UKGOSOC as well. This is probably one of the main drivers of increasing laparoscopic surgery in gynaecological oncology. Surgical complexity however was not a significant predictor of postoperative unlike intraoperative complications. Instead duration of surgery (OR=1.3) was significant. This has been noted particularly for postoperative infections in total knee arthroplasty. [83]

In addition to being a significant predictor of intraoperative complications, diabetes (OR=1.6) was also found to be significant in predicting postoperative complications. In the Australian study, while diabetes was significant in univariable analysis, it was not found to be so in multivariable analysis [45]. However studies in other specialties such as plastic surgery (breast reconstruction surgery) and orthopaedic surgery have shown diabetes to be a significant predictor of surgical complications particularly wound infections [81, 82, 84]. Diabetes has also been found to increase the risk of postoperative complications following coronary artery bypass surgery [80]. Our data indicates that the presence of any comorbidity (OR=1.3) predicted postoperative complications on multivariable analysis. Performance status as measured by ASA grade was significant only on univariable analysis. This is in contrast to the Australian study and Aletti's study where ASA grade was a significant independent predictor for overall morbidity [43, 45].

8 Benchmarking of surgical complications in gynaecological oncology surgery

There is a drive within the National Health Service (NHS) to increase transparency and improve quality and safety. To this end, one of the initiatives in surgery has been to publish outcomes data for hospitals and more recently for individual surgeons which have been sourced from national clinical audits in some specialties and in most from administrative data. [85, 86]

While surgical data on a national level has been collected in specialties such as cardiothoracic [50] and orthopaedic [86] surgery and certain cancers such as lung [87], colorectal [51] and head and neck [88], there is paucity of such data in gynaecological oncology.

As mentioned in previous chapters, the overall unadjusted intraoperative complication rate (CR) was 4.7% [89] and the postoperative CR was 25.7%. [90] However use of such observed complication rates (CRs) for centre level comparisons does not take into account patient comorbidity, underlying disease or surgical complexity, all of which can impact on the risk of a complication. [89] The use of unadjusted crude CRs has resulted in significant unease amongst surgeons and hospitals due to the variations in prevalence of surgical risk factors. Concerns have been raised that it might deter surgery being undertaken in 'high-risk' patients with significant comorbidity. This chapter explores the impact of risk-adjustment of surgical CRs on benchmarking of gynaecological oncology surgery at the participating hospitals.

8.1 Statistical Methods

All methods described apply to both intraoperative and postoperative comparisons.

8.1.1 Data description

Cross-tabulations of outcome and categorical risk predictors by hospital were performed. To assist in the easy identification of covariate imbalance across hospitals, chi-squared test statistics and p-values were included in the tables. The p-values were not used as a formal test measure for the predictors with small category counts (<5) at any hospital. Continuous predictors were summarised by within-hospital means and standard deviations and F test statistics and p-values from an analysis of variance similarly used to aid judgement on hospital variation.

8.1.2 Risk prediction and penalised regression

Logistic regression models were a natural choice for the risk prediction, though parameter estimates were based on a penalised method (lasso) [91] rather than maximum likelihood (ML). A fundamental issue involved in prognostic model construction is that of 'events per variable' (EPV) [92], where the number of 'events' in a binary regression model is taken as the total of the less common outcome. A standard rule of thumb is that a fitted model should have an EPV of at least 10[93, 94], where the variable count includes all estimated levels of a categorical variable. The EPV requirement should hold even if variable selection (stepwise methods) is performed, so that the variable count is based on the full model.

A limited sample size (in the EPV sense) can cause potential problems when using ML, as the model becomes over-fitted and prediction error is inflated. This is why many prediction models fail to be successfully validated. [92] Penalised methods that deliberately bias the regression estimates toward zero can give predictions that reduce the mean square error (MSE). The MSE of an estimator, which quantifies prediction error, is a function of the variance as well as the bias of the estimator. Therefore a penalised method can provide better prediction than ML, in spite of the intentional

bias, by using a more 'efficient' estimator and may prove a more appropriate strategy, dependent on the primary goal of the analysis. With model selection procedures there is known selection- or omission-bias [95], whereby weakly significant variables will be infrequently selected, dependent on chance variation, and when selected, they will typically have overestimated coefficients.

The lasso (least absolute shrinkage and selection operator) estimator [91] employs a penalty term in the likelihood function that is then maximised subject to a constraint on the (absolute) sum of the regression coefficients. The penalty term is a function of a shrinkage parameter (λ) chosen by the investigator, which when equal to zero reduces to ML estimation and when tending to infinity results in estimates tending to zero. In contrast to the similar ridge regression method, where all the coefficients of the full model are partially shrunk, the lasso actually performs a type of variable selection. Strong and moderate predictors are shrunk by a certain amount dependent on λ, whilst weak predictors may be shrunk to exactly zero and so drop out of the model. The choice of λ here was based on a grid search that minimised the generalised cross-validation error. [91] The user-written Stata commands *plogit* and *plsearch* were used to fit lasso-shrunk logistic models. Note that inference, such as confidence intervals and p-values, based on standard errors from the lasso variance-covariance matrix should be treated with caution and used only for approximate guidance. Standard errors are not particularly meaningful for (deliberately and quite strongly) biased estimates as they will exclude the inaccuracy caused by bias. [91] Equivalent models fitted by ML are presented for comparison.

From the fitted model with chosen λ, McFadden's R^2 was used to assess improvement on the null model. Model fit was assessed using the Hosmer-Lemeshow test (with the data split into 10 groups based on estimated probabilities). Model specification was considered using the link test, which refits the model using only the linear predictor

from the original model and its square. Significance of the latter term suggests model misspecification. A receiver operating characteristic (ROC) curve plotted the performance characteristics for all possible cut-offs of the predicted probabilities generated by leave-one-out cross-validation (LOO-CV). LOO-CV predicts the risk for each subject in turn based on a model fitted with that subject excluded. Overall performance (discrimination) may be assessed by the area under the curve (AUC). By regressing the outcome on bootstrapped linear predictions (log odds) for each subject, the calibration slope [92, 93] could be estimated as the mean slope (beta) of 1000 bootstrap samples, where a slope close to 1 suggests good calibration and (much) less than one implies over-fitting of the model. An over-fitted model will give predictions that are too narrow.

8.1.3 Hospital rate adjustments

A prediction model may typically be used to help quantify the risk of surgery for a new individual (or at least modify the baseline risk) using suspected risk factors. In addition, we can use them to enable fairer comparisons of complication rates (CR) across different hospitals, by using the model to predict the expected CR for a given set of confounders. A standard approach to institutional comparison is a funnel plot [96, 97], where the hospital's observed CR is plotted against sample size and assessed with respect to confidence bands (which narrow with sample size) that signify unusually high or low complication rates. The funnel plots presented here show 95 and 99% confidence bands that are smoothed 'exact' confidence limits, rather than symmetric normal-based confidence limits.

The prediction model was used to produce expected CRs for each hospital by calculating the predicted risk of each surgery, averaging over the surgeries within each hospital, and multiplying by the number of surgeries per hospital. Note, this will not

equal the sum of predicted risks within hospitals if missing data meant predicted risks could not be calculated for certain surgeries. An alternative method to funnel plots, for assessing hospitals of potential concern, is to compare the expected CR with the observed CR, and if the confidence interval for the observed to expected CR ratio does not contain one, then the hospital may be deemed as having an unusually high (or low) CR.[98, 99] Methods that calculate confidence intervals for observed to expected ratios typically treat the expected value as 'fixed' and ignore any uncertainty in its estimation, such as standardised mortality ratios where the expected rate is taken from published national statistics. Additionally, they are often normal-based [98, 99] which can lead to a lower limit of below zero for a low ratio. To incorporate the uncertainty involved in estimating the expected CR, the sampling distribution of the observed to expected CR ratio was estimated by taking 1000 bootstrap samples of the full dataset. For each bootstrap sample the new 'observed' CR was compared with the new expected CR, based on a refitting of the lasso model, to calculate the bootstrap sample CR ratio for each hospital. A 95% confidence interval for the ratio was based on the appropriate bias-corrected centiles of the bootstrap derived sampling distribution. Note, the grid-search for lambda was performed for each bootstrap sample and so the uncertainty involved in the selection of lambda was also represented in the CR ratio confidence intervals.

8.2 Results

8.2.1 Intraoperative complications

Table 26 shows the primary outcome and risk factor distribution across the 10 hospitals. There is variation across hospitals for most predictors, but particularly for laparoscopic approach, surgeon grade, surgical complexity, final diagnosis, smoking and ASA grade. Despite ranging from 2.0% to 8.0%, there was not strong evidence

that overall the proportion of intraoperative complications varied significantly between hospitals (p=0.052).

8.2.1.1 Modelling and fit

Of the 2948 surgeries 139 had at least one intraoperative complication. However, when fitting the full model, missing data meant only 132 were included out of 2709 surgeries, meaning an EPV of 4.1 given the 32 variables. The grid search yielded a lambda value of 3.4 and resulted in 4 variables out of the 32 being shrunk completely to zero (BMI, and the 3 comorbidities musculoskeletal, neurology-psychiatric and integumentary-dermatology). The resulting lasso-shrunk odds ratios are presented in Table 27, which also give the ML estimates for comparison. As stated in the methods it is unwise to give too much credence to the p-values and confidence intervals but it is apparent that the strongest predictor is surgical complexity (risk increases with complexity), with previous abdominal surgery, diabetes (both increase risk), metabolic-endocrine (decreases risk) and final diagnosis (all cancer types reduce risk relative to ovarian cancer) also predictive of intraoperative complication (all with p-values <0.05 when estimated by ML). McFadden's R^2 was only 0.066, suggesting that the outcome was largely unrelated to the identified risk factors, though the ML version was not much larger at 0.089. Both the goodness of fit test (p=0.502) and the misspecification test (p=0.754) suggested the model was acceptable with regard to these criteria.

Table 26 Full dataset used for intra-operative complications analysis (n=2948)

	Hospital																				Overall		chi2	df	pvalue
	A		B		C		D		E		F		G		H		I		J						
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%			
Intraoperative complications	13	*5.7*	17	*3.5*	10	*4.0*	44	*5.3*	14	*7.7*	4	*2.0*	6	*6.6*	11	*4.6*	8	*2.8*	12	*8.0*	139	*4.7*	16.8	9	0.0517
Postoperative complications (hospital reported)	40	*17.4*	56	*11.4*	30	*12.0*	159	*19.3*	18	*9.9*	26	*12.9*	16	*17.6*	25	*10.3*	32	*11.3*	22	*14.7*	424	*14.4*	32.0	9	0.0002
Previous abdominal surgery	83	*36.1*	168	*34.1*	64	*25.5*	306	*37.1*	42	*23.2*	84	*41.8*	33	*36.3*	109	*45.0*	117	*41.2*	19	*12.7*	1,025	*34.8*	75.6	9	0.0000
Low Albumin	0	*0.0*	5	*1.0*	0	*0.0*	1	*0.1*	0	*0.0*	0	*0.0*	1	*1.1*	3	*1.2*	0	*0.0*	1	*0.7*	11	*0.4*	17.7	9	0.0391
Coagulation-thrombosis	9	*3.9*	16	*3.3*	12	*4.8*	24	*2.9*	8	*4.4*	9	*4.5*	6	*6.6*	17	*7.0*	9	*3.2*	6	*4.0*	116	*3.9*	11.9	9	0.2180
Diabetes	21	*9.1*	52	*10.6*	30	*12.0*	94	*11.4*	12	*6.6*	15	*7.5*	5	*5.5*	30	*12.4*	18	*6.3*	21	*14.0*	298	*10.1*	17.2	9	0.0455
Cardiac	17	*7.4*	55	*11.2*	32	*12.8*	75	*9.1*	21	*11.6*	23	*11.4*	7	*7.7*	29	*12.0*	27	*9.5*	22	*14.7*	308	*10.5*	10.5	9	0.3081
Respiratory	21	*9.1*	58	*11.8*	21	*8.4*	74	*9.0*	14	*7.7*	20	*10.0*	5	*5.5*	37	*15.3*	21	*7.4*	16	*10.7*	287	*9.7*	16.6	9	0.0553
Gastrointestinal	10	*4.4*	10	*2.0*	6	*2.4*	21	*2.6*	9	*5.0*	17	*8.5*	6	*6.6*	13	*5.4*	3	*1.1*	9	*6.0*	104	*3.5*	35.2	9	0.0001
Genitourinary	2	*0.9*	5	*1.0*	2	*0.8*	7	*0.9*	6	*3.3*	5	*2.5*	0	*0.0*	14	*5.8*	8	*2.8*	3	*2.0*	52	*1.8*	37.2	9	0.0000
Musculoskeletal	15	*6.5*	23	*4.7*	15	*6.0*	98	*11.9*	13	*7.2*	19	*9.5*	4	*4.4*	34	*14.1*	21	*7.4*	19	*12.7*	261	*8.9*	38.7	9	0.0000
Neurology-psychiatric	18	*7.8*	37	*7.5*	12	*4.8*	65	*7.9*	8	*4.4*	15	*7.5*	7	*7.7*	17	*7.0*	22	*7.8*	7	*4.7*	208	*7.1*	6.7	9	0.6652
Vascular	4	*1.7*	18	*3.7*	5	*2.0*	18	*2.2*	3	*1.7*	9	*4.5*	4	*4.4*	8	*3.3*	11	*3.9*	6	*4.0*	86	*2.9*	9.5	9	0.3916
Infections	2	*0.9*	8	*1.6*	2	*0.8*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	1	*0.4*	0	*0.0*	13	*0.4*	24.9	9	0.0031
Auto-immune	4	*1.7*	8	*1.6*	2	*0.8*	6	*0.7*	3	*1.7*	5	*2.5*	0	*0.0*	2	*0.8*	5	*1.8*	3	*2.0*	38	*1.3*	8.5	9	0.4874
Metabolic-endocrine	25	*10.9*	47	*9.5*	25	*10.0*	67	*8.1*	15	*8.3*	27	*13.4*	15	*16.5*	35	*14.5*	35	*12.3*	11	*7.3*	302	*10.2*	18.7	9	0.0282
Integumentary-dermatology	4	*1.7*	2	*0.4*	3	*1.2*	6	*0.7*	1	*0.6*	3	*1.5*	0	*0.0*	8	*3.3*	3	*1.1*	0	*0.0*	30	*1.0*	19.7	9	0.0199
Hypertension	61	*26.5*	186	*37.7*	72	*28.7*	257	*31.2*	66	*36.5*	78	*38.8*	19	*20.9*	110	*45.5*	71	*25.0*	53	*35.3*	973	*33.0*	48.4	9	0.0000
Smoking	1	*0.4*	25	*5.1*	15	*6.0*	3	*0.4*	5	*2.8*	10	*5.0*	16	*17.6*	14	*5.8*	1	*0.4*	5	*3.3*	95	*3.2*	113.7	9	0.0000
Other neoplasms	24	*10.4*	15	*3.0*	6	*2.4*	40	*4.9*	11	*6.1*	6	*3.0*	5	*5.5*	16	*6.6*	19	*6.7*	6	*4.0*	148	*5.0*	27.4	9	0.0012
Surgeon grade																							302.4	18	0.0000
General Obstetrics & Gynaecology Trainee	3	*1.3*	22	*4.6*	3	*1.3*	15	*1.8*	25	*15.0*	3	*1.5*	0	*0.0*	2	*0.9*	30	*11.1*	5	*3.4*	108	*3.8*			

Table 26 Full dataset used for intra-operative complications (n=2948) continued….																								
Sub-specialty trainee	87	*37.8*	95	*19.9*	65	*27.2*	172	*20.9*	8	*4.8*	3	*1.5*	23	*25.3*	80	*35.1*	35	*12.9*	5	*3.4*	573	*20.0*			
Consultant	140	*60.9*	360	*75.5*	171	*71.6*	638	*77.3*	134	*80.2*	192	*97.0*	68	*74.7*	146	*64.0*	206	*76.0*	136	*93.2*	2,191	*76.3*			
Laparoscopic approach	109	*47.4*	40	*8.1*	44	*17.5*	208	*25.2*	8	*4.4*	11	*5.5*	26	*28.6*	62	*25.6*	152	*53.5*	21	*14.0*	681	*23.1*	373.2	9	0.0000
ASA Grade																							145.5	27	0.0000
ASA grade 1	44	*19.2*	142	*28.8*	107	*43.3*	194	*23.5*	32	*17.7*	58	*28.9*	23	*25.3*	19	*7.9*	97	*34.2*	38	*25.3*	754	*25.6*			
ASA grade 2	149	*65.1*	262	*53.1*	115	*46.6*	438	*53.1*	93	*51.4*	101	*50.3*	56	*61.5*	156	*65.0*	138	*48.6*	79	*52.7*	1,587	*54.0*			
ASA grade 3+	36	*15.7*	89	*18.1*	25	*10.1*	193	*23.4*	56	*30.9*	42	*20.9*	12	*13.2*	65	*27.1*	48	*16.9*	33	*22.0*	599	*20.4*			
Surgical complexity																							228.9	36	0.0000
Complexity score 1&2	97	*42.2*	149	*30.2*	160	*63.8*	395	*47.9*	118	*65.2*	72	*35.8*	48	*52.8*	124	*51.2*	181	*63.7*	54	*36.0*	1,398	*47.4*			
Complexity score 3&4	79	*34.4*	199	*40.4*	62	*24.7*	276	*33.5*	38	*21.0*	88	*43.8*	39	*42.9*	79	*32.6*	70	*24.7*	52	*34.7*	982	*33.3*			
Complexity score 5&6	41	*17.8*	111	*22.5*	17	*6.8*	105	*12.7*	23	*12.7*	37	*18.4*	3	*3.3*	35	*14.5*	19	*6.7*	39	*26.0*	430	*14.6*			
Complexity score 7&8	9	*3.9*	24	*4.9*	5	*2.0*	34	*4.1*	2	*1.1*	4	*2.0*	1	*1.1*	3	*1.2*	6	*2.1*	5	*3.3*	93	*3.2*			
Complexity score >8	4	*1.7*	10	*2.0*	7	*2.8*	15	*1.8*	0	*0.0*	0	*0.0*	0	*0.0*	1	*0.4*	8	*2.8*	0	*0.0*	45	*1.5*			
Final diagnosis																							274.2	36	0.0000
Ovarian	94	*40.9*	123	*25.0*	99	*39.4*	305	*37.0*	57	*31.5*	82	*40.8*	27	*29.7*	78	*32.2*	64	*22.5*	60	*40.0*	989	*33.6*			
Uterine	70	*30.4*	119	*24.1*	73	*29.1*	243	*29.5*	56	*30.9*	51	*25.4*	37	*40.7*	60	*24.8*	62	*21.8*	49	*32.7*	820	*27.8*			
Cervical	18	*7.8*	19	*3.9*	20	*8.0*	82	*9.9*	16	*8.8*	9	*4.5*	5	*5.5*	16	*6.6*	11	*3.9*	11	*7.3*	207	*7.0*			
Vulval	3	*1.3*	18	*3.7*	14	*5.6*	69	*8.4*	12	*6.6*	12	*6.0*	4	*4.4*	20	*8.3*	12	*4.2*	12	*8.0*	176	*6.0*			
Benign	45	*19.6*	214	*43.4*	45	*17.9*	126	*15.3*	40	*22.1*	47	*23.4*	18	*19.8*	68	*28.1*	135	*47.5*	18	*12.0*	756	*25.6*			
Estimated blood loss																							246.2	27	0.0000
<500ml	155	*67.4*	400	*82.0*	196	*78.7*	709	*87.4*	93	*51.4*	161	*80.9*	69	*75.8*	198	*81.8*	261	*93.2*	93	*62.0*	2,335	*79.9*			
500ml-1000ml	50	*21.7*	49	*10.0*	33	*13.3*	62	*7.6*	69	*38.1*	23	*11.6*	12	*13.2*	31	*12.8*	11	*3.9*	38	*25.3*	378	*12.9*			
1000ml-2500ml	19	*8.3*	33	*6.8*	16	*6.4*	37	*4.6*	17	*9.4*	15	*7.5*	7	*7.7*	10	*4.1*	7	*2.5*	13	*8.7*	174	*6.0*			
>2500ml	6	*2.6*	6	*1.2*	4	*1.6*	3	*0.4*	2	*1.1*	0	*0.0*	3	*3.3*	3	*1.2*	1	*0.4*	6	*4.0*	34	*1.2*			
	mean	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**F**	**df***	**pvalue**
Age at surgery	58.6	*13.8*	59.5	*15.4*	58.4	*15.7*	60.6	*15.0*	63.2	*12.1*	63.1	*13.6*	57.2	*12.0*	63.3	*16.0*	59.6	*14.4*	64.1	*14.0*	60.6	*14.8*	5.2	9	0.0000
BMI	27.6	*6.7*	28.8	*6.9*	28.2	*8.3*	29.1	*7.2*	30.0	*6.8*	28.5	*6.1*	29.6	*8.4*	29.2	*6.7*	28.9	*6.4*	28.4	*6.7*	28.8	*7.0*	2.1	9	0.0304
Duration of surgery (hrs)	141	*59.1*	114	*53.7*	151	*85.1*	159	*83.4*	116	*52.0*	122	*57.0*	136	*56.8*	121	*58.8*	101	*47.9*	128	*55.9*	133.3	*69.9*	31.4	9	0.0000

Table 27 Risk prediction model for intra-operative complications

Variables	Lasso				Maximum Likelihood				Shrinkage
	OR	p-value*	L95% CI*	U95% CI*	OR	p-value	L95% CI	U95% CI	
Age at surgery	1.000	0.977	0.985	1.015	1.001	0.859	0.986	1.017	-84.0%
BMI	*removed*				1.003	0.867	0.974	1.032	-100.0%
Previous abdominal surgery	1.426	0.058	0.988	2.057	1.459	0.045	1.008	2.111	-6.0%
Low albumin	3.916	0.118	0.709	21.645	4.461	0.080	0.836	23.799	-8.7%
Coagulation-thrombosis	1.052	0.910	0.436	2.540	1.148	0.755	0.483	2.729	-63.1%
Diabetes	1.804	0.032	1.052	3.095	1.923	0.018	1.118	3.306	-9.7%
Cardiac	1.462	0.205	0.812	2.632	1.572	0.128	0.878	2.814	-15.9%
Respiratory	0.676	0.266	0.339	1.348	0.573	0.133	0.277	1.185	-29.8%
Gastrointestinal	1.065	0.893	0.425	2.668	1.188	0.703	0.490	2.879	-63.5%
Genitourinary	0.699	0.679	0.129	3.805	0.486	0.483	0.065	3.651	-50.4%
Musculoskeletal	*removed*				1.091	0.791	0.574	2.071	-100.0%
Neurology-psychiatric	*removed*				1.028	0.940	0.501	2.109	-100.0%
Vascular	0.849	0.775	0.276	2.607	0.675	0.527	0.199	2.286	-58.3%
Auto-immune	1.968	0.253	0.617	6.282	2.132	0.191	0.685	6.642	-10.6%
Metabolic-endocrine	0.412	0.027	0.187	0.906	0.329	0.010	0.141	0.768	-20.3%
Integumentary-dermatology	*removed*				0.964	0.965	0.191	4.873	-100.0%
Hypertension	1.239	0.325	0.808	1.899	1.279	0.263	0.831	1.969	-13.0%
Smoking	0.978	0.969	0.323	2.961	0.828	0.760	0.246	2.788	-88.2%
Other neoplasms	1.506	0.246	0.755	3.004	1.590	0.182	0.805	3.140	-11.8%
Laparoscopic approach	1.021	0.935	0.618	1.689	1.240	0.403	0.749	2.051	-90.2%
ASA									
ASA grade 1	1				1				
ASA grade 2	1.103	0.699	0.670	1.816	1.250	0.401	0.742	2.106	-56.0%

Table 27 Risk prediction model for intraoperative complications continued…

Variables	Lasso				Maximum Likelihood				Shrinkage
	OR	p-value*	L95% CI*	U95% CI*	OR	p-value	L95% CI	U95% CI	
ASA grade 3+	1.039	0.908	0.539	2.003	1.183	0.628	0.599	2.336	-77.0%
Surgeon grade									
Consultant	1				1				
Sub-specialty trainee	0.716	0.604	0.202	2.535	0.614	0.460	0.168	2.243	-31.6%
General Obstetrics & Gynaecology Trainee	1.286	0.673	0.399	4.144	1.243	0.720	0.378	4.083	15.8%
Surgical complexity									
Complexity score 1&2	1				1				
Complexity score 3&4	1.097	0.692	0.695	1.731	1.263	0.325	0.794	2.009	-60.4%
Complexity score 5&6	1.905	0.016	1.130	3.212	2.208	0.003	1.298	3.756	-18.6%
Complexity score 7&8	2.666	0.012	1.242	5.725	3.080	0.004	1.434	6.612	-12.8%
Complexity score >8	4.005	0.003	1.626	9.865	4.561	0.001	1.850	11.242	-8.6%
Final diagnosis									
Ovarian	1				1				
Uterine	0.600	0.050	0.360	1.001	0.504	0.011	0.296	0.856	-25.5%
Cervical	0.834	0.636	0.393	1.769	0.696	0.361	0.320	1.514	-49.9%
Vulval	0.289	0.049	0.084	0.993	0.195	0.026	0.046	0.826	-24.1%
Benign	0.567	0.041	0.329	0.976	0.508	0.017	0.291	0.887	-16.2%
Constant	0.033	0.000	0.007	0.146	0.025	0.000	0.004	0.145	-32.8%
* for approximate guidance only									

The ROC curve based on leave-one-out cross validation produced an AUC= 0.663 (95% CI: 0.616-0.710), which was only slightly larger than an equivalently generated AUC using ML=0.659 (95% CI: 0.611-0.706), although ROC curves are affected only by rank order and not magnitude. The mean bootstrapped calibration slope of 0.871 suggested a slight narrowness of predictions, although the 2.5^{th}-97.5^{th} centile of the slopes (0.717-1.068) did contain the optimum value of one. In contrast, a ML equivalent slope=0.712 (95% CI: 0.364-0.887) indicated that the prediction range was very limited, and hence the model over-fitted, without parameter shrinkage.

8.2.1.2 Hospital rate adjustments

Figure 9a shows the funnel plot allowing a simple comparison of observed intraoperative CRs by hospital. Hospital F, outside the 95% confidence bounds, would appear to have an unusually low CR; whereas, although Hospitals J and E are clearly higher than the overall CR, the moderate number of surgeries performed at these hospitals (150 and 181, respectively) means that one may be less sure of their outlier status.

Figure 9b shows the observed to expected CR ratio, based on the prevalence of the risk factors amongst the 10 hospitals. Actual values can be found in Table 28, and show the spread of expected CRs for hospitals is between 3.9% and 5.4%. In Figure 9b Hospital F is confirmed as having an unusually low intraoperative CR. The confidence interval for Hospital E is entirely above the line of equality (observed=expected), marking it out as a high CR of potential concern. The ratio for Hospital G is also high at 1.8, though has wide confidence intervals. Hospital J, which had the highest crude (observed) CR, only has the 3^{rd} highest ratio, indicating that its high CR is partially mitigated by a relatively high risk case-mix of surgeries.

Figure 9 Observed and expected intraoperative complication rates for individual hospitals

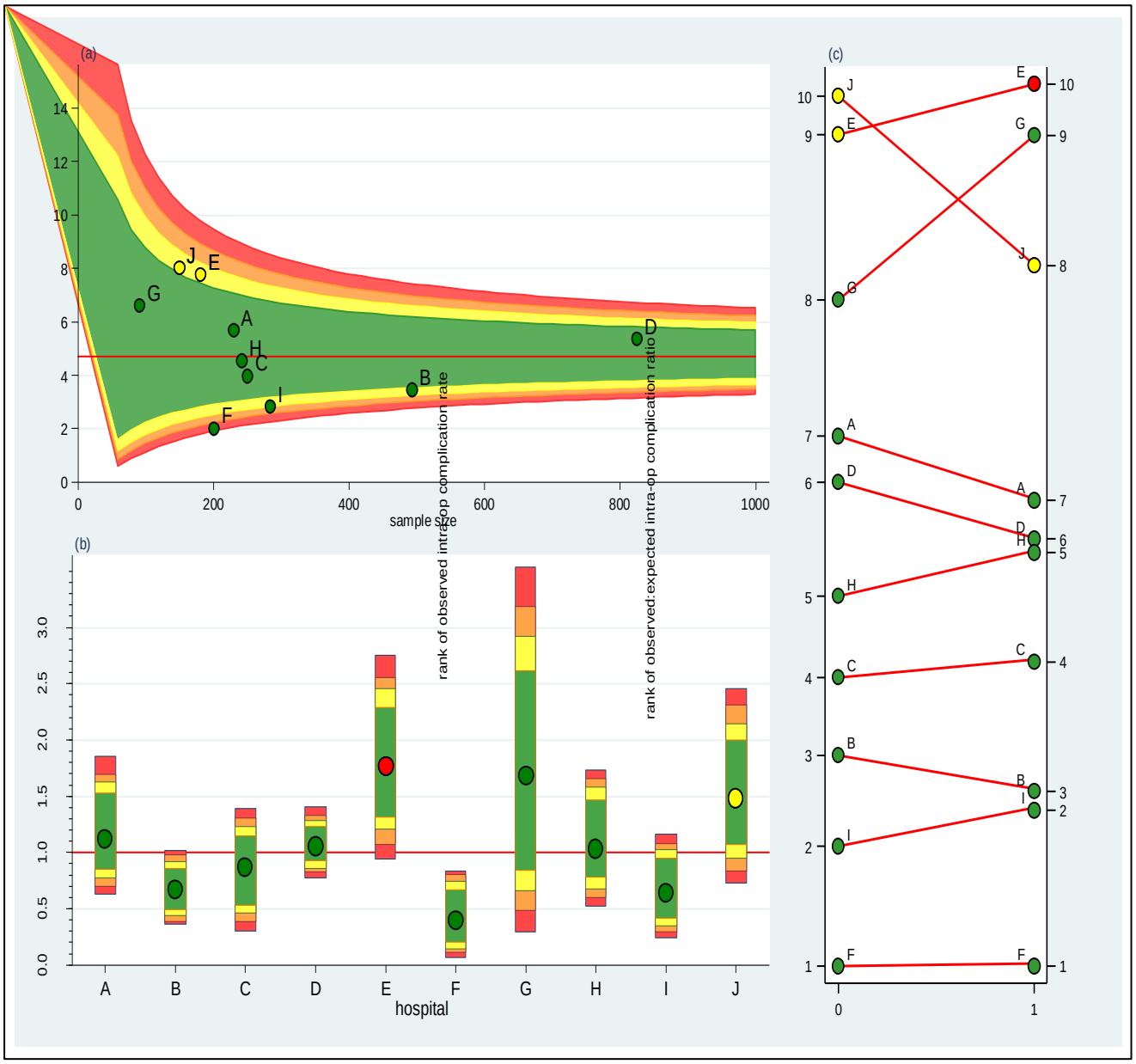


Figure 9c displays this adjustment process by plotting the rankings over the 10 hospitals for the observed intraoperative CR (left axis) and the observed:expected intraoperative CR ratio (right axis) with the placement on each axis reflective of the standardised differences in values. For example, although there is little change in terms of rank order, hospital G can be seen to have a notably higher CR ratio than observed CR, relative to the other hospitals.

Table 28 Summary of intraoperative complications by hospital

Hospital	No. of surgeries	No. of IO[1] complications	Observed IO CR[2]	Expected number IO complications	Expected IO CR	O/E[3] IO CR ratio	Lower 95% CI[4] for O/E ratio	Upper 95% CI for O/E ratio
A	230	13	5.7%	11.7	5.1%	1.116	0.689	1.698
B	493	17	3.4%	25.6	5.2%	0.664	0.390	0.977
C	251	10	4.0%	11.6	4.6%	0.865	0.389	1.307
D	825	44	5.3%	41.7	5.1%	1.055	0.826	1.333
E	181	14	7.7%	8.0	4.4%	1.761	1.072	2.554
F	201	4	2.0%	10.2	5.1%	0.393	0.102	0.804
G	91	6	6.6%	3.6	3.9%	1.681	0.481	3.189
H	242	11	4.5%	10.6	4.4%	1.035	0.598	1.659
I	284	8	2.8%	12.6	4.4%	0.635	0.298	1.081
J	150	12	8.0%	8.1	5.4%	1.479	0.838	2.313

1-Intra-operative complications; 2-Complication Rate; 3-Observed/Expected ratio; 4-Confidence interval

8.2.2 Post-operative complications

Table 29 repeats the by-hospital statistics of Table 26 but restricted to the subset (n=1462) used for the postoperative analysis. The findings are similar to those for the full dataset and estimated blood loss and duration of surgery also vary notably by hospital. BMI is not significantly different however, and neither is the postoperative complication rate (p=0.096) even though they vary from 15.6% to 36.2%.

Modelling and fit

Of the 1462 surgeries where both patient and hospital records were available, 376 had at least one postoperative complication. However, when fitting the full model missing data meant only 346 events were included out of 1371 surgeries, meaning an EPV of 9.9 given the 35 variables. Low albumin could not be included in the model as there was only one instance of it amongst the 1462 surgeries. The grid search yielded a lambda value of 12.2 and resulted in 15 variables out of the 35 being shrunk completely to zero (the comorbidities: cardiac, respiratory, genito-urinary, auto-immune, metabolic-endocrine, smoking, integumentary-dermatology, hypertension,

other neoplasms; both ASA grade levels, both surgeon grade levels, benign diagnosis and surgical complexity score 5-6). The resulting lasso-shrunk odds ratios are presented in Table 30, which also give the ML estimates for comparison. Only duration of surgery appears to be a strong predictor of postoperative complications, though from the ML model coagulation-thrombosis, diabetes, musculoskeletal (all increase risk), laparoscopic approach (decreases risk) and final diagnosis (cervical and vulval cancer increase risk relative to ovarian cancer) were significant at the 5% level and still retain some predictive power in the lasso model. McFadden's R^2 was just 0.027, whilst the ML version was 0.056. Both the goodness of fit test (p=0.130) and the misspecification test (p=0.385) suggested the model was acceptable with regard to these criteria.

The ROC curve based on leave-one-out cross validation produced an AUC= 0.659 (95% CI: 0.585-0.733), significantly larger than an equivalently generated AUC using ML=0.569 (95% CI: 0.487-0.652) as tested using a method by DeLong et al [(100)] (p=0.0003). By way of contrast, ROC curves based on full sample estimates (no cross-validation) generated a smaller AUC of 0.644 for the lasso penalised model, but a considerably larger AUC of 0.630 for the ML-based model. The mean bootstrapped calibration slope for the lasso-based model of 1.008 (95% CI: 0.799-1.264) suggested near perfectly calibrated predictions. However, the ML-based calibration slope=0.689 (95% CI: 0.562-0.835) strongly indicated that the prediction range was too narrow, and hence the model was over-fitted.

Table 29 Subset used for postoperative complication analysis where both hospital and patient-reported data was available n=1462

	Hospital																				Overall		chi2	df	pvalue
	A		B		C		D		E		F		G		H		I		J						
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%			
Intraoperative complications	3	*3.7*	10	*3.5*	2	*5.6*	22	*5.6*	10	*7.8*	3	*2.7*	3	*6.7*	8	*4.9*	5	*3.2*	2	*3.5*	68	*4.7*	7.1	9	0.6276
Postoperative complications (hospital and patient reported)	20	*24.4*	76	*26.7*	12	*33.3*	110	*27.9*	30	*23.3*	29	*25.7*	7	*15.6*	44	*27.2*	27	*17.1*	21	*36.2*	376	*25.7*	14.8	9	0.0960
Previous abdominal surgery	23	*28.1*	99	*34.7*	13	*36.1*	141	*35.8*	30	*23.3*	42	*37.2*	14	*31.1*	70	*43.2*	66	*41.8*	9	*15.5*	507	*34.7*	27.9	9	0.0010
Low Albumin	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	1	*0.6*	0	*0.0*	0	*0.0*	1	*0.1*	8.0	9	0.5311
Coagulation-thrombosis	3	*3.7*	9	*3.2*	2	*5.6*	12	*3.1*	7	*5.4*	3	*2.7*	3	*6.7*	11	*6.8*	5	*3.2*	1	*1.7*	56	*3.8*	8.3	9	0.4997
Diabetes	7	*8.5*	28	*9.8*	5	*13.9*	43	*10.9*	6	*4.7*	7	*6.2*	3	*6.7*	22	*13.6*	13	*8.2*	11	*19.0*	145	*9.9*	15.8	9	0.0713
Cardiac	5	*6.1*	36	*12.6*	10	*27.8*	29	*7.4*	15	*11.6*	12	*10.6*	3	*6.7*	17	*10.5*	18	*11.4*	8	*13.8*	153	*10.5*	20.4	9	0.0157
Respiratory	7	*8.5*	40	*14.0*	3	*8.3*	26	*6.6*	9	*7.0*	11	*9.7*	2	*4.4*	22	*13.6*	10	*6.3*	4	*6.9*	134	*9.2*	19.0	9	0.0254
Gastrointestinal	1	*1.2*	3	*1.1*	1	*2.8*	12	*3.1*	8	*6.2*	7	*6.2*	5	*11.1*	7	*4.3*	1	*0.6*	4	*6.9*	49	*3.4*	26.7	9	0.0016
Genitourinary	2	*2.4*	2	*0.7*	0	*0.0*	2	*0.5*	4	*3.1*	1	*0.9*	0	*0.0*	11	*6.8*	6	*3.8*	0	*0.0*	28	*1.9*	34.3	9	0.0001
Musculoskeletal	7	*8.5*	17	*6.0*	2	*5.6*	57	*14.5*	8	*6.2*	11	*9.7*	3	*6.7*	28	*17.3*	13	*8.2*	7	*12.1*	153	*10.5*	26.4	9	0.0017
Neurology-psychiatric	5	*6.1*	14	*4.9*	1	*2.8*	22	*5.6*	5	*3.9*	7	*6.2*	2	*4.4*	12	*7.4*	16	*10.1*	4	*6.9*	88	*6.0*	8.0	9	0.5329
Vascular	2	*2.4*	9	*3.2*	1	*2.8*	6	*1.5*	3	*2.3*	4	*3.5*	2	*4.4*	5	*3.1*	6	*3.8*	2	*3.5*	40	*2.7*	4.1	9	0.9046
Infections	0	*0.0*	6	*2.1*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	1	*0.6*	0	*0.0*	7	*0.5*	20.8	9	0.0136
Auto-immune	1	*1.2*	3	*1.1*	1	*2.8*	4	*1.0*	3	*2.3*	2	*1.8*	0	*0.0*	1	*0.6*	2	*1.3*	0	*0.0*	17	*1.2*	4.4	9	0.8794
Metabolic-endocrine	9	*11.0*	22	*7.7*	4	*11.1*	32	*8.1*	12	*9.3*	14	*12.4*	7	*15.6*	23	*14.2*	22	*13.9*	5	*8.6*	150	*10.3*	11.3	9	0.2567
Integumentary-dermatology	2	*2.4*	0	*0.0*	1	*2.8*	1	*0.3*	1	*0.8*	1	*0.9*	0	*0.0*	6	*3.7*	1	*0.6*	0	*0.0*	13	*0.9*	23.7	9	0.0048
Hypertension	25	*30.5*	113	*39.7*	12	*33.3*	127	*32.2*	47	*36.4*	47	*41.6*	12	*26.7*	74	*45.7*	51	*32.3*	17	*29.3*	525	*35.9*	17.2	9	0.0458
Smoking	0	*0.0*	14	*4.9*	0	*0.0*	1	*0.3*	2	*1.6*	2	*1.8*	7	*15.6*	9	*5.6*	1	*0.6*	1	*1.7*	37	*2.5*	58.1	9	0.0000
Other neoplasms	10	*12.2*	9	*3.2*	1	*2.8*	27	*6.9*	6	*4.7*	3	*2.7*	3	*6.7*	13	*8.0*	10	*6.3*	5	*8.6*	87	*6.0*	15.6	9	0.0768
Surgeon grade																							201.5	18	0.0000
General Obstetrics & Gynaecology Trainee	2	*2.4*	17	*6.2*	1	*2.9*	6	*1.5*	21	*17.8*	3	*2.7*	0	*0.0*	2	*1.3*	19	*12.5*	3	*5.3*	74	*5.2*			

Table 29 Subset used for postoperative complication rate analysis where both hospital and patient-reported data was available continued…..																								
Sub-specialty trainee	35	*42.7*	55	*20.2*	16	*47.1*	82	*20.8*	5	*4.2*	1	*0.9*	15	*33.3*	58	*38.2*	21	*13.8*	1	*1.8*	289	*20.4*			
Consultant	45	*54.9*	201	*73.6*	17	*50.0*	306	*77.7*	92	*78.0*	107	*96.4*	30	*66.7*	92	*60.5*	112	*73.7*	53	*93.0*	1,055	*74.4*			
Laparoscopic approach	37	*45.1*	21	*7.4*	4	*11.1*	99	*25.1*	8	*6.2*	6	*5.3*	15	*33.3*	43	*26.5*	91	*57.6*	9	*15.5*	333	*22.8*	220.3	9	0.0000
ASA Grade																							49.1	18	0.0001
ASA grade 1	10	*12.4*	80	*28.1*	12	*33.3*	90	*22.8*	23	*17.8*	29	*25.7*	9	*20.0*	15	*9.3*	45	*28.5*	17	*29.3*	330	*22.6*			
ASA grade 2	58	*71.6*	155	*54.4*	21	*58.3*	230	*58.4*	70	*54.3*	64	*56.6*	32	*71.1*	106	*65.8*	82	*51.9*	29	*50.0*	847	*58.0*			
ASA grade 3+	13	*16.1*	50	*17.5*	3	*8.3*	74	*18.8*	36	*27.9*	20	*17.7*	4	*8.9*	40	*24.8*	31	*19.6*	12	*20.7*	283	*19.4*			
Surgical complexity																							125.8	36	0.0000
Complexity score 1&2	36	*43.9*	89	*31.2*	25	*69.4*	179	*45.4*	87	*67.4*	41	*36.3*	22	*48.9*	84	*51.9*	106	*67.1*	21	*36.2*	690	*47.2*			
Complexity score 3&4	30	*36.6*	115	*40.4*	9	*25.0*	143	*36.3*	27	*20.9*	46	*40.7*	20	*44.4*	53	*32.7*	38	*24.1*	23	*39.7*	504	*34.5*			
Complexity score 5&6	11	*13.4*	60	*21.1*	1	*2.8*	50	*12.7*	13	*10.1*	22	*19.5*	2	*4.4*	23	*14.2*	10	*6.3*	14	*24.1*	206	*14.1*			
Complexity score 7&8	3	*3.7*	16	*5.6*	0	*0.0*	15	*3.8*	2	*1.6*	4	*3.5*	1	*2.2*	2	*1.2*	1	*0.6*	0	*0.0*	44	*3.0*			
Complexity score >8	2	*2.4*	5	*1.8*	1	*2.8*	7	*1.8*	0	*0.0*	0	*0.0*	0	*0.0*	0	*0.0*	3	*1.9*	0	*0.0*	18	*1.2*			
Final diagnosis																							163.5	36	0.0000
Ovarian	39	*47.6*	70	*24.6*	17	*47.2*	157	*39.9*	39	*30.2*	46	*40.7*	11	*24.4*	54	*33.3*	34	*21.5*	14	*24.1*	481	*32.9*			
Uterine	25	*30.5*	68	*23.9*	13	*36.1*	124	*31.5*	40	*31.0*	33	*29.2*	22	*48.9*	41	*25.3*	40	*25.3*	21	*36.2*	427	*29.2*			
Cervical	7	*8.5*	7	*2.5*	0	*0.0*	29	*7.4*	12	*9.3*	4	*3.5*	3	*6.7*	10	*6.2*	3	*1.9*	5	*8.6*	80	*5.5*			
Vulval	0	*0.0*	14	*4.9*	1	*2.8*	26	*6.6*	7	*5.4*	6	*5.3*	0	*0.0*	10	*6.2*	8	*5.1*	7	*12.1*	79	*5.4*			
Benign	11	*13.4*	126	*44.2*	5	*13.9*	58	*14.7*	31	*24.0*	24	*21.2*	9	*20.0*	47	*29.0*	73	*46.2*	11	*19.0*	395	*27.0*			
Estimated blood loss																									
<500ml	54	*65.9*	237	*84.0*	24	*68.6*	331	*86.0*	68	*52.7*	91	*80.5*	35	*77.8*	135	*83.3*	148	*94.9*	39	*67.2*	1,162	*80.3*	140.4	27	0.0000
500ml-1000ml	20	*24.4*	25	*8.9*	8	*22.9*	35	*9.1*	46	*35.7*	14	*12.4*	5	*11.1*	21	*13.0*	4	*2.6*	17	*29.3*	195	*13.5*			
1000ml-2500ml	7	*8.5*	17	*6.0*	3	*8.6*	17	*4.4*	13	*10.1*	8	*7.1*	3	*6.7*	4	*2.5*	4	*2.6*	2	*3.5*	78	*5.4*			
>2500ml	1	*1.2*	3	*1.1*	0	*0.0*	2	*0.5*	2	*1.6*	0	*0.0*	2	*4.4*	2	*1.2*	0	*0.0*	0	*0.0*	12	*0.8*			
	mean	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**mean**	***sd***	**F**	**df***	**pvalue**
Age at surgery	59.6	*12.2*	60.5	*14.4*	62.1	*12.8*	62.8	*12.8*	63.1	*11.7*	63.8	*12.3*	59.1	*11.8*	64.5	*14.8*	62.0	*12.9*	65.4	*13.3*	62.4	*13.3*	2.4	9	0.0107
BMI	27.8	*7.8*	28.8	*6.7*	31.1	*8.8*	28.5	*6.8*	29.7	*6.6*	28.3	*5.5*	30.2	*10.0*	29.2	*6.9*	29.1	*6.3*	28.6	*6.3*	28.9	*6.9*	1.2	9	0.2625
Duration of surgery (hours)	148.9	*60.6*	110.6	*51.3*	146.1	*91.2*	161.8	*80.8*	110.3	*51.0*	121.3	*55.4*	138.8	*53.4*	122.6	*56.6*	95.1	*42.6*	114.4	*34.8*	128.9	*66.2*	23.7	9	0.0000

Table 30 Risk prediction model for postoperative complications

Variables	Lasso				Maximum Likelihood				Shrinkage
	OR	p-value*	L95% CI*	U95% CI*	OR	p-value	L95% CI	U95% CI	
Age at surgery	0.997	0.552	0.986	1.008	0.991	0.160	0.979	1.003	-57.3%
BMI	1.012	0.213	0.993	1.031	1.020	0.059	0.999	1.041	-38.6%
Previous abdominal surgery	1.008	0.954	0.774	1.313	1.096	0.501	0.838	1.434	-90.4%
Coagulation-thrombosis	1.510	0.202	0.802	2.842	2.130	0.022	1.115	4.072	-45.1%
Diabetes	1.355	0.145	0.901	2.038	1.565	0.038	1.024	2.392	-31.3%
Cardiac	*removed*				1.036	0.878	0.660	1.627	-100.0%
Respiratory	*removed*				1.146	0.536	0.744	1.763	-100.0%
Gastrointestinal	0.916	0.798	0.467	1.796	0.673	0.291	0.322	1.405	-77.4%
Genitourinary	*removed*				1.371	0.490	0.560	3.354	-100.0%
Musculoskeletal	1.254	0.265	0.842	1.868	1.555	0.033	1.037	2.333	-50.3%
Neurology-psychiatric	0.908	0.722	0.533	1.546	0.693	0.217	0.387	1.241	-69.0%
Vascular	0.926	0.847	0.423	2.024	0.692	0.412	0.287	1.669	-78.6%
Auto-immune	*removed*				0.531	0.366	0.134	2.098	-100.0%
Metabolic-endocrine	*removed*				1.120	0.586	0.744	1.688	-100.0%
Integumentary-dermatology	*removed*				0.981	0.977	0.262	3.672	-100.0%
Hypertension	*removed*				1.129	0.431	0.834	1.530	-100.0%
Smoking	*removed*				1.341	0.467	0.609	2.955	-100.0%
Other neoplasms	*removed*				1.167	0.577	0.678	2.009	-100.0%
Laparoscopic approach	0.739	0.084	0.525	1.042	0.649	0.020	0.451	0.935	-28.7%
ASA									
ASA grade 1	1								
ASA grade 2	*removed*				0.942	0.745	0.659	1.348	-100.0%
ASA grade 3+	*removed*				0.812	0.407	0.497	1.328	-100.0%
Consultant	1								

Table 30 Risk prediction model for Postoperative complications continued…

Variables	Lasso				Maximum Likelihood				Shrinkage
	OR	p-value*	L95% CI*	U95% CI*	OR	p-value	L95% CI	U95% CI	
Surgeon Grade									
Sub-specialty trainee	*removed*				0.864	0.658	0.453	1.648	-100.0%
General Obstetrics & Gynaecology Trainee	*removed*				0.873	0.656	0.480	1.588	-100.0%
Surgical complexity									
Complexity score 1&2	1								
Complexity score 3&4	1.112	0.437	0.851	1.454	1.322	0.078	0.969	1.804	-61.8%
Complexity score 5&6	*removed*				1.054	0.819	0.670	1.659	-100.0%
Complexity score 7&8	1.056	0.881	0.516	2.163	1.480	0.313	0.691	3.169	-83.3%
Complexity score >8	1.004	0.970	0.828	1.217	1.748	0.322	0.579	5.279	-90.6%
Final diagnosis									
Ovarian	1								
Uterine	0.982	0.911	0.719	1.343	0.951	0.790	0.658	1.376	-82.5%
Cervical	1.606	0.094	0.923	2.794	2.099	0.016	1.148	3.836	-33.4%
Vulval	1.779	0.030	1.056	2.999	2.274	0.003	1.311	3.943	-27.7%
Benign	*removed*				1.058	0.775	0.720	1.554	-100.0%
Duration of surgery (hrs)	1.086	0.003	1.028	1.146	1.081	0.018	1.014	1.152	6.5%
Estimated blood loss									
<500ml	1								
500ml-1000ml	1.267	0.208	0.876	1.833	1.405	0.077	0.963	2.048	-32.1%
1000ml-2500ml	1.052	0.860	0.600	1.843	1.249	0.442	0.709	2.202	-76.4%
>2500ml	0.997	0.962	0.867	1.146	0.506	0.417	0.098	2.623	-86.6%
constant	0.167	0.000	0.066	0.422	0.179	0.003	0.057	0.564	-25.5%

*for approximate guidance only; low albumin not included as only one instance in 1462 surgeries

Hospital rate adjustments

Figure 10a compares the observed CRs of the 10 hospitals using a funnel plot. No hospital appears to have a postoperative CR that is worryingly high relative to the overall CR of 25.7%, although the postoperative CRs are generally considerably larger than for intraoperative. Hospital J has the CR of most concern (36.2%), though based on only 58 surgeries. Hospital C is the only other CR over 30% (33.3%, n=36). Hospitals G and I have an approximately equally low CR (15.6% and 17.0%) though it is for the latter that the evidence of an unusually low CR is stronger, given the larger sample size – only hospital I lies outside either 95% or 99% confidence bands. Figure 10b shows the observed to expected postoperative CR ratio, with actual values found in Table 31 .The range of expected CRs was from 20.1% to 28.5%. None of the hospitals have a CR ratio significantly different from one. Figure 10c shows that hospital J is now a little further away from the average when considering the CR ratio. For the middle ranked hospitals there is some swapping of rankings using the CR ratio, but little real change in their relative rating. By contrast hospitals C, G and I maintain their original rankings but are the biggest movers in terms of standardised deviation. Notably, hospital I does not have a significantly low CR when factoring for the case-mix of their surgeries.

Figure 10 Observed and expected postoperative complication rates for individual hospitals

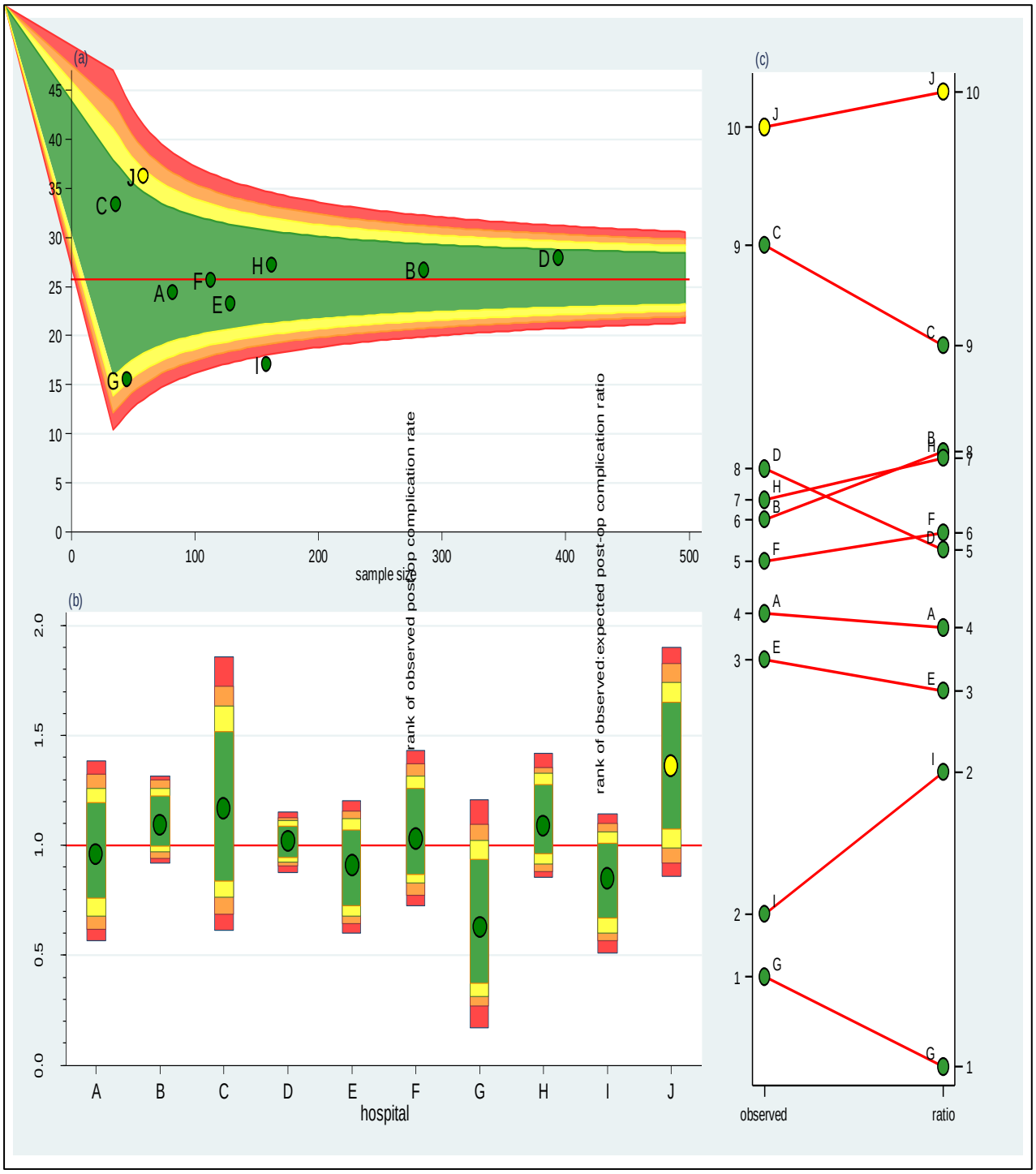


Table 31 Summary of postoperative complications by hospital

Hospital	Number of surgeries	Number PO[1] complications	Observed PO CR[2]	Expected number PO complications	Expected PO CR	O/E[3] PO CR ratio	Lower 95% CI[4] for O/E ratio	Upper 95% CI for O/E ratio
A	82	20	24.4%	20.9	25.4%	0.958	0.616	1.325
B	285	76	26.7%	69.7	24.4%	1.091	0.942	1.296
C	36	12	33.3%	10.3	28.5%	1.171	0.688	1.723
D	394	110	27.9%	108.2	27.5%	1.017	0.902	1.128
E	129	30	23.3%	33.0	25.5%	0.910	0.638	1.157
F	113	29	25.7%	28.2	24.9%	1.029	0.769	1.370
G	45	7	15.6%	11.1	24.8%	0.628	0.265	1.098
H	162	44	27.2%	40.5	25.0%	1.086	0.881	1.355
I	158	27	17.1%	31.8	20.1%	0.850	0.562	1.099
J	58	21	36.2%	15.4	26.6%	1.361	0.917	1.828

1-Postoperative complications; 2-Complication Rate; 3-Observed/Expected ratio; 4-Confidence interval

8.3 Discussion

Published data comparing CRs across gynaecological oncology centres is sparse and limited to a small retrospective study from the United States, comparing outcomes of ovarian cancer surgery between three tertiary cancer centres. (44) However, such data is available nationally in other specialties such as cardiac surgery(50), colorectal(101), head and neck (88) and lung (87) cancer.

This is the first large study in gynaecological oncology to develop risk-adjusted CRs for comparison of outcomes between gynaecological oncology centres. The overall intraoperative (≈5%) and postoperative (≈26%) CR derived from this study could be used to benchmark performance in gynaecological oncology.

The main finding is that while adjustment for risk did not make a difference for majority of hospitals, it helped better delineate the outliers. The shaded funnel plots and observed versus expected ratios generated made comparisons easy to comprehend. It is important to note that where hospital under-reporting is common as for

postoperative complications, use of patient reported outcomes was crucial to ensure a valid comparison between institutions.

By accounting for the prevalence of potential surgical complication risk factors it might be possible to (partially) mitigate an institution's observed CR if it appears, say, unusually high. Likewise, it may also be found that a hospital's CR is more concerning than it perhaps initially appears. For this dataset adjustment for confounding of risk resulted in only moderate differences to the crude CRs. Even with ML estimation not many of the proposed risk factors appeared strongly predictive of the outcome.

Risk factors for intraoperative CR were largely different from that for postoperative CR and even after adjustment there was no concordance between hospital intraoperative and postoperative CR. Therefore for benchmarking hospitals, it may be important to calculate intraoperative and postoperative CRs separately.

Based on the ML based p-values, for intraoperative CRs only surgical complexity, previous abdominal surgery, diabetes, metabolic-endocrine and final diagnosis were significant at the 5% level. For postoperative CRs on the other hand, only duration of surgery, coagulation-thrombosis, diabetes, musculoskeletal, laparoscopic approach and final diagnosis were significant at the 5% level. Indeed, only diabetes had a consistent effect on both intraoperative and postoperative CR. With regards to final diagnosis, ovarian cancer was the riskiest diagnosis for intraoperative complications but cervical and vulval cancers were considerably riskier diagnoses for postoperative complications.

These mitigating risk factors are by intention factors that are out of the hospital's or surgeon's control. It could be argued then, that surgeon grade should not be controlled for as the hospital could in theory have the highest graded surgeons always performing. There was, perhaps surprisingly, little evidence that surgeon grade was related to adverse surgical outcome though this could be due to more junior surgeons

being allocated ‘easier’ surgical procedures. All other intraoperative factors, regardless of their estimated risk implication, were entirely exogenous to the surgical environment. For postoperative complications, the additional factors duration of surgery and estimated blood loss of course may in part be reflective of surgical skill, but generally are proxies for the exogenous issue of surgical requirement and difficulty. Duration of surgery was in fact the one clearly important factor in predicting postoperative risk.

Few of the factors appeared important across either model and this reflected the difficulty of the task in developing risk prediction models. The collection of data for 2948 gynaecological surgeries was a major time-consuming undertaking, yet this still only meant 139 intraoperative complications which had significant implications for estimation given the large number of risk factors under consideration. The intraoperative EPV rate was far less than the usual guideline of 10 (=4.1), and any attempt to model the full set with standard methods would inevitably lead to over-fitting and poor predictions. The calibration statistic using the ML estimates demonstrated this clearly (0.712 for intraoperative; 0.689 for postoperative) showing the need for parameter shrinkage that would bias the estimates but improve predictions. In fact ML estimation only gives unbiased estimates asymptotically and for several of the comorbidity factors, where the prevalence was very low, a different cause of bias is introduced. Low predictor counts may lead to near perfect prediction (or ‘separation’) and greatly biased estimates, if estimation is even possible. In this scenario a different form of penalised regression [(102)] would be more suitable if well estimated odds ratios were the research goal.

The lasso method was used to produce better predictions, but as can be seen from the diminished pseudo-R^2 statistics, even less of the outcome is predicted and the observed to expected CR ratios will be typically less affected as a consequence. The

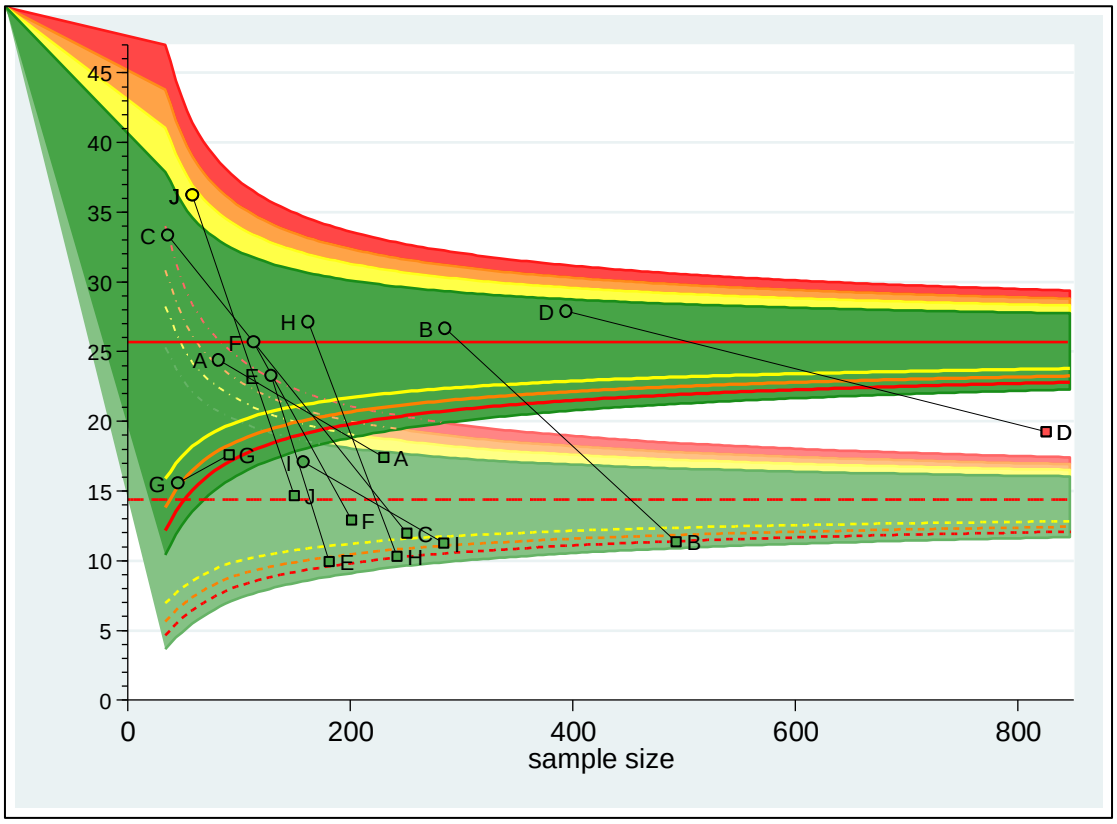
EPV (=9.9) for postoperative complications was considerably higher yet conversely there was more shrinkage performed (larger lambda). A different criterion to the generalised cross-validation statistic might have resulted in differing penalty terms, but the lack of association for the postoperative predictors will be a major cause of the greater shrinkage. It demonstrates effectively that the EPV is very much an approximate guideline, and in reality the requirement may be quite different from dataset to dataset.

Given that most of the predictors appeared to have minimal impact on outcome it therefore might seem tempting to conclude that the adjustment process is not strictly necessary. However it is felt that where feasible, adjustment is still worthwhile in safeguarding against an excess of surgical complications at a given hospital, as it will help define that level of excess better. Hospital E only became flagged as having a statistically high intraoperative CR following adjustment. Figures 9c and 10c show that relative performances for most hospitals are moderately affected by the adjustment process, especially regarding postoperative complications, even if the overall conclusions and rankings seem unaffected. It was noted that statistically the intraoperative and postoperative CRs did not vary significantly between the ten hospitals, so that for the majority the observed CRs were comfortably inside the funnel plot confidence limits. In future scenarios, where hospitals may have a larger spread of CRs or quality control has been compromised at a certain hospital, this could mean more institutions close to or beyond the simple safety bounds, and therefore the need for a more exacting assessment of their performance. In stark contrast, nearly all the predictors varied considerably by hospital, especially those involving an element of surgical decision (laparoscopic approach, surgeon grade and surgical complexity). This by-hospital variability in risk factor prevalence is a strong argument in itself for the need to attempt adjustment for fairer comparison. That many of the factors were not

apparently important will partially be a result of the lack of statistical power, and with the accumulation of additional data it may well be shown that some of these factors make a telling contribution to CR prediction, both statistically and clinically. The lack of association between CR and certain factors like BMI, especially after open surgery, are contrary to previous reports [103, 104].

The other important finding of this study was the difference in ranking order of hospitals for intraoperative and postoperative complications. Hospitals G and E had high intraoperative CRs (both crude and risk-adjusted) and low postoperative CRs. This discrepancy between intraoperative and postoperative CR ranking could be due to a variety of factors including surgical skill, postoperative care in wards and under reporting of postoperative complications. Analysis of only hospital-reported postoperative complications demonstrated that hospital D, which had contributed the largest number of surgeries, also had the highest postoperative CR (Figure 11). However, when the surgical subset with both hospital and patient-reported data was analysed, hospital D was no longer an outlier but hospital J's rate had increased from close to the 50th to the 95th centile, suggesting that perhaps hospital D had been more diligent at recording all postoperative complications when compared to the other institutions. These findings substantiate the need for including patient-reported postoperative complications to overcome the issue of under reporting by hospitals. Despite limiting analysis to operations with both hospital and patient-reported postoperative complications to calculate the risk-adjusted rates, the reversal in the ranking for hospitals G and E persisted. This finding would suggest that intraoperative and postoperative complications are different entities as they have different contributing factors, as already shown.

Figure 11 Comparison of observed postoperative complication rates against colour-coded funnel plots. Bright colour-coding and circle markers represent patient-reported statistics and faded colour-coding and square markers represent hospital reported statistics only



Therefore it is important to rank hospitals separately for intraoperative and postoperative complications and combining the two would perhaps mask the deficiencies inherent in the perioperative care in certain hospitals.

Despite this recommendation it is evident that much of the outcome variability is related to unmeasured (and probably even unobservable) phenomena. This was anticipated, and it is not expected for a surgical complication to be ever predicted with a high degree of confidence. Individual surgeon scoring not based on status but hitherto historical performance may be one (though potentially unpopular), possibility in improving surgical risk prediction.

A non-trivial issue for the funnel plots was that of the overall CR the confidence limits were built around. An internal measure (the observed overall rate) was used in lieu of a pre-specified target rate based on external data and expert opinion. Clearly, using

the observed overall rate is data-dependent and a hospital with a particularly high rate will help push up that value to which all hospitals are compared to. Unfortunately there was not sufficient data regarding gynaecological cancer surgery to utilise a prior target rate.

A related issue was that the data used to estimate the prediction model was the same to which the model was then applied to. Cross-validation methods were used to determine the calibration and discrimination of the predictions, but not for the expected hospital CRs. Penalised regression methods help to limit the influence of the specific dataset the estimates were based upon, by not over-fitting to each 'feature' of the data. Ideally, there would be a validation set to demonstrate the model predictions, but even the full dataset had a limited EPV rate and proper validation of a risk prediction model requires a fully external dataset anyway. By using the same dataset a hospital's own surgical history can influence the model parameters which are in turn used to mitigate their performance via the expected rate. However, this is analogous to the overall rate being used as the target rate; an expected rate based on a null model with no predictors would be the same for all hospitals and equal to the observed overall rate.

By using a shrinkage method it may appear that the potential of this dataset and model forming the basis of a routine risk adjustment process in the future is limited. The EPV requirements deem all initial predictors as part of the variable count, so selection methods that appear to trim a model to a parsimonious and 'useful' subset do not obviate this need. In a limited event situation it is known that selection methods will drop some moderate predictors, and even include some noise predictors [(95)]. It was therefore not preferable to produce a reduced-variable risk model with 'nicely rounded' coefficients that allow simple hand calculation, as for example the Risk of Malignancy index (RMI) used to preoperatively predict the nature of ovarian masses [(105)]. However, it is straightforward to input predictor values into, say, an Excel sheet pre-prepared

with the necessary inverse logit formula to calculate risk scores (Appendix 9 and 10) and it would be easy for an appropriate hospital employee to perform this provided they are prepared to record the data. Admittedly, use of bootstrapping methods is not an easy proposition in a clinical setting, but for approximate inference it is simple enough to use the confidence limits described by DeLong et al, treating the expected rate as fixed.

Since morbidity is the main yardstick being used to benchmark surgical performance, moving forwards, it would be important to have complete and accurate data in a national database. Although it would be more acceptable to clinicians, the main drawback of clinician-led databases is that they rely on voluntary data entry and therefore may not be complete. [4] Also, as demonstrated by Almoudaris et al, there is the possibility that centres with high rates of morbidity may be hesitant to voluntarily enter all their data into these databases. [106] The alternative might be to source information from an administrative database like Hospital Episode Statistics (HES) where all surgical episodes are automatically recorded. Although Nouraei et al [88] found complication rates derived from HES comparable to that in the clinician-led head and neck surgery database, this has not been the case with other surgical specialties [73]. An audit of complications post UKGOSOC in one of the participating centres also demonstrated that the morbidity rates were higher than that reported on HES but comparable to that in UKGOSOC. [107] Therefore in future, a reasonable compromise may be to have a combination of the two so that the data fields requiring entry by surgeons is kept to a minimum to ensure completeness. In addition to disclosing outcomes data for hospitals it is now becoming a requirement to publish data for individual surgeons as well [85] and it is hoped that this will act as an impetus for surgeons to ensure data on their surgical procedures is complete and accurate.

9 Discussion

This study has demonstrated that multi-centred contemporaneous data collection on surgery and complications is feasible to allow calculation of crude and risk-adjusted complication rates for the purpose of benchmarking in gynaecological oncology surgery.

The key findings of the study are as follows:

- The overall unadjusted intraoperative complication rate was 4.7% (95% CI 4.0 - 5.6).
- The unadjusted hospital-reported postoperative complication rate was 14.4% (95% CI 13.2-15.7) which increased to 25.9% (95% CI 23.7-28.2) when both hospital and patient reported postoperative complications were included.
- The predictors for intraoperative complications were different to that for postoperative complications, except for diabetes which was common to both.
- The significant contributing factors for intraoperative complications were surgical complexity, diabetes, ovarian cancer diagnosis, previous abdominal surgery.
- The significant contributing factors for postoperative complications were age, duration of surgery, open approach (compared to laparoscopic), vulval cancer diagnosis and diabetes.
- Risk adjustment had a modest effect on the rankings of the individual centres based on their complication rates. However, the adjusted complication rates for individual centres ensured a fairer comparison.
- There was no concordance between intraoperative and postoperative complications rates of the participating centres. Centres with high intraoperative

complication rates were found to have some of the lowest postoperative complication rates.

Strengths of this study include prospective data collection using standard forms, large sample size and multi-centre design with ten participating gynaecological cancer centres. An online database, accessible to the clinical team whether they were in theatre, wards or outpatient departments facilitated capture of surgical data and complication events contemporaneously. Validity of the data was ensured by weekly review by an independent clinician at the coordinating centre, who contacted the teams on a regular basis to retrieve missing data and “clean” erroneous entries.

Prior to UKGOSOC, data on surgical complications were limited to a single centre study from Australia [45] and a small three centre study from the US on ovarian cancer surgery. [44] This is the first time that such data on approximately 3000 surgeries involving ten centres has been collected. A database was specifically designed and refined to collect data on comorbidity, surgery and complications. To account for the various procedures often performed for gynaecological cancers and to have a standardised approach to collect this data across the ten centres, a score to grade surgical complexity was developed based on Aletti’s surgical complexity score [43] for ovarian cancer surgery. This scoring system however requires validation in future studies.

In order to define a complication, one of the definitions suggested by D Sokol was adopted which stated that a surgical complication was ‘an undesirable and unintended result of an operation affecting the patient that occurs as a direct result of the operation’. [6] However, in some instances it was not clear whether the event was a direct consequence of surgery. For example, an exacerbation of a pre-existing condition like atrial fibrillation (AF) which had been quiescent could have flared up after

surgery. Although by definition, AF in this situation was not a direct consequence of the operation, surgery had certainly contributed to its exacerbation and therefore was included as a complication.

The one intraoperative complication that was particularly difficult to define/determine was intraoperative haemorrhage. Some studies have used the need for intraoperative [45] or postoperative blood transfusion as a marker of significant intraoperative haemorrhage. This definition could not be used as there were women in this study having surgery soon after chemotherapy which often causes anaemia and such women would have been transfused during or soon after surgery. Therefore the indication for transfusion in these cases would not necessarily be intraoperative blood loss. Also, the threshold haemoglobin level for transfusion would not have been the same across the ten hospitals. Taking these issues into account, estimated intraoperative blood loss of >2500mls was defined as intraoperative haemorrhage in this study. Although a threshold of >2.5litres might seem a bit excessive for a simple hysterectomy it may not be so for a radical debulking surgery involving bowel resection, upper abdominal surgery etc. Various thresholds could have been used for individual procedures depending upon their complexity for a more accurate assessment of haemorrhage, but this would not have been easy to capture uniformly across the ten centres and would have been open to individual interpretations. For example, for an abdominal hysterectomy one would expect the blood loss to be <500mls but not all hysterectomies are the same and the blood loss could have varied depending on uterine size, presence of adhesions, endometriosis etc., and not just be a reflection of surgical skill.

Comorbidity was captured according to the various organ systems. The advantage of this method was that the effect of individual comorbidity on complications could be

analysed. As a result, diabetes was identified as a key predictor. The disadvantage of this approach was that the severity of individual illnesses was not accounted for. In addition to the ASA grade which was easily available for all patients undergoing surgery, the ACE-27 score was built into the database to capture comorbidity. However this could not be used due to the issue with licensing for the individual centres. Towards the end of the study, the Charlson index was incorporated into the database. However, by the time it was tested and ready for use, the study was nearing to an end. Future studies in gynaecological oncology could use this index to capture comorbidity as it has been used to capture comorbidity in patients with gynaecological cancers and also in those undergoing surgery in other specialties. [108-110] Studies have also shown that it is feasible to derive Charlson scores from administrative databases like HES [111]

Postoperative complications were defined as those complications occurring up to eight weeks after surgery although in reality there would have been some complications that occurred after this period. For e.g. incisional hernias from laparotomies could present months after an operation. Instead of a one off follow-up letter, a series of follow-up letters to patients at regular time intervals would have been necessary to capture these late complications.

Patient follow-up was invaluable to this study and was a very efficient way of obtaining information on complications treated in primary care or the local hospital. Patient-reported complications were found to significantly impact on the post-operative complication rate both overall and also for individual hospitals. [90] One of the hospitals which had contributed the most number of cases also had the highest hospital-reported postoperative complication rate. However when patient reported data was

included the postoperative complication rate for this hospital was no longer the highest highlighting the need to include patient reported complications.

The questions in the follow-up questionnaire (developed during the course of the study), were designed in such a way that complications could be easily graded according to the Clavien and Dindo system [8] which was used in the study. During the development of the questionnaire non-medical colleagues and lay volunteers were asked to choose between two versions of the questionnaire and the one with the most votes was chosen. Although in the patient feedback none of the women expressed any difficulty in understanding the questions, it would be important to include women/patients in the development of future versions. Also, complications have been traditionally defined by clinicians and this was the case in this study as well. However, as more emphasis is now being given to patient reporting and patient experience, there probably needs to be patient involvement in defining what a complication is, and, in determining which complications are important to patients. It is possible that complications which matter to patients may not always be the same as those which clinicians think are significant.

Since prior consent had not been obtained from the women, it was not possible to contact their general practitioners (GPs) to verify the patient-reported complications. However when the centres were contacted, they were able to verify all the major complications with serious sequelae like re-operation/admission to intensive care and around half of those complications managed with medical therapy in primary care or the local hospital. Very few of the verified complications had been erroneously reported by patients suggesting that in most instances patients accurately report complications and therefore are a valuable resource.

The response rate for the follow-up letters was 68% which could perhaps have been improved by re-sending the letters to the non-responders. However sending the follow-up letters was not always straight forward. Prior to sending the letters, the centres had to be contacted in cases of missing information, and for an update on whether any of the patients from the list had deceased, as a good proportion of the patients were elderly with co-morbidities and cancer. Despite adopting this policy, letters were inadvertently sent to some deceased patients causing distress to their families.

Given the added value of patient reporting, it would be essential for future studies to incorporate this in addition to hospital data. However it requires additional resources, clinician input to analyse patients' responses and may not be an easy undertaking on a larger scale. Use of a questionnaire format would help with easy interpretation and data entry, and, one way of routinely collecting this information might be to add the follow-up questionnaire to patient reported outcome measures (PROMs) questionnaires [18] which may become a requirement for cancer surgery in future.

One of the main drivers of this study was the need for risk adjusted rates as there was much unease amongst the clinicians that patient comorbidity and surgical risk factors were not being accounted for when calculating complication rates for benchmarking purposes. Therefore the aim of creating a risk prediction model was to predict risk as accurately as possible, taking into account all the risk factors so that fair comparisons could be made between the centres. The problem with previous risk-prediction models like the POSSUM index has been that that they tend to over predict risk and therefore failed to be validated. [47] To avoid this problem, the Lasso method of penalised regression was used in this study. [67] Even though the relative performances for most hospitals were only moderately affected by the adjustment process, adjustment was

still important as it helped to better define the level of excess surgical complications at a given hospital. With a larger dataset the findings might be different due to a wider variation in the patient cohort, skill mix of the surgeons and complication rates between hospitals.

There was little concordance between the intraoperative and postoperative complication rates of individual centres. Centres with high rates for intraoperative complications were found to have low postoperative complication rates. This would suggest that they are two different entities and therefore should not be combined. This was further strengthened by the finding that the predictors for intraoperative complications were different from those for postoperative complications. Also, other factors such as perioperative management of the patient and the standard of postoperative care on the wards could vary from one hospital to another. Therefore it was felt that the two should not be combined and could in turn help in identifying the deficiencies in certain aspects of patient care in hospitals.

This study was very much led by the clinicians. The advantage was that clinicians had control over the data that was entered and therefore there was less room for any errors that tend to happen with administrative databases where clinical coders have to rely on the operating notes and other patient records for information. However it heavily relied on junior doctors who had to enter data during their busy clinical schedules. Also, as the doctors changed firms every 4-6 months, new doctors had to be familiarised with the database, given passwords for access, all of which had a knock on effect on the continuity of data entry. Such heavy reliance on clinicians may not be feasible in the long run and could result in incomplete data entry which has been shown in a study comparing clinician-led database with HES for the purpose of revalidation of clinicians. [(4)] The other disadvantage of a purely clinician led database

is that it could be open to manipulation by the clinicians. A study in colorectal cancers demonstrated that hospitals with higher morbidity rates were less likely to voluntarily enter complete data. [106]

Morbidity rates for individual surgeons will soon be a requirement for all surgical specialties and will be accessible to the public.[86] This requirement is likely to encourage surgeons to ensure data on their individual operations is accurate and complete, but on the other hand, it could deter surgeons from entering all their complications into the database. It could also deter some surgeons from undertaking high risk surgery or surgery on patients with significant co-morbidities that could potentially impact on their complication rates. However this has not been the case with cardiac surgery which has a database that is very much clinician led and has published complications data for individual surgeons since 2004. [50]

The National Surgical Quality Improvement Programme (NSQIP) in the US continues to be so successful from its inception in 1994 to this day due to its robust organisational structure and dedicated staff. [48] The trained clinical nurse reviewers at every centre work closely with the chief of surgery at that centre to ensure accurate collection and timely transmission of data to the coordinating centre. There is also regular contact between the coordinating centre and the medical centres to address any issues with data collection and transmission. To have a similar organisation to collect data in gynaecological oncology in the UK would require funding and may not be feasible in an already cash strapped NHS. The success of UKGOSOC was down to the determination of all the participating clinicians arising from their desire to have robust morbidity data for future benchmarking purposes. However in order for it to be successful in a large scale in the long term, it would be essential not to rely so heavily on clinicians. Some of the data fields like comorbidity could be automatically populated

from HES. A study by Aylin et al found that the predictors for mortality derived from HES was comparable to that in clinician led databases. [111] Other data fields such as surgical procedures and intraoperative complications would still need to be entered by the surgeons. Instead of a long exhaustive list of complications, limiting the list to four or five key postoperative complications might help with completeness of data capture. It would also be essential to have a national body such as the National Cancer Intelligence Network (NCIN) or the British Gynaecological Cancer Society (BGCS) to coordinate, monitor, analyse and publish the outcomes data. The ultimate aim of such a national database would be to move the focus away from judgment towards improvement. Studies in other specialties have demonstrated that publishing outcomes data over a period of time actually helps in reducing morbidity and mortality rates. [49] In addition to being a national repository for outcomes data, such a database would also provide valuable information for future research.

9.1 Conclusion

This the first large multi-centre prospective study to investigate the morbidity associated with gynaecological oncology surgery. There are significant patient and surgical factors which influence the risk of developing a complication. Patient follow-up is vital to obtain a more realistic estimate of the postoperative complication rate. Although risk adjustment had a modest effect on the complication rate of individual centres, by accounting for the prevalence of potential risk factors for surgical complications we were able to estimate an adjusted institutional complication rate that ensured fairer comparison. The contributing risk factors for intraoperative and postoperative complications were different and in future studies it would be important to report on the intraoperative and postoperative complication rates separately. It is envisaged that the robust complications and risk-adjusted data generated from this

study will be utilised for future benchmarking of surgical practice in gynaecological oncology.

10 Appendices

Appendix 1 Consent Form

UKGOSOC

United Kingdom Gynaecological Oncology Surgical Outcomes and Complications (UKGOSOC)

Coordinating Centre Team
R Iyer/ Prof Usha Menon / Dr Alex Gentry-Maharaj / Mr Robert Liston
Gynaecological Cancer Research Centre, Maple House 1st Floor
149 Tottenham Court Road
London W1T 7DN; 020 7380 6925 (telephone)

A national audit to assess outcomes of major gynaecological surgery is being undertaken in 10 Gynaecological Oncology Centres in the NHS. The Trust where you are undergoing treatment is participating in this audit. The aim of the audit is to provide information that we can use to monitor the quality of surgery and improve the care we provide. To do this, the audit will collect information on the types of major gynaecological operations performed around the country, the severity and frequency of any complications and the effect of pre-existing medical problems on surgical outcomes.

What does this mean for you?

In the course of the audit, information regarding the details of your surgery, any complications during or after your operation and final diagnosis will be forwarded to a central database, for analysis and comparison with patients from around the United Kingdom. Sometimes problems arise after discharge and in order to ensure a complete record of events is collected, we will send you a post card about 6-8 weeks after your surgery. It will ask you for details of any problems you may have had following your discharge from hospital. We would be grateful if you would ensure you complete this post card when it arrives, and return it to the address marked on the card.

Your information will be held securely on a central NHS computer at Trent Cancer registry and **will remain strictly confidential**. In addition to your local team, the Gynaecological Cancer Research team at University College London who are conducting the audit will have access to the data. If you do not want information which can identify you to be made available to the audit team in London running the audit, please let your nurse/doctor know. We will then ensure that only data about your surgery, complications and diagnosis is sent to the national team with your identity concealed. Also do let the team know if you do not want any of your data to be included in this surgical audit. However, we hope that everyone will agree to all of the confidential information being sent to the national team, for this would make the audit more accurate and therefore more effective in improving the quality and standards of care for women in the future.

The results of the audit will be available in due course. If you would like to see these, please ask your clinician who will provide you a summary of the report. If you have any queries, you could contact:

UKGOSOC

Consent : Please tick appropriate option

☐ I am willing for information which can be used to identify me in relation to my operation and any complications that may arise to be collected and analysed in the UKGOSOC audit by the University College London gynaecological oncology research team. I understand that I will receive a postcard in 6-8 weeks asking about any complications that I may have experienced following my operation.

☐ I am willing to participate in the UKGOSOC audit of my operation and any complications that may arise BUT do not want any information that will identify me to be made known to the UKGOSOC audit team at University College London gynaecological oncology research team.

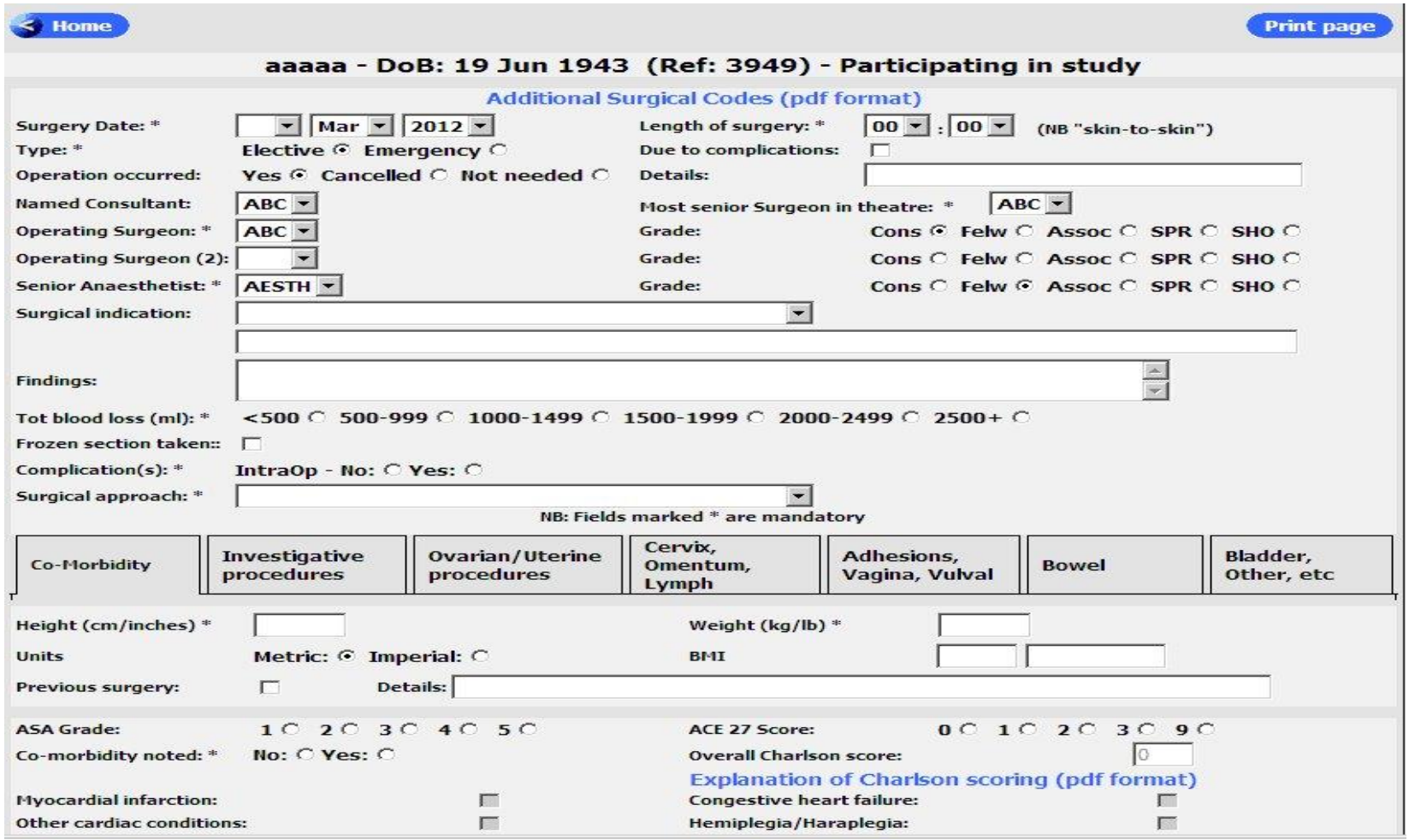
☐ I do not want any of my data included in the national audit (UKGOSOC) of gynaecological oncology operations and any complications that may arise.

SIGNED: **WITNESS:**

NAME: **NAME (WITNESS):** **DATE:**

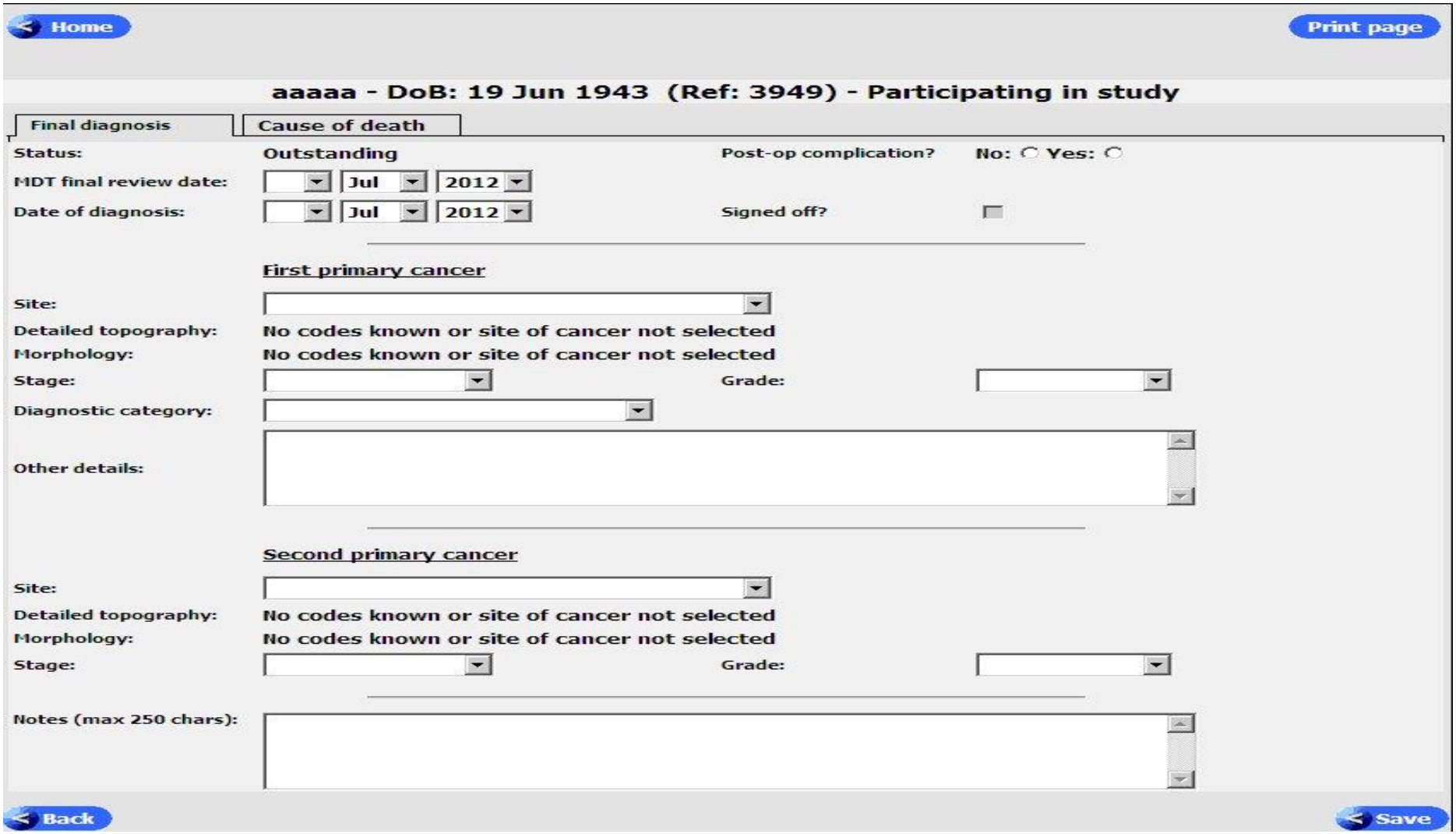
Appendix 2 Screen shot- Patient details

Appendix 3 Screen shot- Surgery details



Appendix 4 Screen shot- Intraoperative complications

Appendix 5 Screen shot- Diagnosis details



Appendix 6 Screen shot- Patient report

Home

Print page

aaaaa - DoB: 19 Jun 1943 (Ref: 3949) - Participating in study

Please print in landscape format for best results

Address:

FinalDiagnosis (Status: Outstanding)

MDM review date:		Post-op complications?	No	
First primary cancer:	Site:	Benign disease (specify)	Stage:	Grade:
	Topography:		Morphology:	
	Other details:	normal ovaries and tubes		
	Diagnostic cat:	Normal		
2nd primary site:	Site:		Stage:	Grade:
	Topography:		Morphology:	
Died within 30 days?	Unknown			

Date of admission:		Date of discharge:	Type: Elective
Reason:	Elective surgery		
Follow up:	(Outstanding)		
Follow-up card sent:		Received back:	

Surgery during this admission

Date: 01/03/2012 - Status: Completed - Named Consultant: ABC - Type: Elective

Length of surgery: 1 hr :0 min
Senior Surgeon: ABC
Operating Surgeon: ABC (Consultant) - Senior Anaesthetist: AESTH (Fellow)
Total blood loss: < 500 ml BMI: 17.5 (Underweigth (<18.5)) h:151cm w:40kg
Clinical indication: Risk reduction surgery
Procedure(s): (Q22.1) Bilateral salpingo-oophorectomy - Laparoscopic and vaginal
Co-morbidity: ASA grade 2 (Patient with mild systemic disease)
ACE 27 score 9 (Unknown)
No co-morbidity noted
No complications noted

Admissions

Appendix 7 Free text format Follow-up letter

UKGOSOC

United Kingdom Gynaecological Oncology Surgical Outcomes and Complications (UKGOSOC)

Private and Confidential

Ms «First_Name» «Last_Name»
«Address1»
«Address2»
«Town»
«County»

Date

Dear Ms «Last_Name»,

UKGOSOC Reference number: «UKGOSOC_Ref»

Thank you for participating in this audit.

You might recall your consultant (or one of the members of the team) mentioning that we would be writing to you following your surgery, to find out if you had any problems (complications) relating to your operation.

We would be grateful if you could fill in the tear-off slip at the bottom of this letter and return it to us in the FREE POST envelope provided. We look forward to hearing from you.

Yours sincerely,

(On behalf of the co-ordinating centre team)

If you have any queries, please contact your local hospital on the following phone numbers:

✂ -

Name: «Patient_Name» **UKGOSOC Ref No:**

Please tick as appropriate

□ No, I did not have a complication following my gynaecological surgery

□ Yes, I had a complication following my gynaecological surgery

If the answer is yes, please describe below the complication you had following your operation. Please use additional paper if you would like to.

If you are willing to be contacted for any clarification, please enter your telephone number below. ________________________

Appendix 8 Questionnaire format of follow-up letter

A surgical complication may be defined as *'an undesirable and unintended result of an operation affecting the patient that occurs as a direct result of the operation'*.			
• Below is a list of 11 common complications experienced by patients			
• Even though the list appears long, it should only take approximately five minutes of your time.			
• Please choose the complication/s that is most appropriate and indicate the treatment you required.			
• You may choose more than one option.			
• However if your complication is not on the list, please use the free text space provided. Please use additional paper if necessary			
1	**Did the wound get infected or did it break down?**	**Yes**	**No**
	If the answer is yes, how was it treated?		
	a. Antibiotics	Yes	No
	b. Regular dressing of the wound	Yes	No
	c. Required re-admission to hospital	Yes	No
	d. Cleaning (debridement) in the operating theatre	Yes	No
	e. Re-suturing in the operating theatre	Yes	No
	f. Other (please give details)	Yes	No
2	Excluding a wound infection, have you had **any other infection** following your surgery?	**Yes**	**No**
	a. Urine infection	Yes	No
	b. Chest Infection or Pneumonia	Yes	No
	c. Other (please give details)	Yes	No
	How was the infection treated?		
	a. With antibiotics	Yes	No
	b. Required re-admission to hospital	Yes	No
	c. Required other treatment (please give details)	Yes	No
3	Did you develop an **abscess or a haematoma (collection of blood)** in your pelvis or abdomen following surgery?	**Yes**	**No**

	If so how was this managed?		
	a. Resolved spontaneously	Yes	No
	b. Treated with antibiotics	Yes	No
	c. Required drainage in the x-ray / radiology department	Yes	No
	d. Required drainage in the operating theatre	Yes	No
	e. Other (please give details)	Yes	No
4	Light vaginal bleeding is common after most gynaecological procedures. Have you had **heavy vaginal bleeding** following surgery?	**Yes**	**No**
	If so, how was this managed?	Yes	No
	a. It settled spontaneously	Yes	No
	b. It was treated with antibiotics	Yes	No
	c. It required re-admission to hospital	Yes	No
	d. It required packing of the vagina	Yes	No
	e. It required being taken back to the operating theatre	Yes	No
	f. Other (please give details)		
5	**Lymphoedema** is a build-up of lymph fluid which can occur as a result of lymph nodes being removed at surgery. It is commonly seen in the legs. Have you had lymphoedema following surgery?	Yes	No
	If so, how was this managed?		
	a. With compression stockings	Yes	No
	b. Other (please give details)	Yes	No
7	Have you been troubled with **constipation** after surgery? (*please do not fill this if you had this problem before surgery*) If so how was this managed?	Yes	No
	a. Diet	Yes	No

	b. Laxatives	Yes	No
	c. Required re-admission to hospital for treatment	Yes	No
	d. Other (please give details)	Yes	No
8	Have you had any other **problems related to your bowels**? *(please do not fill this if you had this problem before surgery*) If so, please give details	Yes	No
9	Have you had any problems with your **bladder** since the surgery *(please do not fill this if you had this problem before surgery)*	Yes	No
	a. Difficulty in emptying the bladder	Yes	No
	b. Loss of sensation to empty bladder	Yes	No
	c. Leaking with coughing / sneezing / walking etc. (Stress incontinence)	Yes	No
	d. An urgent need to pass urine with occasional leakage of urine (urge incontinence)	Yes	No
	e. Inability to pass urine requiring insertion of a catheter (urinary retention)	Yes	No
	f. Required re-admission to hospital for treatment	Yes	No
	g. Other (please give details)	Yes	No
10	Did you develop a blood clot in your legs **(deep vein thrombosis)** after surgery? If so, what sort of treatment did you receive?	Yes	No
	a. Daily injections for blood thinning (heparin)	Yes	No
	b. Blood thinning tablets (Warfarin)	Yes	No
	c. Required re-admission to the hospital for treatment	Yes	No
	d. Other (please give details)	Yes	No
11	Did you develop a clot in the lung (**pulmonary embolism**) following surgery? If so, how was this treated?	Yes	No
	a. Daily injections for blood thinning (heparin)	Yes	No
	b. Blood thinning tablets (Warfarin)	Yes	No
	c. Required re-admission to hospital	Yes	No
	d. Other (please give details)	Yes	No

12	If you have had **any other complication** not listed here, please give details below regarding the nature of the complication, how this was treated and whether you required re-admission into hospital for this. Please use additional paper if necessary.	Yes	No

We would be grateful if you could provide a little more information about yourself.

1. What is the main language spoken in your home?

☐ English

☐ Other, please specify……

2. Is this questionnaire in a language that you can easily understand?

☐ Yes

☐ No

☐ No, I don't understand the language but I had help from a friend or family member to fill in this questionnaire

3. What is the highest level of education you have achieved?

☐ Finished school at or before the age of fifteen

☐ Completed GCSEs, O-levels or equivalent

☐ Completed A levels or equivalent

☐ Completed further education but not a degree

☐ Completed a Bachelor's degree / master's degree / PhD

☐ Other, please specify……..

4. If you are willing to be contacted for any clarification, please enter your telephone number below.

……

……

5. If you have any suggestions on how we could improve this questionnaire, please write your comments overleaf.

Appendix 9 Intraoperative risk prediction calculator

Variables	Odds Ratio	Beta Coefficient	INPUT VALUE (1 for categorical indicator)	
Age at surgery	1.000	0.000225974	50	0.011299
BMI	*removed*	0	20	0
Previous abdominal surgery	1.426	0.354740775		0
Low albumin	3.916	1.365177205		0
Coagulation-thrombosis	1.052	0.050917424		0
Diabetes	1.804	0.590046332		0
Cardiac	1.462	0.380077554		0
Respiratory	0.676	-0.3910953		0
Gastrointestinal	1.065	0.062959776		0
Genitourinary	0.699	-0.357729071		0
Musculoskeletal	*removed*	0		0
Neurology-psychiatric	*removed*	0		0
Vascular	0.849	-0.163887984		0
Auto-immune	1.968	0.677039648		0
Metabolic-endocrine	0.412	-0.886688484		0
Integumentary-dermatology	*removed*	0		0
Hypertension	1.239	0.214281196		0
Smoking	0.978	-0.022255732		0
Other neoplasms	1.506	0.409210751		0
Laparoscopic approach	1.021	0.021004846		0
ASA Grade				
ASA grade 1	1	0		0
ASA grade 2	1.103	0.098371852		0
ASA grade 3+	1.039	0.038729246		0
Surgeon grade				

Consultant	1	0		0	
Sub-specialty trainee	0.716	-0.334224145		0	
General Obstetrics & Gynaecology Trainee	1.286	0.251685137		0	
Surgical complexity					
Complexity score 1&2	1	0		0	
Complexity score 3&4	1.097	0.092363114		0	
Complexity score 5&6	1.905	0.644478334		0	
Complexity score 7&8	2.666	0.980736749		0	
Complexity score >8	4.005	1.387667168		0	
Final diagnosis					
Ovarian	1	0		0	
Uterine	0.600	-0.510855458		0	
Cervical	0.834	-0.181421282		0	
Vulval	0.289	-1.24149331		0	
Benign	0.567	-0.567497568		0	
constant	0.033	-3.420303751		-3.4203	"=Linear prediction"
				-3.40901	**"=Predicted Risk"**
				0.032015	

Appendix 10 Postoperative risk prediction calculator

Variables				
Age at surgery	**Odds Ratio**	**Beta Coefficient**	**INPUT VALUE (1 for categorical indicator)**	
BMI	0.997	-0.003276361	50	-0.16382
Previous abdominal surgery	1.012	0.011984893	20	0.239698
Coagulation-thrombosis	1.008	0.007733023		0
Diabetes	1.510	0.412101042		0
Cardiac	1.355	0.303676723		0
Respiratory	*removed*	0		0
Gastrointestinal	*removed*	0		0
Genitourinary	0.916	-0.087944503		0
Musculoskeletal	*removed*	0		0
Neurology-psychiatric	1.254	0.22645885		0
Vascular	0.908	-0.096767982		0
Auto-immune	0.926	-0.077126539		0
Metabolic-endocrine	*removed*	0		0
Integumentary-dermatology	*removed*	0		0
Hypertension	*removed*	0		0
Smoking	*removed*	0		0
Other neoplasms	*removed*	0		0
Laparoscopic approach	*removed*	0		0
ASA Grade	0.739	-0.302105458		0
ASA grade 1				
ASA grade 2	1	0		0
ASA grade 3+	*removed*	0		0
Surgeon grade	*removed*	0		0
Consultant				0

Sub-specialty trainee	1	0		0
General Obstetrics & Gynaecology Trainee	*removed*	0		0
Surgical complexity	*removed*	0		0
Complexity score 1&2				
Complexity score 3&4	1	0		0
Complexity score 5&6	1.112	0.106170088		0
Complexity score 7&8	*removed*	0		0
Complexity score >8	1.056	0.054954932		0
Final diagnosis	1.004	0.00368819		0
Ovarian				
Uterine	1	0		0
Cervical	0.982	-0.017798661		0
Vulval	1.606	0.473605883		0
Benign	1.779	0.5763077		0
Duration of surgery (hrs)	*removed*	0		0
Estimated blood loss	1.086	0.082342284		0
<500ml				
500ml-1000ml	1	0		0
1000ml-2500ml	1.267	0.236948621		0
>2500ml	1.052	0.050509637		0
constant	0.997	-0.003410308		0
	0.167	-1.788685997		-1.78869
				-1.71281

"=Linear prediction"

"=Predicted Risk"

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