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Implementation of A Perioperative Respiratory Care Bundle to Improve Respiratory Outcomes Following Major Abdominal Surgery

By

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Abstract

Postoperative pulmonary complications (PPCs) commonly occur following major abdominal surgery. There are different approaches to manage and minimise PPCs, one of which is respiratory physiotherapy. Enhanced Recovery After Surgery (ERAS) approach is currently considered within perioperative practice to enhance recovery and decrease postoperative complications in general. However, there a few interventions targeting PPCs in particular within ERAS. Therefore, the aim of this thesis is to assess if implementation a perioperative respiratory care bundle improves postoperative respiratory outcomes following major abdominal surgery.

Three studies were conducted in this thesis. First study aimed to find best respiratory care interventions that would be included within the bundle by a systematic review and meta-analysis. Second study investigated the need for improvement in perioperative practice by an observational study. Third study assessed the success of the implemented bundle by a quality improvement study.

The incidence of PPCs was extremely high in local hospital and was associated with increased morbidities and length of stay. The proposed perioperative respiratory care bundle to be implemented, being called I-COUGH Plus, includes Incentive Spirometry (IS) plus Inspiratory Muscle Trainer (IMT), coughing and deep breathing, oral hygiene, understanding, get out of bed, head of bed elevated. The I-COUGH Plus was proposed aiming to improve respiratory muscle strength and patient outcomes postoperatively. Preliminary results showed that I-COUGH Plus has no effect on improving respiratory muscles and decreasing PPCs. However,

I-COUGH Plus is still considered within perioperative practice hoping to show its effectiveness after recruiting sufficient number of patients.

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Declaration

This thesis is submitted to the University of Birmingham to support my application for the degree of Doctor of Philosophy. I certify it has been entirely composed by myself and contains no material, which, has been accepted for the award of any other degree, or diploma in my name, in any University or other tertiary institution. In chapter 3, an observational study conducted was within the context of the Perioperative Quality Improvement Programme (PQIP) which is a national programme where most of NHS hospitals should share collected data with the PQIP. To the best of my knowledge and belief the thesis contains no material previously published or written by another person, except where the due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for another degree or diploma.

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List of abbreviations

ARDS	Acute Respiratory Distress Syndrome
ASA	American Society of Anesthesiologists
CABG	Coronary Artery Bypass Graft
CCP	Conventional Chest Physiotherapy
CDC	Centres for Disease Control
CG	Control Group
CI	Confidence Interval
CM	Centimetre
cmH2O	Centimetre of Water
COPD	Chronic Obstructive Pulmonary Disease
CPAP	Continuous Positive Airway Pressure
CPT	Chest Physiotherapy
CXR	Chest X-Ray
DB	Deep Breathing
DB&C	Deep Breathing and Coughing
ESA-ESIC	European Society of Anaesthesiology and the European Society of Intensive Care Medicine
F	Female
FEV1	Forced Expiratory Volume in one second
FiO2	Fraction of Inspired Oxygen
FIS	Flow Incentive Spirometry
FVC	Forced Vital Capacity
g/dl	Gram/deciliter
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
HPB	Hepato-pancreatic-biliary
ICU	Intensive Care Unit
IMT	Inspiratory Muscle Training
IQR	Interquartile range
IS	Incentive Spirometry
IV	Intravenous
KG	Kilogram
kPa	Kilopascal
LOS	Length of Stay
M	Male
MEP	Maximum Expiratory Pressure
MeSH	Medical Subject Heading
MGS	Melbourne Group Scale
MIP	Maximum Inspiratory Pressure
ml	Millilitre
mmHg	Millimeters of Mercury
MVV	Maximum Voluntary Ventilation
N	Number of patients
Non-DB&C	Non-Deep Breathing and Coughing
NYHA	New York Heart Association
PACU	Post-Anaesthesia Care Unite

PaO_2	Partial pressure of oxygen
PEEP	Positive End Expiratory Pressure
PEF	Peak Expiratory Flow
PFT	Pulmonary Function Test
PICO	Participant/ Intervention/ Comparator/ Outcome
POMS	Postoperative Morbidity Survey
PPCs	Postoperative Pulmonary Complications
PQIP	Perioperative Quality Improvement Programme
RCT	Randomised Controlled Trials
RMS	Respiratory Muscle Strength
RR	Risk Ratio
SaO_2	Oxygen saturation
SD	standard Deviation
SNIP	Sniff Nasal Inspiratory Pressure
SpO_2	Peripheral capillary Oxygen Saturation
SVC	Slow Vital Capacity
TEDS	Transcutaneous Electrical Diaphragmatic Stimulation
VAPS	Visual Analog Pain Scale
VC	Vital Capacity
VIS	Volume Incentive Spirometry

Chapter One

Introduction

1.1 Definition of postoperative pulmonary complications

Postoperative Pulmonary Complications (PPCs) is a term used to refer to respiratory adverse events which occur after surgery. PPCs are defined either by a single adverse event definition for each complication or a composite outcome measure definition for the category of complication (1). Composite outcome definitions for PPCs include a variety of respiratory complications and encompass respiratory infections, respiratory failure, pneumothorax, bronchospasm, pleural effusion, atelectasis and aspiration pneumonitis (1). These forms of complications have been defined by the American Society of Anesthesiologists (ASA) and are presented in Table 1.1 (2). According to Jammer, et al. (1), the composite definition of PPCs provides more benefits than definition of a single adverse event, mainly increasing the event rate, which may ensure adequate statistical power. Also, composite definitions vary in structure and provide categorical and continuous variables and provide more information about frequency and severity of the complications.

Table 1. 1 American Society of Anesthesiologists definition of PPCs (2)

Complication	Definition
Respiratory Infection	Patient received antibiotics for a suspected respiratory infection and meets one or more of the following conditions: new/changed sputum, new/changed lung opacification, fever, white blood cell count >12x10^9/l
Respiratory failure	Postoperative PaO_2<8kPa on room air or a PaO_2/FiO_2 <40kPa or a SpO_2 <90% and requiring oxygen therapy
Pleural effusion	Chest radiograph demonstrates blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in an upright position, evidence of the displacement of adjacent anatomical structures or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm toward the affected area, and compensatory over-inflation in the adjacent non-atelectatic lung
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura
Bronchospasm	Newly detected expiratory wheezing that is treated by bronchodilators
Aspiration Pneumonia	Acute lung injury after the inhalation of regurgitated gastric contents

FiO2: Fraction of Inspired Oxygen, kPa: kilopascal, PaO_2: Partial pressure of oxygen, PPCs: Postoperative Pulmonary Complications, SpO_2: Peripheral capillary Oxygen Saturation.

Postoperative Morbidity Survey (POMS) is a binary measure of the presence of postoperative complications that are severe enough to require continued hospital admission following major surgery (3). POMS include nine postoperative complications, one of which is PPCs (Table 1.2). POMS defines PPCs as the need for new requirements for patients to receive supplemental oxygen therapy and/or advanced respiratory support, such as invasive and non-invasive mechanical ventilation (4). POMS is a validated outcome measure and showed high inter-rater reliability for fifty one patients who underwent major abdominal surgery (4). A study of validity and reliability on 439 adult patients found POMS is a reliable and valid tool to measure postoperative morbidities following major elective surgery (5). However, the results of Grocott, et al. (5) could not be generalised to vascular, cardiac and paediatrics surgeries as these certain surgeries were excluded.

Table 1. 2 Postoperative Morbidity Survey (POMS) definition (3)

Morbidity	**Definition**
Pulmonary	Patient has developed a new requirement for oxygen and/or respiratory support
Infection	Patient is currently on IV antibiotics and/or had temperature over 38˚C in the past 24 hours
Gastrointestinal	Patient is unable to tolerate enteral diet (oral or tube feeding) and/or experienced nausea, vomiting or abdominal distention in the past 24 hours
Renal	Patient had any of the following in the past 24 hours: Oliguria (urine output less than 50ml), serum creatinine level increased by 30% preoperative level and urethral catheter in-situ not present preoperatively
Cardiovascular	Patient had diagnostic test or therapy for any of the following in the past 24 hours: Hypotension requiring more than 200ml fluid bolus or pharmacological therapy, new myocardial infarction or ischaemia, thrombotic event requiring anticoagulation, arrhythmias and cardiogenic pulmonary oedema
Neurological	Patient developed any of the following in the past 24 hours: new neurological deficit, delirium or confusion, sedative-induced coma and non-sedative associated coma
Wound	Patient had wound dehiscence requiring surgical exploration and/or had drainage of pus from the operative wound, wound ooze or a swab taken
Haematology	Patient required red cell transfusion, fresh frozen plasma, cryoprecipitate or platelets in the past 24 hours
Pain	Patient developed significant pain that required parenteral opioids and/or regional anaesthetics

The definitions of postoperative morbidities are based on patient's status on day 7 postoperatively.
IV: intravenous, ml: millilitre.

The Melbourne Group Scale (MGS) is another composite outcome measure to define PPCs. MGS screens patients daily for 7-days postoperatively to try and identify those that have developed PPCs. The MGS presumes that patients have not developed PPCs if is discharged before the seventh postoperative day (6). The MGS is a valid and reliable tool to screen PPCs following thoracic and abdominal surgeries (7). The MGS clinically defines PPCs by the presence of four or more of the clinical conditions presented in Table 1.3 (6).

Table 1. 3 Melbourne Group Scale (MGS) definition of PPCs (6)

Clinical condition
- Chest radiograph report of consolidation/collapse - Raised temperature >38°C on two or more consecutive days - SpO_2 <90% on room air on two consecutive days - Production of yellow or green sputum which is different to pre-operative assessment - An otherwise unexplained white cell count >11×10^9/L or prescription of an antibiotic specific for respiratory infection - Physician diagnosis of chest infection - Presence of infection on sputum culture report - Abnormal breath sounds on auscultation which differ from pre-operative assessment

Furthermore, another composite definition of PPCs was developed by the European Society of Anaesthesiology and the European Society of Intensive Care Medicine (ESA/ESICM), being called the European Perioperative Clinical Outcome (EPCO) definition (1). The EPCO definition of PPCs is presented below in Table 1.4. The statement of ESA/ESICM also highlighted definitions of PPCs as a single organ outcome measure, including Acute Respiratory Distress Syndrome (ARDS), pneumonia and pulmonary embolism. ARDS is defined according to the Berlin Definition of ARDS as in Table 1.5 (8). Pneumonia is clinically defined according to the Centres for Disease Control (CDC) definition as in Table 1.6 below , while pulmonary embolism is defined as “a new blood clot or thrombus within the pulmonary arterial system” (1).

Table 1. 4 European Perioperative Clinical Outcome (EPCO) definition of PPCs (1)

Complication	Definition
Respiratory infection	Patient has received antibiotics for a suspected respiratory infection and met one or more of the following criteria: new or changed sputum, new or changed lung opacities, fever, white blood cell count > $12X10^{9}$ l^{-1}
Respiratory failure	Postoperative PaO_2<8 kPa (60 mmHg) on room air, a PaO_2:FiO_2 ratio <40 kPa (300 mmHg) or arterial oxyhaemoglobin saturation measured with pulse oximetry < 90% and requiring oxygen therapy
Pleural effusion	Chest radiograph demonstrating blunting of the costophrenic angle, loss of sharp silhouette of the ipsilateral hemidiaphragm in upright position, evidence of displacement of adjacent anatomical structures or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows
Atelectasis	Lung opacification with a shift of the mediastinum, hilum or hemidiaphragm towards the affected area, and compensatory over-inflation in the adjacent non-atelectatic lung
Pneumothorax	Air in the pleural space with no vascular bed surrounding the visceral pleura
Bronchospasm	Newly detected expiratory wheezing treated with bronchodilators
Aspiration pneumonitis	Acute lung injury after the inhalation of regurgitated gastric contents

FiO_2: Fraction of Inspired Oxygen, kPa: kilopascal, mmHg: Millimetres of Mercury, PaO_2: Partial pressure of oxygen

Table 1. 5 Berlin Definition of ARDS (8)

Criteria	**Definition**
Timing	Within one week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging	Bilateral opacities – not fully explained by effusions, lobar/lung collapse or nodules
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload; requires objective assessment (e.g., echocardiography) to exclude hydrostatic oedema if no risk factor is present
Oxygenation	
• **Mild**	PaO_2/FiO_2 between 26.7 and 40.0 kPa (200-300 mmHg) with PEEP or CPAP ≥ 5 cmH_2O
• **Moderate**	PaO_2/FiO_2 between 13.3 and 26.6 kPa (100-200 mmHg) with PEEP ≥ 5 cmH_2O
• **Severe**	PaO_2/FiO_2 ≤ 13.3 kPa (100 mmHg) with PEEP ≥ 5 cmH_2O

ARDS: Acute Respiratory Distress Syndrome, cmH_2O: Centimetre of Water, CPAP: Continuous Positive Airway Pressure, FiO_2: Fraction of Inspired Oxygen, kPa: kilopascal, mmHg: Millimetres of Mercury, PaO_2: Partial pressure of oxygen, PEEP: Positive End Expiratory Pressure.

Table 1. 6 Centres for Disease Control (CDC) definition of Pneumonia (9)

Criteria	**Definition**
Radiology	Two or more serial chest radiographs with at least one of the following (one radiograph is sufficient for patients with no underlying pulmonary or cardiac disease): new or progressive and persistent infiltrates, consolidation and cavitation
Sign and symptoms	At least one of the following conditions: - Fever (>38**°**C) with no other recognised cause - Leukopenia (white cell count $<4\times10^9$/L) or leucocytosis (white cell count $>12\times10^9$/L) - For adults >70 years of age, altered mental status with no other recognised cause In addition to at least two of the following conditions: - New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements - New onset or worsening cough, or dyspnoea, or tachypnoea - Rales or bronchial breath sounds - Worsening gas exchange (hypoxaemia, increased oxygen requirement, increased ventilator demand)

CDC: Centres for Disease Control, L: Litre

The Standardised Endpoints for Perioperative Medicine and Core Outcome Measures in Perioperative and Anaesthetic Care (StEP-COMPAC) group developed a composite definition for PPCs based on pathophysiological mechanisms and severity (Table 1.7) (9). StEP-COMPAC included only atelectasis and pulmonary infection, whereas pulmonary embolism, pleural effusion, cardiogenic pulmonary oedema, pneumothorax and bronchospasm were excluded from the composite definition due to their different biological mechanisms. In addition, StEP-COMPAC used the CDC definition for pneumonia and the Berlin consensus definition for ARDS (Table 1.5 and 1.6). PPCs severity definition was based on the need for supplemental oxygen and mechanical ventilation.

Table 1. 7 StEP-COMPAC definition of PPCs (10)

Criteria	**Definition**
Mechanism	- Atelectasis detected on computed tomography or chest radiograph - Pneumonia using US CDC criteria - ARDS using Berlin consensus definition - Pulmonary aspiration (clear clinical history AND radiological evidence)
Severity	- None: planned use of supplemental oxygen or mechanical respiratory support as part of routine care - Mild: therapeutic supplemental oxygen <0.6 FiO_2 - Moderate: therapeutic supplemental oxygen =>0.6 FiO_2 - Severe: unplanned non-invasive mechanical ventilation, CPAP, or invasive mechanical ventilation requiring tracheal intubation

ARDS: Acute Respiratory Distress Syndrome, CDC: Centers for Disease Control, CPAP: Continuous Positive Airway Pressure, FiO_2: Fraction of Inspired Oxygen

In summary, there are many definitions of PPCs which are either single adverse event definition or definition of composite outcome measures. Composite outcome measures considered as more comprehensive tool that increases frequency and severity rate which therefore, increases the statistical power such as POMS definition. POMS is valid and reliable tool to measure absence or presence of postoperative morbidity including PPCs (4). POMS is also easy to use as an outcome measure in both research and clinical practice without requirement of training.

Despite the large number of definitions, there is no consensus yet between definitions discussed above which vary in frequency, severity and biological mechanism of an adverse event included in the definitions (9). Therefore, clinical trials would use a specific definition that would be applicable to a particular research question as all definitions are not applicable to every circumstances. In addition, some definitions are considered difficult to apply due to requirement of intensive diagnostic test, such as bronchoscopy (9). In general, definitions of composite outcome measures would be more appropriate definition to use owing to the advantages discussed earlier.

1.2 Incidence of postoperative pulmonary complications

Major surgeries are performed frequently worldwide, accounting for more than 200 million operations annually (10). The vast majority of procedures are performed safely with a low risk of postoperative complications. However, some patients are at a high-risk of developing these; roughly 10% of patients undergoing surgery in the United Kingdom account for 80% of postoperative mortality (11).

PPCs are common postoperative complications and are associated with an increased rate of mortality and morbidity, and increased length in hospital stay (12). Jensen and Yang (13) retrospectively screened 315 patients who underwent Coronary Artery Bypass Graft (CABG) for PPCs and demonstrated that almost all patients (99.4%) developed PPCs. This result could be overestimated as PPCs were not clearly defined and they were only identified based on previous clinical diagnosis labelled on progress note and laboratory and imaging reports. In contrast, Naveed, et al. (14) documented that incidence of PPCs was 6.2% after cardiac surgery using a prospective cohort design. However, their definition of PPCs was strictly limited to respiratory failure and the presence of pneumonia. Respiratory failure was defined as the need for mechanical ventilation for more than 48 hours or the need for re-intubation, and pneumonia was identified based on laboratory and imaging reports along with presence of fever and sputum. As a result, PPCs represent only respiratory failure and pneumonia. In both studies, the results would not be reliable due to the unclear or invalid definitions of PPCs used.

PPCs are also extremely common in neurosurgery, as documented by Sogame, et al. (15) and Damian, et al. (16). Sogame, et al. (15) prospectively investigated the incidence of PPCs in 236 patients who underwent elective intracranial surgery. Incidence of PPCs was 24.6% based on clinical signs and symptoms of the following PPCs: pneumonia, tracheobronchitis, atelectasis and bronchoconstriction. Damian, et al. (16) also found that PPCs incidence was 32.7% following head and neck surgery and retrospectively identified PCCs based on critical care and radiographic reports and discharge summaries.

Thoracic surgery also showed considerable association with developing PPCs, in particular pneumonia and atelectasis (17). Agostini, et al. (17) found that incidence of PCCs was 14.5% following thoracic surgery using MGS definition to identify PPCs. Similarly, Lugg, et al. (18), using MGS definition, documented that PPCs incidence was 13% with prolonged hospital stay and poor patient outcomes following thoracic surgery. Both studies documented quite similar PPCs incidence as they both used MGS definition, which is a valid and reliable PPCs definition. Similar incidence of PPCs might also be explained by the use of similar patients' characteristics and research design, a prospective observational study, as well as similar surgery type which is thoracic surgery. In addition, similar incidence of PPCs was also due to the use of similar perioperative practice as both studies were conducted in the same hospital.

A summary of the above discussed studies about PPCs incidence with the used definition of PPCs on different surgical patients is presented below in Table 1.8.

Table 1. 8 Summary of the incidence of PPCs following different surgeries

Study	Study design	Population	Sample size	Definition of PPCs	PPCs incidence
Agostini, et al. (17)	Prospective observational study	Thoracic surgery	- N= 234 - Over one year	Melbourne Group Scale	14.5%
Lugg, et al. (18)	prospective observational study	Lung surgery	- N= 670 - Over four years	Melbourne Group Scale	13%
Jensen and Yang (13)	Retrospective cohort study	CABG	- N= 315 - From January to April 2002	Identifying PPCs based on clinical diagnosis reported on progress notes, diagnostic imaging reports and laboratory reports.	99.4%
Damian, et al. (16)	Retrospective cohort study	Head and neck cancer surgery	- N= 110 - From January 2005 to December 2011.	PPCs definition was according to clinical diagnosis reported on critical care reports, radiographic reports and the discharge summary to identify pulmonary oedema, pneumonia, pneumothorax, pulmonary embolism, and ARDS only.	32.7%
Naveed, et al. (14)	Prospective observational study	Cardiac surgery	- N= 517 - From January 2015 to August 2016	Respiratory failure and pneumonia only considered as PPCs. Respiratory failure was defined as the need for mechanical ventilation more than 48 hours or need for re-intubation. Pneumonia was identified based on chest X-rays and laboratory reports alongside the presence of fever and sputum.	6.2%
Sogame, et al. (15)	Prospective cohort study	Elective intracranial surgery	- N= 236 - Over 24 months	Pneumonia, tracheobronchitis, atelectasis and bronchoconstriction are only considered as PPCs and they were clinically defined as follows: Pneumonia was classified as recent pulmonary infiltration on chest radiography associated with at least two of the following signs: purulent tracheobronchial secretion, a body temperature >	24.6%

				38.3°C, and leukocytes in circulation > 25% above the basal count. Tracheobronchitis was an increase in the volume or a change in the colour or purulent aspect of tracheobronchial secretion with a normal chest radiograph. Atelectasis was evidence on chest radiography of pulmonary atelectasis associated with acute respiratory symptoms. Bronchoconstriction was classified as the presence of wheezing associated with acute respiratory symptoms with a good response to inhalatory bronchodilator medication.	

CABG: Coronary Artery Bypass Graft, N: Number of patients, PPCs: Postoperative Pulmonary Complications

1.2.1 Incidence of postoperative pulmonary complications after major abdominal surgery

PPCs are also common following abdominal surgery, their incidence ranging from 4.7% to 22.5% (Table 1.9) (12, 19-22). Brooks-Brunn (21) prospectively screened 400 patients following abdominal surgery for PPCs defined only to atelectasis and pneumonia and found PPCs incidence was about 22.5% with prolonged length of stay (mean 9.4±5.6 days). In a prospective multicentre study, Canet, et al. (19) showed that PPCs incidence was 7.2% following abdominal surgery when using the ASA definition (Table 1.1). In a retrospective cohort study, incidence of PPCs was 4.7% following gastrectomy for gastric cancer patients (22). In this study, PPCs was reported if patient developed any of the following PPCs forms within the first month after surgery: pneumonia, atelectasis, pneumothorax, prolonged mechanical ventilation (more than 24 hours), pleural effusion or ARDS.

Patel, et al. (12) used the EPCO definition of PPCs (Table 1.4) to prospectively evaluate PPCs and suggested that incidence of PPCs following major abdominal surgery to be roughly 11%. In a large retrospective cohort, the incidence of PPCs was 5.8% for 165,196 patients who underwent major abdominal surgery (20). PPCs was clinically defined as presence of pneumonia, pulmonary embolism and infection, according to the American College of Surgeons' National Surgical Quality Improvement Programme (23).

This variation in incidence of PPCs in the above discussed studies could be due to the use of different PPCs definitions and research designs, as retrospective cohorts showed lower incidence of PPCs compared to prospective cohorts. Robust data collection method is an important factor for accurate detection of PPCs as in case of prospective cohort design.

Conversely, event rate tends to be lower in retrospective design due to poor documentation which would result in missing key measures. The incidence of PPCs following abdominal surgery still needs further investigation in terms of identifying the perioperative risk factors, which may contribute to a reduction in PPCs incidence and an improvement in the current perioperative practice (12).

Table 1. 9 Summary of the incidence of PPCs following abdominal surgery

Study	Study design	Population	Sample size	Definition of PPCs	PPCs incidence
Brooks-Brunn (21)	Prospective cohort study	Abdominal surgery	N= 400 January 1993 to August 1995	Clinical definition for pneumonia and atelectasis. Two criteria of the following are required to be present for longer than 48 hours during the first postoperative week: new productive cough, abnormal breath sounds, high body temperature (>38°C) and documentation of atelectasis or pneumonia based on radiographic reports and/or physician diagnosis.	22.5%
Inokuchi, et al. (22)	Retrospective cohort study	Gastrectomy for Gastric Cancer	N= 1053 Between 1999 and 2011	Clinical diagnosis of the development of one of the following PPCs within 30 days after surgery: pneumonia, atelectasis, pneumothorax, the need for mechanical ventilation longer than 24 hours, mass pleural effusion requiring puncture, or ARDS.	4.7%
Patel, et al. (12)	Prospective cohort study	Major abdominal surgery	N= 268 Over two weeks in December 2014	EPCO definition for PPCs (Table 1.3) (1).	11%
Yang, et al. (20)	Retrospective database review	Major abdominal surgery	N= 165,196 From2005 to 2012	PPCs definition by Association for Academic Surgery-National Surgical Quality Improvement Programme (23).	5.8%
Canet, et al. (24)	Prospective cohort study	Abdominal surgery	N= 726 Over one year	Definition according to the American Society of Anesthesiologists.	7.2%

ARDS: N: Number of patients, EPCO: European Perioperative Clinical Outcome, PPCs: Postoperative Pulmonary Complications

1.3 Impact of postoperative pulmonary complications

In patients who develop PPCs, mortality increases in both the short and long term. In patients who develop PPCs, 30-day mortality rate might reach 30% following major surgery, compared to less than 3% of those who do not have a PPCs (25-30). Ninety-day mortality is significantly increased in patients with PPCs, up to 24.4% (19). By examining two large databases in an observational study, the long-term mortality rate was significantly higher in patients with PPCs compared to those without PPCs (45.9% vs 8.7% at one year and 71.4% vs 41.1% at five years postoperatively) (30).

PPCs also significantly increases morbidity and length of hospital stay, which is extended by 13–17 days (28, 31, 32). For instance, unplanned re-intubation due to postoperative respiratory failure, which could happen within three days of surgery, is linked to considerable increases in LOS and morbidity (26, 32). Consequently, PPCs have a general impact at patient's level such as reduced function and quality of life.

In addition, the development of PPCs will also increase the cost of healthcare, mainly because of an increase in LOS (33). For instance, the cost increased in a Canadian tertiary hospital due to respiratory failure and pneumonia by 41 and 47%, respectively (34). More recently, an evaluation of extra costs which can be attributed to PPCs discovered incremental costs of over $25,000 per admission following gastro-intestinal surgery (35). Therefore, decreasing the incidence of PPCs would be a significant possible source of cost-saving.

1.4 Pathophysiology of postoperative pulmonary complications

The effect of general anaesthesia on respiratory system starts when patient loses consciousness as general anaesthesia causes depression in central respiratory drive which causes apnoea (36). General anaesthesia significantly affects the response to hypoxia and hypercapnia even when a low dose of an anaesthetic drug is administered especially when airway management is challenging, as in the case of airway obstruction. (37).

The function of the respiratory muscles is affected by general anaesthesia as soon as induction starts. Changes in respiratory muscle function cause airway obstruction, change in position and shape of the diaphragm in dependent areas and a reduction in the cross-sectional area of the chest wall. These changes in respiratory muscle function lead to functional residual capacity (FRC) being reduced by 15–20% in comparison to the awake subject (36). Reduction in FRC, together with distribution of normal ventilation during positive pressure ventilation, which causes reduction in cardiac output, results in ventilation perfusion (V/Q) mismatch (36).

One of the greatest effects of a reduction in lung volume regarding PPCs is developing atelectasis (36). This was found to occur in more than 60% of patients who received general anaesthesia with neuromuscular blocking drug, which can easily be seen on computerised tomography (CT) scans in the dependent lung areas, regardless of the patient's position (38). Physiological elements which contribute to development of atelectasis include direct

compression of lung tissues by displacement of the diaphragm, airway closure when FRC is reduced to less than the closing volume, and rapid gas absorption from alveoli in lung regions when the airways are closed or narrowed. In addition, these elements are worsened when high fractional inspired oxygen (FiO_2), especially at FiO_2 of 100%, is used due to denitrogenation when high FiO_2 replaces nitrogen with oxygen (36). For instance, preoxygenation with an FIO_2 of 100%, 80% and 60% results in 5.6%, 1.3%, and 0.2% atelectasis, respectively, a few minutes after induction (39).

Hypoxia commonly occurs in recovery room immediately after surgery, which is considered as PPCs (40). There are a number of factors which contribute to desaturation following surgery, the most common being airway obstruction (36). Residual anaesthetic and opioid drugs which impact on the central respiratory drive cause respiratory failure as do the residual effects of neuromuscular blocking drugs (41).

The impact of general anaesthesia on oxygenation and FRC is usually resolved within a few hours following minor surgeries; however, this is not the case for major surgery. In a randomised controlled trial, CT scans were taken 20 minutes after extubation from 30 patients who had peripheral surgery under general anaesthesia (42). The results showed presence of atelectasis, which was even worse when using FiO_2 of 100% during surgery. In another small sample of patients undergoing either open cholecystectomy or inguinal hernia surgery, CT showed presence of atelectasis in 90% of patients at one (1) hour and in 50% of

patients at 24 hours postoperatively (43). CT scans also showed that atelectasis occurs more commonly in morbidly obese patients at first postoperative day (44).

Following major surgery, a normal alveolar-to-arterial oxygen difference might take a few days to reach full restoration, and hypoxaemia can frequently occur. For instance, FRC is usually at the lowest value at one to two days following upper abdominal surgery, gradually returning to normal values after five to seven days (45-47). As mentioned above, atelectasis can be observed on a CT scan for at least 24 hours in the majority of patients following major surgery.

Pulmonary function test measurements, such as functional residual capacity (FVC), forced expiratory volume at one second (FEV_1), and peak expiratory flow rate, are all decreased postoperatively, especially when the patient is in pain (47). The majority of respiratory muscles, including the airway and abdominal muscles, and diaphragm, are negatively affected following major surgery (48). Many factors contribute to these muscles dysfunctions, including neuromuscular blocking drugs, anaesthetic agents, postoperative analgesic drugs (especially opioids), disruption to sleep patterns, pain, and inflammatory responses to surgery (48).

The effect of surgery and anaesthesia may last for a few weeks after surgery, with, for instance, a low ventilatory response to hypoxia and hypercapnia (49). It has been found in

one study that the ventilatory response retained some degree of impairment for six weeks after surgery, when the effect of pain, inflammation and analgesic use were not present (49). This indicates that it may take some time for normal respiratory control mechanisms to be restored.

Sputum retention frequently occurs after surgery, especially with the use of endotracheal tube, which results in impairment of sputum production through the airways, which may continue into the postoperative period (50). Sputum retention is also caused by inhaled anaesthetics, high oxygen concentration, inadequate humidification of inspired gases and pain which results in poor cough (50).

All the above interacting factors, including impaired respiratory control, an ineffective cough, residual atelectasis, and reduced FRC, create an ideal condition for the development of PPCs.

1.5 Risks factors of postoperative pulmonary complications

The current literature identifies several perioperative factors that increase the risk of developing PPCs (2). These risk factors can be classified as patient-related, anaesthesia-related or surgical-related factors. Summary of risk factors is presented in Table 1.10.

1.5.1 Patient-related factors

The patient's pre-existing health status is strongly associated with the development of PPCs (2). Patient-related factors include advanced age, American Society of Anesthesiologists class ≥2, functional dependence, poor exercise capacity, chronic obstructive pulmonary disease (COPD), obstructive sleep apnoea (OSA), respiratory symptoms, Asthma, low oxygen saturation, respiratory infection, congestive heart failure, anaemia and smoking (51-57). Many studies have documented that advanced age (more than 60 years) is high risk factor of developing PPCs (21, 29, 54, 57). A meta-analysis indicates that OSA patients have double the chance of those without OSA for developing respiratory failure following non-cardiac surgery (58).

Smoking is one of the main risk factors for PPCs, as smoking negatively effects pulmonary function due to airway obstruction, inflammation and sputum retention (20, 21, 26, 59, 60). In a meta-analysis by Mills, et al. (61), current and previous smokers (stopped smoking for more than four weeks) were compared and the results showed significant reduction in PPCs for previous smokers [relative risk (RR) 0.81, CI 0.70–0.93]. The American College of Surgeons' NSQIP database was used by several studies to quantify postoperative complications in

current smokers, ex-smokers (stopped more than one year), and never smoked patients who underwent major surgery (61-64). The results showed that current smokers were at higher risk of developing PPCs in comparison to previous smokers, who were also at higher risk of having PPCs than those who had never smoked. The risk of having PPCs for ex-smokers increased in those with a more than 10 packs-year smoking history (64). This is also applicable in active smokers as the risk of PPCs increases with the number of pack-year smoked (65).

Anaemia is common Europe, and is found in about 30% of patients who present to pre-assessment clinics (66). Patients with preoperative anaemia (haemoglobin <100g litre^{1}), who are at high risk of requiring intraoperative blood transfusion, are at three times more at risk of developing PPCs compared to patients without anaemia (19).

1.5.2 Anaesthesia-related factors

General anaesthesia usually contributes to physiological changes in respiratory function and causes an immediate reduction in FRC, which results in atelectasis in the dependent regions of the lung (52). As described above, atelectasis occurs during general anaesthesia through three mechanisms, specifically, compression of the lung tissue, absorption of alveolar nitrogen (e.g., absorption atelectasis) and impairment of surfactant function (2). The use of regional anaesthesia, including spinal and epidural anaesthesia, is recommended as an alternative to general anaesthesia in order to reduce the incidence of PPCs (67). Patients undergoing surgeries requiring general anaesthesia are at higher risk for developing PPCs compared to patients undergoing surgeries requiring regional anaesthesia (36). In addition,

research indicates that, even for similar surgical procedures, general anaesthesia is still an independent PPCs risk factor which carries higher risk in comparison to regional anaesthesia. For instance, a Cochrane systematic review showed that regional anaesthesia contributes to significant reduction in postoperative pneumonia [RR (CI) 0.45 (0.26–0.79)] (68). Similarly, a large cohort study for patients undergoing major non-cardiac surgery showed higher odds ratio (OR) (CI) of 1.56 (1.36–1.80) for general anaesthesia compared to regional anaesthesia in relation to development of PPCs (59). Another prospective multicentre study found incidence of PPCs is higher with general anaesthesia compared to without (7.5% vs 2.0%, respectively) (19). Furthermore, a cohort study suggests avoiding general anaesthesia for patients with COPD, as regional anaesthesia showed a lower incidence of PPCs, such as pneumonia, prolonged ventilator dependence and unplanned intubation (69).

Anaesthesia, analgesics and other perioperative drugs may contribute to exacerbate PPCs, as they affect the central regulation of breathing and change the neural drive of the chest wall muscles and upper airways (2). In addition, the immunosuppressant effect of anaesthetics and intraoperative transfusion may also contribute to the development of PPCs (2).

Mechanical ventilation is one of the most important intraoperative factors that contribute to the development of serious PPCs, such as ARDS and ventilator-induced lung injury (VILI) (70, 71). In a well-conducted clinical trial, the use of low or no positive end expiratory pressure (PEEP) can induce atelectasis (72). Neto, et al. (73) also suggested the use of intraoperative lung-protective strategies (e.g., low tidal volume, high PEEP and recruitment manoeuvres) to prevent PPCs and to improve postoperative outcomes. In contrast, in a large multicentre trial, the PROVHILO, examined high PEEP (12 cmH_2O) with recruitment manoeuvre vs. low PEEP (2

cmH_2O) without recruitment manoeuvre in regard to the development of PPCs following open abdominal surgery (74). The results of the PROVHILO trial showed that high level of PEEP with recruitment manoeuvre does not protect from PPCs. More recently, a PROBESE trial on obese patients showed that high level of PEEP (12 cmH_2O) with recruitment manoeuvre does not reduce incidence of PPCs following non-cardiac surgery (75).

Expiratory flow limitation during mechanical ventilation was recently studied and reported as an intraoperative risk factor for developing PPCs following major abdominal surgery, which increases the risk by 50% (76). Spadaro, et al. (76) found expiratory flow limitation to be associated with increased incidence of postoperative pneumonia and acute respiratory failure, as well as increased length of hospital stay. The presence of intraoperative expiratory flow limitation may participate in developing atelectasis by absorption of the trapped gas in the obstructed area of the lung. Limited expiratory flow can also impair cough and secretion removal which consequently increase the risk of pulmonary infection (76).

1.5.3 Surgery-related factors

The surgical site is one of the most important surgery-related factors that greatly contribute to the development of PPCs (2). Surgical sites that carry the highest risk of developing PPCs include aortic surgery, thoracic surgery and abdominal surgery (59). Generally, the risk of developing PPCs increases when the surgery site is closer to the diaphragm (77). For example, the risk of developing PPCs after open abdominal aortic aneurysm repair may be as high as 25%. Oesophageal surgery is also a risk factor for developing PPCs (20). Other types of surgeries, including ear, nose, and throat, lower abdominal, urological and peripheral vascular

surgeries, carry low risk of developing PPCs (36). Laparotomy with upper abdominal incision contributes to higher risk of developing PPCs compared to laparoscopic procedures, as small incisions decrease the systemic inflammation response and postoperative pain (77). The risk of PPCs in upper abdominal surgery is 15 times the risk of PPCs with lower laparotomy (21, 28).

In addition to the surgical site, emergency surgery has a strong contribution to developing PPCs, reaching six times the risk of PPCs with elective surgery, as emergency surgery is usually performed for critically ill patients (19, 28, 53, 57). Lack of proper perioperative management and preoperative patient's health optimisation due to limited timing may link between emergency surgery and developing PPCs. Prolonged surgery duration is also considered a risk factor for developing PPCs (77).

Table 1. 10 Risk factors of postoperative pulmonary complications

Patient-related factors	**Anaesthesia-related factors**	**Surgery-related factors**
- Advanced age - ASA class ≥2 - Functional dependence - Poor exercise capacity - Chronic obstructive pulmonary disease (COPD) - obstructive sleep apnoea (OSA) - Respiratory symptoms - Pulmonary hypersensitivity - Low oxygen saturation - Respiratory infection - Congestive heart failure - Anaemia - Smoking	- General anaesthesia - Analgesics - Mechanical ventilation - Intraoperative fluid management	- Surgical site - Surgical incision causes pain and inflammation - Major surgery - Prolonged surgery duration - Emergency surgery

ASA: American Society of Anesthesiologists

1.5.4 Prediction of postoperative pulmonary complications

Preoperative assessment for developing PPCs is essential as patients undergo different surgeries with different demographics and preoperative health conditions. Considering risk factors for developing PPCs would help in preoperative evaluation for predicting high-risk patients, which, therefore, enables best perioperative management to avoid PPCs (36). Several risk prediction models for PPCs have been developed previously; however, these models were developed based on retrospective studies and focused on a single adverse event rather than considering all PPCs forms (27, 59, 78-84). Therefore, these limitations of previously published prediction models would be impractical to use within preoperative assessment (36).

Furthermore, there are more reliable and valid risk prediction models for PPCs, such as the ARISCAT (assess respiratory risk in surgical patients in Catalonia) scoring system, which have been developed by multicentre trials and used more valid PPCs definition (85). ARISCAT included seven risk factors, each with a different score, using EPCO definition for composite outcomes in order to classify patients at low- medium- and high-risk for developing PPCs (Table 1.11). These independent factors include low preoperative oxygen saturation (SpO_2 <96%), respiratory infection in the last month, age, preoperative anaemia, intrathoracic/upper abdominal surgery, surgery duration more than two hours and emergency surgery. The incidence of PPCs in the risk groups, low, medium and high risk was 1.6, 13.3 and 42.1%, respectively. Accordingly, ARISCAT score composed of the total score categorises patients into: low risk (score <26), medium risk (score 26-44) or high risk (score ≥45) (85).

Table 1. 11 ARISCAT (assess respiratory risk in surgical patients in Catalonia) scoring system

Risk factor		**Score**
1- Age (in years)	- ≤50	0
	- 51-80	3
	- >80	16
2- Preoperative SpO_2 (in %)	- ≥96	0
	- 91-95	8
	- ≤90	24
3- Respiratory infection in the last month		17
4- Preoperative anaemia (≤10 g/dl)		11
5- Surgical incision	- Peripheral	0
	- Upper abdominal	15
	- Intra-thoracic	24
6- Duration of surgery (in hours)	- ≤2	0
	- >2 to 3	14
	- >3	23
7- Emergency procedure		8

G/dl: gram/decilitre, SpO2: Peripheral capillary Oxygen Saturation

1.6 Strategies to reduce postoperative pulmonary complications

Many of the above risk factors are modifiable, such as smoking, COPD, anaesthesia techniques and mechanical ventilation strategy, and can be avoided or managed by specific perioperative interventions (Table 1.12). There are different perioperative interventions which would help in reducing the incidence of PPCs, especially for those who are at high risk of developing PPCs (2). The first step to minimise the incidence of PPCs is preoperative assessment to identify the previously discussed risk factors associated with PPCs, such as smoking, anaemia, respiratory symptoms and pre-existing cardiovascular and respiratory diseases.

Preoperative smoking cessation is beneficial with the degree of benefit correlating to the duration of cessation, the age at the time of smoking cessation and the number of cigarettes smoked (2). A number of studies have examined the effectiveness of smoking cessation programmes in reducing PPCs incidence (86-88). However, these studies failed to adequately show the effectiveness of the used smoking cessation programmes as they were small studies with lack of methodological rigour. In contrast, a meta-analysis documented that patients who stopped smoking for more than four weeks before surgery had significant reduction in PPCs compared to current smokers [(RR) 0.81, CI 0.70–0.93] (61). Duration of cessation is important and can impact on the effectiveness of preoperative smoking cessation. It has been suggested that smoking cessation reduces PPCs by 23% when cessation is for >4 weeks and by 47% for >8 weeks, meaning that maximising the duration of preoperative smoking cessation minimises PPCs (61, 89). Thus, the recommended period of preoperative smoking

cessation is at least four to six weeks (90). Additional research is needed for evaluating the benefits of smoking cessation one to two weeks prior to surgery (36).

Preoperative anaemia is a modifiable risk factor for PPCs and should be optimised preoperatively. Preoperative treatments for anaemia are mainly dietary supplements such as vitamin B_{12} and iron therapy (oral or intravenous) (91). UK national guidelines with regard to anaemia management published some treatment options that mainly depend on cause and severity of anaemia and available time before surgery (92). The recommended anaemia treatments include iron, vitamin B12, folate and erythropoiesis-stimulating agents (ESA) therapy. The guidelines also recommend the use of iron supplementation alongside ESA therapy in order to maximise the efficacy of ESA agents.

Pre-existing morbidities should be optimised before surgery to avoid PPCs. COPD and asthma should ideally be treated with inhaled or oral steroids and bronchodilator (36). Warner, et al. (93) suggested administration of prophylactic bronchodilators would help in prevention of PPCs for patients with COPD. A respiratory infection in the last month is a risk factor for developing PPCs; therefore, elective surgery should be delayed until symptoms have disappeared and pulmonary function returns to the baseline, except for when surgery is urgent, whereby individual patient care plan is required, maintaining a balance of the risk for developing a PPC vs delaying surgery (85, 94). Cardiologists should pharmacologically optimise congestive heart failure with the intention of minimising symptoms and maximising functional capacity (95).

Preoperative physiotherapy is a well-documented and recommended intervention to reduce PPCs (96). Preoperative physiotherapy would enhance pulmonary function and strengthen the respiratory muscles, thereby potentially reducing PPCs (77, 97). Grams, et al. (98) suggested that breathing exercises have a positive effect on respiratory muscle strength postoperatively. A systematic review which included 12 trials revealed that pre-operative aerobic exercises and inspiratory muscle training (IMT) reduce PPCs and length of stay following cardiac and abdominal surgery [RR (CI) where PPCs was 0.4 (0.23–0.72)] (99). Further details about respiratory physiotherapy are discussed below in Section 1.6.1.

Intraoperative strategies that help to prevent PPCs are mainly incorporated with anaesthetic technique, intraoperative ventilatory strategy and surgical management. Addition of epidural analgesia to general anaesthesia has a significant benefit in terms of reducing postoperative pneumonia in comparison with the use of systemic opioids alone (68, 100). Epidural analgesia would be more beneficial for COPD patients undergoing major abdominal surgery as it improves analgesia and reduces the consumption of opioid. It has been suggested that epidural analgesia also enhances respiratory function and decreases postoperative ventilation and unplanned re-intubation (101, 102). Epidural analgesia would be greatly helpful to obese patients who are at high risk of having OSA, which increases postoperative respiratory depression (103).

Lung-protective strategy with low tidal volume and PEEP is a suggested ventilation strategy to avoid and manage PCCs, especially atelectasis (2). Lung-protective strategy is a well-

documented ventilatory strategy in ARDS patients (71) and is performed by using low tidal volume, high PEEP, and recruitment manoeuvre. Strong evidence supports that low tidal volume reduces incidence of PPCs, whereas the optimal PEEP level is still controversial, taking into account the impact of high PEEP on haemodynamic status (72, 104-106). PROVHILO and PROBESE trials recently showed that high level of PEEP (12 cmH_2O) with recruitment manoeuvre does not reduce incidence of PPCs following abdominal and non-cardiac surgery (74, 75). In contrast, a meta-analysis suggested that PEEP and recruitment manoeuvre reduce the incidence of PPCs, but only when used in combination with low tidal volume (107). The recommended tidal volume is 6–8 ml/kg for non-obese patients with normal lungs (70). Multicentre studies showed that high tidal volume (>10 ml/kg) is harmful and contributes to 18% incidence of acute lung injury (108, 109). In a small study, Severgnini, et al. (104) showed that low tidal volume (7 ml/kg) and moderate PEEP (10 cmH_2O) with recruitment manoeuvre arterial oxygenation improve pulmonary function and reduce atelectasis without compromising haemodynamic status.

Furthermore, surgical technique is a very important measure to avoid PPCs, such as reducing aggressiveness and duration of the surgery, minimising open surgery, and considering laparoscopic surgery where possible (2). Studies showed that prolonged surgery duration (>2 hours) is strongly liked with development of PPCs (19, 29). Thus, major surgery with prolonged surgery time for high risk patients would best be performed by a senior surgeon in order to minimise surgery duration (19).

Postoperative interventions are essential to manage and avoid PPCs, including administration of supplemental oxygen, which is routinely used to treat early postoperative hypoxemia. Non-invasive ventilation, including continuous positive airway pressure (CPAP) and high-flow nasal oxygen, would be a postoperative intervention in some cases, especially following major abdominal surgery and for patients who are at risk of postoperative atelectasis (110). In 2012, a meta-analysis documented the benefit of postoperative non-invasive ventilation in reducing postoperative pneumonia, length of stay and re-intubation rate following major surgery (111). However, these findings could not be generalised to all major surgeries as the majority of the data were derived from one large randomised controlled trial focusing on cardiac surgery (112). In contrast, a more recent Cochrane review in 2014 suggested insufficient evidence confirming the benefit of non-invasive ventilation in reducing PPCs or mortality following abdominal surgery (113).

Postoperative analgesic technique plays an important role in pain management, which therefore helps in reducing the incidence of PPCs (96). Evidence suggests the use of postoperative epidural analgesia, which effectively reduces the incidence of PPCs; however, the evidence in this subject remains insufficient (2).

Nasogastric tubes are also used postoperatively to reduce the incidence of postoperative pneumonia and atelectasis following abdominal surgery (114). The effectiveness of routine use of nasogastric tube to reduce PPCs, to enhance bowel function recovery and to reduce length of say was assessed by a meta-analysis (115). The results of 37 studies assessed by Verma and Nelson (115) showed no evidence of the effectiveness of the routine use of

nasogastric tube to reduce PPCs and length of stay. Therefore, the routine use of nasogastric tube is not recommended, and it should only be used selectively for patients who have symptomatic abdominal distension and who are at a high risk of aspiration (2).

Nevertheless, although all of the above strategies are used to reduce the incidence of PPCs, only a few strategies are supported with good evidence while the effectiveness of most of the strategies needs to be carefully examined, in particular postoperative strategies. In addition, there are challenges of implementing preoperative strategies in some of the surgeries as in the case of urgent surgeries. These preoperative strategies are usually carried out during a long preoperative time, up to six weeks, such as smoking cessation and rehabilitation programmes.

Table 1. 12 Strategies to reduce postoperative pulmonary complications (2)

Time	**Intervention**
Preoperative	- Preoperative assessment - Smoking cessation (at least 4-6 weeks)
Intraoperative	- Anaesthetic technique (general vs. spinal) - Ventilatory management (lung protective strategy) - Fluid management - Surgical management (duration, open vs. laparoscopic)
Postoperative	- Supplemental oxygen - Postoperative lung expansion - Postoperative analgesia - Nasogastric intubation

1.6.1 Respiratory physiotherapy techniques

Anaesthesia and surgery-related factors contribute to the development of undesirable respiratory events, such as decreased pulmonary function and respiratory muscle strength, diaphragmatic dysfunction, and impaired breathing and cough effort (96). These adverse respiratory events increase the risk of developing PPCs following surgeries, especially major abdominal and cardiothoracic surgeries where PPCs incidence is much higher than with other surgeries (96, 116).

Respiratory physiotherapy may help to overcome these adverse respiratory events and, therefore, leads to the prevention of PPCs. There are different physiotherapy modalities that are regularly used in both pre- and post-operative care, such as lung expansion techniques which incorporate breathing exercises, inspiratory muscle training, Incentive Spirometry (IS), and airway clearance manoeuvres (77, 117). However, the effectiveness of these lung expansion techniques is not demonstrated adequately, and no single technique has been found to be superior to any other in a postoperative setting (118). Therefore, the effectiveness of these interventions is still underreported and needs deeper investigation regarding which, when and how to utilise these respiratory physiotherapy modalities.

Some studies have investigated the effectiveness of preoperative physiotherapy to reduce the incidence of PPCs. In a systematic review and meta-analysis, eight studies were assessed to evaluate the effectiveness of preoperative inspiratory muscle training (IMT) (119). Mans, et al. (119) compared IMT with sham and no IMT on patients awaiting open cardiac, thoracic

and upper abdominal surgeries. The results showed that IMT significantly improves the strength of the inspiratory muscles, which is maintained throughout the postoperative period and which consequently reduces the incidence of PPCs. In a Cochrane review, the effectiveness of preoperative IMT on cardiac and major abdominal surgeries was also evaluated (117). According to Katsura, et al. (117), IMT was associated with a reduction in the incidence of PPCs and the length of hospital stay. However, the effectiveness of IMT in this review might be overestimated due to the poor methodological rigour of the included studies, such as a lack of adequate blinding. In another Cochrane review, the effectiveness of IS was compared with standard care or other respiratory physiotherapy techniques, such as deep breathing exercises, intermittent positive pressure breathing and chest physiotherapy, was extensively evaluated (120). Junior, et al. (120) have found low quality evidence supports the use of IS to decrease incidence of PPCs following upper abdominal surgery. Their result is consistent with another systematic review which found no evidence to support the effectiveness of pre- and post-operative IS on reducing the incidence of PPCs (121). However, IS is still widely used in pre- and post-operative care. The use of breathing exercises in upper abdominal surgery was investigated in a meta-analysis, which failed to draw a clear conclusion about their benefits on lung function and the prevention of PPCs (98). A randomised controlled trial demonstrated that breathing exercises can significantly reduce post-operative hypoxia as measured by SpO_2 (SpO_2 before breathing exercises: 93$\pm$4.3% vs. SpO_2 after breathing exercises: 96$\pm$2.6%; p=0.02) (122). A more recent small study by Lunardi, et al. (123) examined lung expansion techniques, including deep breathing, flow IS and volume IS, in reducing incidence of PPCs. The results suggested that PPCs incidence was, in fact, higher in the lung expansion techniques groups compared to control group (control group=0; flow IS=3; deep breathing=8; volume IS=3 patients). Therefore, the routine use of

tested lung expansion techniques was not recommended. Another randomised controlled trial investigated the efficacy of an intensive preoperative rehabilitation to prevent PPCs following esophagectomy (124). The rehabilitation programme includes respiratory muscle and thoracic cage stretching to enhance lung compliance, deep inspiratory training and diaphragmatic breathing, efficient coughing and huffing with vigorous contraction of abdominal muscles, muscle strength exercises for lower limbs and abdominal muscles and biking for 20 minutes. The preoperative rehabilitation programme was effective in reducing PPCs.

1.7 Current perioperative practice targeting postoperative pulmonary complications

Currently, there is no specific approach implemented to minimise the incidence of PPCs. In the UK, the dominant perioperative approach used is Enhanced Recovery After Surgery (ERAS), which incorporates different interventions aiming to improve recovery and, therefore, minimise postoperative complication in general (125). The specific approaches used postoperatively to decrease PPCs include early mobilisation and incentive spirometer, which are provided by nurses and physiotherapists. Physiotherapy departments provide other modalities to avoid and manage PPCs, such as chest physiotherapy and IMT. However, these modalities are not provided routinely for all postoperative patients and are only prescribed for patients with high risk to develop PPCs. Physiotherapists categorise high risk patients by using the Southampton Physiotherapy Post-Operative Screening Tool (SPPOST) (126).

SPPOST was developed to predict the risk of developing PPCs considering the following factors: inspired oxygen, oxygen saturation, respiratory rate, COPD, obesity/ malnutrition, functional dependency, older age, smoking history and anaesthetic duration. SPPOST uses the valid definition of PPCs by Brooks-Brunn (21), and is shown to be a valid and reliable tool to predict PPCs (126). However, it is not clear how widely is the SPPOST being used in the UK. Patients with SPPOST score more than 10 will be considered at high risk and then will be referred to physiotherapy service to receive respiratory physiotherapy interventions. Patients with SPPOST score of 10 or less will be given incentive spirometer with written instructions by the physiotherapist and encouraged for mobilisation by a nurse. Hence, the aim of SPPOST is to decrease the workload and recourse of the physiotherapy department whereby only high-risk patients are referred to a physiotherapist.

1.8 Gap in knowledge

The current literature does not provide conclusive results on the benefits of respiratory physiotherapy to reduce the incidence of PPCs, which, therefore, indicates the need for a systematic review that would provide clear evidence about the effectiveness of perioperative respiratory physiotherapy on PPCs. All the previously discussed systematic reviews illustrated the need for high quality research on the effectiveness of different respiratory physiotherapy modalities for PPCs reduction, as the literature is lacking high quality research on this subject. In addition, many of these reviews are outdated, such as the reviews by Grams, et al. (98).

Furthermore, some reviews did not evaluate pre-operative and post-operative interventions separately, although the effectiveness of pre-operative and post-operative interventions might be very different. For example, Carvalho, et al. (121) failed to examine precisely pre- or post-operative IS, as studies on both pre-operative IS and post-operative IS were included in the review. Many reviews examined one or more respiratory physiotherapy techniques on PPCs following different types of surgery, which might affect the results about the efficacy of the intervention. For instance, Mans, et al. (119) examined IMT on PPCs following cardiac, thoracic, and upper abdominal surgeries rather than focusing on one specific surgery type. Thus, it would be appropriate if a systematic review were to provide conclusive results on the effectiveness of pre- or post-operative respiratory physiotherapy on PPCs following a specific surgery type.

Currently, there is no gold standard perioperative respiratory physiotherapy technique which targets PPCs reduction following major abdominal surgery. Current practice in the UK relies on adherence with ERAS protocol, which aims to improve recovery and, thereby, reduce length of stay and postoperative complications (125). However, ERAS protocols have few items that would help in reduction of PPCs in particular. Therefore, current practice would require an investigation in terms of the need for improvement. In addition, perioperative respiratory physiotherapy techniques need to be studied in depth in terms of reduction of PPCs following major abdominal surgery.

1.9 Summary

PPCs are common following major surgeries, especially when the surgical incision is close to the diaphragm, as is the case in cardiac, thoracic and abdominal surgeries. PPCs are strongly associated with postoperative mortality and length of stay. Preoperative evaluation to predict high-risk patients would enable best perioperative management and help in avoiding PPCs. Despite there being no consensus on the best PPCs risk prediction model which should be used, the ARISCAT score seems clinically feasible to assess the risk of developing PPCs. Optimising modifiable risk factors, such as smoking cessation and treating preoperative anaemia, should be taken into account before surgery in order to reduce PPCs. Intraoperative interventions, including use of epidural and low tidal volume (6-8 ml/kg), contribute in reduction of PPCs following major surgery. The ideal PEEP level and the benefit of recruitment manoeuvre are still controversial. Postoperative CPAP might reduce postoperative atelectasis, especially in high risk patients such as OSA patients. Breathing exercises and IMT also could also be considered before and after surgery to improve respiratory muscle strength and reduce PPCs. However, there is insufficient evidence about the effectiveness of postoperative lung expansion techniques in reducing PPCs following major abdominal surgery. Thus, high quality research about the effectiveness of postoperative respiratory physiotherapy in reducing PPCs is required. Currently, ERAS protocol is used to reduce postoperative complications in general, but not PPCs in particular. Therefore, a perioperative respiratory care bundle targeting PPCs should be considered within current practice.

1.10 Hypothesis

It was hypothesised that a perioperative respiratory care bundle improves postoperative pulmonary outcomes following major abdominal surgery.

1.11 Aim

The aim of this thesis is to implement a perioperative respiratory care bundle that improves postoperative respiratory outcomes following major abdominal surgery.

1.12 Objectives

Specific objectives of each study are outlined in relevant chapters. The main objectives of the thesis are presented below:

1- To assess available evidence about the effectiveness of postoperative respiratory physiotherapy techniques in reducing PPCs following major abdominal surgery.

2- To investigate the need for improvement in current perioperative practice at Queen Elizabeth Hospital Birmingham by measuring the incidence of PPCs following major abdominal surgery.

3- To assess the success of a perioperative respiratory care bundle in improving respiratory muscle strength following major abdominal surgery.

Chapter two

Effectiveness of postoperative respiratory physiotherapy on minimising postoperative pulmonary complications following major abdominal surgery: systematic review and meta-analysis

Abstract

Introduction: Postoperative pulmonary complications (PPCs) commonly occur following major abdominal surgery. There are different interventions to manage and reduce PPCs, such as respiratory physiotherapy. However, the effectiveness of postoperative respiratory physiotherapy modalities remains uncertain. The aim of this systematic review is to assess the evidence concerning the effectiveness of postoperative respiratory physiotherapy on PPCs after major abdominal surgery.

Methods: Randomised controlled trials that test the effectiveness of postoperative respiratory physiotherapy on minimising PPCs after major abdominal surgery were included in this review. The primary outcome was the incidence of PPCs. Secondary outcomes were pulmonary function and respiratory muscle strength. Databases searched in this review were MEDLINE, Cochrane Library, EMBASE, and CINAHL Plus. Data was narratively synthesised and treatment effect expressed as Risk Ratio (RR) with 95% Confidence Interval (CI). Heterogeneity was measured by I^2 statistics.

Results: Total of five studies (n=312) were included in this review. Two studies showed that lung expansion techniques were not associated with reduction of PPCs incidence. One study found significant improvement in oxygen saturation after chest physiotherapy. One study showed that lung expansion techniques can improve postoperative lung function. Two studies (n=120) were included in meta-analysis to measure the treatment effect of deep breathing exercises compared to control group in terms of PPCs incidence. The results showed no

significant difference between the two groups with high degree of heterogeneity (RR= 3.34; CI 0.27 to 41.63; P= 0.35; I^2 statistics= 64%).

Conclusion: This systematic review shows there is lack of evidence for the effectiveness of postoperative respiratory physiotherapy on reduction of PPCs incidence after major abdominal surgery. Lung expansion techniques and chest physiotherapy improve oxygen saturation and lung function, however there is no evidence that this translates to reductions in PPCs incidence. The overall quality of evidence is very low due to paucity of studies which indicates the need for good quality researches in this field.

2.1 Introduction

Major surgery is defined as a surgical procedure that lasts longer than two hours, or with anticipated blood loss of 500 ml or greater (4) and, globally, account for more than 200 million operations annually (10). The vast majority of these are performed safely with a low incidence of postoperative complications. However, 10% of patients undergoing surgery in the United Kingdom are at high risk of developing postoperative complications, accounting for 80% of postoperative mortality observed (11).

Postoperative pulmonary complications (PPCs) are common postoperative complications, in general. PPCs are a composite end-point that includes atelectasis, hypoxemia, pneumonia, bronchospasm, pulmonary oedema and Acute Respiratory Distress Syndrome (ARDS). A large database showed that PPCs are associated with an increased morbidity and mortality, with a 30-days mortality rate of approximately 22% for patients with PPCs compared to 2% for those without PPCs following different type of surgeries (30).

The incidence of PPCs is considered high, ranging from 6.2% to 32.7% for patients undergoing surgery with general anaesthesia, depending on definition of PPCs used and presence of risk factors (14-18) (Chapter 1.2). Risk factors for the development of PPCs are patient-related factors (e.g.: pre-existing disorders and general health status), anaesthesia-related factors (e.g.: general anaesthesia), and surgery-related factors such (e.g.: surgical site) (1) (Chapter 1.5). The risk of developing PPCs is generally increased when the surgical incisions close to

the diaphragm, as in case with abdominal surgeries (77). Patel, et al. (12) documented the incidence of PPCs at 7th postoperative day to be 11.9% following major abdominal surgery.

A multi-factorial approach is taken to minimise PPCs. These approaches include patient education (e.g.: surgery school), smoking cessation, improvement of preoperative patient's health status, and intraoperative and postoperative interventions (97). Physiotherapy is a well-established perioperative intervention aimed at managing and reducing PPCs (96). These techniques enhance pulmonary function and the strengthen respiratory muscles, thereby potentially modulating PPCs (77, 97). The effectiveness of different respiratory physiotherapy modalities have been assessed in both the preoperative and postoperative settings (98). The review found that breathing exercises have a positive effect on respiratory muscles strength postoperatively. A recent systematic review that assessed the effectiveness of preoperative inspiratory muscle training (IMT) on PPCs following cardiac and major abdominal surgery demonstrated that the use of preoperative IMT significantly reduced PPCs and associated with a reduction of hospital stay (117). A Similar review (119) indicated that preoperative IMT also improves respiratory muscles strength, based on maximum inspiratory pressure measurements, following cardiothoracic and upper abdominal surgery.

A limited number of reviews have assessed the effectiveness of postoperative respiratory physiotherapy on reduction of incidence of PPCs, especially after major abdominal surgery (98, 120, 127). Pasquina, et al. (127) did not recommend the routine use of respiratory physiotherapy after abdominal surgery, pointing out that only a few trials have reported its usefulness. Grams, et al. (98) reviewed only the breathing exercises technique, while Junior,

et al. (120) evaluated trials of incentive spirometry (IS). Consequently, all of these reviews did not deliver conclusive results regarding the effectiveness of most respiratory physiotherapy modalities. In addition, there may have been recent trials illustrating the usefulness of different respiratory physiotherapy techniques after major abdominal surgery in the reduction of PPCs, as in the study by Lunardi, et al. (123) who compared three techniques.

2.2 Objective

The objective of this systematic review is to assess the effectiveness of different postoperative respiratory physiotherapy techniques in reducing PPCs following major abdominal surgery.

2.3 Method

This systematic review was reported in accordance with PRISMA guidelines. The protocol was registered online via PROSPERO (CRD42017055740).

2.3.1 Eligibility criteria

2.3.1.1 Type of studies:

Randomised controlled trials (RCTs) that assess the effectiveness of postoperative respiratory physiotherapy in reducing PPCs were included. Other research designs such as observational and case studies were excluded. RCTs published before 2000 were excluded as they have been included in previous systematic reviews that demonstrated low quality of evidence.

2.3.1.2 Type of participants:

Adult patients undergoing major abdominal surgery, defined as "surgery expected to last more than 2 hours, or with anticipated blood loss more than 500 ml or more" (4). Examples of major abdominal surgery are listed in the table 2.1.

2.3.1.3 Type of intervention:

We included studies that assess at least one of the following postoperative respiratory physiotherapy modalities (Table 2.2):

2.3.1.4 Type of outcome measures:

The Primary outcome was the incidence of PPCs, defined as the presence of any respiratory infection, respiratory failure, pleural effusion, atelectasis, pneumothorax, pneumonia, aspiration pneumonia, acute respiratory distress syndrome (ARDS), or pulmonary embolism, as defined by Jammer, et al. (1). In addition, the definitions of PPCs according to individual studies were also considered. Secondary outcomes were pulmonary function, inspiratory muscles strength, pain intensity, length of postoperative hospital stay, length of postoperative mechanical ventilation, length of postoperative intensive care unit (ICU) stay and mortality.

Table 2. 1 Examples of major abdominal surgery were included in the review

Surgery type	**Examples**
Gastrointestinal	Exploratory laparotomy Partial gastrectomy (+/- excision of surrounding tissue) Total gastrectomy (+/- excision of surrounding tissue) Bypass of oesophagus Oesophagectomy (partial) Oesophagectomy (total)/Oesophagogastrectomy Partial excision of bile duct and anastamosis of bile duct to duodenum/jejunum Resection of duodenal tumour Resection of small bowel tumour Splenectomy (partial/total)
Hepatobiliary	Hemihepatectomy (left/right) Partial hepatectomy (+/- ablation) Pancreatectomy (partial/distal) Pancreatectomy (total) Pancreaticoduodenectomy (Whipple procedure) Resection of lesion(s) of liver
Urological surgery	Cystectomy, prostatectomy and nephrectomy
Laparoscopic surgeries*	Gastric bypass surgery

* Laparoscopic procedures that meet the review's definition of major abdominal surgery were included whilst laparoscopic procedures such as cholecystectomy, hernia repair and appendectomy, were excluded as they are usually considered minor surgeries.

Table 2. 2 List of most common postoperative respiratory physiotherapy modalities

Postoperative respiratory physiotherapy modalities
• Chest physiotherapy • Breathing exercises • Inspiratory muscle training • Incentive spirometry (IS) • Continuous positive airway pressure (CPAP) as lung expansion technique • Airway clearance manoeuvres (assisted cough or expiratory airflow technique)

A new or novel modality was also considered as long as it is used to prevent postoperative pulmonary complications.

2.3.3 Information sources

Literature search was conducted using Medical Subject Heading (MeSH) terms and free text words related to effectiveness of postoperative respiratory physiotherapy in reducing PPCs. We searched MEDLINE (OVID interface, 1948 onwards), Cochrane Library (Wiley interface, current issue), EMBASE (OVID interface, 1974 onwards), and CINAHL Plus (EBSCO interface, current issue).

The recently completed and on-going clinical trials were also searched through ClincalTrials.gov. In addition, PROSPERO was searched for on-going and recently completed systematic reviews.

A snowballing technique was adopted, which involves scanning reference lists of relevant reviews and included studies in order to ensure literature saturation and to gather the most relevant studies.

2.3.3 Search strategy

The search strategy was specifically designed to obtain all available published and unpublished evidence through the databases and sources mentioned above. Only RCTs and studies after 2000 were manually selected, as earlier studies have been part of previous systematic reviews (98, 120, 127). The specific search strategy was created by the systematic review team. A different search strategy was used for each database (Appendix 1). The

keywords and their synonyms/ alternatives used in the search strategies are listed in the below table 2.3.

Table 2. 3 The key concepts based of PICO format and their synonyms/ alternatives

Key concept (PICO)	**Synonym**
P: Major abdominal surgery	General surgery, colorectal surgery, pancreatic surgery, hepatic surgery, gastric surgery, vascular surgery, abdominal aortic aneurysm repair, urological surgery, cystectomy, prostatectomy, nephrectomy
I: Postoperative respiratory physiotherapy	Chest physiotherapy, breathing exercises, Inspiratory muscle training, IMT, Incentive spirometry, IS, continuous positive airway pressure, CPAP, airway clearance manoeuvres, assisted cough, expiratory airflow technique
C: Standard care, other postoperative respiratory physiotherapy	None
O: Postoperative pulmonary complication rate	PPCs, postoperative respiratory events, atelectasis, respiratory infection, pneumothorax, pneumonia, acute respiratory distress syndrome, ARDS, lung injury, hypoxemia, aspiration pneumonia, bronchospasm, pleural effusion

ARDS: Acute Respiratory Distress Syndrome, CPAP: Continuous Positive Airway Pressure, IMT: Inspiratory Muscle Training, IS: Incentive Spirometry, PICO: Participant/ Intervention/ Comparator/ Outcome, PPCs: Postoperative Pulmonary Complications

2.3.4 Data management

The literature search results were transferred to the EndNote software tool in order to remove any duplication of references. RevMan was used for generating graphs, meta-analysis and reporting.

2.3.5 Selection process

Two reviewers independently performed the study selection based on titles and abstracts, which were compared against the inclusion criteria. The records were rescreened on order to remove duplicates and studies published before 2000. The full text was obtained after the titles and abstracts of potential included studies have been screened, with a view to making a final decision on the inclusion of studies. Any concerns regarding study selection were resolved by discussion between the two reviewers and by consulting the third reviewer.

2.3.6 Data collection process

One reviewer performed data extraction using the Cochrane Collaboration Data Collection form. Another reviewer duplicated data extraction in order to minimise errors and reduce potential biases. Consensus was reached through discussion between the two reviewers, as well as by obtaining additional information from the authors of the included studies. The third reviewer was consulted to resolve any disagreement or uncertainty regarding data extraction. Extracted information include study setting, study population and participants' demographic data, details of respiratory physiotherapy techniques used and control/comparator condition,

study methodology, outcome measures, risk of bias assessment, and individual study results (sample size, mean/ median or number of event, and standard deviation or confidence interval).

2.3.7 Risk of bias and quality assessment

The Cochrane Collaboration tool for assessing risk of bias was used in this review to facilitate the process of risk of bias assessment. Six domains were covered in the risk of bias assessment tool: sequence generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data, selective reporting, and other sources of bias. One reviewer performed a risk of bias assessment and the other reviewed and duplicated the assessment. The third reviewer was consulted in case of uncertainty.

2.3.8 Piloting

The Cochrane Collaboration Data Collection form, including risk of bias and quality assessment tool, was piloted on two studies that were randomly selected. The data collection form was revised accordingly by removing irrelevant type of outcome measures.

2.3.9 Data synthesis

Outcomes of studies on the effectiveness of postoperative respiratory physiotherapy after major abdominal surgery in reducing PPCs were compared. Initially, narrative synthesis was conducted, reported in a textual approach and summarised in tables. A meta-analysis was

conducted by calculating the risk ratio for the incidence of PPCs and the mean differences for the length of hospital stay alongside their 95% confidence intervals. Heterogeneity was assessed by I^2 statistic to describe the percentage of variability in the effect estimates between the studies.

2.3.10 Confidence in cumulative evidence

The overall quality of evidence, regarding the effectiveness of postoperative respiratory physiotherapy after major abdominal surgery in reducing the incidence of PPCs, was judged using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) score. A final GRADE score judgment on the quality of the evidence was reported as high, moderate, low, or very low.

2.4 Results

The search yielded 885 records from the database searches (Figure 2.1). After initial screening by title and abstract, we excluded 841 articles, and 44 records were considered for secondary screening by title and abstract for the purpose of including only RCTs and studies published after 2000. A total of 15 full-text articles were obtained, and these underwent further assessment. Of these, ten studies did not fulfil the review's inclusion criteria and were excluded for the reasons described below in figure 2.1.

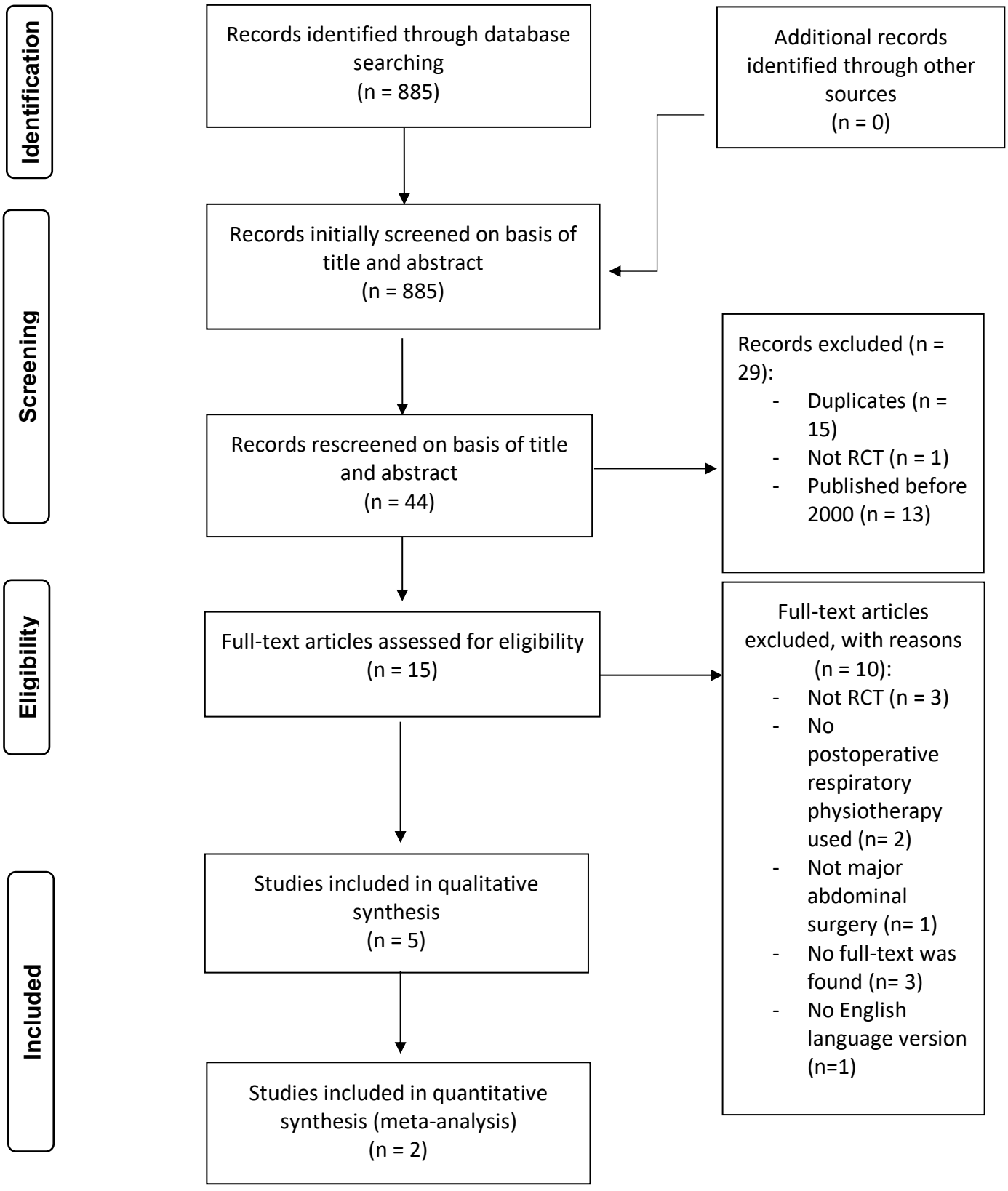

Figure 2. 1 PRISMA flow diagram

The flow diagram illustrates the number of included studies (five studies in qualitative analysis, two studies in quantitative analysis) and excluded studies with the reasons for exclusion at each stage of the review.

2.4.1 Included studies

A total of five studies were included in this review (122, 123, 128-130). These studies included a total of 312 participants. All the included studies were RCTs. The characteristics of the included studies are detailed below and summarised in table 2.4.

2.4.1.1 Type of the study participants:

1. Mackay, et al. (128) studied 50 patients (25 male and 25 female) with a mean age of 69 years for the control group and 63 years for the intervention group. The authors of this study evaluated patients at a high risk of developing PPCs. Patients undergoing abdominal aortic aneurysm repair were excluded in this study due to differences in postoperative management.

2. Manzano, et al. (122) assessed 31 patients (10 male and 21 female) with a mean age of 50.9 years for the control group and 52 years for the intervention group.

3. Forti, et al. (129) included 44 female patients with a mean age of 37 years for both the control and the intervention groups. All patients in this study were obese and underwent a laparoscopic Roux-en-Y gastric bypass. Patient characteristics are poorly reported in this study.

4. Lunardi, et al. (123) evaluated 137 patients (59 male and 78 female) with a mean age of 57, 62, 58, and 55 years for the four different groups in the study.

5. Kumar, et al. (130) studied 50 patients (37 males and 13 females) with a mean age of 59 and 53 years for the two study groups. All patients underwent open abdominal surgery. Inclusion criteria were not reported sufficiently.

2.4.1.2 Type of interventions:

1. In Mackay, et al. (128), the non-deep breathing and coughing (Non-DB&C) group (n= 21) received no additional respiratory physiotherapy. The Non-DB&C group received only standard care, that is, early mobilisation, to increase the restoration of mobilisation and improve pulmonary ventilation. Another group, the deep breathing and coughing (DB&C) group (n= 29), received the same standardised early mobilisation as did the control group in addition to DB&C exercises. The DB&C exercises included at least three coached lateral basal expansion manoeuvres (deep breaths) followed by a cough, huff, or forced expiratory manoeuvre. Patients were encouraged to perform DB&C exercises by themselves once every waking hour.

2. In Manzano, et al. (122), a control group (n=16) received standard care with no chest physiotherapy, and a chest physiotherapy group (n=15) received chest physiotherapy exercises. The protocol of chest physiotherapy includes three breathing exercises: passive and localised exercises, deep diaphragmatic breathing, and chest expansion exercises. These exercises were performed in one session for 30 minutes immediately after the surgery as soon as the patient arrived at the Post-Anaesthesia Care Unite (PACU).

3. In Forti, et al. (129), a Conventional Chest Physiotherapy (CCP) group (n=22) received only CCP exercises. Another group, the CCP plus Transcutaneous Electrical Diaphragmatic Stimulation (CCP+TEDS) group, (n=22) received the CCP exercises in addition to the TEDS. The CCP group received diaphragmatic respiratory exercises, deep inhalation exercises, inhalations fragmented two to three times, and respiratory exercises associated with shoulder flexion movements and extension of the upper limbs. Each exercise was carried out in one series of ten repetitions during each CCP session. The CCP+TEDS group received the same CCP exercises in addition to the TEDS. The TEDS was implemented by placing two pairs of carbon electrodes: one pair was placed on the paraesternal region beside the xiphoid process, and the other pair was placed on the motor points of the diaphragm muscle between the sixth and seventh intercostal spaces in line with the right and left front armpits. The following parameters were used in TEDS: pulse frequency of 30 Hz, respiratory frequency of 14 rpm, ascent time (ramp) of 0.7 s, pulse width of 1.2 ms, and an intensity sufficient to cause a tangible contraction of the diaphragm muscle. During the TEDS session, patients were positioned in a dorsal recumbent position with the bed head raised by 30°, the knees semi-inflected, the feet supported, the arms stretched alongside the body, and the head on the pillow.

4. Lunardi, et al. (123), a control group (CG) (n=35) received no respiratory physiotherapy. Three lung expansion technique groups, specifically, the Flow

Incentive Spirometry (FIS) group (n=33), the Deep Breathing (DB) group (n=35), and the Volume Incentive Spirometry (VIS) group (n=34), received three different lung expansion techniques. All the techniques were carried out in 5 series of 10 repetitions, with a total of 50 repetitions in one session, with 30 seconds of rest between each series. An initial series was achieved before every session in order to determine the target intensity. Then, patients were asked to take breaths as deeply as possible to reach the targeted intensity for at least 5 seconds. All interventions were performed in a seated position. Before every session, the pain level was evaluated by a visual numeric scale in order to achieve best performance during every exercise. If the pain intensity was 3 points and more, a second level of analgesics was required in accordance with World Health Organisation guidelines. The DB technique was performed by asking patients in this group to take deep breaths close to total lung capacity. The lung expansion techniques were performed from the 1st to the 5th postoperative day.

5. In Kumar, et al. (130), the FIS group (n=25) received flow incentive spirometry, and the VIS (n=25) group received volume incentive spirometry. The interventions consisted of three series of five repetitions, which were performed four times a day for five postoperative days. Patients were asked to lie at 45° to the horizontal position with a pillow under the knees during the interventions. Patients were also taught how to perform the exercise in order to repeat the same manoeuvre once every waking hour.

2.4.1.3 Type of outcome measures:

1. Mackay, et al. (128) assessed the incidence of PPCs based on when three or more of the respiratory signs occurred within 14 days. The signs of PPCs were changes on breath sound e.g. crackles or wheezes, body temperature over 38°, increase in amount and/or changes in colour of sputum and changes in chest X-ray e.g. consolidation or atelectasis. Length of hospital stay was also measured in this study as secondary outcome.

2. In Manzano, et al. (122), oxygen-haemoglobin saturation was the primary outcome and pain during chest physiotherapy and pulmonary function were secondary outcomes. All patients were assessed preoperatively and postoperatively, on the 2nd postoperative day. Perioperative assessment consists of anamnesis, physical examination, pulse oximetry and pulmonary function test. These assessments were performed in order to evaluate postoperative SpO_2, pulmonary function including Forced Vital Capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, peak expiratory flow (PEF), and Visual Analog Pain Scale (VAPS).

3. Forti, et al. (129) measured pulmonary function as primary outcome and respiratory muscle strength as secondary outcome. The participants were evaluated three times during the study in order to assess pulmonary function and respiratory muscle strength. The first evaluation was done preoperatively whereas the second evaluation was on the 15th postoperative day and the third evaluation

on the 30th postoperative day. Pulmonary function was evaluated by measuring FVC, FEV, FEV_1/FVC ratio, PEF, Vital Capacity (VC), Slow Vital Capacity (SVC) and Maximum Voluntary Ventilation (MVV). Maximum inspiratory pressure (MIP) and Maximal Expiratory Pressure (MEP) were evaluated in order to measure the respiratory muscle strength.

4. Lunardi, et al. (123) assessed the incidence of PPCs as primary outcome and length of hospital stay as secondary outcome. PPCs incidence was based on the physician's diagnosis of presence of atelectasis, acute respiratory distress syndrome, pneumonia and hypoxemia with SpO_2 <85% with the need of supplemental oxygen.

5. Kumar, et al. (130) measured pulmonary function as primary outcome. Pulmonary function was evaluated by measuring FVC, FEV_1 and PEF. These measurements were taken before the surgery and repeated on every postoperative day until the 5th postoperative day.

Table 2. 4 Characteristics of the included studies

Study	Participants	Study groups and interventions	Outcomes
Mackay, et al. (128) RCT	- N: 50 patients. - M (F): 25 (25). - Mean age, years: 69 for non-DB&C group, 63 for DB&C group	- Non-DB&C group (n= 21): standard care with no respiratory physiotherapy. - DB&C group (n= 29): deep breathing and coughing exercises.	- Incidence of PPCs - Length of hospital stay
Manzano, et al. (122) RCT	- N: 31 patients. - M (F): 10 (21). - Mean age, years: 50.9 for CG, 52 for CPT group.	- Control group (n=16): No chest physiotherapy - Chest physiotherapy group (n=15): immediate postoperative chest physiotherapy for 30 minutes.	- Incidence of PPCs (Oxygen saturation SpO_2) - PFT (FVC, FEV_1, FEV_1/FVC ratio and PEF) - Pain intensity (VAPS)
Forti, et al. (129) RCT	- N: 44 obese patients. - M (F): (44) - Mean age, years: 37 for CCP, 37 for CCP+TEDS *	- CCP group (n=22): conventional chest physiotherapy exercises. - CCP+TEDS group (n=22): conventional chest physiotherapy exercises plus TEDS.	- PFT (FVC, FEV_1, FEV_1/FVC ratio, PEF, VC, SVC, FVC, and MVV) - Respiratory muscle strength (MIP and MEP)
Lunardi, et al. (123) RCT	- N:137 patients. - M (F): 59 (78) - Mean age, years: 57 for CG, 62 for FIS, 58 for DB, 55 for VIS	- Control group (n=35): no intervention. - FIS group (n=33): flow incentive spirometry. - DB group (n=35): deep breathing exercises. - VIS group (n=34): volume incentive spirometry	- Incidence of PPCs - Length of hospital stay
Kumar, et al. (130) RCT	- N: 50 patients - M (F): 37 (13) - Mean age, years: 59 for FIS, 53 for VIS	- FIS group (n=25): flow incentive spirometry. - VIS group (n=25): volume incentive spirometry	- PFT (FVC, FEV_1 and PEF)

DB: Deep Breathing, DB&C: Deep Breathing and Coughing, F: Female, FEV_1: Forced Expiratory Volume in one second, FIS: Flow Incentive Spirometry, FVC: Forced Vital Capacity, M: Male, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, MVV: Maximum Voluntary Ventilation, N: Number of patients, Non-DB&C: Non-Deep Breathing and Coughing, PEF: Peak Expiratory Flow, PFT: Pulmonary Function Test, PPCs: Postoperative Pulmonary Complications, RCT: Randomised Controlled Trials, SpO_2: Peripheral capillary Oxygen Saturation, SVC: Slow Vital Capacity, TEDS: Transcutaneous Electrical Diaphragmatic Stimulation, VAPS: Visual Analog Pain Scale, VC: Vital Capacity, VIS: Volume Incentive Spirometry.

2.4.2 Risk of bias assessment

The results of risk of bias assessment are reported below and are summarised in table 2.5.

2.4.2.1 Allocation:

Random sequence generation was done correctly and reported in Manzano, et al. (122), Mackay, et al. (128), Forti, et al. (129) and Kumar, et al. (130), which were therefore graded at a low risk of bias for this domain. Methods of randomisation for each study were as follows: in Mackay, et al. (128) by random number table; in Manzano, et al. (122) by means of selection according to a randomisation table; in Forti, et al. (129) by drawing lots; and in Kumar, et al. (130) by block randomisation. Only the study by Lunardi, et al. (123) was ranked at an unclear risk of bias, as there was no information reported about randomisation. Allocation concealment was done in Mackay, et al. (128) and Forti, et al. (129), which were therefore ranked at a low risk of bias. The other studies Mackay, et al. (128), Lunardi, et al. (123), and Kumar, et al. (130) did not mention any information regarding allocation concealment, and therefore, they were graded at unclear risk of bias.

2.4.2.2 Blinding:

Three studies (123, 128, 129) reported the process of blinding, and therefore, they were ranked at a low risk of bias. The study by Manzano, et al. (122) did not report whether blinding was conducted for personnel, patients, or outcome assessors and was therefore ranked at an unclear risk of bias. Only one study (130) was ranked at a high risk bias, as there was no blinding for either patients or outcome assessors.

2.4.2.3 Incomplete outcome data:

All studies were considered a low risk of bias as there were no drop outs in 3 studies and in the other 2, the dropout rates were below 20%.

2.4.2.4 Selective reporting:

All the included studies (122, 123, 128-130) were ranked at a low risk of bias, as there was no evidence of selective reporting.

2.4.2.5 Other source of bias:

No other source of bias was identified in any of the included studies and were ranked at a low risk of bias except the study by Kumar, et al. (130) was ranked at a high risk of bias. Kumar, et al. (130) included only obese females, which raises a gender bias.

Table 2. 5 Results of risk of bias assessment

Mackay, et al. (128)		
Bias	**Authors' judgment**	**Support of judgment**
Random sequence generation	Low risk	Random number table.
Allocation concealment	Low risk	Patients and outcome assessor were concealed.
Blinding of participants and personnel	Low risk	Patients were blinded.
Blinding of outcome assessment	Low risk	Outcome assessor was blinded.
Incomplete outcome data	Low risk	Dropout < 20% of sample size.
Selective outcome reporting	Low risk	All outcomes were reported.
Other bias	None	None
Manzano, et al. (122)		
Bias	**Authors' judgment**	**Support of judgment**
Random sequence generation	Low risk	Quote: "The participants were allocated into two groups (control and chest physiotherapy) by means of a draw according to a randomisation table. "
Allocation concealment	Unclear	No information provided.
Blinding of participants and personnel	Unclear	No information provided.
Blinding of outcome assessment	Unclear	No information provided.
Incomplete outcome data	Low risk	All participants completed the intended intervention.
Selective outcome reporting	Low risk	All outcomes were reported.
Other bias	None	None
Forti, et al. (129)		
Bias	**Authors' judgment**	**Support of judgment**
Random sequence generation	Low risk	Randomisation by drawing lots.
Allocation concealment	Low risk	Patients and outcome assessor were concealed.
Blinding of participants and personnel	Low risk	Patients were blinded.
Blinding of outcome assessment	Low risk	Outcome assessor was blinded.
Incomplete outcome data	Low risk	All participants completed the intended intervention.
Selective outcome reporting	Low risk	All outcomes were reported.
Other bias	High risk	Gender bias (only female gender included).

Lunardi, et al. (123)		
Bias	**Authors' judgment**	**Support of judgment**
Random sequence generation	Unclear	No information was provided.
Allocation concealment	Unclear	No information was provided.
Blinding of participants and personnel	Unclear	No information was provided.
Blinding of outcome assessment	Low risk	Blinded outcome assessors
Incomplete outcome data	Low risk	Dropout < 20% of sample size.
Selective outcome reporting	Low risk	All outcomes were reported.
Other bias	None	None
Kumar, et al. (130)		
Bias	**Authors' judgment**	**Support of judgment**
Random sequence generation	Low risk	Block randomisation.
Allocation concealment	Unclear	No information was provided.
Blinding of participants and personnel	High risk	No blinding.
Blinding of outcome assessment	High risk	No blinding.
Incomplete outcome data	Low risk	All participants completed the intended intervention.
Selective outcome reporting	Low risk	All outcomes were reported.
Other bias	None	None

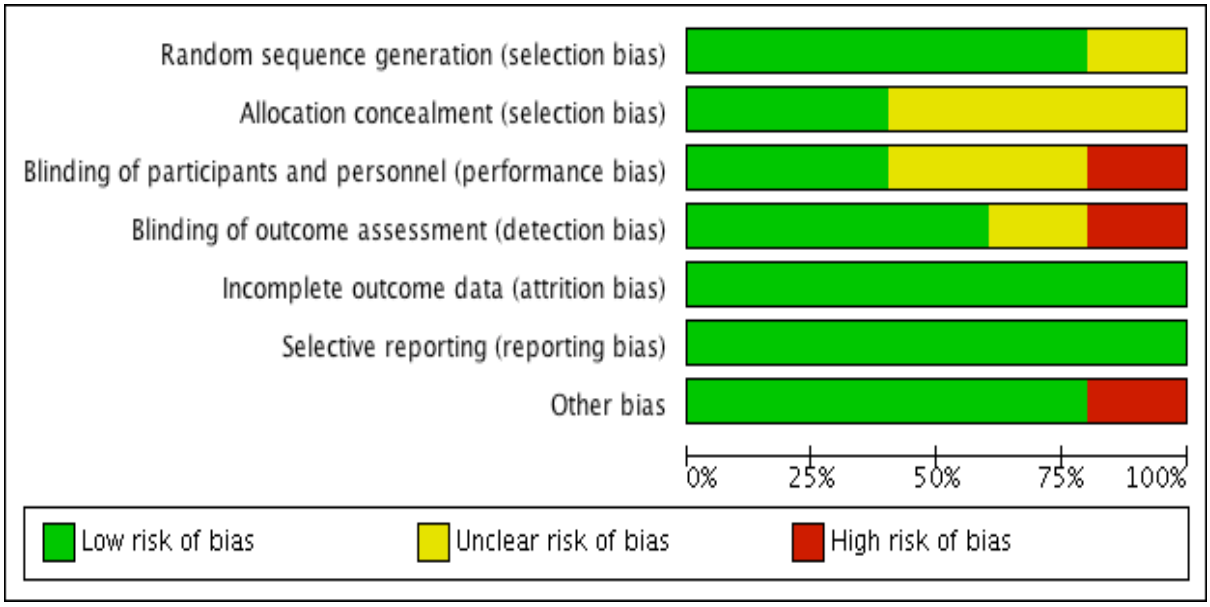

Figure 2. 2 Risk of bias graph demonstrates the percentage of risk of bias of the included studies in each domain

The percentage of studies ranked at a low risk of bias: 100% in incomplete outcome data and selective reporting domains; 80% in the random sequence generation and other bias (gender bias) domains; 40% in allocation concealment and blinding of participants domains; and 60% in blinding of the outcome assessment domain.

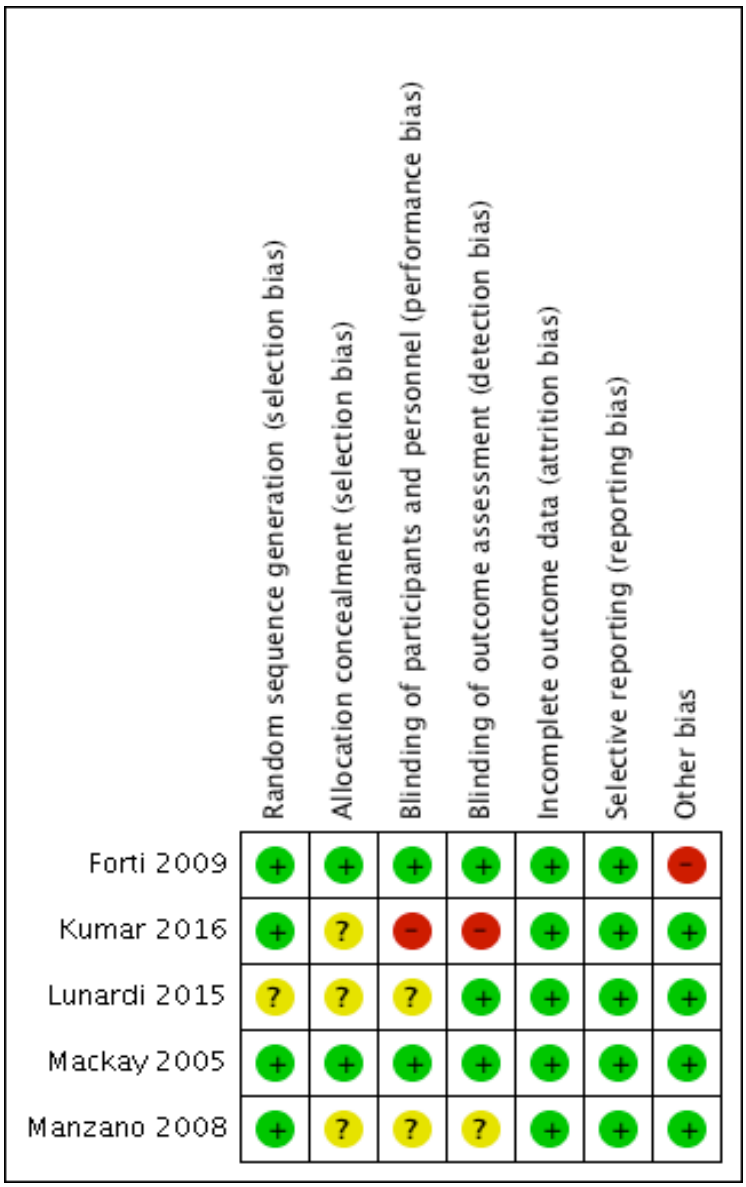

Figure 2. 3 Risk of bias summary

The figure highlights the level of bias (low +; unclear ?; high -) of the studies in each domain.

2.4.3 Excluded studies

We excluded ten studies that did not fulfil inclusion criteria. Reasons for exclusion are listed in the below table 2.6.

Table 2. 6 List of the excluded studies

Study	Reason(s) for exclusion
Westwood, et al. (131)	- Not RCT. - Population: abdominal and thoracic surgeries.
Forgiarini Junior, et al. (132)	- No specific physical therapy technique or respiratory physiotherapy was used.
Lunardi, et al. (133)	- Not RCT.
Ferreyra, et al. (134)	- Critical analysis paper (no full text is available). - No English language version.
Casimire, et al. (135)	- Abstract (no full text is available).
Krishna, et al. (136)	- Laparoscopic minor surgeries.
Silva, et al. (137)	- The comparison was mainly between early and delayed mobilisation not respiratory physiotherapy.
Lunardi, et al. (138)	- Preliminary result no full-text article was found.
Possa, et al. (139)	- Not RCT (before and after study design) to evaluate the implementation of physical therapy guidelines.
Syropoulos, et al. (140)	- No English language version.

RCT: Randomised Control Trial

2.4.4 Primary outcome

The results of the included studies are summarised below in table 2.7.

2.4.4.1 Incidence of PPCs:

Three studies, with a total of 218 participants, assessed the incidence of PPCs after abdominal surgery using different postoperative respiratory physiotherapy techniques (122, 123, 128). Assessment of the primary outcome was based on the defined criteria of PPCs and/or physician diagnosis. Mackay, et al. (128) showed no difference in PPCs incidence between DB&C and standard care (DB&C: 5 (17%); Non-DB&C: 3 (14%); p=0.62). However, Manzano, et al. (122) demonstrated that chest physiotherapy can significantly reduce post-operative hypoxia as measured by SpO_2 (SpO_2 before chest physiotherapy: 93$\pm$4.3 vs. SpO_2 after chest physiotherapy: 96$\pm$2.6; p=0.02). Lunardi, et al. (123) results suggested that PPCs incidence was in fact higher in the lung expansion techniques groups whereas no patient in the control group developed any PPCs (CG=0; in FIS=3; DB=8; VIS=3; p=0.02). Therefore, the routine use of tested lung expansion techniques was not recommended by them.

2.4.5 Secondary outcomes

2.4.5.1 Pulmonary function:

Three studies, with a total of 125 participants, investigated different variables of pulmonary function test that were measured preoperatively and postoperatively (122, 129, 130). The results of Manzano, et al. (122) showed no statistical difference between the chest physiotherapy and control groups. Therefore, chest physiotherapy did not improve pulmonary function after major abdominal surgery. The results of Forti, et al. (129) showed

no significant difference between the CCP and CCP+TEDS groups regarding preoperative and postoperative measurements of pulmonary function. Therefore, CCP alone or with TEDS can prevent the reduction of pulmonary function after Roux-en-Y gastric bypass surgery. Kumar, et al. (130) found no significant difference between the preoperative and the 5th postoperative day measurements for both flow IS and volume IS groups. Therefore, flow IS and volume IS were effective in improving pulmonary function postoperatively.

2.4.5.2 Respiratory muscle strength:

One study, involving 44 obese female patients, reported the effectiveness of respiratory physiotherapy on respiratory muscle strength after abdominal surgery (129). Forti, et al. (129) found that CCP was able to maintain only postoperative inspiratory muscle strength whilst CCP+ TEDS improved both inspiratory and expiratory muscle strength.

2.4.5.3 Pain intensity:

(122) evaluated pain before and after surgery and chest physiotherapy and showed no difference in pain scores seen suggesting that chest physiotherapy was well tolerated with no adverse pain-related outcomes.

2.4.5.4 Length of stay:

Two studies reported length of postoperative hospital stay with conflicting results (123). Mackay, et al. (128) showed a reduction in length of hospital stay in the DB&C group whilst (123) showed no difference in length of stay between the control and lung expansion groups.

Table 2. 7 Summary of the results of the included studies

Study	Comparison	Outcome	Results
Mackay, et al. (128)	DB&C vs. Control	-PPCs -LOS	-Low PPCs in both groups -LOS in DB&C group < control group *
Manzano, et al. (122)	Pre-CPT vs. post-CPT CPT vs. Control	-SpO_2 -PFT -VAPS	- SpO_2 pre-CPT< post-CPT * -No difference in PFT between groups -No difference in VAPS between groups -No difference in VAPS between pre- and post-op CPT
Forti, et al. (129)	CCP+TEDS vs. CCP	-PFT -MIP and MEP	-No difference in PFT between groups -CPT improves only MIP -CCP+TEDS improve both MIP and MEP
Lunardi, et al. (123)	DB vs. FIS vs. VIS vs. Control	-PPCs -LOS	-PPCs are significantly lower in control group (routine use of lung expansion techniques not recommended). * -LOS slightly higher in intervention groups (no statistical difference)
Kumar, et al. (130)	FIS vs. VIS	-PFT	-Improvement in PFT each postop day -No difference between preoperative and 5^{th} postoperative day

* Statistically significant

CPT: Chest Physiotherapy, DB: Deep Breathing, DB&C: Deep Breathing and Coughing, FIS: Flow Incentive Spirometry, LOS: Length of Stay, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, PFT: Pulmonary Function Test, PPCs: Postoperative Pulmonary Complications, SpO_2: Peripheral capillary Oxygen Saturation, TEDS: Transcutaneous Electrical Diaphragmatic Stimulation, VAPS: Visual Analog Pain Scale, VIS: Volume Incentive Spirometry.

2.4.6 Treatment effect

It was not possible to include all the studies in meta-analysis due to variations in interventions and outcomes. Thus, only two studies (123, 128) were included in the quantitative analysis that compared the treatment effect of DB vs. the control group on PPCs incidence and length of hospital stay.

2.4.6.1 PPCs incidence

Two studies (123, 128), involving 120 participants, focused on the outcome 'PPCs incidence'. Pooled analysis showed that DB was associated with an increased risk of developing PPCs compared with the control group, with no respiratory physiotherapy interventions, however, this was with no statistical significance (RR= 3.34; CI 0.27 to 41.63; P= 0.35; I^2 statistics= 64%). A large degree of heterogeneity with wide CI was noted, which indicates the inconsistency and imprecision of the treatment effect (Figure 2.4).

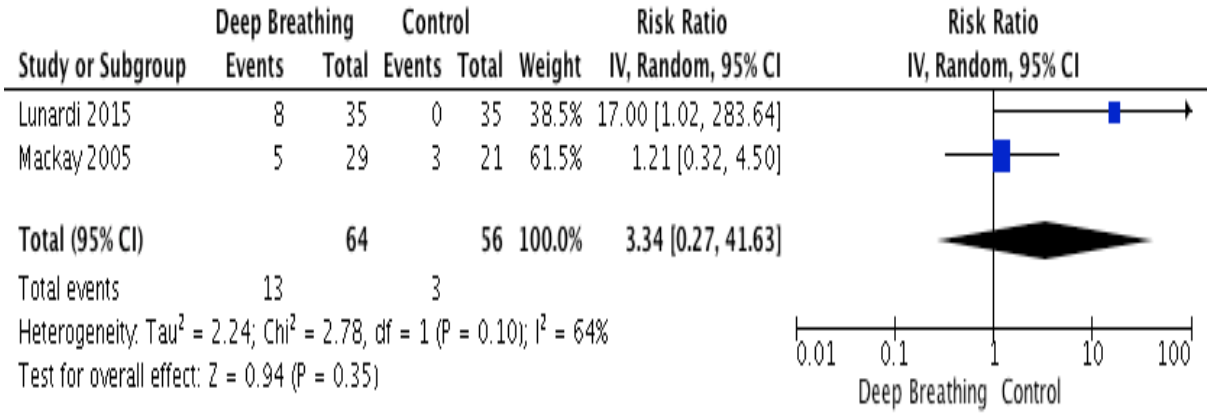

Figure 2. 4 Forest plot of comparison: DB vs Control, outcome: PPCs incidence

CI: Confidence Interval, DB: Deep Breathing, PPCs: Postoperative Pulmonary Complications

2.4.6.2 Length of hospital stay

Two studies (123, 128), involving 120 participants, focused on the outcome 'length of hospital stay'. Pooled analysis showed that DB was associated with reduced length of hospital stay compared with the control group; however, this was with no statistical significance (Mean Difference= -0.61; CI -5.49 to 4.27; P= 0.81; I^2 statistics= 81%). Although the CI was narrow, a large degree of heterogeneity was noted, which also indicates the inconsistency and imprecision of the treatment effect (Figure 2.5).

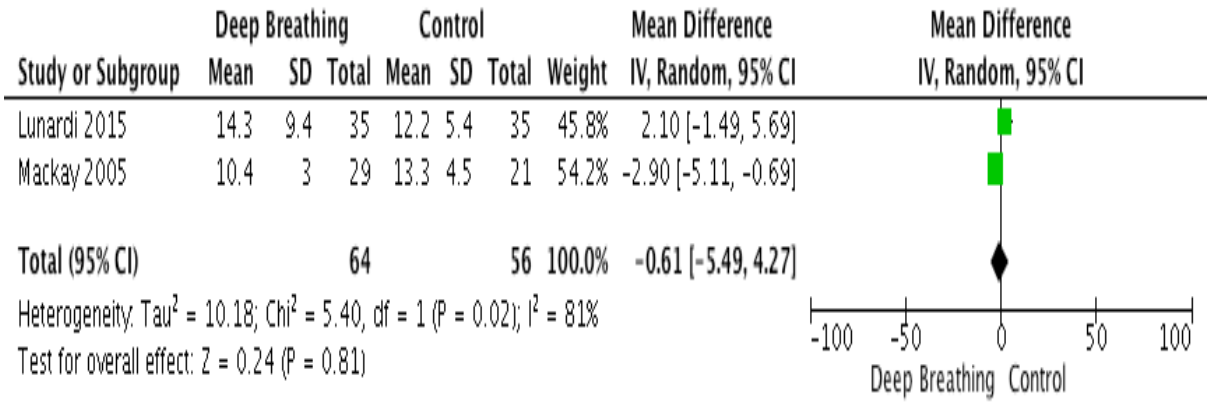

Figure 2. 5 Forest plot of comparison: DB vs Control, outcome: Length of hospital stay

CI: Confidence Interval, DB: Deep Breathing, LOS: Length of Stay

2.4.7 Confidence in cumulative evidence

The overall quality of evidence was assessed based on the GRADE approach for the outcome incidence of PPCs incidence. There was no need for downgrading in the study design item, as all the included studies are RCTs. In addition, there was no need for downgrading in the risk of bias item, as most of the information from the included studies was at a low or an unclear risk of bias, and so was unlikely to alter the results. The inconsistency item was downgraded by two points due to the substantial heterogeneity between the included studies (I^2= 64%). There was no need for downgrading in the indirectness item, as indirectness in the included studies does not appear to be an issue. The imprecision item was downgraded by one point due to the wide confidence interval and the small number of participants (n= 120 participants) in the included studies. Publication bias was not downgraded, as no publication bias was detected. As a result of the GRADE assessment, the overall quality of evidence was graded at a very low level (Appendix 2).

2.5 Discussion

Patients who undergo major abdominal surgeries are at risk of PPCs due to the disruption of the respiratory muscles, normal respiration and infection (141). Respiratory physiotherapy, including lung expansion techniques, is frequently used in postoperative settings in order to help restore normal respiratory function, with the aim of preventing PPCs. The rationale for these techniques is to overcome hypoventilation, hypoxia and to strengthen the respiratory muscles (77). The present review provided a very low quality of evidence about the effectiveness of respiratory physiotherapy in minimising the PPCs after major abdominal surgery. The respiratory physiotherapy modalities assessed in the included studies were applied differently. This variation in practice could be due to the lack of any gold standard postoperative respiratory physiotherapy strategy that would reduce the incidence of PPCs and improve pulmonary function.

The primary outcome, incidence of PPCs was addressed by only three studies (122, 123, 128). Mackay, et al. (128) and Lunardi, et al. (123) failed to prove the benefits of lung expansion techniques, including BD, FIS, and VIS, in reducing the incidence of PPCs. Mackay, et al. (128) and Lunardi, et al. (123) suggested that lung expansion techniques should not be used routinely, as there was no significant difference between the intervention and the control groups in terms of PPCs reduction. However, the validity of their results is questionable, as in both studies, the control group had received other interventions that may reduce PPCs incidence. Mackay, et al. (128) used early mobilisation, which was standard care, to the two groups, and this could help in improving pulmonary function and PPCs reduction. The control group in Lunardi, et al. (123) were asked to take deep breaths in order to measure the

thoracoabdominal mechanics and lung volume. As a result, deep breathing during thoracoabdominal mechanics assessment could participate in the prevention of PPCs in the control group. In addition, the results of the meta-analysis provided inconsistent and imprecise results about the effectiveness of DB in comparison with the control group, owing to the high degree of heterogeneity. However , the review found that lung expansion techniques can improve pulmonary function based on the results of (130). However, the results are prone to a high risk of bias due to lack of blinding in the trial by Kumar, et al. (130), which could affect the reliability of the results.

The review found that chest physiotherapy exercises significantly improve postoperative hypoxia without increasing pain intensity, which might increase with chest physiotherapy (122). Manzano, et al. (122) did not directly assess the incidence of PPCs, however, used postoperative oxygen saturation (SpO_2) as a surrogate outcome measure to assess incidence of PPCs. However, Manzano, et al. (122) failed to statistically compare the differences in postoperative SpO_2 between the chest physiotherapy group and the control group. Chest physiotherapy was also associated with the improvement of pulmonary function and respiratory muscle strength, especially with the addition of TEDS (129).

The small number of studies and the lack of robust methodology of the included studies made it difficult to draw a clear conclusion in this review. Thus, our results are consistent with those of previous systematic reviews that showed a lack of evidence about the benefits of different modalities (98, 120, 127). In the review by Pasquina, et al. (127), a few studies supported the effectiveness of respiratory physiotherapy in minimising PPCs after abdominal surgery while another review by Grams, et al. (98) showed only a slight benefit of deep breathing exercises

on muscle strength. However, Grams, et al. (98) included studies that were poorly conducted where their interventions were applied pre- and post-operatively. Grams, et al. (98) also could not draw a clear conclusion about the usefulness of postoperative deep breathing exercises due to the lack of good quality evidence. Junior, et al. (120) documented that incentive spirometry has no benefits in PPCs avoidance compared with no respiratory physiotherapy or other modalities, such as deep breathing exercises. The present review has attempted to assess all recent trials conducted in the effectiveness of postoperative respiratory physiotherapy to minimise incidence of PPCs and improving pulmonary function. However, the present review agrees with previous systematic reviews that there are few studies in this field in addition to there being variability in applying these modalities due to the lack of any gold standard technique.

A few limitations should be taken into account when reading the results of this review. The review included only RCTs published after 2000 as earlier studies had already been assessed in those previous systematic reviews, which showed a low quality of evidence (120, 127). We excluded one recent trial (140), as an English version was not available. Finally, our results are not conclusive, as we were able to include only five studies in the qualitative synthesis and two studies in the meta-analysis. This was due to the lack of available evidence in this subject.

Consequently, there is an urgent need for good quality research that assesses different postoperative respiratory physiotherapy modalities. Future research should address the effectiveness of postoperative respiratory physiotherapy modalities in minimising PPCs incidence. Such research can help to identify the most effective modalities in order to develop

a gold standard postoperative respiratory physiotherapy strategy that reduces the incidence of PPCs and improves postoperative outcomes after major abdominal surgery.

2.6 Conclusion

The present review could not draw any conclusive results due to the lack of good quality evidence about the effectiveness of postoperative respiratory physiotherapy for minimising PPCs after major abdominal surgery. Lung expansion techniques and chest physiotherapy seem to improve pulmonary function and respiratory muscle strength. The addition of TEDS to chest physiotherapy after major abdominal surgery could be beneficial in improving respiratory muscle strength. No specific modality or technique was shown to be superior to other techniques in reducing PPCs. The literature is lacking in this subject; thus, good quality research is needed in future in order to develop a gold standard strategy that helps in PPCs reduction after major abdominal surgery.

Chapter Three

Postoperative Pulmonary Complications following major Hepato-Pancreatic-Biliary Surgery: A prospective observational study at a large tertiary centre

Abstract

Introduction: Postoperative Pulmonary Complications (PPCs) are common following major abdominal surgery. PPCs are associated with increased morbidity, mortality and length of stay. However, incidence of PPCs is still under-reported and needs further investigation in order to improve the quality of perioperative practice.

Aim: To measure incidence and severity of PPCs following major Hepato-Pancreatic-Biliary (HPB) surgery.

Methods: Patient who underwent major HPB surgery at QEHB and who had been enrolled in the Perioperative Quality Improvement Programme (PQIP) study between May 2018 and May 2019 were included. PQIP is a prospective observational study of patients undergoing major surgery. The primary outcome was the incidence of PPCs at day 7 measured by the Postoperative Morbidity Survey (POMS), with severity of the PPCs determined using the StEP-COMPAC group's definitions. Secondary outcomes were length of stay (LOS) and 30-day mortality. Data analysis was performed using Man-Whitney U test for continuous variables and Chi-Square test for categorical variables.

Results: A total of 145 patients were enrolled in the study with 89 (61.4%) males and 56 (38.6%) females. The median (IQR) age of the patients was 66 (57.5-73) years with most patients classified as ASA grade II (61.3%) or III (38%). The majority of HPB surgery was open (n=130; 89.6%). Based on POMS, PPCs occurred in 18.6% (n=27) of patients. The majority of patients developed PPCs on day of surgery and day 1 postoperatively (n=8; 30%). Atelectasis

was the commonest PPCs (67%), followed by pleural effusion (15%) and pneumonia (11%). Patients who developed a PPC were significantly older (70 (IQR: 64-77) years vs. (65 (IQR 56-72) years, p=0.027). There were no other preoperative differences between the two groups. The majority of PPCs were mild (n=24; 88.9%) requiring only supplemental oxygen, with only 3 patients (11.1%) developing severe PPCs that required ventilatory support. The development of a PPC was associated with a significantly longer LOS (14 (IQR: 9-23) days vs. 6 (IQR: 5-7) days; $p < 0.001$) and higher chance of infectious complications (14 vs 4; $p<0.001$).

Conclusion: This study has shown that using POMS and the StEP-COMPAC group's definitions that PPCs are extremely common following major HPB surgery and that the development of even mild PPCs has a significant impact on patient morbidity and LOS. The use of PQIP has helped to identify major morbidities and risk factors associated with PPCs. Future interventions should focus on reducing PPCs, with interventions targeted perioperatively.

3.1 Introduction

Quality improvement is essential in healthcare where everyone, clinicians, patients and their families, researchers and educators, participate to improve healthcare system and patient outcomes (142). Perioperative Quality Improvement Programme (PQIP) is a national project in the United Kingdom and is led by the National Institute for Academic Anaesthesia's Health Services Research Centre (NIAA-HSRC), based at the Royal College of Anaesthetists (RCoA) (143). PQIP aims to measure complications, patient outcomes and patient-reported outcomes after major surgery in order to improve perioperative practice.

As described in Chapter 1.2, Postoperative Pulmonary Complications (PPCs) are common following abdominal surgery, their incidence ranging from 4.7% to 22.5% (Table 1.8) (12, 19-22). PPCs are associated with increased morbidity, mortality and length of stay following abdominal surgery (12). The variation in the incidence of PPCs was due to different methodology and definitions of PPCs used in the previous studies. Therefore, PPCs following abdominal surgery need further investigation in terms of investigating the impact of PPCs and identifying the modifiable risk factors, which may contribute to a reduction in PPCs incidence and an improvement in the current perioperative practice (12). In this study, PQIP used the Postoperative Morbidity Survey (POMS) to describe morbidity at day-7 following major abdominal surgery (4). POMS measures postoperative complications based on diagnostic items in 9 domains, including pulmonary, infection, gastrointestinal, renal, cardiovascular, neurological, haematological, wound and pain (Table 1.2) (144).

Identifying modifiable risk factors associated with PPCs, such as smoking, anaemia, respiratory symptoms and pre-existing cardiovascular and respiratory diseases, play a crucial role in avoiding PPCs (2). Other intraoperative and postoperative interventions such as respiratory physiotherapy, are considered within current practice to reduce PPCs (97). However, in Chapter two, the systematic review and meta-analysis showed insufficient evidence available in regard with postoperative respiratory physiotherapy techniques used to decrease PPCs. Currently, there is no gold stander intervention targeting PPCs where PPCs are managed based on the severity of PPCs.

Patients with PPCs may require therapeutic supplemental oxygen or non-invasive or invasive mechanical ventilation depending on the severity of PPCs (9). The Standardised Endpoints for Perioperative Medicine (StEP) group and the Core Outcomes Measures in Perioperative and Anaesthetic Care (COMPAC) initiative have recently defined the severity of PPCs (Table 1.6) (9). According to the StEP-COMPAC group (9), severity of PPCs is classified as follow, none: Planned supplemental oxygen or mechanical ventilation with in routine practice; mild: therapeutic supplemental oxygen < 0.6 FiO_2; moderate: therapeutic supplemental oxygen <= 0.6 FiO_2; severe: unplanned non-invasive or invasive mechanical ventilation.

Using PQIP, this study attempted to quantify the incidence of PPCs alongside with measuring risk factors, impact and severity of PPCs following hepato-pancreatic-biliary (HPB). Consequently, this study would provide better understanding about perioperative interventions required to decrease incidence, impact and severity of PPCs in this population.

3.2 Aim and objectives

3.2.1 Aim

- To measure incidence and severity of PPCs following major HPB surgery.

3.2.2 Objectives

- To measure incidence and impact of PPCs using POMS at day 7
- To assess severity of PPCs based on StEP-COMPAC definition of severity of PPCs
- To assess factors that contribute in development of PPCs
- To assess the effect of PPCs on the quality of recovery and patients-reported outcomes

3.3 Methods

This study was conducted through PQIP where more than 70 hospitals are participating in PQIP. PQIP methodology was used in this study and described in detail in this section.

3.3.1 Study design

Prospective observational study using cohort study design was used in this study.

3.3.2 Setting

The study was conducted at Queen Elizabeth Hospital Birmingham (QEHB) which is one of the largest hospitals in the United Kingdom with over 1000 beds. QEHB is a national centre for liver, heart and lung transplantation and is one of the largest HPB surgery centre in the United Kingdom (145).

3.3.3 Ethical considerations

Health Research Authority (HRA) approval was given to University College London (UCL) for the PQIP (Regional Ethics Committee reference: 16/LO/1827). Local Research and Development (R&D) approval was also sought from the QEHB.

All data were collected, stored and processed according to Data Protection Act 1998. All data were entered into electronic data collection form on PQIP website and held on servers managed by UK fast on behalf of RCoA. Raw data were exported from PQIP website to local

site's hard disc as excel document, which was then protected by password. All personal data were kept anonymous where only study team had access to the data.

3.3.4 Recruitment

Patients were recruited from May 2018 to May 2019. Eligible patients were invited to participate and handed Patients Information Sheet (PIS) (Appendix 3) when they attended the pre-assessment clinic. Patients were approached 24-hours prior to the day of surgery to be consented (Appendix 4) and enrolled within the study. This ensured patients had had adequate time to read and understand the information related to the study.

3.3.5 Eligibility criteria

Only patients undergoing major HPB surgery were included this study due to the nature of the procedures which is major surgery and high number of patients attending at the QEHB for HPB surgery. Major HPB surgery is defined as surgery that last more than two hours and/or with anticipated blood lose ≥500 ml. Inclusion and exclusion criteria is described in Table 3.1.

Table 3. 1 Eligibility criteria

Inclusion criteria	**Exclusion criteria**
- Adult patients aged 18 years old and older - Only patients undergoing major HPB surgery that last 2 hours and more - Patients who are able to consent and understand English language	- Patients younger than 18 years old - Patients undergoing minor HPB surgery that last less than 2 hours - Patients who are not able to consent or understand English language - Patients who were already participated in PQIP in another site

HPB: hepato-pancreatic-biliary, PQIP: Perioperative Quality Improvement Programme

3.3.6 Data collection

All data were collected using PQIP data collection form (Appendix 5). Data collection started before operation and finished on discharge, death or withdrawal. Pre-operative clinical data and pre-operative Quality of Recovery (QoR15) questionnaire, were collected on admission before the surgery. Intra-operative data were collected from hospital system and patient's note after the surgery. Recovery data were collected postoperative in the recovery room. Postoperative data and questionnaire were collected on 1st, 3rd and 7th day after the operation in addition to the discharge or death data.

3.3.7 Outcomes

3.3.7.1 Primary outcome

Primary outcome was the incidence and severity of PPCs at day 7 after the operation. Primary outcome, the incidence of PPCs, and other morbidities including infection, gastrointestinal, renal, cardiovascular, neurological, haematological, wound and pain, were assessed by POMS at day 7. POMS was used to define PPCs in this study as most of common morbidities, including PPCs, are considered within the definition to present the overall morbidities at day seven after major abdominal surgery. The specific PPCs form was defined based on physician's diagnosis and chest radiography report. The definitions for the nine domains of postoperative morbidities are listed in table 3.2. POMS is a valid and reliable tool to assess postoperative morbidities (144). Severity of PPCs was classified based on StEP-COMPAC group's definition of PPCs severity (9) (Table 3.3). StEP-COMPAC definition considers PPCs as none when patients receive planned or routine supplemental oxygen which ensure PPCs is severe enough to require supplemental oxygen at day seven after surgery.

Table 3. 2 Postoperative Morbidity Survey (POMS) definition (3)

Morbidity	Definition
Pulmonary	Patient has developed a new requirement for oxygen and/ or respiratory support
Infection	Patient is currently on IV antibiotics and/ or had temperature over 38˚C in the past 24 hours
Gastrointestinal	Patient is unable to tolerate enteral diet (oral or tube feeding) and/ or experienced nausea, vomiting or abdominal distention in the past 24 hours
Renal	Patient had any of the following in the past 24 hours: Oliguria (urine output less than 50ml), serum creatinine level increased by 30% preoperative level and urethral catheter in-situ not present in preoperatively
Cardiovascular	Patient had diagnostic test or therapy for any of the following in the past 24 hours: Hypotension requiring more 200ml fluid bolus or pharmacological therapy, new myocardial infarction or ischaemia, thrombotic event requiring anticoagulation, arrhythmias and cardiogenic pulmonary oedema
Neurological	Patient developed any of the following in the past 24 hours: new neurological deficit, delirium or confusion, sedative-induced coma and non-sedative associated coma
Wound	Patient had wound dehiscence requiring surgical exploration and/ or had drainage of pus from the operative wound, wound ooze or a swab taken
Haematology	Patient had required red cell transfusion, fresh frozen plasma, cryoprecipitate or platelets in the past 24 hours
Pain	Patient developed significant pain that requires parenteral opioids and/ or regional anaesthetics

The definitions of postoperative morbidities are based on patient's status on day 7 postoperatively.
IV: intravenous, ml: millilitre.

Table 3. 3 StEP-COMPAC definition of PPCs severity (11)

Severity	Definition
None	Planned use of supplemental oxygen or mechanical respiratory support as part of routine care
Mild	Therapeutic supplemental oxygen <0.6 FiO_2
Moderate	Therapeutic supplemental oxygen ≥0.6 FiO_2
Severe	Unplanned non-invasive mechanical ventilation, CPAP, or invasive mechanical ventilation requiring tracheal intubation

CPAP: Continuous Positive Airway Pressure, FiO_2: Fraction of Inspired Oxygen, PPCs: Postoperative Pulmonary Complications

3.3.7.2 Secondary outcomes

Secondary outcomes included risk factors and morbidities associated with PPCs, 30-days mortality, quality of recovery and length of postoperative stay. Quality of recovery was assessed by pain level and DrEaMing (Drinking, Eating and Mobilising) at day 1 postoperatively. DrEaMing assesses the proportion of patients that are drinking, eating and mobilising after 1st postoperative day (146). Quality of recovery was also assessed by patient-reported outcomes, QoR15 on admission and 3rd postoperative day (Appendix 6). QoR15 has two parts of questions assessing patient-reported outcomes. First part is asking how patient been feeling at home in the weeks before the operation (preoperative questionnaire) and how patient been feeling since the operation (3rd postoperative day questionnaire). This part has 10 questions about ability to breathe easily, enjoying food, feeling rested, having a good sleep, ability to look after personal hygiene unaided, ability to communicate with family and friends, getting support from hospital doctors and nurses, ability to return to work or usual home activity, feeling comfortable and in control and having a feeling of general well-being. Each question has a scale from 0 (none of the time (poor)) to 10 (all of the time (excellent)). The other part is asking about if the patient had any of the following in the past 24 hours: moderate pain, severe pain, nausea or vomiting and feeling sad o depressed. Each item in this part has a scale from 10 (none of the time (excellent)) to 0 (all of the time (poor)). QoR15 is a valid and reliable questionnaire to assess the quality of recovery from patient's prospective (147)

3.3.8 Data analysis

All collected data were written in PQIP data collection form and inputted into the PQIP website and then imported as excel documents. Afterward, data from the excel sheet were exported to Statistical Package for Social Sciences (SPSS) for appropriated coding. All data were analysed using SPSS version 25.0 and graphs were generated using GraphPad Prism version 8. Data were split into two groups (PPCs vs. No PPCs) to measure the differences. Appropriate statistical tests for differences in continuous variables were used based on the results of Shapiro-Wilk test of normality. Mann-Whitney U test was used for continuous variables as they were non-normally distributed data. Results are reported as median, Interquartile Range (IQR) and p-value. For categorical variables, chi-square test was used, and the results were reported as counts, percentages and corresponding p-values.

Multivariate logistic regression analysis was used to determine the association of perioperative factors on the incidence of PPCs. Factors included in the regression model were age, gender, ASA grade, smoking history, cardiac history, respiratory history, heart failure history, epidural analgesia, postoperative infection. The results were reported as odds ratio with 95% Confidence Interval (CI) and p-value.

Wilcoxon signed-rank test was used for testing the difference between QoR15 admission and 3rd postoperative day as the data were non-normally distributed. Missing data for patients who did not complete QoR15 at 3rd postoperative day were excluded from analysis. The results were reported as median, IQR and p-value.

3.4 Results

Total of 204 patients were screened for their eligibility from May 2018 to May 2019. Of these, 145 patients were recruited to the study and included in the final analysis (Figure 3.1).

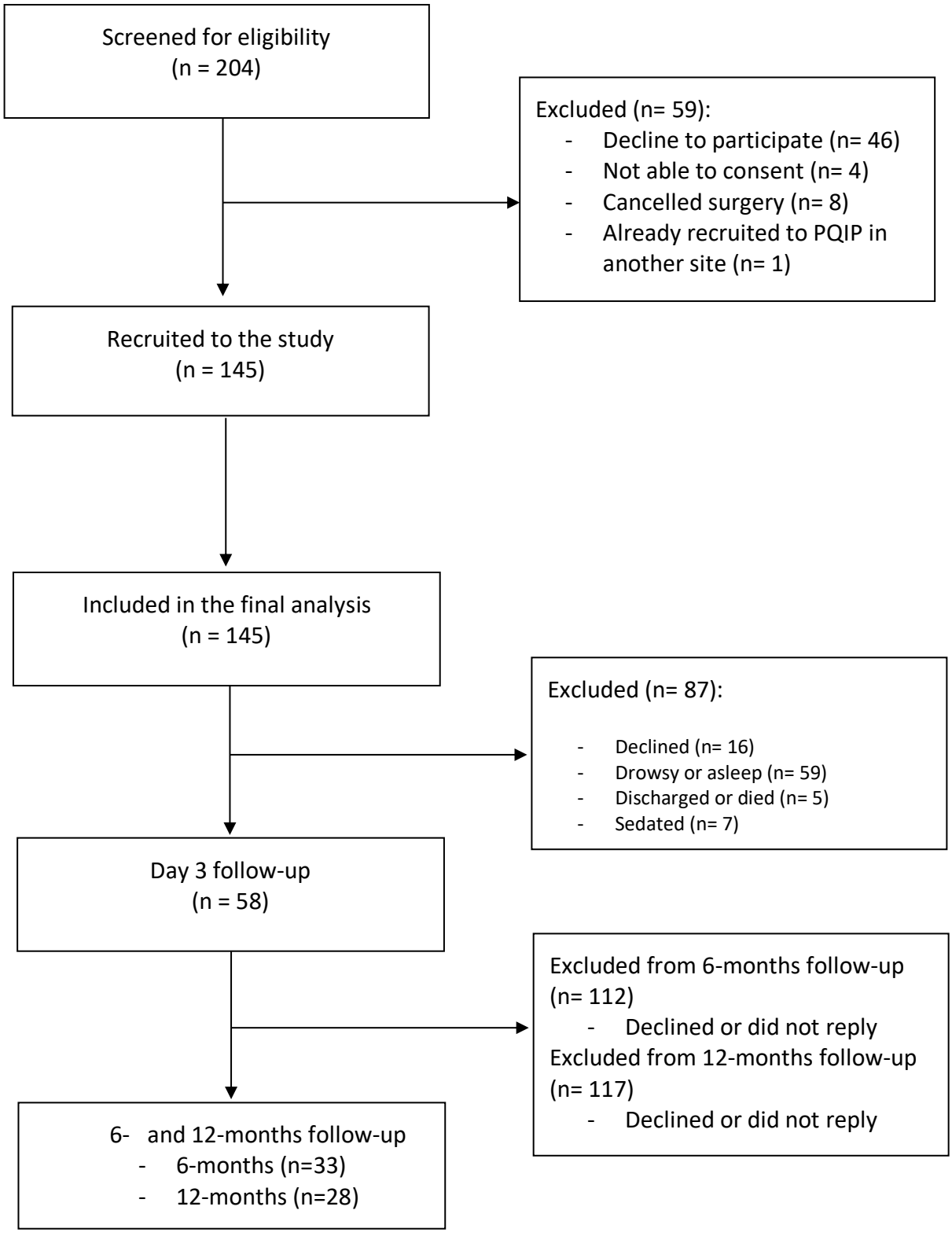

Figure 3. 1 Flow diagram for number of patients who screened, recruited, analysed and followed-up

N: Number of Patients, PQIP: Perioperative Quality Improvement Programme

3.4.1 Basic Demographics and clinical characteristics

Out of the 145 patients recruited, 89 (61.4%) were males and 56 (38.6%) were females. The median age was 66 (IQR 57.5-73) years old (Table 3.4). Most of these patients had open HPB surgery (n=130 (89.7%)) where only 15 (10.3%) patients had laparoscopic surgery.

Table 3. 4 Demographics and clinical characteristics of patients

Variable	**N (%)/ (Median (IQR))**
Gender (M/F)	89 (61.4%)/ 56 (38.6)
Age (years)	66 (57.5- 73)
Height (cm)	170 (163-177)
Weight (kg)	79.5 (69.9-91.5)
ASA - Grade I - Grade II - Grade III	 - 1 (0.7%) - 89 (61.4%) - 55 (37%)
Smoking history - Current smoker - Never smoked - Ex-smoker, stopped > 6 months - Ex-smoker, stopped =< 6 months - Not known	 - 17 (11.7%) - 89 (61.4%) - 28 (19.3%) - 2 (1.4%) - 9 (6.2%)
Cardiac failure history - No failure - Diuretic digoxin antianginal or antihypertensive therapy - Peripheral oedema warfarin therapy or borderline cardiomegaly	 - 136 (93.8%) - 4 (2.8%) - 5 (3.4%)
NYHA Heart Failure Classification - Grade I - Grade II	 - 111 (76.6%) - 34 (23.4%)
Respiratory failure history - No dyspnoea - Dyspnoea on exertion or CXR: mild COPD - Dyspnoea limiting exertion to <1 flight or CXR: moderate COPD	 - 130 (89.7%) - 13 (9%) - 2 (1.4%)
Epidural (Yes/ No)	83 (57.2%)/ 62 (42.8%)
Open vs. Laparoscopic	130 (89.7%) vs. 15 (10.3%)

ASA: American Society of Anaesthesiologists, CM: Centimetre, COPD: Chronic Obstructive Pulmonary Disease, CXR: Chest X-Ray, F: Female, IQR: interquartile range, KG: kilogram, M: Male, N: Number of patients, NYHA: New York Heart Association, PPCs: Postoperative Pulmonary Complications.

3.4.2 Incidence of PPCs, morbidities, mortality and length of stay

The results showed that postoperative morbidities at day-7 were highest in pulmonary, infection and gastrointestinal (n=27 (18.6%), n=18 (12.4%) and n=26 (17.9%), respectively) (Table 3.5). The overall median of the length of postoperative stay was 6 (IQR 5-9) days and 30-day mortality was 2.8% (n=4).

Table 3. 5 Postoperative morbidities based on POMS at day-7

Complication	Yes	No
Pulmonary	27 (18.6%)	118 (81.4%)
Infection	18 (12.4%)	127 (87.6%)
Gastrointestinal	26 (17.9%)	119 (82.1%)
Renal	7 (4.8%)	138 (95.2%)
Cardiovascular	1 (0.7%)	144 (99.3%)
Neurological	6 (4.1%)	139 (95.9%)
Wound	1 (0.7%)	144 (99.3%)
Haematological	1 (0.7%)	144 (99.3%)
Pain	4 (2.8%)	141 (97.2%)

POMS: Postoperative Morbidity Survey

3.4.3 Factors associated with PPCs and Impact of PPCs on patient outcomes

The results showed not statistical difference in basic demographics between patients with and without PPCs except age which was significantly higher in patients with PPCs (PPCs vs. No PPCs: 70 (IQR 64-77) years vs. 65 (IQR 56-72) years, p = 0.027, U=1157) (Table 3.6). Also, there were no statistical difference in preoperative measurements, ASA grade, smoking history, cardiac failure history, NYHA heart failure classification and respiratory failure history (Table 3.6). The results showed significant difference in surgical incision between PPCs (n= 27) vs. No PPCs (n= 118) (open 100% (n=27) and laparoscopic 0% (n= 0) vs. open 87.3% (n=103) and laparoscopic 12.7% (n= 15), p= 0.05, X^2=3.828, respectively). There was no statistical difference in the use of epidural between the two groups (Table 3.6).

Multivariate logistic regression analysis showed that increasing age is associated with the incidence of PPCs (Odds ratio (95%CI): 1.07 (1.01-1.13), p=0.031). The results also showed postoperative infection is strongly associated with incidence of PPCs (Odds ratio (95%CI): 95.35 (13.58- 669.36), p<0.001) (Table 3.7). The Nagelkerke R square for the regression model was 0.51.

The results of morbidities at 7th postoperative day were significantly higher in PPCs group except pain which was not statistically different between the two groups (Table 3.8). The highest postoperative morbidity associated with PPCs was infection (Infection rate: PPCs group 9% (n=14) vs. No PPCs group 2.8% (n= 4), p< 0.001, X^2=47.46). Mortality was not significantly different between the PPCs vs. No PPCs (1.4% (n= 2) vs. 1.4% (n= 2), p= 0.102,

X^2=2.67, respectively). The median (IQR) length of stay was significantly higher in PPCs group (PPCs vs. No PPCs: 14 (9-23) days vs. 6 (5-7) days, p<0.001, U=225) (Figure 3.2).

Table 3. 6 Differences in basic demographics and clinical characteristics between patients with and without PPCs

Variable	**PPCs (n=27)**	**No PPCs (n=118)**	**P value**
Gender (M/F) N (%)	16 (59.3%)/ 11 (40.7%)	73 (61.9%)/ 45 (38.1%)	P=0.802
Age (years) Median (IQR)	70.0 (64-77)	65.0 (56-72)	P=0.027*
Height (cm) Median (IQR)	172.0 (162-176)	169.5 (163-177.25)	P=0.992
Weight (kg) Median (IQR)	79.5 (68.4-87.4)	79.95 (70.2-93.4)	P=0.421
ASA - Grade I - Grade II - Grade III	 - 0 (0%) - 16 (59.3%) - 11 (40.7%)	 - 1 (0.8%) - 73 (61.9%) - 44 (37.3%)	 P=0.851
Smoking history - Current smoker - Never smoked - Ex-smoker, stopped > 6 months - Ex-smoker, stopped =< 6 months - Not known	 - 4 (14.9%) - 18 (66.7%) - 5 (18.5%) - 0 (0%) - 0 (0%)	 - 13 (11%) - 71 (60%) - 23 (19.5 %) - 2 (1.7%) - 9 (0.7%)	 P=0.566
Cardiac failure history - No failure - Diuretic digoxin antianginal or antihypertensive therapy - Peripheral oedema warfarin therapy or borderline cardiomegaly	 - 24 (16.6%) - 1 (3.7%) - 2 (7.4%)	 - 112 (95%) - 3 (2%) - 3 (2%)	 P=0.427
NYHA Heart Failure Classification - Grade I - Grade II	 - 21 (77.8%) - 6 (22.2%)	 - 90 (62.1%) - 28 (19.3%)	 P=0.868
Respiratory failure history - No dyspnoea - Dyspnoea on exertion or CXR: mild COPD - Dyspnoea limiting exertion to <1 flight or CXR: moderate COPD	 - 23 (85%) - 3 (11%) - 1 (3.7%)	 - 107 (91%) - 10 (8.5%) - 1 (0.8%)	 P=0.462

Variable	PPCs (n=27)	No PPCs (n=118)	P value
Epidural (Yes)	19 (70%)	64 (54.2%)	P=0.126
Open vs. Laparoscopic	27 (100%) vs. 0 (0%)	103 (87.3%) vs. 15 (12.7%)	P=0.050*

* Statistically significant

The results showed significant difference in age and surgical incision between patients with PPCs vs. no PPCs (age: P=0.027, U=1157 and surgical incision: P=0.050, X^2=3.828)

ASA: American Society of Anaesthesiologists, CM: Centimetre, COPD: Chronic Obstructive Pulmonary Disease, CXR: Chest X-Ray, F: Female, IQR: interquartile range, KG: kilogram, M: Male, N: Number of patients, NYHA: New York Heart Association, PPCs: Postoperative Pulmonary Complications.

Table 3. 7 Multivariate analysis of perioperative factors associated with the incidence of PPCs

Risk factor	**OR (95% CI)**	**P value**
Increasing age	1.07 (1.01-1.13)	P=0.031*
Male gender	2.88 (0.76-10.89)	P=0.119
Respiratory history (mild-moderate COPD)	6.71 (0.37-123.39)	P=0.200
Smoking history - Current smoker - Ex-smoker	 1.27 (0.14-11.44) 1.07 (0.18-6.32)	 P=0.831 P=0.942
ASA ≥ grade II	0.99 (0.23-4.26)	P=0.992
NYHA Heart failure ≥ class II (slight physical activity limitations)	0.08 (0.01-0.85)	P=0.036*
Presence of cardiac failure	8.51 (0.81-89.43)	P=0.074
Use of epidural	0.54 (0.15-1.92)	P=0.341
Postoperative infection	95.35 (13.58- 669.36)	P<0.001*

* Statistically significant

The results showed only increasing age postoperative infection are significantly associated with development of PPCs.

ASA: American Society of Anaesthesiologists, CI: Confidence Interval, COPD: Chronic Obstructive Pulmonary Disease, NYHA: New York Heart Association, OR: Odds Ratio, PPCs: Postoperative Pulmonary Complications.

Table 3. 8 Morbidity associated with PPCs at day 7 after the surgery

Complication	**PPCs (n=27)**	**No PPCs (n=118)**
Infection	14 (51.8%)	4 (3.4%)
Gastrointestinal	15 (55.6%)	11 (9.3%)
Renal	4 (14.8%)	3 (2.5%)
Cardiovascular	1 (3.7%)	0 (0%)
Neurological	4 (14.8%)	2 (1.7%)
Wound	1 (3.7%)	0 (0%)
Haematological	1 (3.7%)	0 (0%)
Pain	1 (3.7%)	3 (2.5%)

The results showed that all postoperative morbidities at day 7 within POMS, except pain, were higher in patients with PPCs.

PPCs: Postoperative Pulmonary Complications

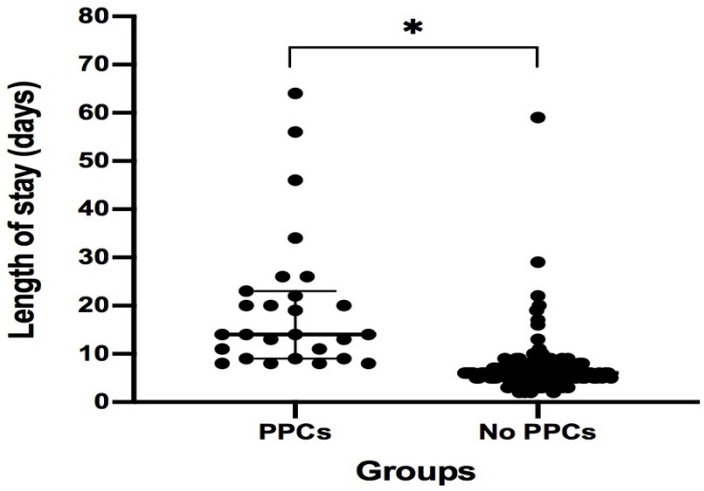

Figure 3. 2 Boxplot for length of postoperative stay

* Statistically significant
The graph shows significant increase in median length of postoperative hospital stay in patients with PPCs compared to patients without PPCs (median (IQR): 14 (9-23) days vs. 6 (5-7) days, p<0.001, respectively).

LOS: Length of Stay, PPCs: Postoperative Pulmonary Complications

3.4.4 Severity and forms of postoperative pulmonary complications

Based on StEP-COMPAC definition of PPCs severity, incidence of PPCs was considered none for patients who received routine supplemental oxygen, 24 patients had mild PPCs as they required low flow oxygen (1-4 l/m O_2) and 3 patients had severe PPCs as they required ventilatory support (Table 3.9). According to clinical diagnosis, the rate for each PPCs form was as follow: Atelectasis 67% (n= 18), Pneumonia 11% (n= 3), Pulmonary oedema 7% (n= 2), Pleural effusion 15% (n= 4) (Figure 3.3). Most of these PPCs occurred on the day of the surgery (n= 5) and first postoperative day (n= 8) (Figure 3.4).

Table 3. 9 Number of patients who had mild, moderate or severe PPCs according to StEP-COMPAC definition of PPCs severity

Severity	**Number of patients**
None: planned use of supplemental oxygen or mechanical respiratory support as part of routine care,	0
Mild: therapeutic supplemental oxygen <0.6 FiO_2	24
Moderate: therapeutic supplemental oxygen ≥0.6 FiO_2	0
Severe: unplanned non-invasive mechanical ventilation, CPAP, or invasive mechanical ventilation requiring tracheal intubation	3

CPAP: Continuous Positive Airway Pressure, FiO_2: Fraction of Inspired Oxygen, PPCs: Postoperative Pulmonary Complications.

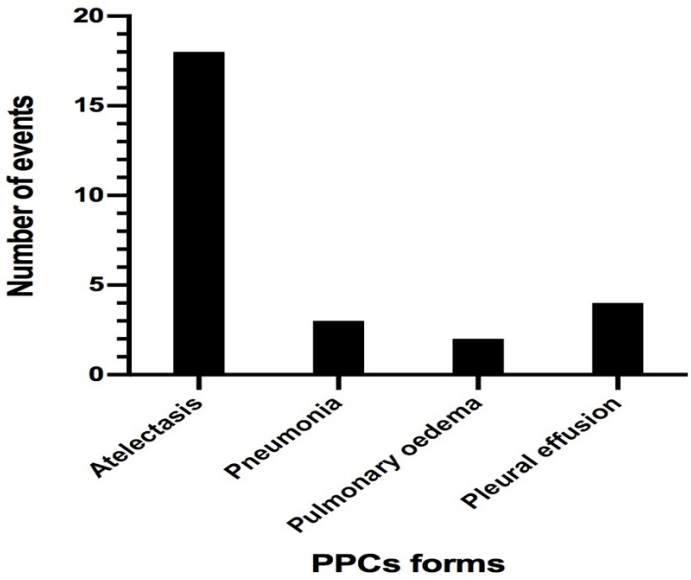

Figure 3. 3 Number of events for specific PPCs forms among the 27 patients who had PPCs

The graph illustrates number of events for PPCs forms. Majority of PPCs were atelectasis (n= 18) followed by pleural effusion (n= 4), pneumonia (n= 3) and pulmonary oedema and (n= 2).

PPCs: Postoperative Pulmonary Complications

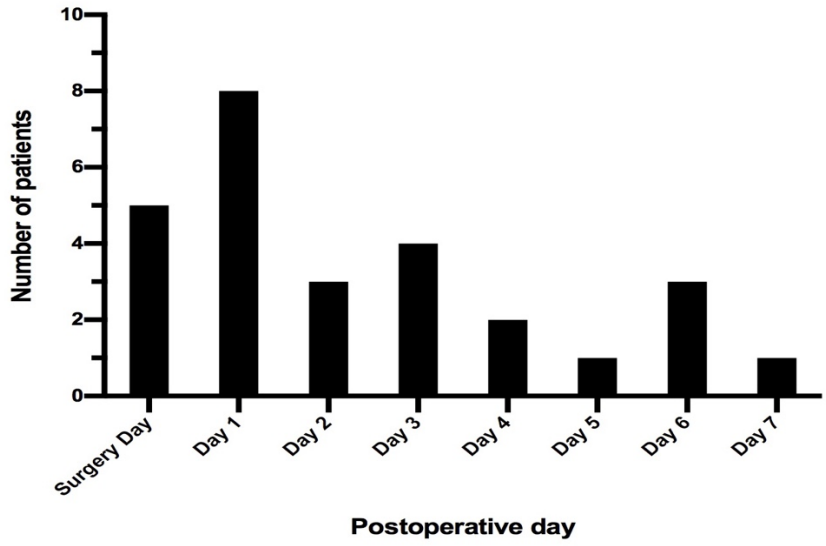

Figure 3. 4 Number of patients had PPCs in each postoperative day

The graph illustrates number of patients had PPCs in each postoperative day, the results as follow: 5 patients on day 0 (day of surgery), 8 patients on day 1, 3 patients on day 2, 4 patients on day 3, 2 patients on day 4, 1 patient on day 5, 3 patients on day 6 and 1 patients on day 7.

PPCs: Postoperative Pulmonary Complications

3.4.5 Quality of recovery

Quality of recovery was evaluated by pain, DrEaMing and QoR15 Questionnaire. The results of pain and DrEaMing, except mobilisation item, were significantly different between PPCs and No PPCs groups as reported in table 3.10.

Quality of recovery was also assessed from patient's prospective by QoR15 questionnaire. Wilcoxon signed-rank test was used to analyse QoR15 questionnaire for only 58 patients as 87 patients did not complete QoR15 in 3rd postoperative day. The reasons for not completing QoR15 in 3rd postoperative day are either patient was declined (n=16), drowsy or asleep (n=59), sedated (n=7) or discharged or died (n=5). The median (IQR) of total QoR15 score was significantly different between admission vs. 3rd postoperative day (118 (101.75-128) vs. 100 (85.75-112.75), $p<0.001$, $Z= -3.86$). The results of the QoR15 showed significant decrease in 3rd postoperative day in the questions related to breathing, enjoying food, ability to look after personal hygiene unaided, communication with family and friends, ability to return to work or usual home activities, feeling comfortable and in control, and general well-being (Table 3.11). In addition, the results showed significant increase in the questions related to having moderate and severe pain, feeling worried and anxious and getting support from hospital doctors and nurses (Table 3.11). Conversely, questions about feeling rested, having good sleep, having nausea and vomiting and feeing sad or depressed, were not significantly different before and after surgery (Table 3.11).

The median (IQR) of the total change in QoR15 after surgery was not significantly different between PPCs vs. No PPCs groups (-27 (-47 – -2) vs. -15 (-28 – 7), $p=0.215$, $U=196$). The median

(IQR) change in all questions of QoR15 after surgery was not significantly different between PPCs and No PPCs groups except the question related to feeling worried and anxious, which was significantly increased in PPCs group (0 (-1.25 – 0) vs. 1 (0 – 3), p=0.019, U=127.5) (Table 3.12).

Table 3. 10 Postoperative pain and DrEaMing

Variable	**Overall (n=145)**	**PPCs (n=27)**	**No PPCs (n=118)**
Pain: - None - Mild - Moderate - Severe - Unable to ascertain (Sedated) - Other	 - 99 (68.3%) - 11 (7.6%) - 11 (7.6%) - 10 (6.9%) - 6 (4.1%) - 8 (5.5%)	 - 17 (63%) - 0 (0%) - 0 (0%) - 3 (11.1%) - 5 (18.5%) - 2 (7.4%)	 - 82 (70%) - 11 (9.3%) - 11 (9.3%) - 7 (5.9%) - 1 (0.8%) - 6 (5%)
Drinking (Yes)	134 (92.4%)	20 (74%)	114 (97%)
Eating (Yes)	113 (77.9%)	14 (52%)	99 (84%)
Mobilising (Yes)	103 (71%)	16 (59%)	87 (74%)

The Chi-square test showed significantly different between PPCs and No PPCs groups in pain and DrEaMing, except mobilisation item.

PPCs: Postoperative Pulmonary Complications

Table 3. 11 The difference in median QoR15 between day of admission and 3rd postoperative day

Question	**Median (IQR)** (n=58)	
	Admission	3rd post-op day
Able to breathe easily	10 (9-10)	8 (7.75-10)
Been able to enjoy food	9 (7-10)	5 (0-8)
Feeling rested	7.5 (5-9)	6 (4-8)
Have had a good sleep	8 (4.75-9)	7 (4.75-9)
Able to look after personal toilet and hygiene unaided	10 (10-10)	5 (1.75-9)
Able to communicate with family and friends	10 (10-10)	10 (9-10)
Getting support from hospital doctors and nurses	10 (8-10)	10 (9-10)
Able to return to work or usual home activities	10 (5.75-10)	0 (0-5)
Feeling comfortable and in control	8 (5-10)	6 (5-8)
Having a feeling of general well-being	8 (5.75-10)	6 (5-8)
Moderate pain	9 (5-10)	5 (3-7)
Severe pain	10 (9-10)	8 (4-10)
Nausea or vomiting	10 (10-10)	10 (6-10)
Feeling worried or anxious	6 (4-9)	8 (4.75-10)
Feeling sad or depressed	9 (5-10)	10 (7-10)
Total QoR15 score	118 (101.75-128)	100 (85.75-112.75)

Wilcoxon signed-rank test showed that median (IQR) of total QoR15 score was significantly different between admission vs. 3rd postoperative day (118 (101.75-128) vs. 100 (85.75-112.75), $p<0.001$, $Z= -3.86$).

IQR: Interquartile Range, Post-op: Postoperative, QoR15: Quality of Recovery 15 questionnaire.

Table 3. 12 The difference in median change in QoR15 after operation between PPCs and No PPCs groups

Question	Median (IQR)		P value
	PPCs (n=11)	No PPCs (n=47)	
Able to breathe easily	-1 (-2.25 – 0)	-1 (-2 – 0)	P=0.668
Been able to enjoy food	-4 (-6.25 – -2.75)	-2(-5 – -1)	P=0.271
Feeling rested	-0.5 (-3.5 – 1)	-1.5 (-3 – 1.75)	P=0.926
Have had a good sleep	0.5 (-2.75 – 1)	-0.5 (-3 – 2)	P=0.992
Able to look after personal toilet and hygiene unaided	-5 (-7.5 – -4.25)	-3 (-8 – -1)	P=0.405
Able to communicate with family and friends	0 (-2.25 – 0)	0 (-1 – 0)	P=0.427
Getting support from hospital doctors and nurses	0 (0 – 2)	0 (0 – 1.75)	P=0.797
Able to return to work or usual home activities	-6.5 (-8.5 – -4.5)	-5 (-10 – -1)	P=0.417
Feeling comfortable and in control	-2 (-5 – 0.25)	-1 (-3.75 – 0)	P=0.756
Having a feeling of general well-being	-2.5 (-3.5 – -1.75)	-2 (-3.75 – 1)	P=0.356
Moderate pain	-1.5 (-8.5 – 1.25)	-3 (-5 – -1)	P=0.844
Severe pain	-2 (-5.25 – 0.25)	-1 (-4.75 – 0)	P=0.745
Nausea or vomiting	0 (-6.25 – 0)	0 (0 – 0)	P=0.172
Feeling worried or anxious	0 (-1.25 – 0)	1 (0 – 3)	P=0.019*
Feeling sad or depressed	0 (-0.25 – 1)	0 (0 – 2.75)	P=0.314
Change in total QoR15 score	-27 (-47 – -2)	-15 (-28 – 7)	P=0.215

* Statistically significant

The median (IQR) of the total change in QoR15 after surgery was not significantly different between PPCs vs. No PPCs groups (-27 (-47 – -2) vs. -15 (-28 – 7), p=0.215, U=196).

IQR: Interquartile Range, PPCs: Postoperative Pulmonary Complications, QoR15: Quality of Recovery 15 questionnaire

3.5 Discussion

This prospective cohort study investigated the incidence and severity of PPCs following major HPB surgery at QEHB within the context of the national PQIP study. The study showed that incidence of PPCs was high. Most of patients developed mild PPCs according to the StEP-COMPAT definition of severity of PPCs. Atelectasis, which mostly occurred at the day of the surgery or 1st postoperative day, was most frequent PPC form. Mortality was not associated with the development of PPCs. The main risk factors associated with PPCs were increasing age at the time of the surgery and preoperative physical activity limitations (NYHA>II). However, the results of NYHA classification would not be reliable due to very wide confidence interval reported which might indicate an inadequate power for this variable.

In this study, PPCs had a great impact on patient outcomes, in particular, increased morbidities and prolonged length of stay. The highest morbidities associated with PPCs were infectious and gastrointestinal complications. PPCs were also associated with a negative impact on quality of recovery, which was explained by DrEaMing, such as developing severe pain and inability to eat or drink at 1st postoperative day. Nevertheless, the quality of recovery described by patient-reported outcomes, the QoR15 questionnaire, was not associated with PPCs. However, the results of QoR15 would not be conclusive as 60% of patients have not completed the QoR15.

The incidence of PPCs in this study is consistent with results of the previous studies which reported incidence of PPCs from 4.7% up to 22.5% (12, 19-22). Another two studies (72, 74) estimated the incidence of PPCs after open abdominal surgery would be as high as 40%. This

variation in the PPCs incidence could be due to different definitions of PPCs used in the studies. For example, Patel, et al. (12) reported that incidence of PPCs was 11% using EPCO definition, which includes a specific clinical definition for each PPC form such as hypoxia, pulmonary infection, pulmonary oedema and ARDS. In this study, incidence of PPCs was defined by POMS definition of PPCs, which is a binary outcome measure of the requirement of supplemental oxygenation or/and ventilatory support. However, POMS is a valid and reliable measure of postoperative morbidities (144).

Another reason of this disparity in the incidence of PPCs would be the type of abdominal surgery included as only major HPB surgery was examined in this study. In a retrospective cohort study, PPCs incidence following gastrectomy for gastric cancer patients was lower (4.7%) in comparison to our results (22). In addition, open and laparoscopic surgeries were examined in this study, where open procedures are associated with prolonged surgery duration which therefore associated with higher PPCs incidence (24). In this cohort, all patients who developed PPCs had open surgery, which suggest a strong relationship between open surgery and increased PPCs incidence.

Low number of patients recruited in PQIP at our site should be considered when interpreting the results of this study, especially results of variable requires larger sample size such as the QoR15. Our results would not be generalised to all major abdominal surgery as only major HPB surgery was selected, as our site is considered one of largest HPB centre in the UK. Long-term postoperative morbidities were considered in PQIP by completing 6 and 12 months follow up questionnaires (the EQ5D-5L and WHODAS questionnaires) (148, 149). However, 6 and 12 months were excluded from analysis in this study due to very high drop-out rate. Out

of 146 patients, only 33 patients completed 6 months follow up and 28 patients completed 12 months follow up (drop-out rate: 78% for 6-months and 81% for 12-months). Of these, only one patients had PPCs which results in unfeasible analysis of the impact of PPCs on long-term morbidities. The reason for this high drop-out rate is either patients declined to complete the questionnaires or patients did not reply to emails/ phone calls.

Routine monitoring of postoperative morbidities, especially PPCs, would be beneficial to improve perioperative practice as in the case of using PQIP. The use of PQIP has helped in measuring the incidence, severity and impact of PPCs as well as identifying risk factors associated with the development of PPCs following major HPB surgery at QEHB which would help to improve current practice. A multifaceted approach that involves different clinical disciplines was recommended by a patient safety summit to reduce the incidence of PPCs (150).

Based on the results of PQIP, improving current perioperative practice in the QEHB should be taken into account by introducing perioperative interventions that are targeting PPCs in particular. For instant, I-COUGH bundle which incorporates incentive spirometry, cough and deep breathing exercises, oral hygiene, patient education, early mobilisation and elevating head of bed postoperatively. The I-COUGH bundle is being used in Manchester and was able to decrease incidence of PPCs by 50% following major surgery, compared to incidence of PPCs before introducing the I-COUGH bundle (151). Optimising pulmonary function and respiratory muscles strength would also help in decreasing incidence of PPCs. In chapter two, the systematic review and meta-analysis showed that lung expansion techniques would improve pulmonary function. Therefore, optimising pulmonary function by using perioperative lung

expansion techniques would directly help in reducing PPCs and improving patient outcomes following major abdominal surgery.

3.6 Conclusion

PQIP has shown that PPCs are common and associated with postoperative morbidities and prolonged length of stay after major HPB surgery. Despite the PPCs were mild, PPCs have a great negative impact on patient outcomes postoperatively. Most of the PPCs occurred on the day of surgery or 1st postoperative day where atelectasis was the commonest. A bundle of perioperative interventions would be required to target PPCs.

Chapter Four

The implementation of I-COUGH Plus bundle to improve respiratory muscles strength following major Hepato-Pancreatic-Biliary surgery: Quality improvement study

Abstract

Introduction: Postoperative pulmonary complications (PPCs) are common following major abdominal surgery. At the Queen Elizabeth Hospital Birmingham (QEHB), the incidence of PPCs was high (18%) following major hepato-pancreatic-biliary (HPB) surgery based on data collected prospectively over one year. Therefore, an improvement in our perioperative practice is required to reduce PPCs. I-COUGH bundle is being conducted in Manchester and we believe enhancing Respiratory Muscles Strength (RMS) perioperatively would help in reducing the incidence of PPCs and improves patient outcomes.

Aim: To assess the success of the I-COUGH Plus bundle in improving respiratory muscles strength and reducing PPCs after major HPB.

Methods: This is a quality improvement study using cohort study design to assess the success of implemented strategy, The I-COUGH Plus bundle. The primary outcome is the change in RMS measurements as a surrogate measure pulmonary function. The RMS measurements include Maximal Inspiratory Pressure (MIP), Maximal Expiratory Pressure (MEP) and Sniff Nasal Inspiratory Pressure (SNIP). Secondary outcomes include postoperative morbidities, mortality rate, length of stay and patient outcomes.

Results: Total of 30 patients were included in the final analysis, 22 patients before implementation vs. 8 patients after implementation (54.5% (n=12) males and 45.5% (n=10) females vs. 50% (n=4) males and 50% (n=4) females). The mean age was 61.91 ± 12.79 years before implementation vs. 69.63 ± 11.08 years after implementation, p=0.431. There was no

significant difference in the changes of RMS measurements between before implementation (n= 22) and after implementation (n= 8). The mean RMS measurements were as follow: MIP change 20.36 ± 12.01 vs. 28.31 ± 17.70, p= 0.180; MEP change 30.14 ± 18.80 vs. 25.00 ± 8.22, p= 0.465; SNIP change 28.55 ± 18.19 vs. 27.63 ± 76, p= 0.892. Also, there was no significant difference in incidence of PPCs between the two groups (22.7% (n=5) before implementation vs. 37.5% (n=3) after implementation, p= 0.418). Mortality rate was 0% in both groups. The results also showed no significant difference in length of stay, morbidities and patients outcomes between the two groups.

Conclusion: The I-COUGH plus bundle has no effect on improving RMS or reducing incidence of PPCs after major HPB surgery. The results are not conclusive as few patients were recruited after implementation of the I-COUGH Plus bundle. Collecting data from sufficient number of patients would provide conclusive results about the success of the implemented strategy.

4.1 Introduction

This is a quality improvement study to assess the success of an implemented intervention. This study is part of Perioperative Quality Improvement Programme (PQIP) (Chapter 3). PQIP is national project that is led by the National Institute of Academic Anaesthesia's Health Services Research Centre (NIAA-HSRC), based at Royal College of Anaesthetists (143).

4.2 Background and rational

Postoperative pulmonary complications (PPCs) are common, with reported incidence of 2% to 40% following major surgery (152). PQIP has shown incidence of PPCs is high, about 18%, after major hepato-pancreatic-biliary (HPB) surgery in our hospital, the Queen Elizabeth Hospital Birmingham (QEHB) (Chapter 3). Enhanced Recovery After Surgery (ERAS) approach for major elective surgery aims to reduce postoperative complications and length of hospital stay (125). ERAS is now a standard postoperative approach for patient undergoing major elective surgery in the United Kingdom aiming to improve postoperative outcomes. However, there are a few interventions within ERAS approach that aim to minimise PPCs in particular (152).

There are different respiratory physiotherapy techniques that are used in an attempt to reduce PPCs after major surgery (77). Systematic reviews have demonstrated that perioperative respiratory physiotherapy techniques are effective in improving pulmonary function and respiratory muscles strength (RMS), therefore, helping to reduce the incidence of PPCs following cardiothoracic and major abdominal surgery (77, 117). These techniques include inspiratory muscles training (IMT), Incentive Spirometry (IS), Deep Breathing (DB) and

coughing (117). Nevertheless, there is no standard technique used currently in perioperative respiratory physiotherapy practice in the UK.

In the United States, a simple respiratory care bundle, called I-COUGH (Incentive Spirometry (IS), Coughing and deep breathing, Oral care, Understanding, Get out of bed, Head of bed elevated), is used to decrease the incidence of PPCs (151). I-COUGH bundle is now incorporated within ERAS Plus approach and being conducted in Manchester, UK (152). I-COUGH approach was able to decrease PPCs by 50% following major surgery (151). In our local hospital the QEHB, data of PQIP (Chapter 3) acknowledged the need for improvement as respiratory care bundle that improves postoperative respiratory outcomes and reduce PPCs was not considered within perioperative practice.

We believed improving respiratory outcome such as pulmonary function and RMS before and after the surgery may reduce PPCs and length of hospital stay after major abdominal surgery. Therefore, we added IMT to the I-COUGH bundle, being called I-COUGH Plus, in order to improve RMS before and after surgery which would help to reduce the incidence of PPCs consequently.

4.3 Aim and objectives

4.3.1 Aim

The aim of this quality improvement study was to implement I-COUGH Plus bundle in our local hospital as well as to assess the success of the implemented strategy in improving RMS following major HPB surgery.

4.3.2 Objectives

- To measure RMS as surrogate measure of pulmonary function order to assess the success of the I-COUGH Plus.
- To measure patient outcomes before and after implementation of the I-COUGH Plus.

4.3.3 Research Questions

- Does I-COUGH Plus bundle improve and preserve RMS postoperatively?
- Does I-COUGH Plus bundle reduce the incidence of PPCs and improve patient outcomes?

4.4 Methods

4.4.1 Study design(153)

This quality improvement study is part of the PQIP, using a prospective cohort study design to assess the success of I-COUGH Plus bundle in improving RMS after major HPB surgery. Major HPB surgery was defined as HPB surgery that last more than three hours as HPB surgery found to last at least three hours for all patients included in previous study (PQIP). RMS were measured instead of direct measure of incidence of PPCs as most of I-COUGH interventions were expected to have direct improvement of RMS. The efficacy of the interventions used would be better explained by RMS measurements which would predict the incidence of PPCs (153).

4.4.2 Setting

The study was conducted at University Hospital Birmingham NHS Foundation trust- Queen Elizabeth Hospital Birmingham (UHB-QEHB) (Chapter 3.3.2).

4.4.3 Eligibility criteria

4.4.3.1 Inclusion criteria:

- Adult patients aged 18 years old or older
- Patients undergoing major HPB surgery that last more than three hours
- Able to give consent
- Able to perform RMS tests

4.4.3.2 Exclusion criteria:

- Patients who are unable or decline to consent
- Patients undergoing minor HPB surgeries that last less than three hours such as cholecystectomy and hernia repair
- Patients who are unable to perform RMS tests
- Patients how are already enrolled in the PQIP in different hospital in the UK

4.4.4 Recruitment

Patients were invited to take part in the study at pre-screening clinic by liver anaesthetists or nurses from May 2019 to August 2019 before implementation of the I-COUGH Plus. After implementing the I-COUGH plus, only patients whose surgeries were scheduled at least 7-days following the pre-screening clinic were invited from August 2019 to March 2020.

Eligible patients were given Participant Information Sheet (PIS) at the pre-screening clinic in order to allow sufficient time for patients to read and understand the study before they decide to take part. Patients were consented and enrolled following adequate time for the PIS to be considered.

4.4.5 Data collection

Data were collected perioperatively from the two groups, standard care group (before implementation) and I-COUGH Plus group (after implementation). Patient's questionnaires and data collection form of PQIP, which includes demographics, perioperative data and

morbidity survey, were used (Appendix 5). In addition, RMS measurements were obtained pre- and post-operatively. All collected data were inputted through a web-based data-entry portal developed by PQIP.

4.4.6 Outcomes

The primary outcome was the change in RMS measurements as a surrogate measure of the incidence of PPCs. Change in RMS is defined as the difference between preoperative RMS measurements and 3rd postoperative day RMS measurements. The primary outcome measure for the RMS are Maximal Inspiratory Pressure (MIP), Maximal Expiratory Pressure (MEP) and Sniff Nasal Inspiratory Pressure (SNIP). MIP and SNIP measure directly inspiratory muscles including diaphragm while MEP measures expiratory muscles including intercostal and abdominal muscles (154).

The RMS was measured by a digital manovacuometer, called Micro Respiratory Pressure Meter (MicroRPM), (MicroRPM, CareFusion Germany 234 GmbH, Leibnizstrasse 7, D-97204 Hoechberg, Germany) (Figure 4.1). MicroRPM is a non-invasive measurement tool that measures MIP, MEP and SNIP to represent the RMS (155). MicroRPM is recommended measurement tool due to its high accuracy in measuring RMS (156). The literature showed that MicroRPM provides reliable and valid measurements of RMS for both clinicians and researchers (155, 156). RMS measurements were obtained preoperatively and then, postoperatively at 1st, 3rd and 7th postoperative day. MIP is measured when patients exhale to Residual Volume (RV) then perform a 'Mueller' manoeuvre, a forced inhalation against the MicroRPM with as much effort as possible for as long as possible (minimum 2 seconds) (157).

MEP is measured when patients inhale to Total Lung Capacity (TLC) then perform a 'Valsalva' manoeuvre, a forced exhalation against the MicroRPM with as much effort as possible for as long as possible (minimum 2 seconds) (157). To measure SNIP, appropriate size of nasal probe should be inserted firmly into a nostril. Afterwards, patients should breathe normally at Functional Residual Capacity (FRC) and then perform a short and sharp voluntary sniffing manoeuvre as much effort as possible (157). The display of the device reported the measurements (MIP, MEP and SNIP) in cmH2O. According to manufacturer guidelines that patients should repeat the MIP, MEP and SNIP tests three times to ascertain a best value.

Secondary outcomes were postoperative morbidities, 30-days mortality, length of stay, quality of recovery. Postoperative morbidity data were collected using validated Postoperative Morbidity Survey (POMS) on 7th postoperative day (144). The quality of recovery was measured by DrEaMing day 1, which assesses the proportion of patients that are drinking, eating and mobilising after 1st postoperative day (Chapter 3.3.7).

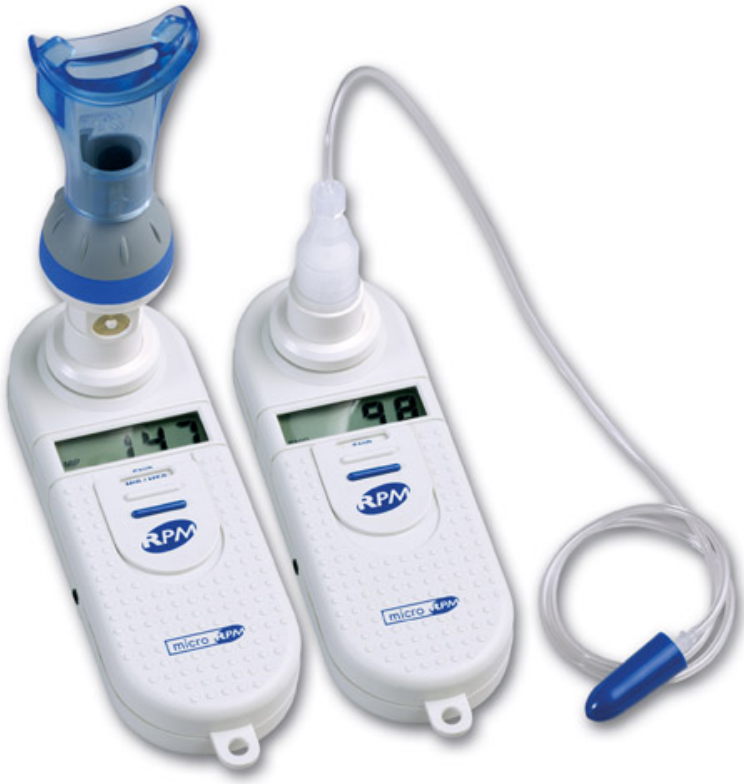

Figure 4. 1 MicroRPM device used to measure RMS (MicroRPM, CareFusion Germany 234 GmbH, Leibnizstrasse 7, D-97204 Hoechberg, Germany).

4.4.7 Implemented strategy (I-COUGH Plus)

The I-COUGH bundle is a perioperative respiratory care bundle that consists of interventions before and after operation. I-COUGH bundle is now incorporated within ERAS Plus (158). I-COUGH bundle includes Incentive spirometry, Coughing, Oral care, Understanding, Get out of bed and Head of bed elevated (151). I-COUGH Plus involves all the earlier interventions in addition to the use of IMT alongside with IS. The interventions within I-COUGH Plus are described in table 4.1. Information about I-COUGH Plus was provided to the patients during an education session, called surgery school, that is conducted preoperatively by a physiotherapist. Surgery school is part of the I-COUGH Plus where Understanding item is achieved. Surgery school provides patients with information about their surgery, what they should expect after surgery and what they should do before and after their surgery for better recovery. In surgery school, patients were educated about the importance and benefits of all the I-COUGH plus items and asked to increase their activities (walking, gardening, dancing or cycling), at least 20 to 30 minutes daily before their surgery. Patients were also asked and encouraged to stop or decrease alcohol intake and smoking before the surgery. During surgery school, patients trained on how to use the IMT and IS devices.

The IS device used in I-COUGH plus is called Spiro-Ball (Spiro-Ball, Leventon, Barcelona, Spain) (Figure 4.2). Sipro-Ball is the IS device that's used routinely in our local hospital. Spiro-Ball used is adult device which has maximum volume of 4000 ml. Patients were asked to use the IS twice daily with 10 breaths each session for at least one week before their surgery. Then, patients had to use the IS on hourly basis with 10 breaths after the surgery until discharge.

The IMT device used in I-COUGH Plus is called POWERbreathe Medic Plus (POWERbreathe Medic Plus, HaB International Ltd, Southam, Warwickship, England, UK) (Figure 4.2). The IMT device has 10 levels with resistance load ranges from 9 cmH_2O to 78 cmH_2O. Patients were asked to use the IMT twice daily before surgery, alongside with the IS, with 3 sets of 10 breaths (total of 30 breaths each session) allowing one-minute rest between each set. The load level to start with for each patient was based on 40% of their baseline MIP. Then, patients had to increase the load level by one level every subsequent day until their surgery. Similarly, patients had to start using the IMT on 1st postoperative day until discharge. Postoperatively, the load resistance patients had to start with was based on their 40% of their MIP at 1st postoperative day. The resistance load of each level is shown in table 4.2 below. POWERbreathe diary was handed to the patients to record number of breaths and load level achieved each session every day in order to ensure patient's adherence with exercises (Appendix 7). The POWERbreathe diary was designed and recommended to be used by the manufacturer for adherence evaluation.

Table 4. 1 Perioperative I-COUGH Plus interventions

ICOUGH item	Preoperative interventions	Postoperative interventions
I- Incentive spirometry (IS) Plus IMT	IS and IMT devices were given to patients to use before the surgery twice a day until the surgery.	IS and IMT devices were given to patients to use after the surgery until they discharged.
C- Coughing with deep breathing	Patients were encouraged to cough out secretion and perform deep breathing before surgery.	Patients were encouraged to cough out secretion and perform deep after surgery. Good pain management was considered in order to help patient to cough effectively.
O- Oral care	Patients had to brush their teeth/dentures at least twice daily with the use of antibacterial 10-15 minutes mouthwash after brushing at least twice daily. Patients had to visit their dentist if they have an active dental problem.	Patients had to brush their teeth/dentures at least twice daily with the use of antibacterial 10-15 minutes mouthwash after brushing at least twice daily.
U- Understanding	Surgery school	Patients were followed up and encouraged to adhere with I-COUGH Plus items after surgery.
G- Get out of bed (early mobilisation)	No intervention was required before surgery.	Patients had to mobilise and get out of bed from first and subsequent postoperative day.
H- Head of bed elevated	No intervention was required before surgery.	Head of bed was elevated at 30°.

IMT: Inspiratory Muscles trainer, IS: Incentive Spirometer

Figure 4. 2 Spiro-Ball (Leventon, Barcelona, Spain) and POWERbreathe Medic Plus (HaB International Ltd, Southam, Warwickship, England, UK)

Table 4. 2 POWERbreathe load levels

Level	0	1	2	3	4	5	6	7	8	9	10
Load (cmH_2O)	9	16	23	29	36	43	50	57	64	71	78

cmH_2O: Centimetre of Water

4.4.8 Ethical considerations

This quality improvement study is part of PQIP to assess the success of implemented improvement, thus, does not need an additional ethical approval. Local ethical approval for PQIP was already sought (Chapter 3.3.3).

All data were collected after obtaining patient's consent. Patients were informed that their participation is voluntary, and they have the right to withdraw any time if they decide to do so after signing the consent. Collection, storage and processing all personal data were according to the requirement Data Protection Act 1998.

This study has very low risk where the patients asked to RMS tests. Performing the RMS tests is considered safe after abdominal surgery where patients only required taking fast deep breaths (159).

4.4.9 Sample size

The sample size calculation was based on the expected improvement of MIP on 3rd postoperative day between the two groups. According to a pilot trial (160), IMT for two weeks preoperatively was able to improve postoperative IMP more than 40% compared to control patients who did not receive IMT. The study showed that median IMP was 42 cmH_2O for control group and 68.5 cmH_2O for IMT group. In this study, preoperative interventions were at least one week before surgery. However, we expect patients to perform IMT for almost two weeks before surgery as usually surgeries performed within one to three weeks from pre-screening clinic visit. Therefore, we expected a 40% improvement in the mean of MIP on 3rd

postoperative day after implementation of I-COUGH Plus. Considering mean ± standard deviation of MIP on 3rd postoperative day for 10 patients recruited before implementation (34.80 ± 15.05), power of 80% and significance level of 5%, a minimum of 20 patients for each group were needed. Accordingly, a value of 22 patients were planned to be recruited before and after implementation of I-COUGH Plus.

4.4.10 Data analysis

All collected data were written in PQIP data collection form and inputted into the PQIP website and then imported as excel documents. Afterward, data from the excel sheet were exported to Statistical Package for Social Sciences (SPSS) for appropriated coding. All data were analysed using SPSS version 25.0 and graphs were generated using GraphPad Prism version 8. Data were split into two groups (standard care vs. I-COUGH Plus) to measure the differences. Paired t-test was used to show the reduction of RMS after surgery. Change in RMS measurements was calculated as (MIP/MEP/SNIP on day 3 minus preoperative MIP/MEP/SNIP) to express the reduction of RMS measurements postoperatively. Shapiro-Wilk test of normality was performed for all continuous variables. Accordingly, t-test was used for age, height, weight and RMS measurements while Mann-Whitney U test for length of stay. Results were reported as mean, standard deviation and corresponding t-test value and p-value for normally distributed data and median, Interquartile Range (IQR) and corresponding Mann-Whitney U value and p-value for non-normally distributed data. For categorical variables, chi-square test was used, and the results were reported as counts, percentages and corresponding X^2 value and p-values.

4.5 Results

Total of 60 patients were invited to take part in the study from May 2019 to March 2020. Of these, 30 patients were excluded from final analysis due to the following reasons: decline to participate, surgery cancellation, already recruited in PQIP by other hospital, withdrew from the study or did not complete RMS tests at 3rd postoperative day (primary outcome measures). Therefore, only 30 patients were included in the final analysis (22 patients before implementation and 8 patients after implementation) (Figure 4.3). The targeted number of patients for each group was 22 patients, but unfortunately, patient recruitment was stopped after implementing I-COUGH Plus due to COVID-19 outbreak as all elective surgeries were suspended.

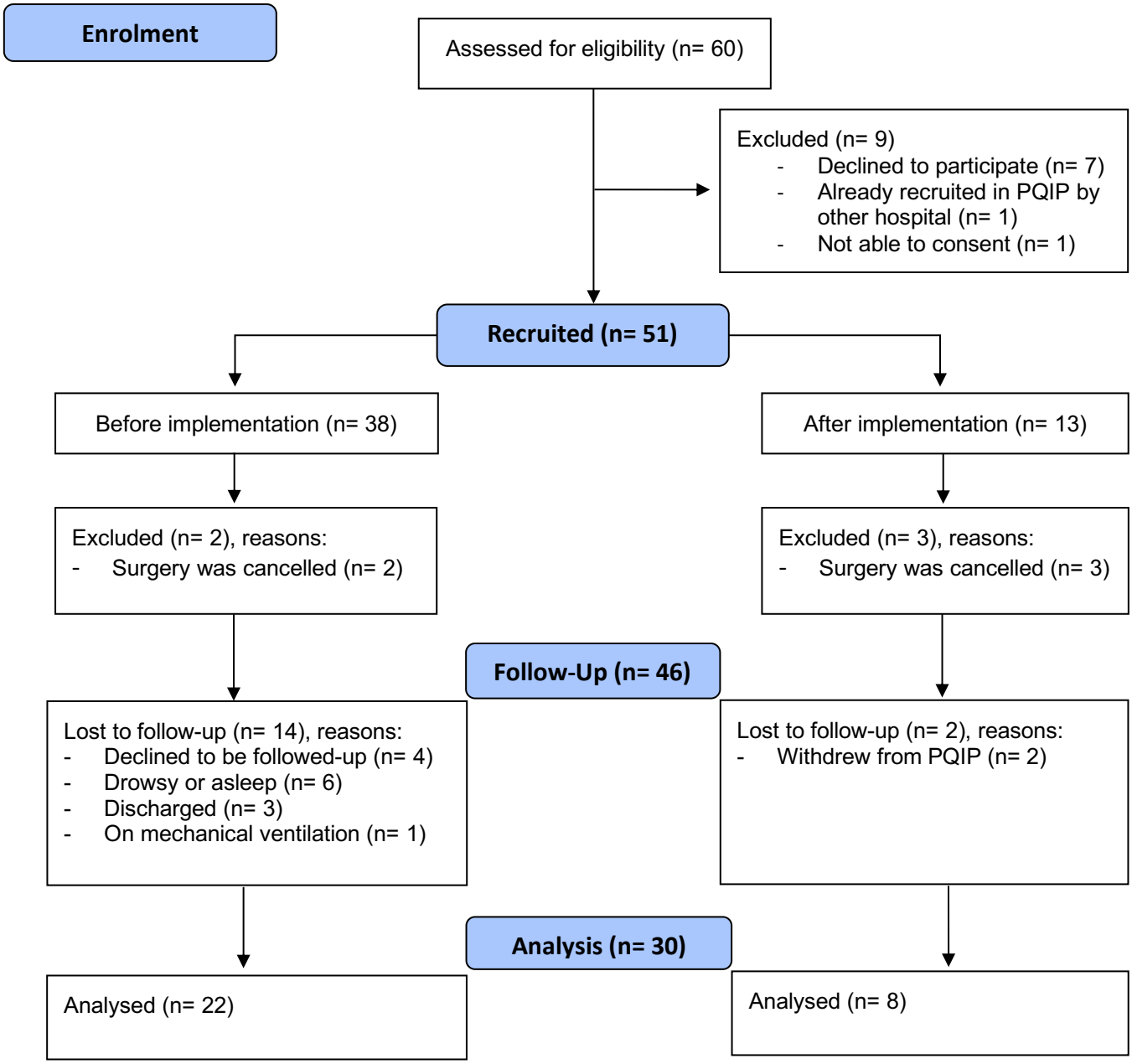

Figure 4. 3 Flow diagram for number of patients who were screened, recruited and analysed

Total of 60 patients were invited to the study. Of these, only 30 patients were included in the final analysis (Before implementation (n=22) vs. After implementation (n= 8)).
N: Number of Patients, PQIP: Perioperative Quality Improvement Programme

4.5.1 Basic demographics and clinical characteristics

The results showed no statistical difference in basic demographics between the patients before and after implementation of I-COUGH Plus. Of these 30 patients included, 22 patients in the standard care group (n=12 (54.5%) males and n=10 (45.5%) females) vs. 8 patients in the I-COUGH Plus group (n=4 (50%) males and n=4 (50%) females), X^2=0.049, p= 0.825. The mean age was 61.91±12.79 years for standard care group vs. 69.63±11.08 years for I-COUGH Plus group, t=-1.508, p= 0.143. Also, there were no statistical difference in preoperative measurements, including ASA grade, smoking history, cardiac failure history, NYHA classification and respiratory failure history (Table 4.3). The surgical incision for all surgeries was not statistically significant between standard care vs. I-COUGH Plus groups (n=19 (86.4%) open upper abdominal and n=3 (13.6%) laparoscopic vs. n=6 (75%) open upper abdominal and n=2 (25%) laparoscopic, X^2=0.545, p= 0.460) (Table 4.3).

Table 4. 3 Demographics and clinical characteristics of patients before and after implementation of I-COUGH Plus

Variable	Mean ± SD or N (%)		P value
	Standard care (n= 22)	**I-COUGH Plus (n= 8)**	
Gender (M/F)	12 (54.5%) / 10 (45.5%)	4 (50%) / 4 (50%)	P= 0.825
Age (years)	61.91 ± 12.79	69.63 ± 11.08	P= 0.143
Height (cm)	170.02 ± 9.11	167.75 ± 8.95	P= 0.549
Weight (kg)	80.29 ± 14.31	80.22 ± 13.60	P= 0.990
ASA - Grade II - Grade III	 - 3 (13%) - 19 (86.4%)	 - 0 (0%) - 8 (100%)	P= 0.271
Smoking history - Current smoker - Never smoked - Ex-smoker, stopped > 6 months - Ex-smoker, stopped < 6 months - Not known	 - 2 (9.1%) - 10 (45.5%) - 10 (45.5%) - 0 (0%) - 0 (0%)	 - 1 (12.5%) - 4 (50%) - 3 (37.5%) - 0 (0%) - 0 (0%)	P= 0.914
Cardiac failure history - No failure - Diuretic digoxin antianginal or antihypertensive therapy - Peripheral oedema warfarin therapy or borderline cardiomegaly	 - 18 (81.8%) - 2 (9.1%) - 2 (9.1%)	 - 8 (100%) - 0 (0%) - 0 (0%)	P= 0.432
NYHA - Grade I - Grade II	 - 9 (40.9%) - 13 (59.1%)	 - 2 (25%) - 6 (75%)	P= 0.424
Respiratory failure history - No dyspnoea - Dyspnoea on exertion or CXR: mild COPD - Dyspnoea limiting exertion to <1 flight or CXR: moderate COPD	 - 12 (54.5%) - 10 (45.5%) - 0 (0%)	 - 6 (75%) - 2 (25%) - 0 (0%)	P= 0.312
Epidural (Yes/ No)	10 (45.5%) / 12 (54.5%)	1 (12.5%) / 7 (87.5%)	P= 0.098
Open vs. Laparoscopic	19 (86.4%) vs. 3 (13.6%)	6 (75%) vs. 2 (25%)	P= 0.460

No significant difference in demographics and clinical characteristics between the before and after implementation groups

ASA: American Society of Anaesthesiologists, CM: Centimetre, COPD: Chronic Obstructive Pulmonary Disease, CXR: Chest X-Ray, F: Female, IQR: interquartile range, KG: kilogram, M: Male, N: Number of patients, NYHA: New York Heart Association, SD: Standard Deviation

4.5.2 Improvement of preoperative RMS and change in RMS measurements on 3rd postoperative day

Paired t-test showed no significant difference in RMS measurements between baseline and preoperative measurements after implementation of I-COUGH Plus (Table 4.4). Paired t-test showed significant difference in RMS measurements between preoperative and 3rd postoperative day measurements in both groups, however, t-test showed no significant difference in preoperative and postoperative MIP, MEP and SNIP between the standard care and I-COUGH Plus groups (Table 4.5). The results also showed no significant difference in RMS reduction on 3rd postoperative day between the standard care and I-COUGH Plus groups. The mean change in RMS measurements for standard care group (n= 22) vs. I-COUGH Plus group (n= 8) was as follow: MIP change -20.36 ± 12.01 vs. -28.31 ± 17.70, t=1.376, p= 0.180; MEP change -30.14 ± 18.80 vs. -25.00 ± 8.22, t=-0.741, p= 0.465; SNIP change -28.55 ± 18.19 vs. -27.63 ± 76, t=-0.137, p= 0.892 (Table 4.6) (Figure 4.4).

Table 4. 4 Difference in RMS measurement between baseline and preoperative RMS measurements for patients after implementation of I-COUGH Plus

RMS measurements	Mean ± SD (n=8)		P value
	Baseline RMS	Preoperative RMS	
MIP (cmH_2O)	63.88 ± 23.35	68.50 ± 23.00	P=0.054
MEP (cmH_2O)	68.75 ± 24.43	68.13 ± 20.69	P=0.789
SNIP (cmH_2O)	62.75 ± 16.25	65.88 ± 16.74	P=0.089

Paired t-test showed no significant difference in RMS measurements between baseline and preoperative measurements after implementation of I-COUGH Plus.

CmH_2O: centimetre of water, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, N: Number of Patients, RMS: Respiratory Muscle Strength, SD: Standard Deviation, SNIP: Sniff Nasal Inspiratory Pressure

Table 4. 5 Difference in preoperative and postoperative RMS measurements for patients before and after implementation of I-COUGH Plus

RMS measurements	**Mean ± SD**		**P value**
	Standard care (n= 22)	**I-COUGH Plus (n= 8)**	
MIP (cmH_2O)			
- Preoperative	56.18 ± 20.74	68.50 ± 23.00	P=0.173
- 3rd postoperative day	35.82 ± 16.40	40.38 ± 10.20	P=0.471
P value for paired t-test	P<0.001*	P=0.003*	
MEP (cmH_2O)			
- Preoperative	73.09 ± 23.61	68.13 ± 20.69	P=0.604
- 3rd postoperative day	42.95 ± 16.71	43.13 ± 21.11	P=0.982
P value for paired t-test	P<0.001*	P<0.001*	
SNIP (cmH_2O)			
- Preoperative	65.55 ± 25.71	65.88 ± 16.74	P=0.973
- 3rd postoperative day	37.00 ± 16.04	38.25 ± 12.89	P=0.845
P value for paired t-test	P<0.001*	P<0.001*	

* Statistically significant

Paired t-test showed significant difference in RMS measurements between preoperative and 3rd postoperative day measurements in both groups. T-test did not show significant difference in preoperative and postoperative RMS measurements between the standard care and I-COUGH Plus groups.

CmH_2O: centimetre of water, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, N: Number of Patients, RMS: Respiratory Muscle Strength, SD: Standard Deviation, SNIP: Sniff Nasal Inspiratory Pressure

Table 4. 6 Difference in RMS reduction on 3rd postoperative day for patients before and after implementation of I-COUGH Plus

RMS Change	**Mean ± SD**		**P value**
	Standard care (n= 22)	**I-COUGH Plus (n= 8)**	
MIP (cmH_2O)	-20.36 ± 12.01	-28.13 ± 17.70	P=0.180
MEP (cmH_2O)	-30.14 ± 18.80	-25.00 ± 8.22	P=0.465
SNIP (cmH_2O)	-28.55 ± 18.19	-27.63 ± 7.76	P=0.892

T-test did not show significant difference in RMS change between the before and after implementation of I-COUGH Plus.

CmH_2O: centimetre of water, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, N: Number of Patients, RMS: Respiratory Muscle Strength, SD: Standard Deviation, SNIP: Sniff Nasal Inspiratory Pressure

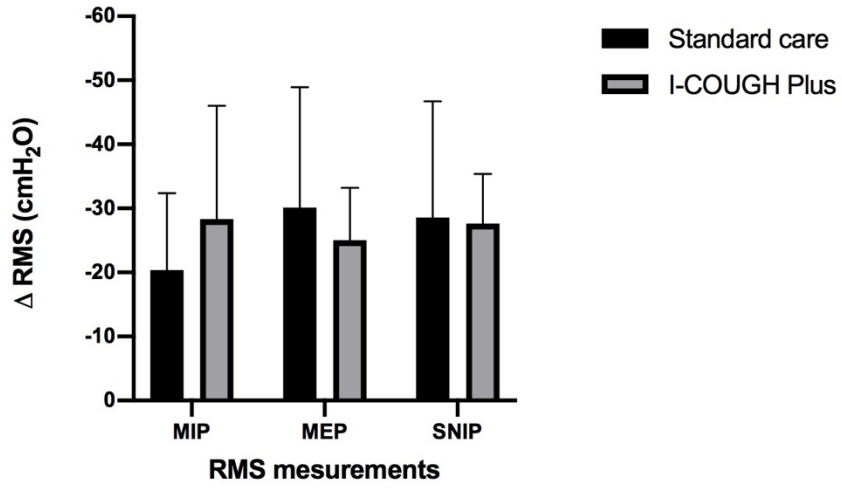

Figure 4. 4 Mean change in RMS before and after implementation of I-COUGH Plus

The graph illustrates the mean reduction in RMS measurements (change between preoperative RMS and 3rd postoperative day) before and after implementation of I-COUGH Plus. The mean ± SD change in RMS measurements for standard care group (n= 22) vs. I-COUGH Plus group (n= 8) was as follow: MIP change 20.36±12.01 vs. 28.31±17.70, p=0.180; MEP change 30.14±18.80 vs. 25.00±8.22, p=0.465; SNIP change 28.55±18.19 vs. 27.63±76, p=0.892.

Δ RMS: Change in RMS measurements = 3rd postoperative day minus preoperative measurements

CmH_2O: centimetre of water, MEP: Maximum Expiratory Pressure, MIP: Maximum Inspiratory Pressure, RMS: Respiratory Muscle Strength, SD: Standard Deviation, SNIP: Sniff Nasal Inspiratory Pressure

4.5.3 Postoperative morbidities, mortality and length of stay

The results showed no significant difference in incidence of PPCs before and after implementation of I-COUGH Plus (22.7% (n=5) in standard care group vs. 37.5% (n=3) in I-COUGH Plus group, p= 0.418). The results also showed no significant difference in all other morbidities except renal complication which was significantly higher after implementation (0% (n=0) vs. 25% (n=2), X^2=5.893, p= 0.015). The rate of infection and gastrointestinal complications were higher before implementation of the I-COUGH Plus but not statistically significant (infection: 4 (18.2%) vs. 1 (12.5%) patients, X^2=0.136, p= 0.712; gastrointestinal: 6 (27.3%) vs. 0 (0%) patients, X^2=2.727, p= 0.099). No patients died in either groups. The median (IQR) of length of stay was not significantly different in both groups (standard care: 6.50 (5.00 – 9.50) days vs. I-COUGH Plus: 9.00 (5.25 – 14.60) days, U=75.500, p= 0.555) (Table 4.7).

Table 4. 7 Postoperative morbidities, mortality and length of stay for patients before and after implementation of I-COUGH Plus

Complication	N (%) or Median (IQR)		P value
	Standard care (n= 22)	**I-COUGH Plus (n=8)**	
PPCs	5 (22.7%)	3 (37.5%)	P= 0.418
Infection	4 (18.2%)	1 (12.5%)	P= 0.712
Gastrointestinal	6 (27.3%)	0 (0%)	P= 0.099
Renal	0 (0%)	2 (25%)	P= 0.015*
Cardiovascular	0 (0%)	1 (12.5%)	P= 0.092
Neurological	0 (0%)	0 (0%)	P= 1.000**
Wound	0 (0%)	0 (0%)	P= 1.000**
Haematological	0 (0%)	0 (0%)	P= 1.000**
Pain	0 (0%)	0 (0%)	P= 1.000**
Mortality	0 (0%)	0 (0%)	P= 1.000**
LOS	6.50 (5.00 – 9.50)	9.00 (5.25 – 14.60)	P= 0.555

* Statistically significant

** Chi-square test could not be computed because variable is a constant (equals 0)

Chi-square test did not show significant difference in morbidities except renal complication which was higher in the I-COUGH Plus group. Mortality rate was zero in both groups. Mann-Whitney test showed no significant difference in the median (IQR) length of stay between the two groups.

IQR: interquartile range, LOS: Length of Stay, N: Number of patients, PPCs: Postoperative Pulmonary Complications

4.5.4 Quality of recovery

The results showed no significant difference in quality of recovery (proportion of patients who had pain or started to be drinking, eating or mobilising at 1st postoperative day) before and after implementation of I-COUGH Plus (Table 4.8).

Table 4. 8 Postoperative pain and DrEaMing for patients before and after Implementation of I-COUGH Plus

Variable	N (%)		P value
	Standard care (n= 22)	**I-COUGH Plus (n= 8)**	
Pain: - None - Mild - Moderate - Sever - Unable to ascertain (Sedated) - Other	 - 15 (68.2%) - 4 (18.2%) - 3 (13.6%) - 0 (0%) - 0 (0%) - 0 (0%)	 - 8 (100%) - 0 (0%) - 0 (0%) - 0 (0%) - 0 (0%) - 0 (0%)	P= 0.190
Drinking (Yes/ No)	20 (90.9%) / 2 (9.1%)	7 (87.5%) / 1 (12.5%)	P= 0.783
Eating (Yes/ No)	18 (81.8%) / 4 (18.2%)	6 (75%) / 2 (25%)	P= 0.680
Mobilising (Yes/ No)	19 (86.4%) / 3 (13.6%)	6 (75%) / 2 (25%)	P= 0.460

Chi-Square test showed no significant difference in proportion of patients who had pain and started drinking, eating and mobilising at 1st postoperative day (quality of recovery).

N: Number of patients

4.6 Discussion

The incidence of PPCs is high following major HPB surgeries in our hospital, with increased length of stay and morbidity rate (Chapter 3). Currently, there is a paucity of data regarding the respiratory physiotherapy modalities targeting PPCs. Systematic review by Pasquina, et al. (127) did not recommend the routine use of respiratory physiotherapy after abdominal surgery. In contrast, other systematic reviews documented that preoperative IMT reduces incidence of PPCs and length of stay as well as improving respiratory muscles strength (117, 119). In chapter two, the systematic review and meta-analysis showed that lung expansion techniques may improve pulmonary function and RMS following major abdominal surgery. Recently, I-COUGH bundle was examined in Manchester and resulted in reduction of PPCs incidence (151). Therefore, we believed adding IMT to I-COUGH, being called I-COUGH Plus, would help more to improve RMS and consequently reduce PPCs following major HPB surgery.

The preliminary results of this study suggested that I-COUGH Plus bundle did not have an effect in improving neither preoperative nor postoperative RMS and reducing PPCs incidence. The results are inconsistent with results of I-COUGH bundle done by Cassidy, et al. (151) in Manchester. We believe that the reason of this contradictory results is the small sample size used, in particular, the difference in number of patients analysed between the two groups in our study. Therefore, our results are not conclusive, and this limitation should be taken into account while reading our results.

ERAS protocol is the standard perioperative practice within our hospital, the QEHB, to decrease postoperative complications and to improve patient outcomes. Moreover, there is no standard interventions targeting PPCs such as perioperative respiratory physiotherapy. Postoperatively, the physiotherapy department screens patients for the need physiotherapy intervention using the Southampton Physiotherapy Post-Operative Screening Tool (SPPOST). Patients with SPPOST score more than 10 will be considered at high risk to PPCs and then will be referred to physiotherapy service to receive respiratory physiotherapy interventions decided by the intensivist based on patient health status. Patients with SPPOST score of 10 or less will be given incentive spirometer with written instructions by physiotherapist and encouraged for mobilisation by critical care nurse.

Regardless of the preliminary results, the I-COUGH Plus is still considered within perioperative practice which hopefully would improve respiratory muscles strength and patient outcomes and reduce PPCs incidence after analysing reasonable number of patients. The I-COUGH Plus bundle has been stopped temporary due to COVID-19 outbreak and will be recommenced after the pandemic.

In the future, more data should be collected, about 22 patients, in order to compare it with the before implementation data concerning respiratory muscles strength improvement as planned in this study. However, expected improvement of 40% used in the sample size calculation in this study would be overestimated as the preliminary results showed about 12% improvement in the mean of MIP on 3rd postoperative day. According to this preliminary result of the 12% improvement, a minimum if 142 patients are needed in each group. Instead, collecting data from 145 patients and then compare it with our previous results in chapter 3

would provide additional knowledge about the effectiveness of I-COUGH Plus in reducing the incidence of PPCs and improving patient outcomes.

4.7 Conclusion

The preliminary results of this quality improvement study showed that I-COUGH Plus has no effect on improving RMS and reduction of PPCs incidence. The results are not conclusive as only 8 patients were recruited after implementation of the I-COUGH Plus and compared with the data of 22 patients before implementation. The I-COUGH Plus is still considered within our perioperative practice and hopefully would have significant improvement in RMS and patients' outcomes and reduction of the incidence of PPCs.

Chapter Five

Discussion

This chapter summarises the discussion points delivered from Chapters two, three and four and attempts to draw a final conclusion about possible future research and implications that would improve current perioperative practice.

5.1 Findings

Postoperative pulmonary complications (PPCs) are common after major abdominal surgery as surgical incision is close to the diaphragm. A variety of different perioperative interventions are used to decrease the incidence of PPCs, such as respiratory physiotherapy. At the time of developing this thesis, the effectiveness of different respiratory physiotherapy techniques in decreasing the incidence of PPCs was unclear. The systematic review and meta-analysis conducted in Chapter two aimed to find the most effective postoperative respiratory physiotherapy techniques that could reduce PPCs after major abdominal surgery. Only five trials were included in the systematic review (122, 123, 128-130) and the techniques examined include chest physiotherapy, deep breathing and coughing, transcutaneous electrical diaphragmatic stimulation (TEDS) and incentive spirometry. The systematic review found the literature is lacking a good quality of researches concerning the effectiveness of postoperative respiratory physiotherapy in reducing the incidence of PPCs. However, chest physiotherapy and lung expansion techniques, such as deep breathing and incentive spirometry, seem to be useful in improving the strength of respiratory muscles and pulmonary function. The systematic review results were consistent with previous reviews as all agree on the deficiency of good quality research and the lack of gold standard techniques targeting PPCs following major abdominal surgery (98, 120, 127).

Furthermore, the thesis also aimed to assess the need for improvement in current perioperative practice in terms of reduction of PPCs and improving patient outcomes. Therefore, an observational study was conducted over one year within the context of the Perioperative Quality Improvement Programme (PQIP) to measure the incidence of PPCs (Chapter 3). The study found that the incidence of PPCs was high (18%) following major hepato-biliary surgeries and also showed that PPCs were associated with prolonged length of stay and other morbidities, such as infectious and gastrointestinal morbidities. The results of this study agree with the findings of Patel, et al. (12) which indicate that PPCs are common and there is a need for implementing perioperative interventions targeting PPCs in our hospital.

Based on the results of Chapter two and three, implementing a care bundle of perioperative respiratory physiotherapy was proposed to improve current perioperative practice in the Queen Elizabeth Hospital Birmingham (QEHB). The I-COUGH approach is incorporated within ERAS Plus and is able to decrease PPCs by 50% following major surgery (151). I-COUGH stands for incentive spirometry (IS), cough and deep breathe, oral care, understanding patient education, get out of bed, and head of bed elevated. In Chapter four, the I-COUGH approach with inspiratory muscles training (IMT), known as I-COUGH Plus, is proposed to be implemented, aiming to enhance respiratory muscle strength perioperatively and, therefore, decrease the incidence of PPCs.

The preliminary results of Chapter four showed that I-COUGH Plus has no effect in improving respiratory muscle strength and incidence of PPCs after major hepato-biliary surgeries. The I-COUGH Plus also has no effect in improving preoperative respiratory muscles strength after

performing breathing exercise interventions for at least one week before surgery. However, these results are not conclusive as only eight patients were recruited after implementation of the I-COUGH Plus. In addition, sample size was calculated based on mean and standard deviation of 10 patients recruited before implementation while expected improvement in mean of maximum inspiratory pressure (MIP) 3rd postoperative day was 40%, which might be overestimated as preliminary results showed an improvement of only 12% with no statistical difference. In addition, the expected improvement in mean MIP of 40% was based on results of a pilot study which investigated the effect of the IMT for two weeks preoperatively. In chapter four, the preoperative interventions were carried out for at least one week preoperatively. Thus, 40% improvement in postoperative MIP could not to be reached as preoperative interventions were carried out over various time depending on waiting time for surgery.

As mentioned in chapter four, a minimum of 142 patient would be required to find significant improvement in postoperative MIP. The I-COUGH Plus is currently no longer being implemented in the QEHB due to COVID-19 outbreak as all elective surgeries have been suspended. It will be recommenced when elective surgeries resume again and, hopefully, will have great benefit after recruiting sufficient number of patients. Despite the results of chapter four is not conclusive, IMT which is incorporated with I-COUGH Plus bundle is found to be effective in improving MIP and reducing PPCs and length of stay following major abdominal surgery (117, 119). Cassidy, et al. (151) collected data over two years, a year before and a year after implementing I-COUGH bundle, and found I-COUGH was effective in reducing PPCs and unplanned intubation.

5.2 Limitations

The limitations of each study have been pointed out fully in the relevant chapters. However, the general limitations of our methodology and outcome measures are summarised in this section. The aim of this thesis is to implement a new care bundle of perioperative respiratory physiotherapy to reduce PPCs and improve patient outcomes following major abdominal surgery. The aim was reached by conducting three studies, systematic review and meta-analysis, prospective observational study and quality improvement study.

The systematic review and meta-analysis aimed to find the most effective respiratory physiotherapy techniques that reduce the incidence of PPCs following major abdominal surgery. This systematic review was limited to only randomised controlled trials that were published from 2000 to 2017, when the review was conducted. The systematic review included trials that only examined postoperative interventions. Due to these limitations, the systematic review included only five studies in the narrative analysis and two studies in the meta-analysis. However, other studies that were excluded by these limitations were sufficiently discussed in the literature. Several systematic reviews have examined the pre- and post-operative lung expansion techniques which have shown to be effective in reducing incidence of PPCs and improving respiratory muscle strength following major abdominal surgery (98, 117, 119). This systematic review also suggested the use of lung expansion techniques to improve respiratory muscle strength and pulmonary function postoperatively. Therefore, perioperative lung expansion techniques, including IMT, IS and deep breathing, were incorporated within the I-COUGH Plus. In chapter three, most of PPCs were occurred at

day of surgery and 1st postoperative day which indicates the need to commence intervention preoperatively as demonstrated in chapter four.

Thereafter, the observational study within the PQIP was conducted aiming to investigate the incidence and severity of PPCs in order to quantify the need for improvement. Incidence of PPCs was measured at day 7 postoperatively by the Postoperative Morbidity Survey (POMS, which is a binary outcome measure that quantifies the presence of morbidities. As stated in Chapter 3, POMS was completed on day 7 postoperatively and patients who were discharged before day 7 were considered to have no complications. It is likely to be discriminative to consider patients who were discharged earlier to have had no complications. However, patients who did not complete the POMS as they were discharged before day 7 recovered very well. POMS at day 7 is a well-validated morbidity outcome measure following elective surgeries (5, 144). In addition, results from Chapter three showed that the majority of patients who completed the POMS at day 7 developed postoperative complications, in particular PPCs which were also associated with prolonged length of stay. Therefore, patients who developed complications are expected to stay in hospital for longer than 7 days. Major limitation of this study is missing some risk factors that could have serious impact on development of PPCs such as previous chemotherapy and immunosuppressants, respiratory co-morbidities, duration of mechanical ventilation, fluid management, and surgery duration. In this study, the respiratory co-morbidities were limited only to mild or moderate COPD. In addition, duration of surgery was recorded as less than two hours, between two to three hours and more than three hours. However, all surgeries in this study lasted more than three hours.

The results of Chapter three cannot be generalised to all major abdominal surgeries as only patients who underwent major hepato-biliary surgery were recruited. However, the QEHB is one of the largest hepato-biliary centres in the United Kingdom where a large percentage of major abdominal surgeries are hepato-biliary.

In Chapter four, the new perioperative respiratory physiotherapy bundle, I-COUGH Plus, was examined in terms of improving respiratory muscle strength and patient outcomes after major hepato-biliary surgery. The main limitation in this quality improvement study is the small sample size collected after implementation of I-COUGH Plus. Data were collected only from patients who agreed to enrol into the PQIP, wherein recruitment rate was very low due to surgery cancellation and patients' withdrawal. Therefore, the targeted sample size could not be reached within the limited time period of the completion of this thesis. However, results were promising, and improvements are expected after collecting a sufficient number of patients.

It should be taken in account that incidence of PPCs could not be used as primary outcome in this study due to low effect size, as a huge sample size would be required. The required sample size for the outcome incidence of PPCs would require more than three years to be completed, which could not be accomplished during this thesis. Instead, respiratory muscle strength was used as a surrogate outcome measure of incidence of PPCs in this study. Systematic reviews have documented that strengthening respiratory muscles before and after surgery contributes to subsequent reduction of PPCs and length of stay (117, 161). Interventions using the I-COUGH Plus bundle mainly target respiratory muscle strength, which

is valid outcome to measure the success of this bundle in terms of improving respiratory muscle strength postoperatively.

5.3 Future work

PQIP is still ongoing nationally, investigating the need for improvement in current perioperative practice. The incidence of PPCs is still high following major abdominal surgery and is associated with increased postoperative hospital stay and presence of other morbidities. Thus, future work should seek continuous monitoring and improvement of current perioperative practice regarding PPCs, length of stay, morbidity and mortality.

1. The effectiveness of postoperative respiratory physiotherapy techniques is still unclear and randomised controlled trials are needed to find the most effective techniques with regard to PPCs reduction and improvement in patient outcomes after major abdominal surgery. Effective techniques would help in modifying the I-COUGH Plus bundle in the event additional improvement is needed.
2. An updated systematic review should be conducted concerning new perioperative respiratory physiotherapy techniques in reducing PPCs and improving pulmonary function and respiratory muscle strength following major abdominal surgery.
3. PQIP helps in investigating postoperative morbidities, in particular PPCs, mortality, length of stay and patient outcomes after implementation of the I-COUGH Plus bundle. Therefore, continuous evaluation of the perioperative practice through PQIP is required with consideration of additional risk factors such as previous chemotherapy. This would provide better understanding of risk factors associated with PPCs and help in improving postoperative patient outcomes and recovery. Quality improvement studies would also help in cost-saving by enhancing recovery as in the case of reducing the incidence of PPCs, which is strongly associated with prolonged hospital stay.

4. Effectiveness of the I-COUGH Plus should be investigated in improving respiratory muscle strength following major abdominal surgery, as Chapter four provided only preliminarily results. This should be done by collecting data from the 22 patients to be compared with the data collected before the implementation of I-COUGH Plus in Chapter four. In addition, a correct power calculation would provide more appropriate number of patients needed as expected improvement used in chapter 4 was overestimated. Furthermore, measuring incidence of PPCs over one year would also provide better understanding about the impact of I-COUGH Plus on reducing incidence of PPCs.
5. Implementation of the I-COUGH Plus bundle would be better conducted by a complex framework through different phases such as development, feasibility, evaluation and implementation.

5.4 Conclusion and Implications

This thesis aimed to investigate the need for improvement in current perioperative practice and to test the effectiveness of the I-COUGH Plus bundle in strengthening the respiratory muscles and reducing PPCs following major abdominal surgery. The systematic review highlighted that lung expansion techniques, e.g. inspiratory muscles training and deep breathing, are effective in improving respiratory muscle strength and pulmonary function following abdominal surgery. However, the literature is still lacking robust clinical trials that assess the effectiveness of postoperative respiratory physiotherapy in reducing PPCs following major abdominal surgery.

PQIP has helped in investigating the need for improvement in our perioperative practice as incidence of PPCs was extremely high, which was strongly associated with prolonged length of stay following major hepato-biliary surgery. The majority of PPCs were atelectasis, which occurred in the first postoperative day. Therefore, a perioperative respiratory physiotherapy bundle targeting PPCs, such as I-COUGH Plus, was required. Accordingly, the I-COUGH Plus bundle was implemented in our local hospital for patients undergoing major hepato-biliary surgery. The results showed I-COUGH Plus has no effect on improving respiratory muscle strength or reducing PPCs. However, these were only preliminary results as more data need to be collected for final analysis.

The main implication of this thesis is that the implementation the I-COUGH Plus bundle, which is still under investigation, can hopefully help to improve respiratory muscle strength and, therefore, reduce PPCs following major hepato-biliary surgery. PQIP enables continuous

evaluation of perioperative practice and indicates the need for improvement. Thus, after revealing its success in major hepato-biliary surgery, PQIP would potentially help in implementing I-COUGH Plus following all major abdominal surgeries.

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7 Appendixes

Appendix 1: Search strategy for each database

Medline search strategy:
1. colorectal surgery/ or general surgery/ or urology/ 2. digestive system surgical procedures/ or portoenterostomy, hepatic/ or gastrectomy/ or hepatectomy/ or liver transplantation/ or pancreatectomy/ or pancreaticoduodenectomy/ or pancreaticojejunostomy/ 3. Aortic Aneurysm, Abdominal/su [Surgery] 4. cystectomy/ or kidney transplantation/ or nephrectomy/ 5. Abdomen/su [Surgery] 6. 1 or 2 or 3 or 4 or 5 7. physical therapy modalities/ or breathing exercises/ or chest wall oscillation/ 8. respiratory therapy/ or drainage, postural/ 9. Incentive Spirometry.mp. 10. respiratory muscles/ or diaphragm/ or intercostal muscles/ 11. Continuous Positive Airway Pressure/ 12. Lung expansion.mp. 13. pulmonary ventilation/ or forced expiratory flow rates/ or forced expiratory volume/ or maximal voluntary ventilation/ 14. postoperative respiratory physiotherapy.mp. 15. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 16. postoperative pulmonary complication.mp. 17. lung diseases/ or lung injury/ or pneumonia/ or pulmonary atelectasis/ or pulmonary edema/ or pulmonary embolism/ or respiratory distress syndrome, adult/ 18. Hypoxia/ 19. 16 or 17 or 18 20. 6 and 15 and 19
Cochrane search strategy:
#1 abdominal surgery #2 general surgery #3 colorectal surgery #4 pancreatic surgery #5 gastric surgery #6 splenectomy #7 hepatic surgery #8 abdominal aortic aneurysm repair #9 urological surgery #10 cystectomy #11 prostatectomy #12 nephrectomy #13 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12

#14	postoperative respiratory physiotherapy
#15	chest physiotherapy
#16	deep breathing exercise
#17	inspiratory muscles training
#18	CPAP
#19	continuous positive airway pressure
#20	incentive spirometry
#21	lung expansion
#22	airway clearance manoeuvre
#23	assisted cough
#24	expiratory airway technique
#25	#14 or #15 or #16 or #17 or #18 or #19 or #20 or #8 or #21 or #22 or #23 or #24
#26	postoperative pulmonary complication
#27	#13 and #25 and #26

CINAHL search strategy:

S1. abdominal surgery
S2. general surgery
S3. colorectal surgery OR pancreatic surgery OR spleenectomy OR gastric surgery OR hepatic surgery
S4. abdominal aortic aneurysm repair
S5. urological surgery OR cystectomy OR nephrectomy OR prostatectomy OR renal surgery
S6. S1 OR S2 OR S3 OR S4 OR S5
S7. postoperative respiratory physiotherapy OR chest physiotherapy OR deep breathing exercises OR inspiratory muscle training OR incentive spirometry OR airway clearance techniques OR assisted cough
S8. postoperative pulmonary complications OR atelectasis OR pneumonia
S9. pneumothorax OR aspiration pneumonia OR hypoxemia OR hypoxia
S10. S8 OR S9
S11. S6 AND S7 AND S10

Embase search strategy:

1. abdominal surgery/
2. colorectal surgery/
3. pancreas surgery/ or gastrointestinal surgery/ or pancreas duct ligation/ or pancreas transplantation/ or pancreaticoduodenectomy/ or pancreaticojejunostomy/
4. stomach surgery/ or gastrointestinal surgery/ or gastrectomy/ or gastroduodenostomy/ or gastroenterostomy/ or gastrojejunostomy/ or gastropexy/ or gastroplasty/ or gastrostomy/ or gastrotomy/ or percutaneous endoscopic gastrostomy/ or pyloromyotomy/ or pyloroplasty/ or pylorus ligation/ or stomach bypass/ or stomach fundoplication/ or stomach pouch/
5. descending aorta surgery/ or aorta surgery/
6. urologic surgery/
7. cystectomy/
8. prostatectomy/
9. nephrectomy/

10. liver surgery/ or hepatic artery ligation/ or hepatocyte transplantation/ or liver resection/ or liver transplantation/
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. breathing exercise/
13. lung expansion.mp.
14. breathing muscle/ or muscle strength/ or muscle training/ or inspiratory muscle training.mp.
15. positive end expiratory pressure/
16. spirometry/ or incentive spirometry.mp.
17. lung clearance/
18. TENS.mp.
19. lung disease/ or atelectasis/ or postoperative complication/ or lung complication/ or postoperative pulmonary complication.mp.
20. bacterial pneumonia/ or pneumonia/ or aspiration pneumonia/
21. hypoxemia/ or hypoxia/
22. 12 or 13 or 14 or 15 or 16 or 17 or 18
23. 19 or 20 or 21
24. 11 and 22 and 23

Appendix 2: GRADE assessment

Outcome: incidence of PPCs

GRADE criteria	Rating	Reasons for down- or upgrading	Overall quality of evidence
Study design	**RCT (starts as high quality)** Non-RCT (starts as low quality) **High ++++**	RCT	**Very low +OOO**
Risk of bias	**No** serious (-1) very serious (-2) **High ++++**	Most of the information from included studies were at low or unclear risk of bias that unlikely to alter the results	
Inconsistency	No serious (-1) **very serious (-2)** **Low ++OO**	Substantial heterogeneity (I^2= 50% to 90%)	
Indirectness	**No** serious (-1) very serious (-2) **Low ++OO**	Not at all	
Imprecision	No **serious (-1)** very serious (-2) **Very low +OOO**	Small number of participants wide CI in on study out of two studies	
Publication bias	**Undetected** Strongly suspected (-1) **Very low +OOO**	No publication bias detected	
Other (upgrading)	Large effect (+1 or +2) Dose response (+1 or +2) No Plausible confounding (+1 or +2) **Very low +OOO**	No upgrading	

Appendix 3: Patient Information Sheet

Perioperative Quality Improvement Programme

Participant Information Sheet

We may invite you to consent to taking part in a national study aimed at improving the quality of NHS surgical care. Please read the information below and ask any questions you would like to.

What is PQIP?

PQIP stands for the Perioperative Quality Improvement Programme. "Perioperative" refers to the time before, during and after surgery. Our aim is to improve the care and treatment of patients undergoing major surgery in the United Kingdom. We do this by collecting and studying information about you, your surgery, and then your recovery afterwards.

How does PQIP help patients?

The information collected by PQIP is used by doctors, nurses and medical researchers to:
Produce information on the quality of care received by patients undergoing major surgery in NHS hospitals.
Ensure that any changes or improvements to our services benefit patients
Learn about the best ways in which doctors and nurses can use patient information to improve quality of care
Understand better what happens to patients after they leave hospital after having a major operation, and whether the surgery has had a beneficial effect on their longer-term health.

What would taking part involve?

We collect information about you, your surgery, and then your recovery afterwards, both in hospital and at home. This information does not affect the care you receive. Some of this information is provided directly by you, about how you feel about your general health. Other information will be completed by your doctors and nurses, and includes information about the type of surgery, anaesthesia and care your receive before, during and after surgery.

If you consent, we would like you to complete three short questionnaires now, before your surgery. These will take about 20 minutes to complete. We will then contact you the day after your operation, and again on day 3 after surgery to answer some of these questions again (we will either visit you on the ward, or phone you at home if you have been discharged) – these questions should only take 10 minutes to complete.

We will also email or telephone you to ask some questions again 6 months and one year after your operation. These questions should take 10 minutes to answer. All of these questions are aimed at understanding how you feel about your general health and quality of life. This information will help us provide better information for future patients about what to expect from their surgery and how they will recover afterwards. If you later decide not to answer these questions, you do not have to.

Why does PQIP need my personal details?

To help PQIP provide an in-depth picture of your care, we send your personal details (NHS number, date of birth, postcode) to NHS Digital (England), NHS Wales Informatic Service (Patient Episode Database for Wales, Wales) or NHS National Services Scotland (Scotland). These organisations will link information to individual participants in the study which will tell us if you have (for example) been readmitted to hospital after you went home. In addition NHS Digital, NHS Wales Informatic Service, and National Services Scotland are able to provide us with information about people who may have passed away in order that we do not make contact and cause any distress to relatives. This information includes date and cause of death which is sourced from civil registration data on behalf of the Office for National Statistics. The linked information is returned to the PQIP study team in a digital file. The only identifiable details included in this file are your study ID and any information provided on the date and cause of death.

The personal details (listed below) are only shared with NHS Digital, NHS Wales Informatic Service (Patient Episode Database for Wales) or NHS National Services Scotland to enable the linkage to the information held by them. Your details will not be shared with anyone else outside the NHS or research team.
Personal details needed by PQIP are:

✔ Name ✔ Date of birth ✔ Postcode ✔ NHS number

The information collected by PQIP is only used for research after it has been made anonymous.

Who will be able to access my information?

Your information will be anonymised before it is analysed by the study team. Your personal details (detailed above)
are only shared with NHS Digital, NHS Wales Informatic Service (Patient Episode Database for Wales) or NHS
National Services Scotland to enable the linkage to the information held by them. Your details will not be shared
with anyone else outside the NHS or research team.

Only doctors and approved researchers will be able to access the anonymised information which is collected through the PQIP study .

Is my information safe?

Yes. Very strict rules and secure procedures are in place to ensure that your information is kept safe. These systems
and procedures comply with international standards and will be continuously monitored and adapted as necessary
to maintain security over the lifetime of the project.

How long will the study last?

The study will last for 4 years but your involvement will only be for the 12 months following the time of surgery.
Data collected by the PQIP study, and linked data from NHS Digital, NHS Wales Informatic Service and National
Services Scotland will be kept for 30 years in order to track your long term recovery after surgery.

What are the possible benefits of taking part?

It is unlikely that you will benefit directly. Future patients may benefit from an improved NHS as a result of the
information we have collected about you and your care.

What are the risks of taking part?

This is a very low risk study recording your routine care and your experience as a patient. There are no risks.

Can I stop being in the study?

You can decide to stop participating at any time – please contact a member of the research team at your local
hospital or at the central office listed below.

What other choices do I have if I do not take part in the study?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no
penalty to you. Your care will not be affected either way.

What are the costs of taking part in the study? Will I be paid for taking part in this study?

There are no costs to you for taking part in this study. You will not be paid for taking part in this study.

Who is organizing and funding this study?

The study is being led by the Royal College of Anaesthetists. The details are being organised by a

multidisciplinary
project team consisting of anaesthetists, surgeons, physicians, nurses and patients. The research costs for the study
have been supported by the Royal College of Anaesthetists and the Health Foundation.

Who has reviewed this study?

The study design has been reviewed by the South East Coast Research Ethics Committee before any patients were
approached to participate.

What will happen to the results?

The results will be analysed and written up for publication in scientific journals, professional literature, social media
and conference presentations. Participants will not be able to be identified in any publication.

What if there is a problem?

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by
members of staff you may have experienced due to your participation in the research, National Health Service or
UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more
information on this. Your hospital's Patient Advisory Liaison Service (PALS) may also be able to help.
In the unlikely event that you are harmed by taking part in this study, compensation may be available. If you suspect
that the harm is the result of the Sponsor's (University College London) or the hospital's negligence then you may be
able to claim compensation. After discussing with your research doctor, please make the claim in writing to Dr
Ramani Moonesinghe who is the Chief Investigator for the research and is based at University College London
Hospital. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may
have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Finding out more

PQIP Website	Email
www.pqip.org.uk	pqip@rcoa.ac.uk

PQIP Helpline
0207 092 1678 Mon-Fri, 9am to 5pm (excluding public holidays)

PQIP Centre
National Institute for Academic Anaesthesia's Health Services Research Centre,
Royal College of Anaesthetists, Churchill House, 35 Red Lion Square, London, WC1R 4SG

Giving your consent is voluntary and more information is available if you are unsure.

Appendix 4: Consent form

Perioperative Quality Improvement Programme

Patient Consent Form

One copy should be given to the participant, one copy placed in their medical notes and one copy retained by the research team

PQIP Perioperative Quality Improvement Programme

Patient Details

Surname

_____

Forename

_____

Date of Birth

_____

Phone number (for contact on Day 3 if discharged from hospital)

_____

Email address (for contact for questionnaires at 6 months and 12 months after surgery)

_____

Would you prefer to be contacted by telephone or email to complete questionnaires in 6 and 12 months time?

Phone ☐ Email ☐ Don't mind ☐

I would like to receive updates on PQIP from the study team, approximately once a year, by email:

Yes please ☐ No thanks ☐

To be completed by the hospital

Hospital

_____

NHS number

_____

	Please initial
1. I confirm that I have read the participant information sheet dated 16/06/2017 (version 0.9) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. If I choose to withdraw, I understand that no further information will be collected about me, but anonymous information provided may still be used for research.	☐
3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the Royal College of Anaesthetists, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
5. I understand that personal details will be shared with NHS Digital (England), NHS Wales Informatic Service (Patient Episode Database for Wales, Wales) or NHS National Services Scotland (Scotland) to obtain information held by them and the Office for National Statistics in order to provide details about my health status and hospital admissions that are not otherwise collected by the PQIP study (see patient information sheet for more details).	☐
6. I agree to take part in the above study.	☐

NAME: _____ SIGNATURE: _____ DATE: _____

To be completed by the hospital (person accepting patient consent)

Name Signature

_____

Position Date

_____

Appendix 5: CRF

CRF is available at PQIP website

https://pqip.org.uk/pages/study_documents

Appendix 6: QoR15

Patient Booklet – Page 5

Please complete before surgery

QOR15: Quality of Recovery questionnaire

Perioperative Quality Improvement Programme

We are surveying how well our patients are recovering from their surgery, from a patient's perspective. We believe that this will improve the quality of our service, and your experiences in the future. We would like you to complete this questionnaire before your operation so that we understand how your health is now, and will ask these questions again in 3 days' time.

Part A

How have you been feeling at home in the weeks before your operation?
(0 to 10, where: 0 = none of the time [poor] and 10 = all of the time [excellent])

1. Able to breathe easily	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
2. Been able to enjoy food	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
3. Feeling rested	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
4. Have had a good sleep	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
5. Able to look after personal toilet and hygiene unaided	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
6. Able to communicate with family or friends	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
7. Getting support from hospital doctors and nurses	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
8. Able to return to work or usual home activities	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
9. Feeling comfortable and in control	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time
10. Having a feeling of general well-being	None of the time	0	1	2	3	4	5	6	7	8	9	10 All the time

Part B

Have you had any of these in the last 24 hours?
(10 to 0, where: 10 = none of the time [excellent] and 0 = all of the time [poor])

11. Moderate pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All the time
12. Severe pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All the time
13. Nausea or vomiting	None of the time	10	9	8	7	6	5	4	3	2	1	0 All the time
14. Feeling worried or anxious	None of the time	10	9	8	7	6	5	4	3	2	1	0 All the time
15. Feeling sad or depressed	None of the time	10	9	8	7	6	5	4	3	2	1	0 All the time

Appendix 7: POWERbreathe Training diary

POWERbreathe Training diary

The table below is an example of the diary and it shows the minimum load and breaths number you should use by first week of training.

Example

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
1	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning		30		30		30		30		30		30		30
Evening		30		30		30		30		30		30		30

L: Load, B: Number of Breaths

Please try to adhere with the minimum load and breaths for the morning and evening sessions every day. Please have a rest for 1 minute after every 10 breaths. Please increase the load by 1 level every day or as much as tolerated higher than the minimum load in the above table.

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
1	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
2	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
3	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
4	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
5	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
6	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
7	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
8	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
9	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths

Week No	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
10	L	B	L	B	L	B	L	B	L	B	L	B	L	B
Morning														
Evening														

L: Load, B: Number of Breaths