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ADVANCING SURGICAL CARE

# Freemasonry Research Fellows

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## The Freemasons' Fund for Surgical Research



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## Frailty and futility in emergency laparotomy

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### Background

An emergency laparotomy is an invasive surgical procedure carried out through an incision in the abdomen to treat a variety of emergency general surgical conditions, such as a blocked bowel (bowel obstruction) or perforated bowel. It has one of the highest mortality rates of any general surgical procedure. Older people (those aged 70 and over) account for nearly half of all emergency laparotomy patients.

It is projected that by 2050 there will be more than 11 million people aged over 70 living the United Kingdom, therefore the number of emergency laparotomies performed each year are expected to continue to grow. The importance of this research arises from the significant gaps in evidence-based shared-decision making, highlighting the necessity for quantitative data to inform patients comprehensively.

### Aims and objectives

The original objective of my work was to improve the outcomes of older patients having an emergency laparotomy by studying key unknown patient populations. Such as very high or extreme-risk patients and patients that have the least benefit from surgery as they die either during the operation or in the first 72 hours after their operation.

Alongside this our aim was to compare the outcomes of very high risk, older and frail patients having emergency surgery with similar patients who have conservative or best supportive management. However, the data approvals for this aspect of the project from the Healthcare Improvement Partnership have gone through extensive revisions and have not yet been granted.

### Results / outcomes

Our research unearthed previously undiscovered insights, identifying gaps in evidence that impede truly informed decision-making.

Before this research the incidence of death during emergency laparotomy and the characteristic of these patients was not known. We found one in four hundred emergency laparotomies results in intra-operative death, a critical insight, revealing these patients often have a good functional baseline but are acutely and critically unwell at presentation.

### Project impact

Our findings stressed the significance of arterial lactate, surgical pathology like bowel ischaemia and perforation, and clinical frailty score as predictive factors for surgical futility, highlighting their absence in current risk scoring systems. The incorporation of these factors could fortify pre-operative assessments and refine shared decision-making conversations, ultimately aiding in better patient outcomes and potentially averting futile surgical interventions.



Moreover, our research endeavoured to provide a nuanced understanding of surgical risk to patients and their families, emphasizing the need for improved communication about potential complications and impacts on independence. The project redefined the framework to elucidate outcomes of extreme-risk patients, emphasizing the indispensability of concise risk communication.

## Next steps

Quality of life outcomes are a vital next step in emergency laparotomy research, as well as longer term outcomes such as 1-year outcomes. Further work around the decision-making process starting with patient and public involvement to understand more about how decision-making conversations are approached, what information patients are given and how their decisions were reached as well as the patient perspective of futility in surgery.

The project's realisation was contingent upon RCS Fellowship funding; without it, conducting pivotal research would have been challenging. The continuity of this scheme is paramount; it is a catalyst for ground-breaking research with direct repercussions on patient outcomes, enabling advancements in medical science and care that are essential for addressing a myriad of health challenges.

Personally, the research grant has been formative; I (Hannah) have had opportunities to sit on the project team of a national audit, to see how national level best practise is maintained. I have presented nationally and internationally representing my own research and the National Laparotomy Audit, and I have made countless connections with other general surgeons across the United Kingdom and Europe with an interest in emergency laparotomy patient outcomes.



## Novel biomarkers in Pancreaticobiliary Cancers

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### Background

Pancreatic Cancer is a lethal disease with only 1 in 20 patients diagnosed living for more than 5 years and is the fourth most common cause of cancer death in Europe. Despite medical improvements, survival rates for pancreatic cancer have improved by only 4-5% in the past 20 years.

The topic of our research project utilises the recent advances in cancer cell biology, specifically the release of small “particles” called extracellular vesicles (EVs) into the bloodstream and bile which play a large role in protecting and transmitting genetic signals.

### Aims and objectives

The aim of this research project was to discover a small, stable marker for pancreatic (and bile duct) cancer that could detect this disease better and by looking at these particles (EVs) we have a new, unexplored avenue for research.

### Results / outcomes

We were able to recruit 241 patients in total before their diagnosis and this was used to set up a large database from which we have been able to compare patients before their treatment commenced.

Samples were processed using a unique method (Size Exclusion Chromatography) which can be adapted to any other types of fluid and recent advances in genetic analysis have allowed for easier and faster analysis. Currently our research into these markers has led to several promising results which are highly specific to pancreatic and bile duct cancer.

The results of these are still being written for publication and are to be presented to an international audience.

### Project impact

This study has contributed to the basic science understanding of the nature of EVs released by cells in pancreatic and bile duct cancers. As a translational project, we hope to evaluate the role of this as a clinical test, but as yet the results have not made a direct impact on patient care.

This research has developed a novel approach to obtaining EV and analysing the genetic material through the use of size exclusion chromatography which could be used clinically to obtain these markers in a hospital setting within 24 hours. The markers identified were not previously identified in bile and have a role in the development of cancer metastasis. It is hoped these markers could be picked up in blood samples at an early stage and allow more patients to undergo treatment.

An additional specific marker for pancreatic or bile duct cancers would give patients and their families additional information to help them decide treatment options. It is also hoped that more information about the cancer will allow for tailored chemotherapy options.



## Next steps

This is an ongoing project headed by Mr Adam Frampton based at Imperial College London in collaboration with the University of Surrey, University of Southampton, University of Birmingham, & University of Glasgow.

We are currently also working with the VU University Medical Center (Prof Elisa Giovanetti,) to validate a 5-marker panel we have detected in blood. We hope that this research will give more patients the chance at curative treatment and assist those with an uncertain diagnosis contemplating major surgery.

The next stage of our project is dependent on funding and will involve confirmation of these markers (Plasma EV miR-200 family) in a further prospective multicentre cohort study. It may be possible that with recent advances in RNA sequencing and bedside tests arising from COVID-19 that we are able to develop a diagnostic panel using plasma EV miRNAs in the next 5-10 years.