



Liver, Renal,
Urology, Transplant,
Gastroenterology and
Gastrointestinal Surgery
Clinical Academic Group

King's Health Partners

King's Health Partners brings together:

- three of the UK's leading NHS Foundation Trusts
- a world-leading university for health research and education
- nearly 4.8 million patient contacts each year
- 40,000 staff
- nearly 30,000 students
- a combined annual turnover of more than £3.7 billion
- services provided across central and south London and beyond, including nine mental health and physical healthcare hospitals and many community sites
- a comprehensive portfolio of high-quality clinical services with international recognition in cancer, diabetes, mental health, regenerative medicine, transplantation, cardiac and clinical neurosciences
- a major trauma centre and two hyper-acute stroke units

About King's Health Partners

King's Health Partners Academic Health Sciences Centre brings together one of the world's top research-led universities, King's College London, and three of London's most prestigious and highly regarded NHS Foundation Trusts – Guy's and St Thomas', King's College Hospital and South London and Maudsley.

Our partnership provides a powerful combination of complex clinical specialties that cover a wide range of physical and mental health conditions and a breadth of research expertise that spans disciplines from medicine and biomedical sciences to the social sciences and humanities.

There are three parts to our mission: excellence in research, education and clinical care.

To support our mission, we are delivering programmes of work to:

- join up mental and physical healthcare so that we treat the whole person, mind and body;

- increase the value of the care we provide and the outcomes we achieve for our patients and service users;
- integrate care across local primary, secondary and social care services to make it easier for people to get the care and support they need;
- improve the public health of our local community by tackling inequalities and supporting people to live healthy lives;
- bring together our collective strength and expertise in a range of specialist areas to deliver world-leading care, research and education.

We are uniquely structured to deliver our mission for excellence. Our 22 Clinical Academic Groups (CAGs) bring together all the clinical services and staff from the three trusts with the relevant academic departments of King's College London.

Foreword



At King's Health Partners we are committed to improving outcomes for our patients and service users and achieving maximum value for money in everything we do. We believe that being open and transparent about the care and outcomes we deliver results in a culture of improvement across our partnership.

This is why we are publishing a series of outcomes books that will help patients, service users, carers, referring clinicians and commissioners to make better informed decisions. They will also help our staff to drive up the quality of the care we provide. The books report key outcomes for treatments provided by our 22 clinical academic groups. CAGs form the building blocks of our Academic Health Sciences Centre. By bringing together our clinical and academic staff across teaching, training and research, we can use their combined expertise to achieve better outcomes for our patients and service users.

Our books are designed for a clinical and lay audience and contain a summary of clinical outcomes, educational activities, research innovations and publications. They also focus on other important measures, such as staff satisfaction and wellbeing.

The primary purpose of King's Health Partners is to improve health and wellbeing locally and globally. We must deliver this goal in a challenging economic environment with rising demand for, and costs of, healthcare. We will only achieve sustainable health improvement if we strive to increase value. We define value in terms of outcomes that matter to patients, over the full cycle of care, divided by the cost of producing those outcomes. By publishing outcomes books, we have more information to support us measuring the value of the healthcare we provide.

Our goal is to use these books to allow us to reflect on and demonstrate where we are driving improvement and innovation.

Please send comments and suggestions to us at kingshealthpartners@kcl.ac.uk

For more information please visit our website kingshealthpartners.org

A handwritten signature in black ink that reads "John Moxham". The signature is fluid and cursive.

Professor John Moxham
Director of Clinical Strategy, February 2018

Contents

	The value of partnership at King's Health Partners	07
	Introduction	12
	Team	17
	Range of services	18
	Aims and ambitions across the Clinical Academic Group	25
	Transplantation and regenerative medicine	28
	Liver medicine	41
	Hepatobiliary and neuroendocrine tumours	55
	Kidney medicine	69
	Urology	82
	Gastrointestinal – upper GI	96
	Gastrointestinal – lower GI	100
	Digestive diseases – endoscopy services	110
	Digestive diseases – gastroenterology	126
	Bariatric surgery	133
	Nursing prowess	138
	Research in focus	151

Highlights

Transplantation and regenerative medicine p28

- UK's largest live donor kidney transplant programme;
- UK's first paediatric antibody-incompatible live donor kidney transplant, with colleagues at Great Ormond Street Hospital;
- UK's largest experience of kidney transplantation in HIV positive recipients.

Liver medicine p41

- An exemplary viral hepatitis service across all sites of King's Health Partners, with development of a large clinical trials programme in viral hepatitis;
- Continued support and excellence in hepatobiliary medicine through the delivery of endoscopic services in conjunction with gastroenterology across King's Health Partner sites;

- Initiation of protocol driven clinical practice in liver medicine commencing with the management of alcohol-related liver disease, followed by liver cancer (hepatocellular carcinoma).

Hepatobiliary p55

- Largest number of pancreatic surgical resections in England;
- Unique Neuroendocrine Tumour (NET) clinical trials portfolio;
- The KHP NET service is the second largest in the country and one of the larger centres within Europe.

Kidney medicine p69

- Joint renal HIV service has facilitated access to transplantation for this often disadvantaged group;

- Large programme of clinical and basic science research focusing on the mechanism of renal fibrosis in chronic kidney disease;
- Specialist clinics focussing on cystinosis and cystinuria and pre-pregnancy kidney disease.

Urology p82

- A vibrant Professorial unit, Urology at King's Health Partners is designed around a custom-built £4m one-stop clinical hub;
- Largest urological cancer centres in the UK and the highest volume robotics institute;
- Developing and publishing the first standardised international curriculum for training in robotic surgery.

Gastrointestinal – upper GI p96

- Largest volumes of complex procedures in the country with excellent patient outcomes;
- Portfolio of clinical research projects aimed at improving outcomes in patients with oesophageal and gastric cancer;
- International collaborations with research groups at the Karolinska Institute in Stockholm.

Gastrointestinal – lower GI p100

- In the past 2 years the King's College Hospital Colorectal Team have managed over 300 colorectal cancer patients with referrals from both tertiary and local sources;
- High quality specialist multi-disciplinary pathways and rapid access to specialist teams has enabled the King's Colorectal cancer service to achieve a 2 year survival rate of over 85%;
- Multi-professional virtual clinic' allows patients with no identified pathology remote consultation enabling early patient discharge and timely referral back to the GP, reducing delays to patients receiving results and a reduction in unnecessary outpatient appointments.

Digestive diseases – endoscopy services p110

- Comprehensive endoscopy services covers diagnosis and treatment for all diseases of the digestive tract;
- Only centre in the United Kingdom to offer Peroral endoscopic myotomy (POEM) routinely;
- Endoscopy services have attained the highest standards determined by the GRS and JAG accreditation initiative.

Digestive diseases – gastroenterology p126

- Renowned service for treating inflammatory bowel disease (IBD) receiving referrals from throughout the UK with strong focus on personalised medicine;
- Broad portfolio of world-leading translational research;
- Investigator led and commercial clinical trials supported by 3 clinical research nurses.

Bariatric surgery p133

- Experimental studies have provided evidence that has transformed bariatric surgery from a weight loss therapy into a novel surgical discipline aimed at treating diabetes and metabolic illnesses;
- The Bariatric and metabolic surgery service is one of the largest programmes in this specialty in the UK;
- Establishment in 2013 of the first university chair in Metabolic and Bariatric Surgery in the world.

Nursing prowess p138

- The viral hepatitis clinical nurse specialist's (VHCNS) provide an extensive range of services supporting the largest clinical viral hepatitis service in the UK, accounting for 40% of Liver Outpatients activity;
- HPB nurses provide expert, specialised, holistic care for people with liver, pancreatic and biliary disorders;
- Large research portfolio with 41 current research studies in various specialties supported by the nursing team.

The value of partnership at King's Health Partners

King's Health Partners aims to create a centre where world-class research, education and clinical practice (the 'tripartite mission') are brought together for the benefit of patients.

We want to make sure that the lessons from research are used swiftly, effectively and systematically to achieve better patient outcomes, improve public health and join up health and care services for people with physical and mental health problems.

By working together in this way, integrating care across different organisations and sectors, we can not only improve the health of the people we care for, but we can also achieve better value for money.

Integrating mental and physical health

The mind and body are inseparable, and mental and physical health conditions are often connected. The average life expectancy for someone with a long-term mental health illness or learning disability is 15–20 years shorter than for someone without, often due in part to smoking, obesity, diabetes or alcohol misuse. Likewise, many people with long-term physical health conditions suffer from depression or other mental health conditions. Despite this, health services separate care into physical and mental and often fail to share patient information.

At King's Health Partners we are working to overcome these barriers by treating the whole person, through our Mind and Body Programme. We are committed to caring for vulnerable patients with both physical and mental ill health in an integrated manner with better, faster diagnosis and treatment because we know that addressing mental ill health improves physical health outcomes and vice versa. We will treat the whole person by:

- Screening all patients with chronic physical diseases for mental health conditions, and using the learning from this to improve the care we provide;
- Improving our understanding of the physical health needs of people with severe mental ill health;
- Addressing the traditional distinctions between the mind and body in research and education allowing us to train students and staff to deliver more integrated care;
- Better organising and expanding current training provision for physical and psychiatric comorbidity;
- Working with our local commissioners to find new ways of commissioning integrated services;
- Linking IT systems across our partner trusts so that clinicians have access to a person's physical and mental healthcare records;

- Investing in innovative programmes such as IMPARTS (Integrated Mental and Physical Healthcare: Research, Training and Services), 3DfD (3 Dimensions of care for Diabetes) and 3DLC (3 Dimensions of care for long-term conditions);
- Recognising the importance of employee mental and physical health and wellbeing.

Public health

Public health is one of our biggest challenges. At the root of much of the ill health in south London is a high incidence of smoking, alcohol abuse and obesity. With our health and social care partners, we are developing strategies to tackle these public health priorities. We are also developing plans for an Institute for Urban Population Health and care, a collaboration with local partners to bring about transformational change to health in local communities. We want to achieve a measurable improvement and impact on health gain and local management of physical and mental health problems through new evidence based interventions.

Alcohol strategy – key aims

- Developing appropriate resources for clinical staff and patients;
- Developing and implementing training for all staff on harmful drinking, supporting early identification and intervention;

- Establishing ourselves as a centre of excellence for integrated research, training and practice in the management and prevention of alcohol misuse;
- Monitoring the impact of the strategy on indicators of alcohol related harm.

Tobacco strategy – key aims

- Supporting all clinical sites to remain smoke-free after our successful multi-site implementation in 2015, followed by the university in 2016;
- Developing an informatics structure for routinely and systematically recording smoking status;
- Support, referrals and treatment uptake for smoking cessation across the partnership;
- Co-producing clinical care pathway for nicotine dependence treatment;
- Developing and implementing training packages for smoking cessation interventions for all our healthcare professionals;
- Monitoring the impact of our smoking cessation strategy in relation to knowledge and uptake of skills by staff, uptake of smoking interventions, outcomes of interventions, user satisfaction, prevalence of smoking, cost-effectiveness of interventions.

Informatics

Informatics is at the heart of our plans to join up care, research and education. Data is one of our most important assets at King's Health Partners and we have unique strengths in using informatics to improve care, public health, and the efficiency of our health system. Our aim is to use our strength to improve coordination of patient care, across physical and mental health, increase ownership by patients of their own health records, and to enhance clinical decision making through research and planning. We work with our partners across south east London to develop and test new opportunities to use informatics to advance how we care for our local population.

Systems have been developed to enable electronic healthcare records to be shared across our partner organisations and with other healthcare organisations. Our work includes the award-winning 'HealthLocker' programmes, Cogstack, the Clinical Record Interactive Search (CRIS) and the Local Care Record. We are working with patients to make electronic patient information available in an anonymised format between partner trusts, primary care and social care. Together we have a powerful information resource for both practitioners and researchers.

Value Based Health Care

King's Health Partners Value Based Health Care programme is focused on supporting our partner organisations to deliver excellent and consistent health outcomes whilst protecting our NHS resources.

We believe that in order to deliver transformational health improvements that are patient-centred, population-based and sustainable, we must make the best use of every pound available by continually focusing on value for patients and carers across the full cycle of care.

At King's Health Partners, our goal is to:

- Develop meaningful and consistent patient-centred metrics, based on outcomes defined by patients, service users and carers;
- Quantify the potential impact that investment decisions have on our patients, carers, the local health economy and wider society;
- Ensure that the mental, physical and psychosocial needs of people are treated as one;
- Evaluate and learn from the outcomes that we achieve through research and transparent use of data to reduce variation.

We are working with clinical teams across the partnership to redesign pathways of care based on the above principles.

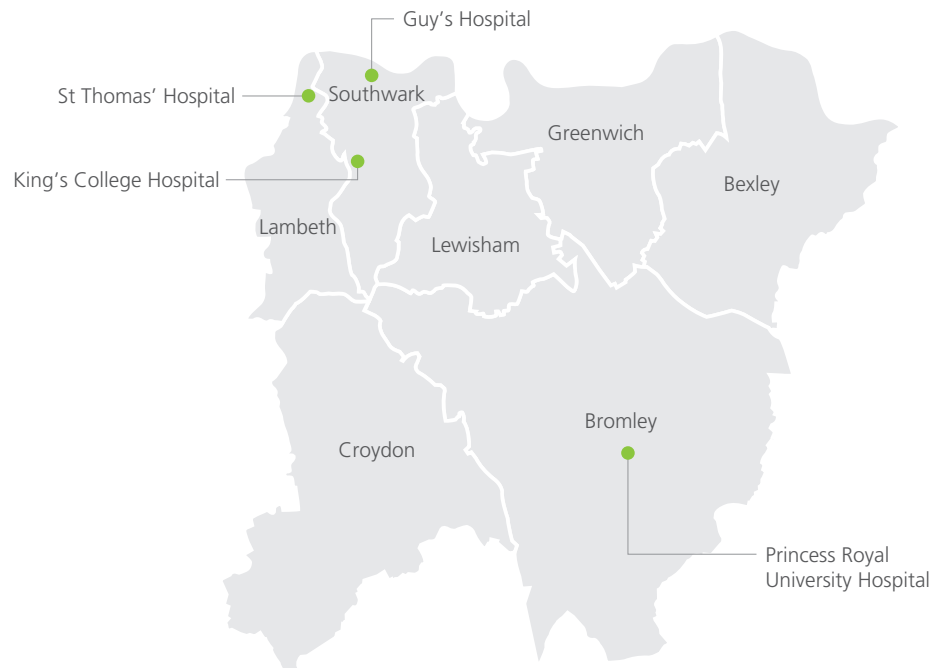
Foreword from the Clinical Academic Group

Our clinical-academic grouping (CAG) covers a wide range of patient-focused activities. It has distinctive programmes in solid organ transplantation and incorporates some of the latest advances in cell and protein therapy research. Large programmes in kidney, pancreas, liver and small bowel care aim to lower the risk of organ failure and to promote return to health following transplantation. The Medical Research Council (MRC) Centre for transplantation embedded in our CAG ensures that new discoveries in immune treatment and monitoring are brought forward through pioneering research and international networking. A centre for prostate disease and complex urological problems promotes early detection and expert treatment including highly regarded research on robotic surgery and linked medical training. An emerging specialist centre for the treatment of inflammatory bowel disease builds on strengths in genetics, immunology,

microbiology, and therapeutics, coupled with state of the art provision for endoscopic, surgical and nutritional services that complete a comprehensive digestive diseases centre. We have recognised expertise in upper gastrointestinal surgery and specialist pelvic floor management skills bringing together the wider experience of the CAG. The CAG oversees the delivery of major cancer services particularly in the fields of urology, hepatobiliary and pancreatic, and upper and lower gastro-intestinal malignancy. Mental health services are an integral part of the CAG, most notably in alcoholic liver disease, obesity and adolescent-to-adult transition clinics, relevant to our clinical practice.

Introduction

Where we provide services from

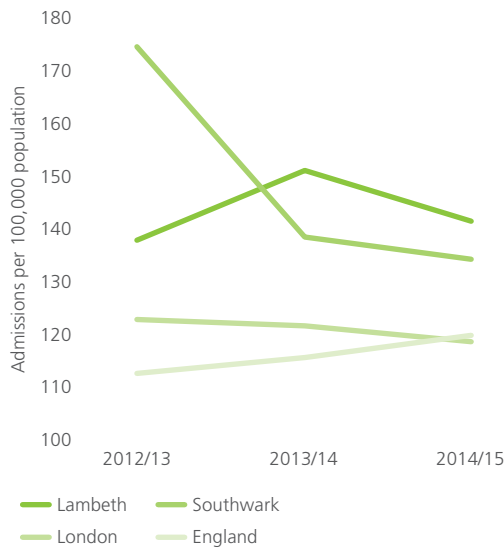


Our clinical academic group incorporates the following:

- Clinical programme of solid organ transplantation in adults and children;
- Clinical programmes of cell transplantation (islets and hepatocytes);
- Integrated Medical Research Council (MRC) Centre for Transplantation and component of UK Regenerative Medicine Programme's Immunology Hub;
- Research division and National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) theme for patients with liver, kidney and pancreatic disease and contribution to cell transplants for patients with metabolic disease including stem cell innovation for tissue repair and acceptance;
- Comprehensive digestive diseases centre, aligned diagnostic and interventional endoscopy services and training centre of excellence in cancer and inflammatory bowel disease;
- Comprehensive specialist urological service based on three sites, with distinctive cancer, robotic surgery, research and training in urology;
- Major coordinated programme in obesity surgery;
- Research on protein and cell therapeutics, biomarker and clinical evaluation, enabled by patient engagement and several national and international networks that keep patient-orientated innovation on the leading edge;
- Institute of Liver studies with international profile for disease management;
- Comprehensive range of renal services focusing on acute kidney injury, glomerulonephritis, vasculitis and genetic disorders;
- Pioneering programmes of alcohol management;
- Colorectal surgery offering a wide range of skills including minimally invasive resection for cancer.

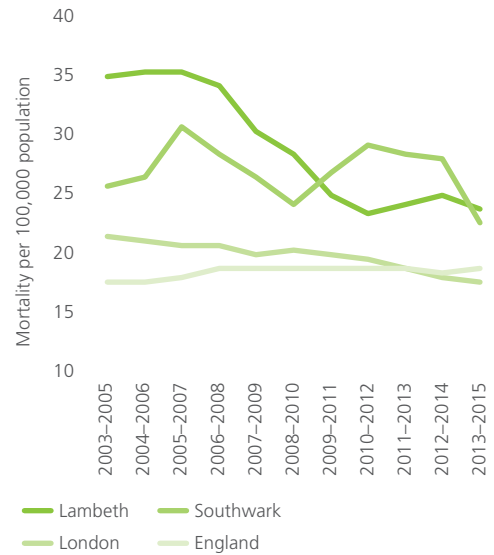
Public health; liver disease and obesity

Figure 1 | Hospital admission rates due to liver disease (all adults)



Rates for Lambeth and Southwark are substantially higher than the London and England averages.

Figure 2 | Under 75 mortality rates for liver disease (adults)



Lambeth and Southwark rates are higher than the London and England averages over the last 10 years for liver disease mortality.

Figure 3 | Alcohol-specific hospital admission rates

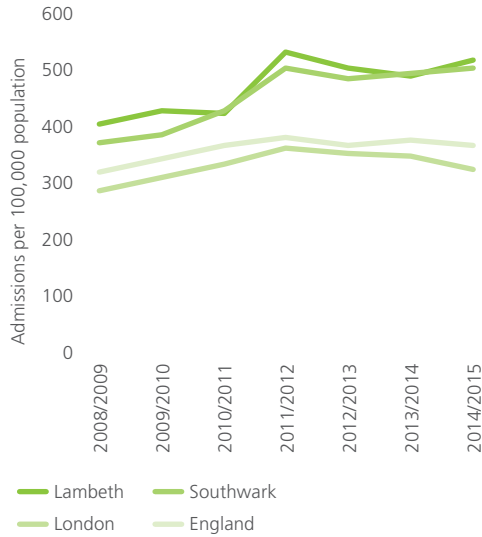
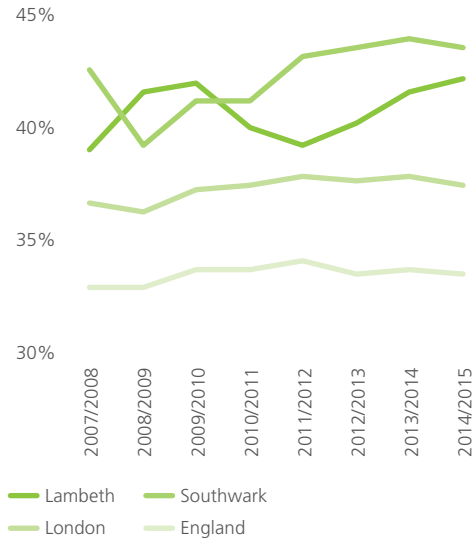
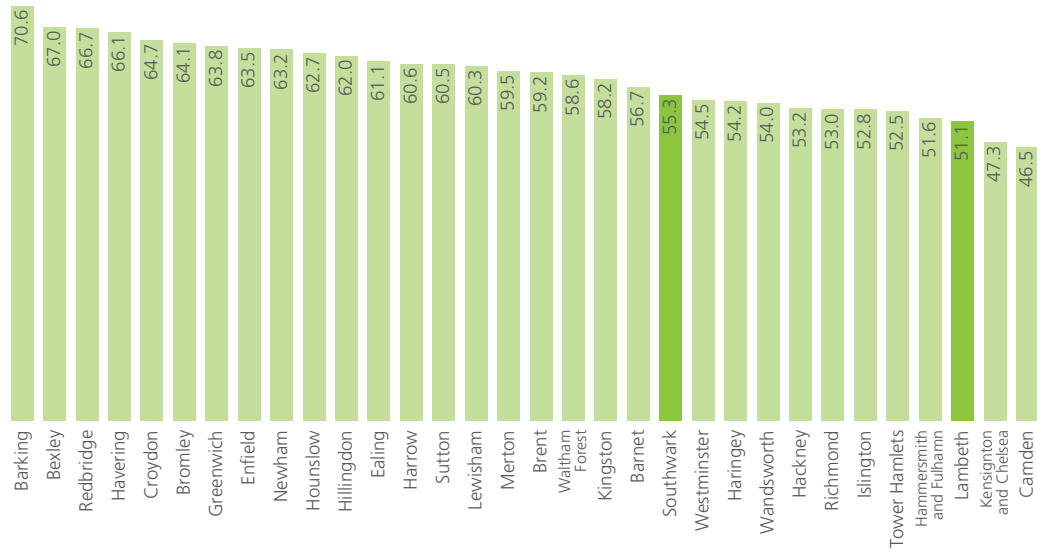


Figure 4 | The percentage of children aged 10–11 with excess weight



A major concern is that the levels of obesity persist into adulthood creating a possible epidemic in years to come putting added pressure on the National Health Service. Percentage of children aged 10–11 classified as overweight or obese. Children are classified as overweight (including obese) if their BMI is on or above the 85th centile of the British 1990 growth reference (UK90) according to age and sex.

Figure 5 | Excess weight in adults from 2013–2015 per 100,000 population



Team



Steve Sacks
CAG Lead



Nigel Heaton
CAG Lead

Transplantation and regenerative medicine	Steve Sacks Academic Lead KCL	Geoff Koffman Service Lead GSTT	Nigel Heaton Service Lead KCH
Liver medicine	Alberto Sanchez-Fueyo Academic Lead KCL	Michael Heneghan Clinical Director KCH	
Hepatobiliary	Alberto Sanchez-Fueyo Academic Lead KCL	Kosh Agarwal Clinical Lead KCH	
Kidney medicine	Claire Sharpe & Iain MacDougall Academic Leads KCL	David Gane Service Lead GSTT	Katie Vinen Service Lead KCH
Urology	Prokar Dasgupta Academic Lead KCL	Kay Thomas Service Lead GSTT	Christian Brown Service Lead KCH
Gastrointestinal surgery: upper GI	Jeremy Sanderson Academic Lead KCL	James Gossage Service Lead GSTT	Andreas Prachalias Service Lead KCH
Gastrointestinal surgery: lower GI	Andy Williams Academic Lead KCL	Andy Williams Service Lead GSTT	Amyr Hajj Service Lead KCH
Digestive diseases: endoscopy	Jeremy Sanderson Academic Lead KCL	Mark Wilkinson Service Lead GSTT	Amyr Hajj Service Lead KCH
Digestive diseases: gastroenterology	Jeremy Sanderson Academic Lead KCL	Mark Wilkinson Service Lead GSTT	Bu Hayee Service Lead KCH
Integration of mental and physical health		John O'Grady Academic Lead KCL	
Nursing prowess	Ian Norman Academic Lead KCL	Rachel Muir Service Lead GSTT	Jacky Sinclair Service Lead KCH

Range of services

Transplantation and regenerative medicine – repairing cell or tissue damage caused by disease or injury

- Liver: living donor and deceased donor;
- Kidney: living donor and deceased donor, antibody incompatible regional service;
- Pancreas;
- Small bowel;
- Multivisceral – more than one organ transplant;
- Cell transplantation: islets and hepatocytes.

Liver medicine – diagnosing and treating liver disease

- Viral hepatitis;
- Autoimmune diseases;
- Alcohol;
- Liver intensive care/acute liver failure;
- Hepatocellular carcinoma – common form of liver cancer.

Hepatobiliary – treating liver, gall bladder and bile ducts disorders

- Hepatobiliary cancer-abnormal growths occurring on or in the liver, bile ducts and biliary tract;
- Pancreatic cancer;

- Neuroendocrine tumours (EU accredited) – rare tumours that can occur in the cells of the neuroendocrine system. It consists of nerve and gland cells and produces and releases hormones into the bloodstream;
- Regional pancreatitis service – inflammation of the pancreas.

Kidney medicine – diagnosing and treating kidney diseases

- Vasculitis and lupus – vasculitis is an inflammation of the blood vessels, lupus a collection of autoimmune diseases in which the human immune system becomes hyperactive and attacks healthy tissues;
- Glomerulonephritis – a group of diseases that injure the part of the kidney that filters blood;
- Acute kidney injury;
- Genetic kidney disease;
- Chronic renal disease management;
- Anaemia services;
- Dialysis;
- Optimised immunosuppression clinic;
- End-of-life care.

Urology – disorders of the kidneys, ureters, bladder, prostate and male reproductive organs

- Cancer services: kidney (open and laparoscopic), bladder, prostate;
- 'One stop' model of care;
- Advanced laparoscopic and robotic surgery;
- Minimally invasive/loco-regional therapies, where treatment is limited to a specific site within the body.

Gastrointestinal surgery – surgery of the stomach and intestines

Upper gastrointestinal

- Cancer services: stomach and oesophagus;
- Academic Research (linked with Karolinska Institute, Sweden);
- Oesophageal Physiology Centre;

- Management of Barrett's Oesophagus, radiofrequency ablation (RFA) and endoscopic mucosal resection;
- Benign disease (Hiatus hernia, achalasia and gastro-oesophageal reflux disease);
- Complex revisional surgery and oesophageal reconstruction.

Lower gastrointestinal

- Cancer care;
- Minimally invasive endoscopy/ laparoscopy/surgery;
- Complex pelvic floor surgery;
- Ano-rectal functional assessment.

Digestive diseases – treating diseases of the digestive system

Endoscopy services

- Diagnostic: oesophago-gastro duodenoscopy; colonoscopy; cancer screening; bile duct SpyGlass visualisation system;

- Interventional: stenting; photodynamic therapy; endoscopic ultrasound imaging/ mucosal resections.

Gastroenterology

- Inflammatory bowel disease;
- Subspecialty clinics and clinical trials;
- Research: genetics and biomarkers especially pharmacogenomics;
- Intestinal failure management.

Bariatric surgery

- Our bariatric and metabolic surgery service is one of the largest programmes in this specialty in the UK;
- Surgical procedures include gastric bypass, sleeve gastrectomy, gastric banding, biliopancreatic diversion, revisional bariatric surgery for failed weight loss and novel endoluminal interventions.

Nursing prowess

- Personalised support for self-management of alcohol-related liver disease;
- Renal exercise and weight management services.

Shared care services

- Sickle cell/renal disease;
- Renal/obstetric clinic;
- Combined liver/kidney transplant clinic;
- Combined kidney/pancreas transplant clinic;
- Exercise and diet management;
- Adolescent and young adult transition service for transplant and chronic liver and kidney diseases.

Integrating mental and physical healthcare

- Integrating Mental and Physical healthcare: Research, Training and Services (IMPARTS);
- Alcohol management.

Translational support – translating scientific findings into new ways to diagnose and treat patients

- Biomarker research teams: support the validation and clinical utility studies for biomarkers of transplant tolerance, rejection, ischaemia reperfusion injury, liver regeneration, tumour diagnosis, and immunosuppressive treatment responses;
- Development of advanced organ perfusion techniques: e.g. Organox (collaboration with Oxford University) and extracorporeal membrane oxygenation (ECMO), aiming to improve the function of organs used in kidney and liver transplantation;
- Advanced therapies: biotechnology and clinical trial resources including statistical support and institutional good manufacturing process (GMP) facilities for evaluating new cellular and protein approaches to improve clinical outcomes in transplantation, autoimmune diseases and cancer;

- Whole body imaging programme (with imaging sciences CAG): applying innovative techniques to visualise innate and adaptive immune responses as an aid to clinical decision-making;
- Ethics research and policy development: to incorporate public expectations for medical innovation and enhance patient recruitment and organ availability in transplantation.

Commitment to education and training

A core ambition of King's Health Partners and our CAG is the provision of excellent education and training for healthcare professionals, students and support staff. This is vital in ensuring that our workforce remains skilled and equipped to deliver improvements in healthcare, and also for training and educating the next generation of clinicians and academics. Training our staff and students in research techniques and methodologies is also important for achieving research excellence. Education and training across the CAG ensures consistent standards of excellence, the sharing of good practice and innovation, and making the best use of resources. We ensure this through the delivery of multiple education programmes at all levels (undergraduate, postgraduate clinical, postgraduate taught courses, continued professional development courses, postgraduate research).

Undergraduate Medicine (phases 1+2)

Academic staff within the Division of Transplantation Immunology and Mucosal Biology (DTIMB) contribute to pre-clinical teaching in phases 1+2 Undergraduate Medicine (phase 3): the abdominal CAG supplies the majority of "firms" for the abdominal rotation during phase 3. The CAG also supplies a large number of clinical advisers and has taken part in the review of the MBBS curriculum.

Intercalated Bachelors of Science (iBSc) and Masters of Science (MSc)

DTIMB offer the Translational Medicine iBSc and MSc and the new Masters of Research in transplantation started this year; there are over 60 students registered for a Doctorate of Philosophy (PhD; postgraduate research degree). Strong links have been established between liver and palliative care including a shared supervised NIHR PhD Fellowship. In addition, the Institute of Liver Studies (ILS) have joined the NIH sponsored Global Alcoholic Hepatitis Consortium opening up research, collaborative and educational opportunities between the USA, Europe and UK. DTIMB and the MRC Centre for Transplantation run a collaborative programme and a fellowship scheme with the Emory Medical Centre in Atlanta, USA. An innovative clinical-academic programme in urology has been launched, with good cross-site cooperation.

Foundation training

We have foundation level doctors in most of our specialties and recognise this as an important area of focus. Whilst some sectors have proved very successful we recognise others as challenging, such as colorectal surgery. Having appointed an educational coordinator, and strengthened supervision, we have seen significant progress in trainee feedback. Rising to the challenge of community-facing training, renal F1s at Guy's are attached to the home therapies team for 2 weeks.

Core training

Core medical and surgical trainees together with intensive care medicine (ICM), acute care common stem (ACCS) and CT-level Trust doctors rotate through our CAG. We have ensured that Educational and Clinical Supervisors have the required training to ensure good supervision of our trainees. We use the "careflow" platform to improve communication amongst our CTs to enhance learning opportunities and also administration such as induction and rotas.

Specialist training

The abdominal CAG has been very successful in the MDECS process under the King's Health Partners banner. A truly King's Health Partners endeavour, supported by nominated Trusts we are now the Lead Provider for the whole of South Thames in higher training for Renal Medicine, Hepatology and Gastroenterology; we offer a coordinated medical and surgical programme

training in inflammatory bowel disease. The last year has seen a transition from Deanery to local process. We can now concentrate on delivering our vision.

Visiting doctors

The Institute of Liver Studies (ILS), King's Liver Unit and Liver Intensive Care unit continue to attract a huge tranche of external visitors both clinical and non-clinical including visiting fellows, surgeons, intensivists and professors. We have seen commendable progress in this area in renal, transplantation and urology.

Short courses and continued professional development (CPD) courses

The Kings Liver course organized by the ILS at King's College Hospital in London has run annually for decades. The objective of the latest course was to discuss the latest developments and best practice in managing both Hepatitis B and Hepatitis C. Feedback from delegates was excellent. The Frontiers in Transplantation CPD course organised by DTIMB and the MRC Centre for Transplantation has run annually since 2011. Feedback is excellent and the course was accredited by the Royal College of Pathologists and also by King's Health Partners via the SCAF process. The MRC Centre for Transplantation also runs an Ethics of Organ Transplantation programme.

Simulation

Six Gastroenterology Simulation Training Days were held in the King's College Hospital Simulation Suite. Three were dedicated to multidisciplinary training within the Trust and three were dedicated to training South Thames gastroenterology SpRs. Feedback was excellent from all six days. Simulation has been a real success. We need to work on the "community of educators" who are trained, appraised and remunerated to take this forward in the other workstreams. A comprehensive programme of simulation training has already been piloted and integrated into the renal medicine and urology postgraduate training schemes. Other notable achievements within our CAG simulation portfolio include the creation of the Institute of Robotic Surgery at King's College London in collaboration with the Vattikuti Foundation, the delivery of award-winning programmes for e-learning and robotics in urology and a surgical sciences intercalated BSc simulation module successfully launched in 2012.

The CAG's *Communication and Public Engagement Strategy* aims to promote stakeholder, staff and public engagement by disseminating research outcomes and knowledge, providing advice, as well as encouraging discussion and dialogue. We want to make sure that the lessons from research are used more swiftly, effectively and systematically to improve healthcare services for people with physical and mental health care problems. Our intended audiences, therefore, will include the general public, basic scientists and clinical staff, stakeholders, partners and patients and their families.

The *Athena SWAN* is a Charter which recognises excellence in an institution's commitment to gender equality. Over the past decade, the principal focus of Athena SWAN has been on the progression of women academics and researchers in the disciplines of science, technology, engineering, mathematics and medicine (STEMM). King's College London has been a member of the Athena SWAN Charter since 2007 and gained its Bronze institutional award in 2008. The university's Bronze award was renewed in September 2013 for a further three years. In 2014, King's' STEMM Divisions and Faculties began to submit for their own Athena SWAN awards, and the Division of Transplantation Immunology & Mucosal Biology received its Silver award in April 2016. Working with the Charter is helping the university to identify and implement best practice for the working environment of all staff, not just women.

Aims and ambitions across the Clinical Academic Group

Our achievements

Our liver transplant outcomes are among the best in the UK, and our renal and bone marrow stem cell transplant programmes aim to improve our already excellent clinical results.

We have made significant advances combining expertise in basic immunology and transplantation biology.

We manage some of the largest transplant-patient cohorts in Europe, delivering excellence in research and clinical trials.

Research for use of stem cells in treatment, and stem cell and islet transplantation, makes us one of the most prestigious centres in the UK for the treatment of liver and pancreas disorders.

In the next five years, we will:

- Conduct a series of first-in-man trials of novel immunotherapies designed to improve transplant and patient survival;
- Develop a programme of regenerative medicine, growing tissues from stem cells to repair organ damage;
- Implement a personalised medicine approach for transplantation based on genotyping recipients and donors.

Examples of excellence

Improved care pathway for urology

Urology services within the CAG have transformed into a model of service provision enriched by a unified teaching and research plan. As a result, the advanced access clinic is now seeing 140 plus new referrals a week, and further progress has been made with the rationalisation of urological oncology across sites. Alongside the joined-up clinical service is a leading programme of simulated teaching and robotics research, which has won a number of awards and national accolades. Urology research is embedded within the MRC Centre for Transplantation and BRC Transplant theme, and has made several new appointments to develop biochemical and physical targeting procedures for the delivery of localised therapeutics in patients with cancer of the urinary tract.

Progress in the management of chronic anaemia

Expertise has evolved within the CAG on the management of chronic anaemia in kidney patients. This is based on national and international leadership in the clinical development of therapeutics designed to restore erythropoietin deficiencies in kidney patients, as reported in several New England Journal of Medicine papers. Through the CAG, we have extended the scope

of research to include chronic gastrointestinal disease, such as inflammatory bowel disease. Our plans include new management protocols to elucidate the size of the problem in our local patient population and intervention studies to measure the effect of corrective treatment.

Bring cell-protective therapeutics to man

The CAG has forged a partnership between the MRC, BRC and NHS teams, which has enabled progress with advanced therapy to move from the bench to the bedside. There are two aspects to these new treatments: one, the development of therapeutic human proteins that reduce ischaemic damage to donor kidneys; two, the development of cell therapy based on human T cells that inhibit the immune response. Both are designed to reduce graft damage due to inflammation and immunity and to prolong the life of the graft, with minimum side effects of treatment. Through the internal collaborations forged by the CAG, two clinical trials in our patients, both of which are supported by MRC developmental awards, began in 2015.

Clinical implementation of biomarker-based immunosuppression in liver transplantation

The Liver Transplant Unit has pioneered the use of a transcriptional liver tissue-based biomarker to stratify long-term recipients on the basis of their need for lifelong immunosuppressive therapy. This is currently being tested within a multi-national NIHR-funded clinical trial sponsored by KHP.

Integration of mental and physical healthcare

Integrating Mental & Physical healthcare: Research, Training & Services (IMPARTS) is an initiative funded by King's Health Partners to integrate mental and physical healthcare across KHP. The inflammatory bowel disease (IBD) advice line gives direct access to the clinical nurse specialists (CNS) via telephone or email to provide services including psychological support, lifestyle guidance and self-management of conditions. Urology services also offer nursing-led initiatives to identify & reduce incidences of regret in patients post-operation.



Trans-
plantation
and regen-
erative
medicine

Transplantation and regenerative medicine

Our renal and pancreas transplant programmes at Guy's continues to expand whilst maintaining high quality services. Over the last three to five years there has been significant expansion in the Guy's deceased donor kidney transplant programme, particularly in the use of organs from donation after circulatory death (DCD) donors. Guy's is now one of the three largest users of DCD kidneys in the UK. The waiting list for deceased donor kidney transplantation has dropped by 25% as a result.

The Guy's living donor kidney transplant programme remains one of the biggest and most innovative in the UK, with a high proportion of antibody-incompatible transplants. This had led to requests to provide these ground breaking transplants to patients across the UK; these patients were previously considered to be untransplantable. Advances in technology and clinical experience have now led to the use of antibody-incompatible live donor kidney transplants in children, provided at Great Ormond Street Hospital and the Evelina Hospital by the Guy's team.

The pancreas transplant programme receives referrals from across London and the Southeast, and increasingly attracts referrals from the Midlands and south west England. The pancreas transplant unit works closely with the King's islet transplant programme, and joint clinics are in place to provide diabetic patients with a seamless service, providing patients with a wider range of management options and optimal outcomes.

The liver transplant programme at King's College Hospital is the UK's largest and one of the largest in Europe, performing between 200 and 250 adult and paediatric transplant procedures per year. The total volume of liver transplantation activity at KCH is in excess of 4,500 transplants. This includes a combination of cadaveric and live related transplant surgery. It has one of the most mature and largest experiences in reduced liver transplantation, auxiliary liver transplantation and has in excess of 15 years' experience dealing with organs retrieved after cardiac death. Data from NHS-Blood & Transplant indicate that KCH liver transplant services provide the highest overall patient and graft survival in the UK.

KCH has the only paediatric liver transplant service in the UK that works closely with adult services to provide a smooth transition for patients as they move from adolescence into adulthood. Furthermore, specific treatment options such as auxiliary liver transplantation and liver cell transplantation are available almost exclusively at King's. The liver transplant services have national and international outreach with clinics in Plymouth, Belfast, Cyprus, Ireland, Qatar, Abu Dhabi and Dubai.

The transplant teams from Guy's and King's work closely together, particularly in the care of those patients requiring simultaneous liver and kidney transplantation.

Key aims

Introduction of novel organ perfusion technologies, enabling prolonged organ preservation times and the use of previously un-transplantable organs.

Research and innovation

CAG members have been instrumental in developing the UK's largest experience with antibody-incompatible kidney transplantation. This programme involves the transplantation of live donor kidneys into patients with high levels of circulating anti-donor antibodies. Removal of the antibodies prior to transplantation, along with careful post-transplant monitoring, enables good outcomes in recipients who would previously have been considered to be non-transplantable.

CAG members have played an active role in the introduction of novel monoclonal antibody therapies to enable expansion of our leading antibody-incompatible live donor kidney transplant programme. The UK's first antibody-incompatible live donor kidney transplant into a paediatric recipient was carried out, in conjunction with colleagues at Great Ormond Street Hospital.

CAG members at King's College Hospital have pioneered the use of normothermic machine perfusion in human liver transplantation by performing the first 10 liver transplants using this technology ever conducted.

Translational research has resulted in multi-centre clinical trials in advanced protein therapeutics targeted at the complement system. These agents will be trialled in deceased donor kidney transplantation to determine if they are able to reduce the rate of delayed function of the renal transplant post-operatively. In addition, a novel biomarker of operational tolerance in liver transplantation is currently being tested within a multi-national biomarker-guided immunosuppression withdrawal study sponsored by King's College London and King's College Hospital.

Members of the MRC Transplant Centre have pioneered the use of high-throughput molecular profiling techniques to investigate the mechanisms of chronic allograft damage in long-term surviving liver recipients.

The CAG's strength in cellular transplantation and cell therapies has been recognised by its participation in a novel multi-centre US and European trial aimed at evaluating the feasibility and efficacy of T regulatory cells in living donor kidney transplantation, and in the performance of the first-in-man clinical trial of T regulatory cells in the setting of liver transplantation.

Current trials in kidney and liver disease transplantation

Researchers at the MRC Centre for Transplantation at Kings College London are working hard to solve the problems associated with organ transplantation. The Centre brings together researchers from many fields of immunology, genetics, stem cell biology and imaging and helps them to work with clinicians to take their scientific discoveries from the bench to the bedside.

The following link will direct you to the detail of the very interesting trials that are currently taking place at the MRC centre including the following:

- A controlled trial of a novel anti inflammation drug, called Mirococept developed within the MRC Centre designed to paint the inside of kidneys before transplantation to protect them from immediate damage caused by the immune system;
- Development of an early warning signal that identifies patients at risk of acute rejection, so that rejection can be prevented;

- A study to investigate the psychosocial aspects of living donation with the view to understanding both the positive and negative outcomes after surgery;
- A multi-centre randomised controlled trial of biomarker-guided immunosuppression withdrawal in liver transplantation;
- A first-in-man phase I trial to test the safety and efficacy of regulatory T cells in liver transplantation.

Figure 8 | CAG commercial income – contract value (£) 2012–2017

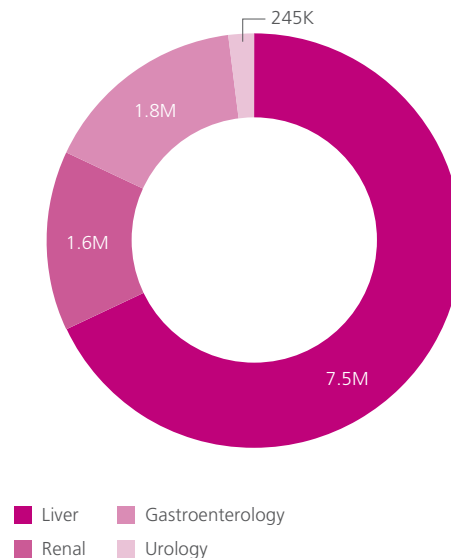


Figure 9 | CAG research income 2014–2015

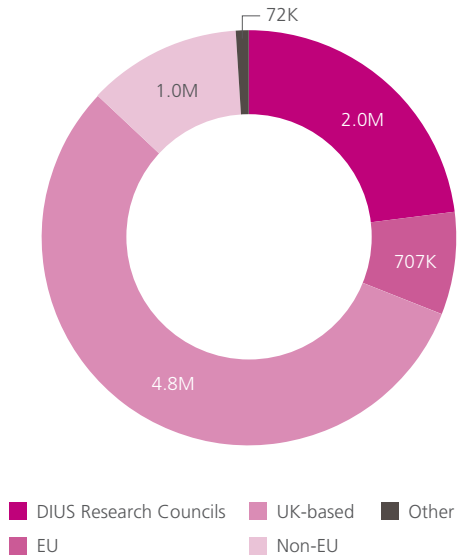
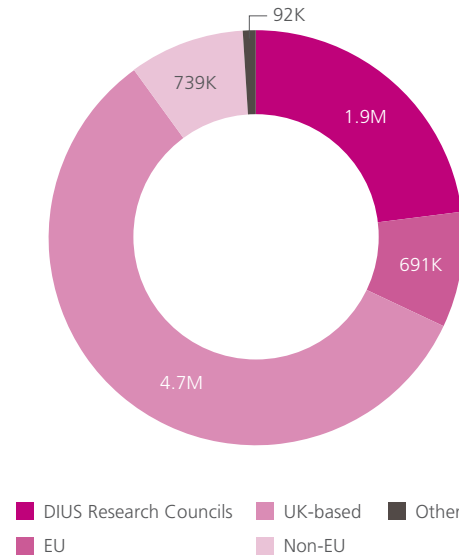


Figure 10 | CAG research income 2015–2016



Education and training

In recent years hepatology and nephrology trainees within the CAG have gone on to occupy professorial, senior lecturer and consultant posts in leading UK Centres including King's Health Partners, reflecting global recognition for the training and academic programme in kidney and liver disease and in transplantation.

Each year, we host a number of visiting fellows from different parts of the developed and less developed world, who come for a period of research or clinical observership. In recent years we have hosted over twenty such fellows from Brazil, India, Hong Kong, Italy, Greece, Spain and other countries. In addition, the MRC Centre participates in an education and training programme jointly with other health science centres at Emory, Duke and Harvard universities in the USA.

Clinical outcomes

We have the UK's largest adult and paediatric kidney transplant programme, and our risk-adjusted outcomes meet or exceed other UK units. Our patient survival from the time of listing for a deceased donor kidney transplant is well above the national average.

Pancreas transplant outcomes

Our risk-adjusted patient and graft survival rates after pancreas transplantation are above the national average.

Table 1 | Transplantation survival rates for patients between 2011–2015

Type of transplant	Description	1-year survival (2011–2015)	1-year survival (2011–2015)	5-year survival (2007–2011)	5-year survival (2007–2011)
		KHP	UK	KHP	UK
Simultaneous pancreas–kidney transplant	Patient survival rates for deceased donor	96% (n=104)	97% (n=661)	94% (n=84)	88% (n=614)
Pancreas graft	Graft survival rates for deceased donor	84% (n=106)	87% (n=679)	82% (n=85)	75% (n=639)

Type of transplant	Description	1-year survival (2011–2015)	1-year survival (2011–2015)	5-year survival (2007–2011)	5-year survival (2007–2011)
		KHP	UK	KHP	UK
Kidney	Patient survival rates for deceased donor	97%	96%	90%	88%
Kidney graft	Graft survival rates for deceased donor	94%	94%	87%	86%
Kidney	Patient survival rates for living donor	99%	99%	95%	95%
Kidney graft	Graft survival rates for living donor	99%	98%	93%	92%

Figure 11 | Liver survival rates – adult elective deceased donor

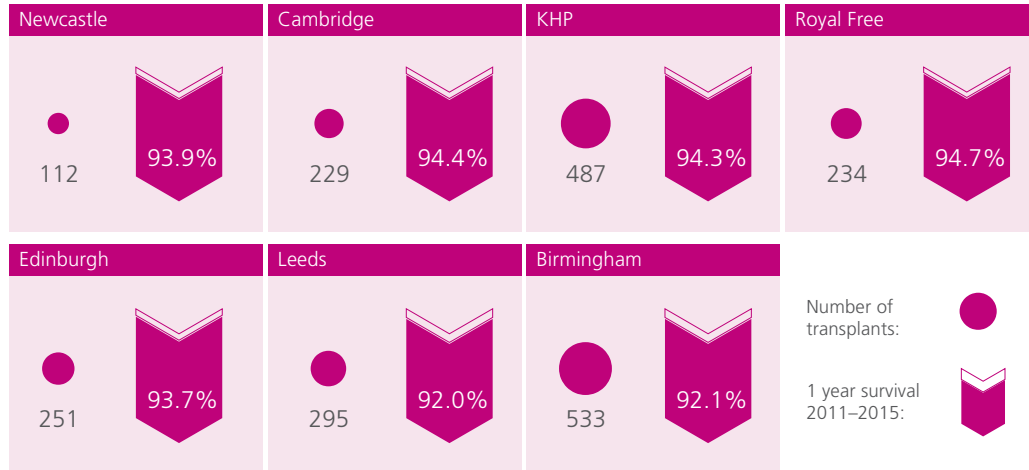
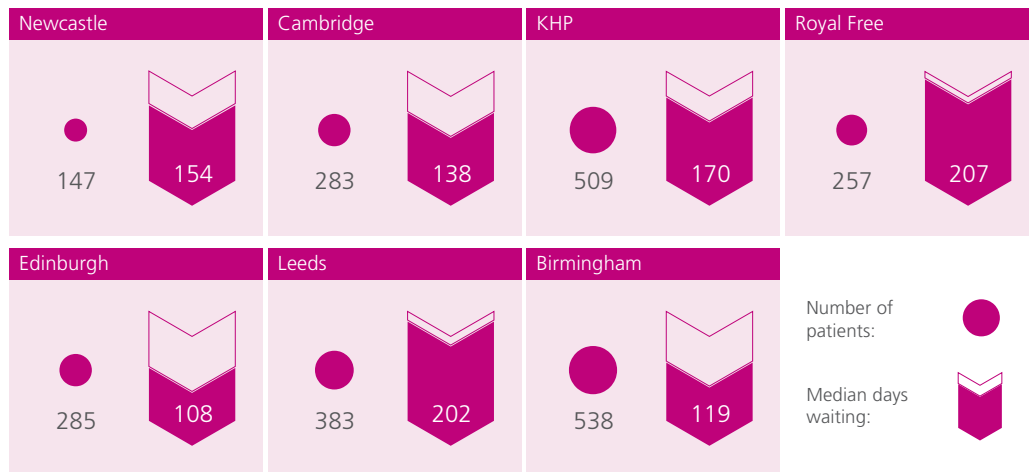


Figure 12 | Median waiting times for deceased donor liver only transplants compared to other NHS trusts between 2010 and 2013



In the offering sequence of a transplant, transplanted livers from deceased donors are either accepted by a liver transplant centre on the first offer and transplanted, or declined by

one or more centres before being accepted for transplantation. The rate at which liver offers are declined at King's College Hospital is amongst lowest in the country.

Figure 13 | Adult elective liver offer decline rates that resulted in a whole liver only first transplant from Donation after Brain Death (DBD) donors, 1 April 2013 and 31 March 2016

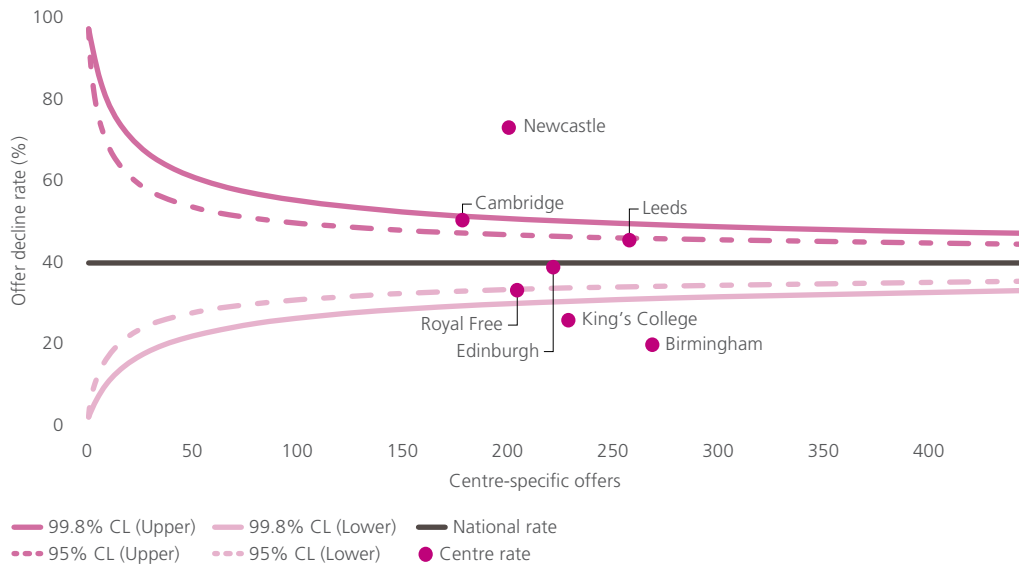
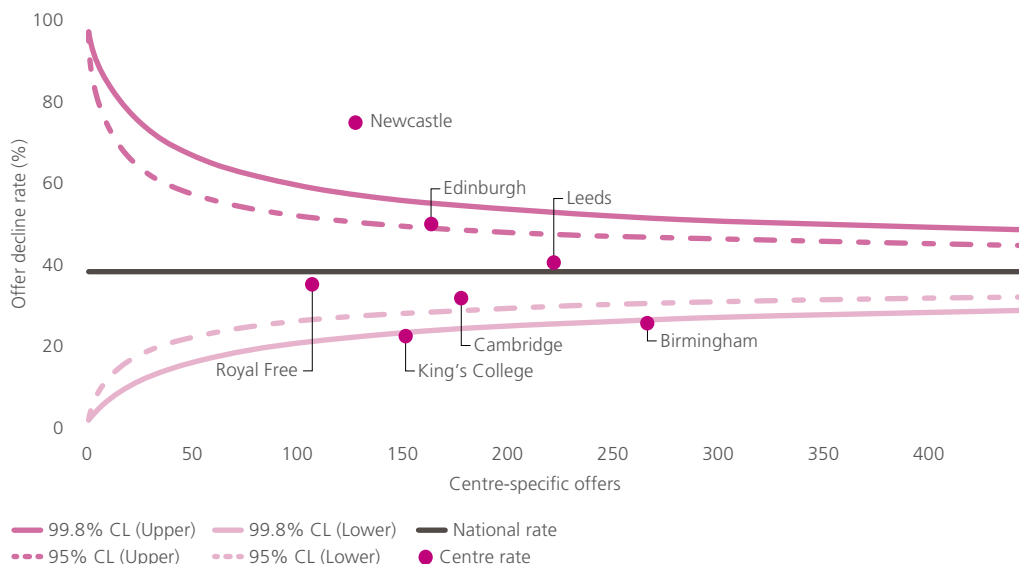


Figure 14 | Adult elective liver offer decline rates that resulted in a whole liver only first transplant from Donation after Cardiac Death donors, 1 April 2013 and 31 March 2016 (a donor who has suffered devastating and irreversible brain injury and may be near death, but does not meet formal brain death criteria)

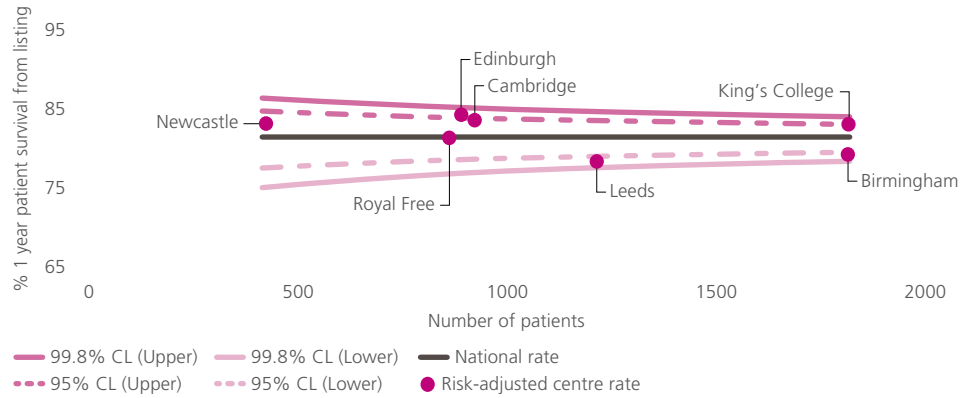


The most common reasons for declining liver offers from either DBD or DCD donors whose liver was subsequently transplanted were donor related, followed by logistical issues and the lack of any suitable recipients.

Survival from listing was analysed for patients aged ≥ 18 years registered for the first time for a liver transplant between 1 January 2004 and 31 December 2015.

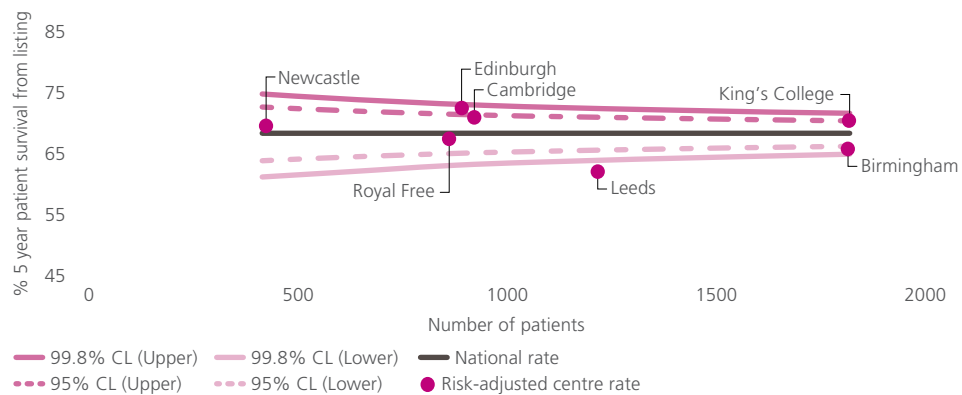
At one year King's College has a risk adjusted survival rate of 83%.

Figure 15 | Risk-adjusted 1 year patient survival rate from the time of listing for adult elective first liver registrations 1 January 2004–31 December 2015. At five years King's College has a risk adjusted survival rate of 71%.



In this analysis, adult patients are defined as 18 years old and older.

Figure 16 | Risk-adjusted 5 year patient survival rate from the time of listing for adult elective first liver registrations 1 January 2004–31 December 2015. At ten years King's College has a risk adjusted survival rate of 62%.



In this analysis, adult patients are defined as 18 years old and older.

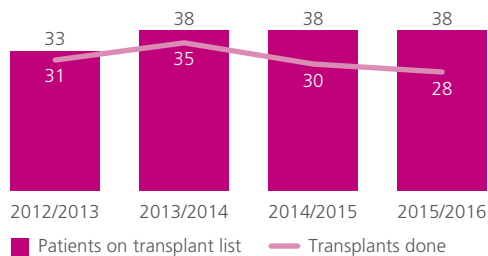
Figure 17 | Risk-adjusted 10 year patient survival rate from the time of listing for adult elective first liver registrations 1 January 2004–31 December 2015



In this analysis, adult patients are defined as 18 years old and older.

Performance measures

Figure 18 | Number of pancreas transplants over the last five years at King's Health Partners



Top grants awarded

Award details	Amount	Year
PI: Dr Giovanna Lombardi, Dr Greg Mullen, Co-investigators: Professor Robert Lechler. <i>Manipulating regulatory T cells to promote clinical transplant tolerance.</i>	£1,255,592	2008
PI: Dr Maria Hernandez Fuentes, Co-investigators: Professor Sir Robert Lechler, Professor Graham M Lord, External co-applicants: Professor Vicki Seyfert-Margolis, Professor Laurence Turka. <i>Biomarkers of clinical transplantation tolerance. GAMBIT study.</i> British Heart Foundation.	£1,134,858	2009
PI: Professor Graham M Lord, Dr Alfonso Martin-Fontecha, External co-applicant: Dr Tom MacDonald. <i>Defining the molecular and cellular pathogenesis of ulcerative colitis.</i> Medical Research Council.	£1,179,374	2009
PI: Professor Giovanna Lombardi, Co-investigators: Dr Maria Hernandez Fuentes, Professor Robert Lechler, Professor Randolph Noelle. <i>The ONE Study: a unified approach to evaluating cellular immunotherapy in solid organ transplantation.</i> EC – European Commission.	£816,001.70	2010
PI: Professor Randolph Noelle, Co-investigator: Professor Steven Sack, External co-applicants: Dr Ethan Dmitrovksy, Dr Leo Lefrancois. <i>The cellular and molecular basis for the impact of vitamin A on immunity.</i> Wellcome Trust.	£4,692,044	2010
PI: Professor Steven Sacks, Dr Wilson Wong. Co-investigators: Mr Conrad Farrar <i>Development of OPN-305 as an orphan drug for the treatment of Delayed Graft Function post solid organ transplantation – MABSOT.</i> EC – European Commission.	£882,950.04	2010
PI: Dr Claudia Kemper, Co-investigators: Professor Andrew Cope, Dr Paul Lavender. <i>The molecular and cellular basis of complement-mediated T helper 1 (TH1) differentiation and regulation.</i>	£857,612	2011
PI: Professor Steven Sacks, Dr Richard Smith, External Co-applicant: Mr Martin Drage. <i>Developmental clinical studies - investigation into the efficacy of mirococept in renal transplantation.</i> Medical Research Council.	£1,724,717	2011
PI: Dr Maria Hernandez Fuentes, Dr Irene Rebollo Mesa, Dr Alberto Sanchez Fueyo, Dr Maria Hernandez Fuentes. <i>BIO-DrIM Personalized minimization of immunosuppression after solid organ transplantation by biomarker-driven stratification of patients to improve long-term outcome and health-economic data of transplantation.</i> EC – European Commission.	£679,728	2012
PI: Professor Kaspar Althoefer, Professor Prokar Dasgupta, Co-investigators: Dr Hongbin Liu, Dr Thrishantha Nanayakkara, Professor Lakmal Seneviratne. <i>STIFF-FLOP – STIFFness controllable Flexible and Learn-able manipulator for surgical Operations.</i> EC – European Commission.	£1,139,265.22	2012
PI: Professor Randolph Noelle. <i>To better understand the role of VISTA in innate and adaptive immunity.</i> ImmuNext, Inc.	£1,041,569	2012

Award details	Amount	Year
PI: Professor Steven Sacks. <i>MRC Centre for Transplantation</i> . Medical Research Council .	£1,694,050.02	2012
PI: Professor Paul Sharpe. <i>Wnt signalling and stem cell mobilisation in tissue injury repair</i> . Medical Research Council .	£692,944	2012
PI: Dr Richard Smith. Co-investigators: Professor Anthony Dorling, Professor Steven Sacks. <i>Development of cytotopically modified antithrombotic agent for prevention of acute intra-graft thrombosis in transplantation</i> . Wellcome Trust .	£1,580,495	2013
PI: Professor Anthony Dorling. <i>Optimized Tacrolimus and MMF for HLA Antibodies after Renal Transplantation (the OutSMART study): a randomized controlled clinical trial to determine if a combined screening/treatment programme can prevent premature failure of renal transplants due to chronic rejection in patients with HLA antibodies</i> . NIHR – National Institute for Health Research .	£1,665,711	2013
PI: Professor Giovanna Lombardi, Co-investigators: Dr Varuna Aluvihare, Mr Nigel Heaton, Professor Robert Lechler, Professor Janet Peacock, Dr Irene Rebollo Mesa, Dr Niloufar Safinia, Dr Alberto Sanchez Fueyo. <i>ThRIL: a 'first-in-human' study, evaluating the safety, tolerability with an investigation into the efficacy of Tregs in liver transplant recipients</i> . Medical Research Council .	£2,042,677	2013
PI: Professor Giovanna Lombardi. Co-investigators: Professor Robert Lechler. <i>Optimising the efficacy of regulatory T cells: informing clinical application</i> . British Heart Foundation .	£1,602,706	2013
PI: Dr Claudia Kemper. <i>Complement receptor signalling in Th1-immunity</i> . Wellcome Trust .	£1,519,891	2014
PI: Professor Fiona Watt. Co-investigators: Professor Francesco Dazzi, Professor Frederic Geissmann, Professor Giovanna Lombardi, Professor Steven Sacks. <i>Overcoming immunological barriers to regenerative medicine (UK Regenerative Medicine Hub Immunology)</i> . Medical Research Council .	£1,752,315	2014
PI: Professor Prokar Dasgupta, Co-investigator: Dr Christine Galustian, Dr Richard Smith. <i>Design of Novel Immunotherapies for Prostate Cancer – from Bench to Bedside</i> . Prostate Cancer Research Centre .	£1,500,000	2014
PI: Professor Graham M Lord. <i>T-bet as a master regulator of mucosal immunity and inflammatory bowel disease</i> . Medical Research Council .	£1,137,695	2014



Liver
medicine

Liver medicine

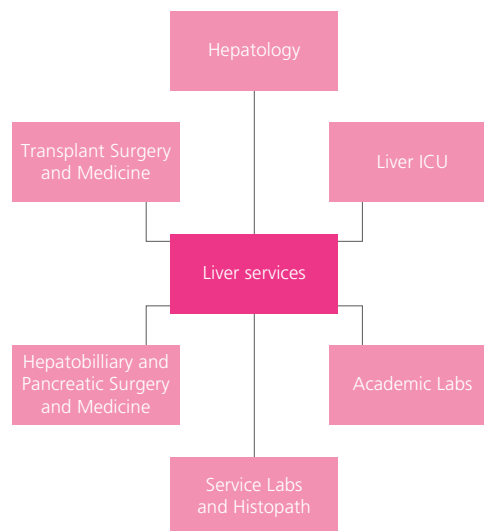
Liver Services at King's Health Partners are located across two main campuses. King's College Hospital facilities operate an integrated care plan of medical and surgical services including liver medicine and surgery, dedicated intensive care unit, pathology services and strong interests in viral hepatitis, complex hepatology, autoimmune liver disease, transition/adolescent hepatology, and oncology.

King's College Hospital also provides services at the Princess Royal Hospital in Orpington, Kent, including liver and bile duct endoscopy. Research laboratories are incorporated into the King's College Hospital facility, offering opportunities in translational research that have served clinical innovation well.

In addition, Liver Services based at the Guy's and St Thomas' campus include inpatient and outpatient facilities and integrated subspecialty clinics and a fibroscan service that incorporates key academic interests. There is close collaboration between services at Guy's and King's, and in particular there are effective working relationships in the viral hepatitis service across King's Health Partners and between the Guy's and St Thomas' liver physicians and King's College Hospital hepatobiliary surgeons

and radiologists. Liver histopathology has been centralised on a King's Health Partners basis, and an efficient diagnostic service benefits from regular joint King's College Hospital and Guy's and St Thomas' histopathology multidisciplinary meetings. Guy's and St Thomas' serves the local community through a community blood borne virus health inclusion team.

Figure 19 | King's Health Partners liver services



The combined service and the breadth of specialist services offered at King's College Hospital, including paediatric hepatology and liver failure management, serve as a national and international referral base for complex disorders, reflected in the large proportion of cases transferred in from other centres throughout the country. Liver services at King's Health Partners therefore acts as a quaternary, tertiary and secondary provider for a large patient sector.

Ambitions

In the next five years we will:

- Continue to develop liver transplant services at King's Health Partners through network development and combined appointments across the network;
- Further embed the provision of comprehensive alcohol services across all King's Health Partners sites in conjunction with South London and Maudsley partners and other local stakeholders;
- Extend the role of subspecialty clinics in conjunction with other clinical academic groupings across King's Health Partners.

Through partnership with The Foundation for Liver Research, continue to build a platform for translational research in liver medicine across King's Health Partners sites.

Hepatitis B

The King's College Hospital Viral Hepatitis service is an exemplar for providing care to both local and tertiary patients.

In line with the World Health Organisation target of hepatitis elimination by 2030, we are focused on innovative models of care incorporating substance misuse services, GPs, antenatal clinic, and prison healthcare services.

We manage over 3,890 patients with chronic hepatitis B; of whom about 5–8% are co-infected with hepatitis delta (Byrne R et al. Hepatology 2016). Over 1,250 individuals are established on long-term antiviral therapy (entecavir or tenofovir). The efficacy and safety outcomes of antiviral therapy at KCH have been reported (Carey I et al. Hepatology 2015).

We have an active clinical trial programme; currently over 70 HBV patients are participating in phase I–IV clinical trials to confer a 'functional cure' of HBV infection (Agarwal K et al. Lancet Gastro Hepatol 2016) and since 2015, 133 patients have been recruited to HCV phase II and III trials.

We continue to strengthen primary and secondary care interfaces whilst maintaining our network profile as an international centre of excellence.

The local population of Guy's and St Thomas' has a higher prevalence of hepatitis B due to a high proportion of people born in sub-Saharan Africa and South East Asia. The antenatal

seroprevalence of hepatitis B is approx 2%. Currently Guy's and St Thomas' have 2,971 outpatients with chronic hepatitis B, and 280 patients on long-term antiviral therapy (entecavir or tenofovir).

The efficacy of hepatitis B therapy at Guy's and St Thomas' has been published in abstract format (Blaker PA et al. Gut 2011 60 A211), and Guy's and St Thomas' was the second largest recruiter of patients to the Collaborative UK Study of Chronic Hepatitis B (Clin Infect Dis. 2013 Apr;56(7):951–960).

Hepatitis C

With the advent of new treatment for hepatitis C we became the lead hub site of the largest operational delivery network (ODN) in the UK, at the forefront of the 'Early Access Program' (Foster et al. J Hepatol 2016) and subsequently treating 649 patients from 2015–2017, accounting for 12% of all patients treated for HCV in the UK. Our cure rate is 96%.

In conjunction with St Georges Hospital, an operational delivery network has been created that will account for the treatment of all patients in South London. This hub is located at Kings College Hospital under the direction of Dr Kosh Agarwal. It will account for 9.8% of all treatment activity for hepatitis C virus infection in the United Kingdom and in addition will coordinate the delivery of novel therapies across its network including Guy's and St Thomas' Hospital, Lewisham, Croydon, Woolwich and

all other hospitals across the sector. Additionally, King's College Hospital is responsible for coordination of the NHS England commissioned operational delivery network for Kent. This will provide care in terms of hepatitis C treatment for 1.8% of the total UK population. All outcomes will be reported to King's College Hospital from the sector in London and in Kent. An extensive networking arrangement is now in place which incorporates weekly multidisciplinary meetings coordinated from King's College Hospital through tele-medicine involving all hospitals that are within the network.

The hepatitis C service of Guy's and St Thomas' comprises of three main services- the general hepatitis C clinic, HIV-HCV co-infection, and the haemophilia reference centre.

The number of new patient referrals with HCV RNA positivity seen at Guy's and St Thomas' in the general hepatitis C clinic and HIV co-infection clinics vary between 110 and 149 per year.

The haemophilia reference centre at Guy's and St Thomas' currently has 311 registered patients with haemophilia A or B. Of these 169 have been infected with hepatitis C. As part of joint Clinical Academic Group working there is a fortnightly joint hepatology-haemophilia multidisciplinary clinic and a fortnightly multidisciplinary meeting. 109 have achieved a sustained virological response (SVR) with hepatitis C therapy. 60 patients remain HCV RNA positive of whom 20 are cirrhotic (fibroscan liver stiffness measurement > 13kPa).

The outcome of hepatitis C therapy at Guy's and St Thomas' have been presented and the SVR rates are equal to, or better than the pivotal registry studies.

Liver Critical Care

KCH Liver Intensive Care Unit (LITU) is the largest dedicated liver intensive care unit in Europe (15 bedded facility). KCH LITU was rated as outstanding by the care quality commission in 2015. It has the world's largest experience in the management of patients with acute liver failure, and has pioneered the implementation of novel therapeutic strategies, development of prognostic scores, and performance of mechanistic studies aiming at elucidating the immunopathogenesis of acute liver failure.

Autoimmune liver disease

The autoimmune service at King's College Hospital is one of the largest in the world with over 600 patients with autoimmune hepatitis. In addition, it has major cohorts of primary biliary cholangitis, autoimmune sclerosing cholangitis, primary sclerosing cholangitis and IgG4 related cholangiopathy. These patients are involved in a range of clinical studies including the UK AIH, UK PBC and UK PSC platforms.

Dr Michael Heneghan, was one of the founder members of the UK PBC and UK AIH consortia and is also on the steering committee of the Wellcome trust funded genome wide

association screening programme for primary biliary cholangitis. The service also links in with transition and has contributed greatly to the literature. Dr Heneghan Co-Authored the British Society of Gastroenterology Clinical Practice Guidelines on autoimmune hepatitis in addition to Co-Authoring the European Association for the Study of the Liver, Clinical Practice Guidelines.

Hepatic steatosis

Guy's and St Thomas' is a study site for several clinical trials in non-alcoholic steatohepatitis including the centaur study, and a study of carbalive, a novel nanocarbon therapeutic agent, in NAFLD.

As part of a joint clinical academic group initiative the hepatology department and the St John's Institute of Dermatology have recruited 480 patients into a study of comorbidities in psoriasis. This study has detected a high proportion of psoriasis patients with hepatic steatosis and steatohepatitis related fibrosis.

Research and innovation

Our intention is to fully combine the strengths and distinctive areas of research across King's Health Partners, so as to deliver a world class base for innovation in liver disease management and support translational research. Permissive structures include the integration of adult and paediatric hepatology and dedicated histopathology, diagnostic and support services that have been exemplified across King's Health Partners, and we will consider the extent to which this can feasibly combine on a single campus, matched to patient care. New recruitment has and will be essential to this goal, and additional impact will be achieved by alignment through relocation of the Foundation for Liver Research into a new research building on the Denmark Hill campus. Increasing involvement in teaching and educational activities across the liver teams on both sites provides a good starting point for improving educational standards, in tune with the ambitions of King's Health Partners.

Strategic alignment is therefore seen as a fundamental basis for innovation to meet the changing needs of our patient populations. A forum for research project development is already in development, and this includes detailed research plans for hepatitis C, alcoholic liver disease, non alcohol related fatty liver disease and autoimmune hepatitis, which all have massive health and economic importance in our local community and nation, and where we can excel to meet the King's Health Partners targets for integrated mental and physical health. As an underpinning resource, plans are

afloat to improve and broaden existing biobank facilities through recruitment of a dedicated research nurse and new methods of annotating banked samples including tumour biopsy material to enable research.

Education and training

King's Health Partners runs substantial training programmes in hepatology and gastroenterology, supporting nationally allocated advanced trainee posts in hepatology and at least 10 other deanery allocated posts accredited for gastroenterology. These are based at King's College Hospital and at the Guy's and St Thomas' and Princess Royal University Hospital sites. In addition the King's College Hospital site supports a large number of visiting fellows from overseas who come for additional training in liver medicine and research. These include trainees from India, Egypt, Spain, Hong Kong, Baltic states and Romania. We have been able to provide clinical and research training in the areas of transplant hepatology, viral hepatitis, autoimmune liver disease, hepatocellular carcinoma and hepatobiliary medicine including hepatobiliary endoscopy. At any one time, three to four clinical observers are present.

Development of cross-CAG multidisciplinary clinics

1. **Viral hepatitis/infectious disease.** This model operates across King's College Hospital and Guy's and St Thomas' sites, bringing together liver, HIV and pharmacy specialists to care for co-infected patients and to enable clinical research and treatment trials.
2. **Liver and kidney medicine.** Run on the King's College Hospital site, this provides care for patients with renal dysfunction and coexisting liver disease ranging from polycystic disease to complicated glomerulonephritis. Joint protocols have emerged to facilitate combined liver and renal transplantation.
3. **Liver medicine/dermatology.** Based on the Guy's and St Thomas' site, this provides hepatology input into patients with psoriasis who are on medications that are potentially damaging to the liver. The provision of fibro-scanning in this patient group has provided new opportunities for clinical research including trials of new therapy.
4. **Hepatology/obstetrics.** A specialist clinic on the King's College Hospital site combines obstetric care with hepatology for patients who are planning pregnancy or for patients with decompensated liver disease who become pregnant. A unique patient cohort identified through this service has contributed to a national prospectively collected dataset that supports research.
5. **Hepatology/haemophilia.** At the Guy's and St Thomas' site, this service is currently for 169 patients with hereditary haemophilia

who have contracted hepatitis C through transfusion related exposure, of whom a substantial proportion have responded to antiviral therapy and a significant proportion have developed cirrhosis. This cohort has allowed the development of models of care and research including monitoring by fibroscan for liver stiffness.

6. **Hepatology/sickle cell disease.** King's College Hospital provides care for 70% of patients with sickle cell disease in the UK. A specialist clinic is focused on sickle cell disease patients developing liver complications. A prospective protocol is in place to assess the role of liver transplantation in this setting.

Development of an effective clinical trials infrastructure

Since 2009, liver services across both sites, supported by a clinical trials team, have contributed patients into a range of clinical trials, which are summarised in the table below. Most involve novel treatments for hepatitis B and hepatitis C but some drug trials involve new treatments for hepatocellular carcinoma or for liver fibrosis. We estimate the drug savings are in excess of £7 million and the cost of clinic visits due to viral hepatitis has been reduced by at least £0.5 million.

In addition to commercial trials, the trials support team also participates in investigator led studies, which in the same period included studies in viral hepatitis (10), hepatocellular carcinoma (10), and other aspects of liver medicine (61) such

as autoimmune liver disease, acute liver failure, alcohol related liver disease, and encephalopathy.

The income generated has also enabled recruitment of medical and nursing staff, further

enhancing the ability to innovate in patient care. A system of governance, good clinical practice guidelines and quality control has developed during the last three years increasing our ability to produce meaningful data.

Table 2 | Number of trials in the liver service since 2009

Year	Number of trials			Number of patients seen			Generated income (£)	Broader health economy	
	Hepatitis	HCC	Others	Hepatitis	HCC	Others		Drug saving (HCV, £)	Clinic visits (HCV, £)
2009	6	5	6	560 (12)	210	100	82,805	180,000	24,000
2010	9	6	6	650 (17)	220	100	112,701	255,000	48,000
2011	12	7	7	1,000 (38)	250	120	206,106	570,000	76,000
2012	17	7	7	1,500 (45)	300	150	730,729	675,880	90,000
2013	23	7	8	1,700 (77)	420	200	868,723	2,695,000	154,000
2014	26	9	14	2,000 (76+)	500	250	Estimated 1,000,000	Estimated 3,108,000	Estimated 255,360
Total	93	11	48	7,410 (265)	1,900	920	3,001,064	7,483,880	699,360

Hepatocellular Carcinoma (HCC) Service

There has been a large increase in the number of patients referred with suspected liver cancer in recent years (see Figure below), reflecting trends in other developed countries and associated with a large rise in mortality. In the last five years this has resulted in dramatic expansion of caseload at King's Health Partners. Consequently, there has been a large increase in the number of treatments delivered to our patients, with 903 treatments

for liver cancer (excluding transplantation) in 2013/2014 representing a five-fold increase since 2008. King's College Hospital treats more patients with HCC than any other UK centre, with excellent outcomes.

The range of treatments available at KHP meets international standards shown to increase patient survival. These include surgical treatments (i.e. resection, transplantation), local-regional therapies (i.e. percutaneous ablation, transarterial chemoembolisation) and systemic

agents (i.e. sorafenib). There is also an active clinical trials programme of studies evaluating novel systemic agents and devices for patients at different stages of the disease.

As shown in the Figure below, the majority of treatments delivered for HCC involve transarterial chemoembolization (TACE), which is delivered by specialist interventional radiologists. The second most common local-regional therapy is radiofrequency ablation (RFA), also delivered by specialist interventional radiologists. Less frequent treatments include conventional chemotherapy and surgery, excluding transplantation. A multidisciplinary team involving liver physicians, surgeons, oncologists, radiotherapists, radiologists, clinical nurse specialists and palliative care physicians underpin the quality of the service.

There has been growth in the use of oral chemotherapy with sorafenib in our patients. The continued involvement of liver specialists in the cancer treatment ensures that issues related to treatment toxicity are effectively managed in this group of vulnerable patients.

Figure 20 | Treatment breakdown

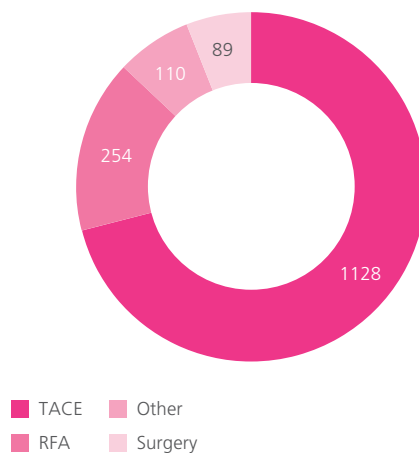
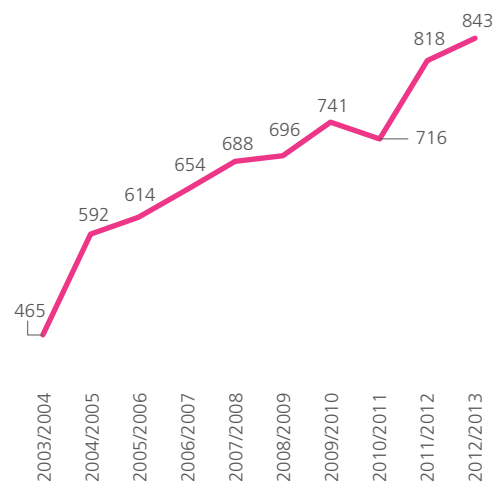


Figure 21 | Admissions between 2003 and 2013 for HCC



Going forward

The volume of work and excellent patient outcomes place Kings Health Partners as a leading UK institution in the management of acute and sub-acute liver failure, whilst developing translational research in monocyte biology and evaluation of large datasets. As quality indicators, multiple high-profile reviews in the New England Journal of Medicine, and the Lancet, and original publications in the core hepatology literature has arisen from the clinical cohorts managed through the service.

During the last 12–18 months period the number of “non-liver” admissions has increased. This is partly explained by novel services which have been introduced, such as the King's ECMO service which is a joint initiative of liver and general intensive care and staffed by medical and nursing specialists across critical care and liver, but also by the acute bed pressures within the trust posed by an expansion of acute and tertiary services.

In recent years the number of paracetamol induced liver failure admissions has dropped considerably. At the same time a significant increase in patient admissions with hypoxic hepatitis induced ALF has been observed – approximately 20% of all ALF admissions over the last 24 month period. There also appears to be a noticeable increase in recreational drug induced liver failure cases (metamphetamine derivatives “ecstasy”), as well as “metabolic” multiple organ failure with liver involvement,

particularly in patients with underlying haematological disease.

The number of admissions following liver transplantation has increased by 10 to 15% over the past two years with a year-on-year increase in transplant activity. In contrast, admissions from decompensated chronic liver disease have remained relatively static. There has been a noticeable increase in admissions and in particular bed occupancy due to the increased hepatobiliary surgical workload. As HPB activity has risen year on year, the number of complications following surgery with associated need for level two and three support has increased in parallel, as expected.

The complexity of the transplant and HPB workload at King's poses significant challenges in terms of infection control, as many patients are hospitalised for prolonged periods of time. The clinical need for often prolonged antimicrobial therapy and transfer from areas where multi-resistant germs are endemic means that many patients are colonised or at risk of acquiring infections with difficult to treat multi-resistant organisms such as Vancomycin-Resistant Enterococci (VRE) and increasingly Carbapenem-Resistant Enterobacteriaceae (CRE).

The layout of the ITU and lack of co-location of the Short Stay High Dependency Unit (SSDU) is a particular challenge in terms of infection control and patient safety. The Liver Intensive Care Unit (LITU) “new build”/refurbishment in 2002/2003 was accomplished on an old footprint of a “Nightingale” ward. The high equipment need and desperate lack of space, as well as absence

of isolation facilities pose exquisite challenges in terms of safe day to day routine working practice which is further compounded by the very high patient throughput.

In the long term, consideration has to be given to strengthening the provision of liver critical care services. Commissioning will mandate a more evolved service and King's Health Partners is well placed to deliver the expansion of this flagship service. Moreover, academically the service is well positioned to maintain its role as the leading single institution in the management of acute and sub-acute liver failure, whilst developing translational research interests in monocyte biology, evaluation of large datasets and interrogation of "big data".

The experience of staff and patients in our service

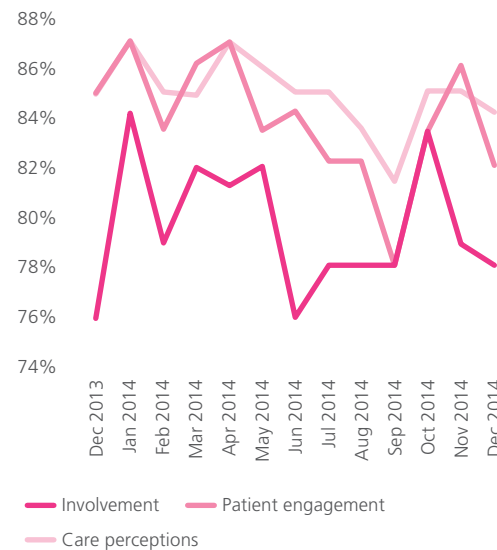
This graphic summarises how we are doing in relation to care perception, patient engagement and environment. Environmental issues are most difficult to address as a consequence of ward layout and historical configuration of wards as nightingale units.

Specialist clinics

Due to the large volume of work, the outpatient facilities provided by the liver service at King's

College Hospital has grown in the period since 2010 and this has stimulated the growth of specialist clinics including the provision of joint clinics, for example with obstetrics, renal services and haematology.

Figure 22 | Patient experience between December 2013 and December 2014



As an illustration, attendance at the specialist Hepatitis clinic at King's College Hospital was 9,105 in 2012/2013, which is a growth of 45% compared with 2008/2009. This has accompanied an increase in the number of inpatient episodes. The figures for patients with hepatitis B (see figure below) include a substantial number from outside our local catchment area of Lambeth and Southwark, increasing the national importance of our service.

The hepatitis service at King's College Hospital sees about 450 new cases of hepatitis B and 350 new cases of hepatitis C virus each year. Over 800 patients with hepatitis B virus infection are on oral therapy.

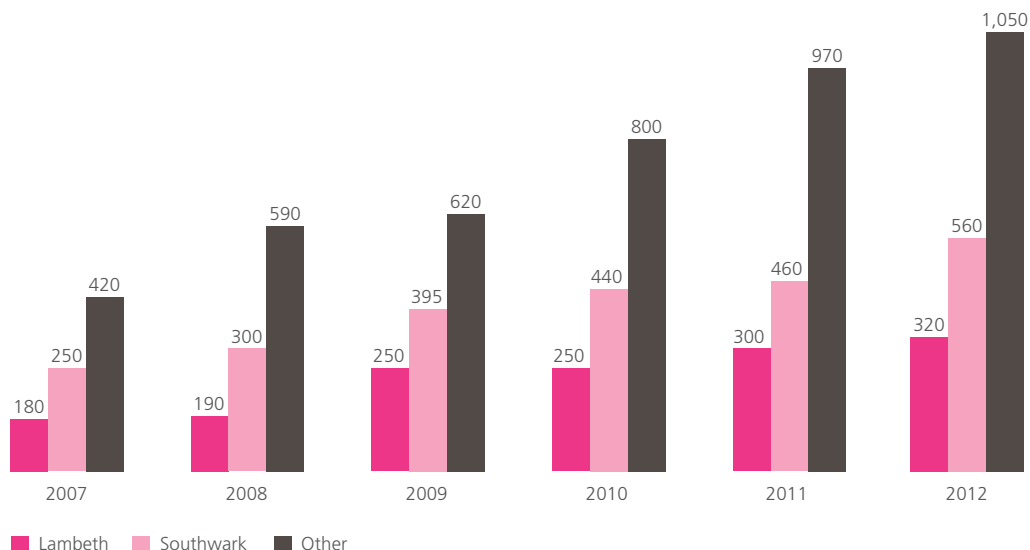
The Hepatitis C clinic at Guy's and St Thomas' sees about 110–150 new referrals per year. The community blood borne virus health inclusion team based out of Guy's and St Thomas' currently have 887 clients with hepatitis C. Clinical outcomes in this patient population have been documented and are equal to, or better than the pivotal registry studies.

The local population served by Guy's and St Thomas has a high prevalence of hepatitis B

virus, with antenatal sero-prevalence of hepatitis B of about 2%. Guy's and St Thomas' currently have 2,971 outpatients with chronic hepatitis B, and have 280 patients on long term antiviral therapy. The efficacy of hepatitis B therapy at Guy's and St Thomas' has been documented (Blaker PA et al. Gut 2011 60 A211). Guy's and St Thomas' was the second largest recruiter of patients to the Collaborative UK Study of Chronic Hepatitis B (Clin Infect Dis. 2013 Apr;56(7):951–960).

Nurse-led services at both King's College Hospital and Guy's and St Thomas' sites play an important and increasing role in the delivery of high-volume, protocol-driven care, which is shared across King's Health Partners sites.

Figure 23 | Hepatitis B patients by region



Fatty liver service

The fatty liver service, primarily run at Guy's and St Thomas' has an ambitious, nationally recognised programme of clinical management at the leading edge of the field. Contributions through basic science embrace the pathogenesis of non-alcoholic fatty liver disease (NALD) and autonomic control of liver regeneration and have led to several high impact publications (e.g. *Hepatology*. 58:128–138, October 2013). Clinical trials such as the current CENTAUR trial looking at the efficacy and safety of cenicriviroc in patients with non-alcoholic steatohepatitis (NASH) and liver fibrosis are also contributing to therapeutic innovation in this area.

The five-year plan is to extend the scope of the service through: including patients at the Evelina Hospital and King's College Hospital; commencing a joint service for endoscopic treatment of fatty liver combining intra-gastric balloon (now at the Guy's and St Thomas') and the EndoBarrier (now on King's College Hospital site); incorporating an exercise therapy service; initiating a patient support group aligned to the endoscopic fatty liver service. In addition, a fatty liver service will be established at King's College Hospital through a collaboration with the Foundation for Liver Research. One of the goals of the KCH fatty liver disease service will be to explore the role of bariatric surgery in improving liver-related outcomes in collaboration with Prof. F. Rubino's Metabolic Surgery Unit.

Incorporation of palliative care

A marker of quality, particularly in the care of patients who have end-stage disease, is the appropriate use of palliative care services. Over a one-year period 2012–2013, the liver speciality made 156 new referrals to the palliative care team, illustrating the importance of end-of-life care and symptom control amongst liver unit patients. These referrals provided support relevant to a range of patients, including 104 patients with a diagnosis of hepatocellular cancer, pancreatic cancer or bile duct cancer.

Commitment by liver services to further integration with palliative care services over the forthcoming years will improve the patient experience and increase academic impact on patient management. It is also clear that early involvement of palliative care services in patient management improves the quality of care. We are determined that the knowledge gained will lead to further improvements in non-cancer terminal care.

Top grants awarded

Award details	Amount	Year
Dr Jude Oben. As part of the Carbalive European Consortium in January 2015 an award was made to investigate the utility of a novel nanocarbon therapeutic agent in cirrhosis and NAFLD. Dr Oben leads the UK NAFLD part of this Consortium.	£5,900,000	2015
Dr Debbie Shawcross. Defining the pathogenic role of cellular immune responses to alcohol dehydrogenase in severe alcohol-related liver disease. WT101722AIA. Laura Blackmore, Yun Ma, Debbie Shawcross Supervisor of Wellcome Trust Fellowship.	£223,077	2013–2016
A placebo controlled single centre double blind randomised trial to investigate the efficacy of rifaximin versus placebo in improving systemic inflammation and neutrophil malfunction in patients with cirrhosis and chronic hepatic encephalopathy, Norgine.	£403,593	2013–2015
InTeam Consortium – Integrated Approaches for Identifying Molecular Targets in Alcoholic Hepatitis. Human Biorepository Core NIHR grant to Dr Shawcross as part of consortium, Ramon Bataller (UNC-CH) (CI/Director) Sidney Barritt (UNC-CH) Debbie Shawcross (King's) Michael Lucey (U of Wisconsin) Samuel B. Ho (UCSD) David Brenner (UCSD) Bernd Schnabl (UCSD) Phillipe Mathurin (Lille U) Alexandre Louvet (Lille U) Robert Brown Jr (Columbia U) Guadalupe Tsao Garcia (Yale U).	\$150,000	2013–2018



Hepato-
biliary and
neuro-
endocrine
tumours

Hepatobiliary and neuroendocrine tumours

Introduction and headline about this speciality

The hepatobiliary and pancreas (HBP) service at King's College Hospital provides a full range of surgical, interventional radiology and medical treatments for benign and malignant hepatobiliary diseases, and coordinates a network of 9 satellites centres in which combined multidisciplinary meetings take place and from which patients are referred. Kings College Hospital Hepatobiliary service has a catchment population of 3.5–5 million. It performs the largest number of pancreatic surgical resections in England. It is one of the largest liver resection centres in England as well. In addition to pancreatic adenocarcinomas, hepatocellular tumours and other hepatobiliary tumours there is a large neuroendocrine tumour

service based across KHP. In the year 2016/2017 alone, there were a registered 1,136 new patients and 4,873 follow-ups for HBP service, with a 40% increase in referrals in our HBP services from 2014–2017.

Overall HPB services are in high demand with a year on year increase in the number of operations being performed. Patient experience is recorded monthly thorough a number of surveys. Overall in 2017 the experience of service has remained high in line or above the national benchmark (see below).

In addition, the number of major liver procedures for cancer (by cases) has remained high in recent years compared to other leading centres as well as the delivery of chemotherapy for pancreatic cancer.

Figure 24 | Admissions to services and number of operations from 2014–2017

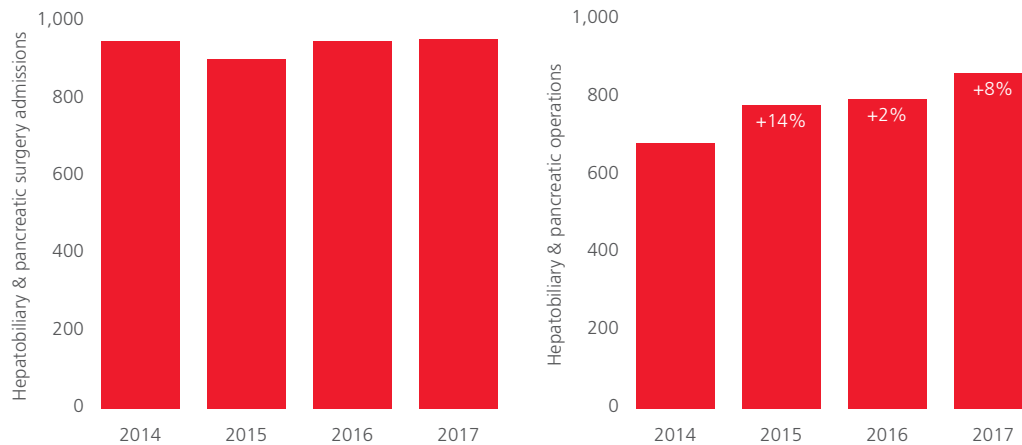


Figure 25 | Monthly survey performance heat map 2017

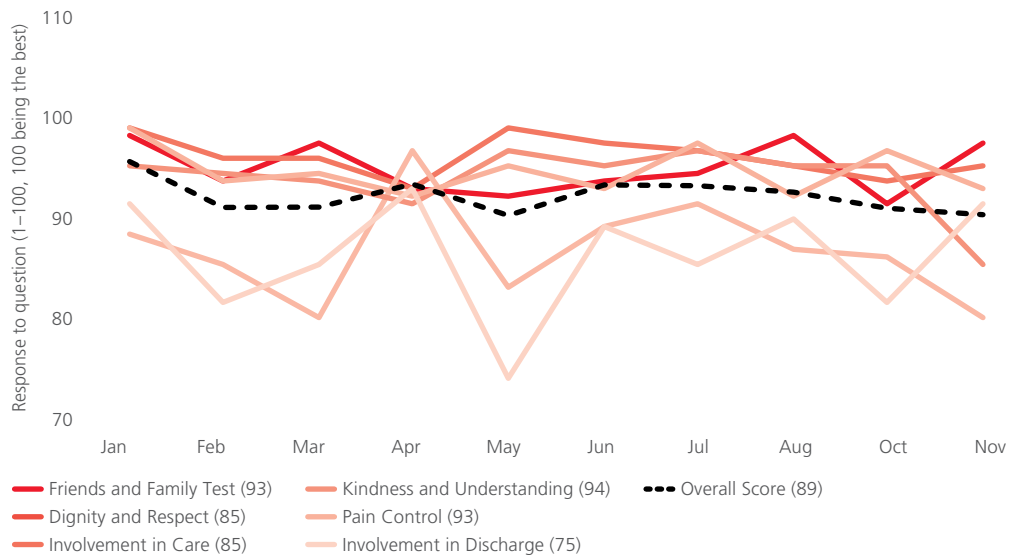


Table 3 | Number of major liver procedures for cancer by England NHS Providers
2012/2013 to 2014/2015

	2012/2013	2013/2014	2014/2015	
	Cases	Cases	Cases	Catchment population
University Hospitals Birmingham NHS Trust	193	133	166	4,518,137
Royal Free London NHS Foundation Trust	142	127	150	4,082,654
Leeds Teaching Hospitals NHS Trust	185	188	139	3,783,259
Hampshire Hospitals NHS Trust	110	122	138	3,756,042
King's College Hospital NHS Foundation Trust	164	173	134	3,647,171
Central Manchester University Hospitals NHS Foundation Trust	69	75	105	2,857,858
University Hospital Southampton NHS Foundation Trust	102	97	104	2,830,640
Nottingham University Hospitals NHS Trust	80	79	100	2,721,769
Plymouth Hospitals NHS Trust	100	83	92	2,504,028
Royal Surrey County Hospital NHS Foundation Trust	95	90	85	2,313,504
The Newcastle Upon Tyne Hospitals NHS Foundation Trust	91	109	81	2,204,633
Aintree University Hospital NHS Foundation Trust	95	86	81	2,204,633
Sheffield Teaching Hospitals NHS Foundation Trust	54	54	73	1,986,892
University Hospitals of Leicester NHS Trust	71	58	70	1,905,239
Imperial College Healthcare NHS Trust	51	60	67	1,823,585
Cambridge University Hospitals NHS Foundation Trust	61	78	66	1,796,368
Pennine Acute Hospitals NHS Trust	73	68	64	1,741,932
Oxford University Hospitals NHS Foundation Trust	50	59	63	1,714,715
Barts Health NHS Trust	60	59	57	1,551,409
University Hospitals Bristol NHS Foundation Trust	67	68	48	1,306,449
University Hospitals Coventry and Warwickshire NHS Trust	27	43	46	1,252,014
East Lancashire Hospitals NHS Trust	45	50	42	1,143,143
The Royal Marsden NHS Foundation Trust	35	32	36	979,837
Norfolk and Norwich University Hospitals NHS Foundation Trust	30	24	19	517,136
Total (providers less than 10 procedures 2014/2015)	46	20	39	1,061,490
Total (England)	2,142	2,055	2,104	57,266,027

Source: HES data extracted February 2016

Figure 26 | Number of chemotherapy cycles delivered by provider trust across London and Greater Manchester 2014/2015 for pancreatic cancer



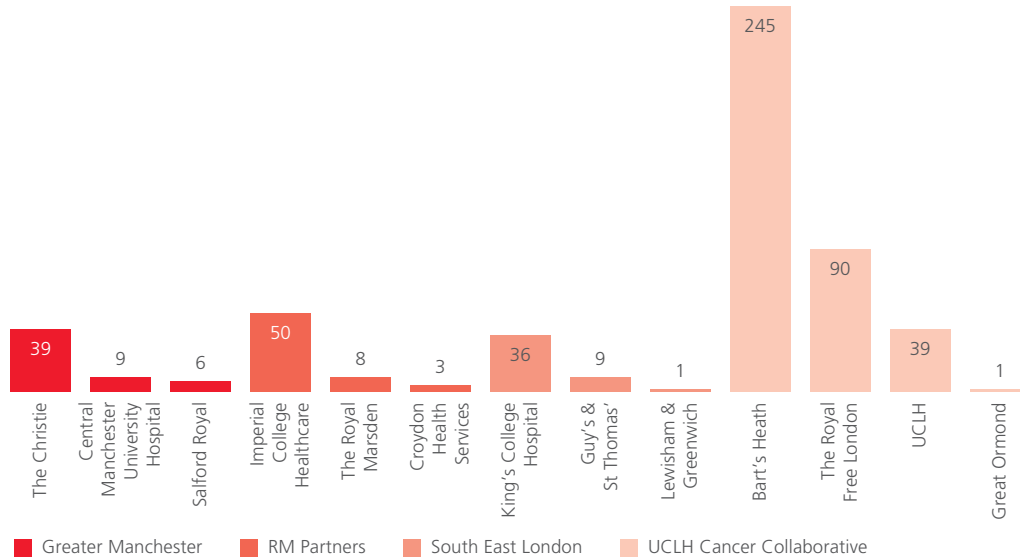
Recruitment into National Institute for Health Research (NIHR) trials

Firstly, it should be noted that these figures do not include commercial trials so may not reflect a provider trusts full clinical trial activity also that often clinical trials are recruited to at specialist centres, and patients under the care or diagnosed at other providers which then may be referred to the specialist centre to be entered into the clinical trial. Therefore, a low number

of patients recruited at an individual provider should not be interpreted as a low level of access to clinical trials for patients under the care of that provider.

Several trials are classed as 'multiple' as these cover several tumour sites. These are not included in these tumour specific figures as it is not possible to distinguish the type of cancer for these trials.

Figure 27 | Number of patients recruited into NIHR HPB cancer (including endocrine) clinical trials in 2015/2016 by provider trust in London and Greater Manchester



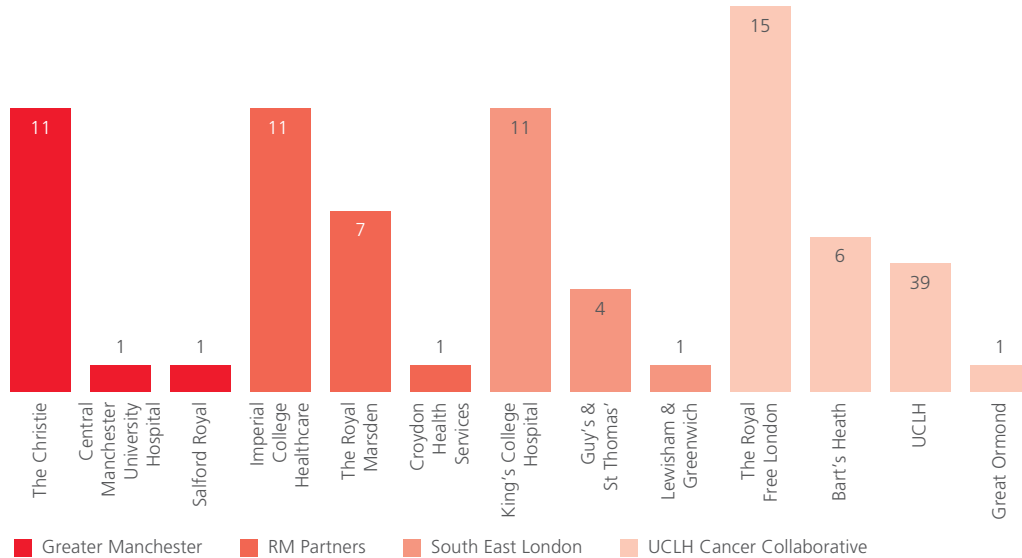
Research and innovation around these specialities

Neuroendocrine tumours (NETs) have historically been regarded as rare tumours and obtaining significant grant funding has been challenging. Globally there are very few centres with large research programmes dedicated to study of NETs. At KHP we have focussed on clinical research, primarily on epidemiology and optimising outcomes for patients with NETs, quality of life and psychological health of patients with NETs and basic science focussed on biomarkers in NETs.

Recent projects investigating epidemiology have been in collaboration with Public Health England to determine the true incidence of NETs in the UK. A grant from the national NET society has enabled us to investigate the incidence of NETs within the bowel cancer screening colonoscopy programme.

Over the last 3 years we have published several articles examining the role of surgery in pancreatic NETs. 1st prize abstract was awarded at the European Annual meeting in both 2014, 2015. Over 400 abstracts are submitted for this meeting annually.

Figure 28 | Numbers of unique NIHR HPB cancer (including endocrine) clinical trials with patients recruited by London and Greater Manchester trust 2015/2016



Professor Ramage is an international expert in Quality of Life and a member of the European Organisation for Research and Treatment of Cancer (ORTC) Quality of Life Group. At King's we have been involved in a number of Quality of Life projects and most recently, following an unconditional grant, we are analysing quality of life in patients undergoing peptic receptor therapy.

The mental health of our patients has been an emphasis defined by KHP. We have looked at the effect of carcinoid syndrome and disease burden on mental health and quality of life. As a participant in the Integrating Mental and

Physical healthcare: Research, Training and Services (IMPARTS) – an initiative funded by King's Health Partners to integrate mental and physical healthcare in research, training and clinical services at Guy's, St Thomas' and King's College Hospitals, as well as South London and Maudsley NHS Foundation Trust – we routinely collect QoL data and screen for anxiety and depression in our patients.

Historically clinical trials in NETs have been rarely performed, however, with the development of the European Neuroendocrine Tumour Society (ENET) and development of a NCRI NET subgroup more clinical trials have been

performed in NET. The KHP NET centre has run all the major commercial clinical trials over the last 5 years. Phase 1 trials are run at GSTT and all other trials are run between GSTT and KCH. 8% of all patients are enrolled in clinical trials.

Education and training

There are currently four Senior Fellows and one National trainee in the Unit and they are responsible to the Clinical Lead in HPB Mr Andreas Prachalias and Mr Krishna Menon as the Educational Lead for Liver Surgery. The National trainee post is for one year and the trainee is directly responsible to Mr Krishna Menon for the appraisals and the end of year final assessment. All Fellows are involved in all aspects of clinical care and are encouraged to do clinical studies and publish their work.

They are supported through the PGMDE for their study leave and expenses for National and International meetings. In addition, there are seven Junior Clinical Fellow posts that provide the on-call for HPB through the week. These are clinical posts but the Junior Fellows are also encouraged to do clinical projects and publish their work.

Separately in NET there is a clinical research fellow who is enrolled at KCL for a MD(Res). In addition a undergraduate medical student has been undertaking research with the NET team for the last 3 years and successfully published an article and won a number of international prizes for best abstracts.

Annually the KHP NET Network holds an educational meeting supported by educational grants from pharmaceutical companies. This meeting has grown on an annual basis with international speakers and a high delegate attendance. The feedback has been excellent, reporting a very useful training opportunity for clinicians and allied health professionals involved in the management of NET patients.

A number of the core members of the NET team are Key Opinion leaders and give talks at national and international meetings. In addition the national and European guidelines are co-authored by members of the KHP Network.

Key clinical outcomes

The main quantitative outcomes that we collect are related to patient numbers referred and treated per annum and interventional outcomes for surgery and chemotherapy. In addition we collect survival outcomes of the different subtypes of NETs.

In 2015 we received 170 new referrals of which 92 were seen in the KCH NET clinic. 65% of these patients had their treatment at KCH. There are currently 412 patients under active follow up within the KHP network and 244 of these have been seen in the NET clinic this year.

Surgical outcomes

- 30 day mortality for NET patients post-surgery: $0/64 = 0\%$
- 90 day mortality for NET patients post-surgery: $1/64 = 1.56\%$
- Re-admission rate (within 30 days) for NET patients post-surgery: $2/64 = 3.12\%$

Breakdown

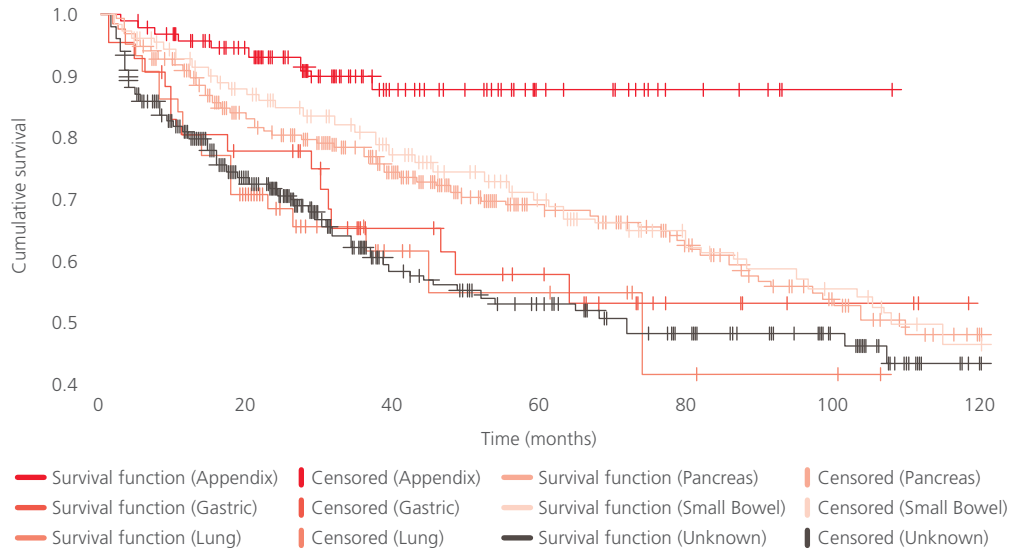
- 30 day mortality in hepato-biliary surgeries for GEP NET patients: $0/10 = 0\%$
- 90 day mortality in hepato-biliary surgeries for GEP NET patients: $0/10 = 0\%$
- Re-admission rate (within 30 days) for GEP NET patients that have had hepato-biliary surgery: $2/10 = 20\%$
- 30 day mortality in pancreatic surgeries for GEP NET patients: $0/24 = 0\%$
- 90 day mortality in pancreatic surgeries for GEP NET patients: $0/24 = 0\%$
- Re-admission rate (within 30 days) for GEP NET patients that have had pancreatic surgery: $0/24 = 0\%$
- 30 day mortality in colo-intestinal surgery for GEP NET patients: $0/30 = 0\%$

- 90 day mortality in colo-intestinal surgery for GEP NET patients: $1/30 = 3.33\%$
- Re-admission rate (within 30 days) for GEP NET patients that have had colo-intestinal surgery: $0/30 = 0\%$

Chemotherapy outcomes

- Number of NET patients undergoing chemotherapy = 14
- Percentage of discontinuation of cytotoxic therapy in NET Patients = 0
- Percentage mortality after cytotoxic chemotherapy in NET patients (after 30 days) = 0

Figure 29 | Survival data is created from the database of KCH patients. As a comparator the median survival for patients with Gastroenteropancreatic Neuroendocrine Tumour (GEP NET) is approximately 60 months.



Primary	Mean*				Median			
	Estimate	Std. error	95% confidence interval		Estimate	Std. error	95% confidence interval	
			Lower bound	Upper bound			Lower bound	Upper bound
Appendix	96.789	3.497	89.935	103.643	–	–	–	–
Gastric	73.972	8.396	57.516	90.429	–	–	–	–
Lung	61.507	7.667	46.480	76.534	73.710	25.442	23.844	123.576
Pancreas	82.179	2.735	76.819	87.538	103.520	–	–	–
Small bowel	84.433	3.040	78.474	90.392	107.770	–	–	–
Unknown	68.479	3.528	61.564	75.393	67.760	18.303	31.885	103.635
Overall	79.714	1.645	76.490	82.937	105.570	–	–	–

*Estimation is limited to the largest survival time if it is censored.

What the patients and staff think of the service

There is an annual cancer patient survey, however, historically this has not incorporated patients with Neuroendocrine tumours. Consequently, the national patient charity, the NET patient foundation, sponsored a national survey of NET patients attending centres around the UK. Kings performed very well in this survey and the national data was also good. The summary inserted below covers some of the areas asked about with patients and their response.

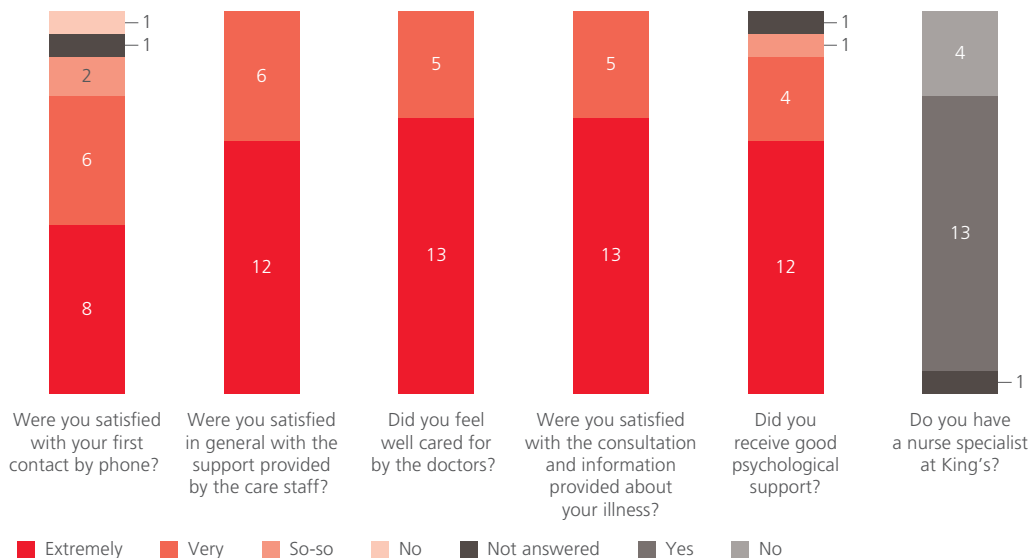
NET service patient questionnaire – 2015

Questionnaire handed out over a 3 month period (Oct–Dec 2015), with a 36% return rate.

Key results

The graph below, demonstrates that majority of patients surveyed are extremely happy with the service that they received.

Figure 30 | NET service patient questionnaire – 2015



Areas for investigation included, patients understanding of a clinical nurse specialist (CNS), as all patients are allocated a CNS, however 4/18 respondents stated they did not have one.

Comments regarding the patient environment, include "need more toilets and seating", "I think you do a great job, in particular the staff at all levels, better than the physical building".

We have moved from the old outpatients department to a new one in February 2016.

Comments regarding waiting times

Comments regarding waiting times, showed that patients did not experience long waits in the outpatient department, "Usually seen within acceptable waiting times", "Not aware of having to wait", "Delays at liver outpatients, very busy sometime, didn't bother me, treatment ok".

Other comments received were very positive

"I could not have asked for better care", "Very pleased with all aspects of care and organisation received, hopefully ongoing treatment will continue to the same high standard", and "My nurse specialist brought it all together – great help and service, thanks to Nicki Jervis and team".

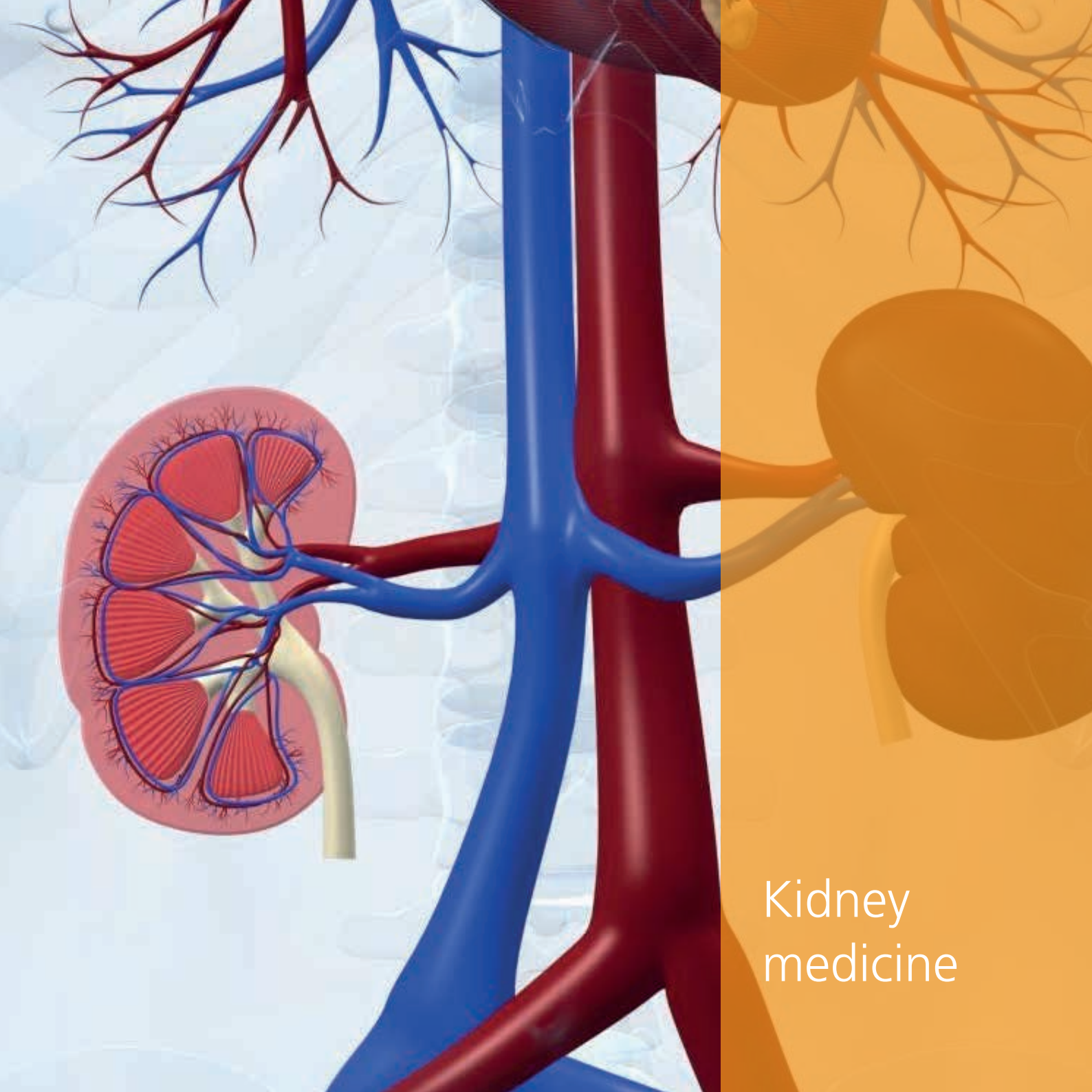
In terms of external assessment of the service, the ENET Centre of Excellence auditors praised the service offered.

Table 4 | Clinical trials in neuroendocrine tumours over last 3 years

Protocol(year)	PI's name	Study design
CRAD001C2324(2008)	Dr Ross	A randomized double-blind phase III study of RAD001 10 mg/d plus best supportive care versus placebo plus best supportive care in the treatment of patients with advanced pancreatic neuroendocrine tumor (NET).
TELESTAR(2014)	Dr Srirajaskathan	A Phase 3, Randomized, Placebo-controlled, Parallel-group, Multicenter, Double-blind Study to Evaluate the Efficacy and Safety of Telotristat Etiprate (LX1606) in Patients with Carcinoid Syndrome Not Adequately Controlled by Somatostatin Analog (SSA) Therapy.
CAM-NET(2014)	Dr Srirajaskathan	A Phase IV, Multicentre, Open label, Single Group Exploratory Study to Assess the Clinical Value of Enumeration of Circulating Tumour Cells (CTCs) to Predict Clinical Symptomatic Response and Progression Free Survival in Patients receiving Deep Subcutaneous Administrations of Somatuline® (lanreotide) Autogel® to treat the Symptoms of Functioning Midgut NeuroEndocrine Tumours (NET).
TELECAST(2014)	Dr Srirajaskathan	A Phase 3, Randomized, Placebo-controlled, Multicenter, Doubleblind Study to Evaluate the Safety and Efficacy of Telotristat Etiprate (LX1606) in Patients with Carcinoid Syndrome.
AAA-III-01(2013)	Dr Srirajaskathan	A multicentre, stratified, open, randomized, comparator-controlled, parallel-group phase III study comparing treatment with 177Lu-DOTA0-Tyr3-Octreotate to Octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive, midgut carcinoid tumours.
Oblique(2014)	Dr Ramage	A Phase IV, Observational study to assess Quality of Life in patients with Pancreatic Neuroendocrine Tumors receiving treatment with oral 10mg Everolimus (Afinitor®) o.d.
TELEPATH(2015)	Dr Srirajaskathan	A Multicenter, Long-term Extension Study to Further Evaluate the Safety and Tolerability of Telotristat Etiprate (LX1606) – Expanded Treatment for Patients with Carcinoid Syndrome Symptoms.
LUNA	Dr Sarker	3-arm trial to evaluate Pasireotide LAR/Everolimus alone/in combination in patients with lung of thymus NET (LUNA trial).
RADIANT4	Dr Sarker	EVOROLIMUS plus best supportive care versus placebo plus best supportive in the treatment of patients with advanced neuroendocrine tumours (GI/Lung origin) (RADIANT4).
BEZ	Dr Sarker	<ol style="list-style-type: none"> 1. BEZ235 Phase II Trial in Patients With Advanced Pancreatic Neuroendocrine Tumors (pNET) After Failure of mTOR Inhibitor Therapy; 2. Randomized phase II study of BEZ235 or everolimus in advanced pancreatic neuroendocrine tumours.

Top grants awarded

Award details	Amount	Year
Grants awarded to KHP NET centre between 2011–2016:		
1. Novartis unrestricted educational grant awarded	£42,000	2013
2. Imaging Equipment limited unrestricted grant awarded 2015	£75,000	2015
3. Ipsen, Pfizer and Novartis meeting sponsorship	£27,000	2015
EORTC grant awarded 2015 for QoL research	€60,000	2015
TransNet/UKINET research grant	£30,000	2014
IPSEN unrestricted educational grant	£7,000	2016
Ipsen, Pfizer, Novartis and Imaging Equipment meeting sponsorship	£20,000	2016



Kidney
medicine

Kidney medicine

Introduction and headline about this speciality

The Renal units of Guy's and St Thomas's and King's College Hospitals work in close collaboration within the King's Health Partners Academic Health Sciences Centre. This is particularly true in the care of renal transplant patients. Together the units serve the renal patients of South East London as well as a wider population extending into Kent. The Guy's campus provides kidney care to the Channel Islands whilst both units receive national and international referrals of highly complex specialised patients. While core services remain a strength at both sites, there are several distinctive areas that complement each other on each site.

King's College Hospital

The KCH campus has approximately 300 staff and focuses on the delivery of excellent clinical care through strong multi-disciplinary working. The main renal unit is based at the Denmark Hill campus, and in addition the service provides care to patients at 7 haemodialysis units across South East London, has three community teams and, in partnership with local teams, provides renal

care at Darent Valley Hospital, Princess Royal University Hospital and Queen Elizabeth Hospital.

The delivery of a well-developed Acute Kidney Injury (AKI) service to KCH extends to patients who develop acute kidney injury whilst admitted to the tertiary liver, cardiac and haematology services and to patients from other hospitals in South East London. The unit hosts a specialised team of acute kidney injury nurses.

A full range of chronic kidney disease care is available to its 650 dialysis patients including one of the largest, most innovative peritoneal dialysis programmes in the country, which supports complex, co-morbid and frail patients in this dialysis modality permitting optimum quality of life. The wide network of community-based haemodialysis units run by the centre aims to provide local treatment with a particular focus on shared care. The unit has also developed an internationally recognised programme of end of life care for renal patients caring both for those following a maximally supportive non-dialysis pathway and for those becoming increasingly frail whilst receiving dialysis.

The unit serves a complex and much deprived local population and has developed a large range

of specialist joint services which are responsive to the specific needs of the local populations or collaborate with local expertise. The renal sickle clinic provides joint care to the large local sickle population. In addition, a joint renal HIV service has facilitated access to transplantation for this often disadvantaged group. The renal liver clinic receives national referrals for patients with complex disease and supports the combined liver/renal transplant programme based on the King's site. The renal obstetric clinic works in collaboration with the internationally acclaimed department of foetal medicine. The renal obesity and exercise programmes led by a consultant dietician and a consultant physiotherapist are considered exemplars in their field.

The unit based at KCH also hosts a large programme of clinical and basic science research focusing on the treatment of renal anaemia and the understanding of, and intervening in, the mechanism of renal fibrosis in chronic kidney disease.

Guy's & St Thomas' Hospitals

The Department of Nephrology and Transplantation based at Guy's is one of the largest and busiest in the UK with 365 WTE staff. The unit has one of the largest kidney transplant programmes in Europe and also provides a comprehensive range of services for its local population, from management of mild kidney disease through to acute kidney injury (AKI). The renal unit offers a full range of

peritoneal and haemodialysis therapies, both at home and through a network of satellite units (approximately 690 dialysis patients in total). In addition, the unit has strong clinical links with both the Evelina and Great Ormond Street Children's Hospitals and aims to progressively develop these.

The unit has developed a network model of care that is, as far as possible, delivered close to home for patients. Outreach renal clinics at Lewisham University Hospital, Queen Mary's Hospital, Sidcup and at our 'Kidney Treatment Centre' in Tunbridge Wells have been opened to support this goal.

The GSTT surgical team provides a regional service for patients of KCH, Kent and Canterbury Hospital and the Channel Islands. A team of 7 Consultants supported by six surgical trainees enables day-case surgery at these sites, so patients can have their care closer to home. Onsite and satellite clinics offer one-stop assessment including dedicated duplex ultrasound evaluation.

The service incorporates a strong team dedicated to advanced kidney care, with multidisciplinary support and community cover. The team oversees all aspects of treatment for patients with advanced kidney disease including anaemia, metabolic bone disease and blood pressure control as well as introducing various options for renal replacement therapy (through regular teaching sessions). The team is involved in providing palliative care in the community for patients who opt for this treatment.

A dedicated glomerulonephritis clinic and a combined rheumatology/renal clinic cater for patients with complex disease, including lupus and other forms of vasculitis. This has been effective in allowing focused management of these patients as well as providing an opportunity to enrol them in national and international clinical trials.

In addition the unit runs outpatient speciality clinics for patients with cystinosis and cystinuria. There is a dedicated pre-pregnancy clinic for patients with kidney disease who are planning to become pregnant as well as a young adult transition clinic (in collaboration with the Evelina Children's Hospital). A dedicated clinic looks after transplant patients with a failing graft and there is a specialist clinic for patients with HIV who need a transplant or have been transplanted. A specialised clinic caters for patients who have had a kidney transplant for over 8 years. This is to seek out and prevent complications of long term immunosuppression such as skin cancer in this population and to modify cardiovascular risks and investigate and treat bone disease.

The umbrella of renal services provided at the KCH and Guy's & St Thomas' sites prides itself on the range and quality of services provided to an ethnically and economically diverse sector of the Southeast of England. It will continue to develop shared protocols, for example, for anaemia management, immunosuppressive treatment and transplant research, in order to optimise patient benefit for the local community and beyond.

Our achievements

On the KCH Campus

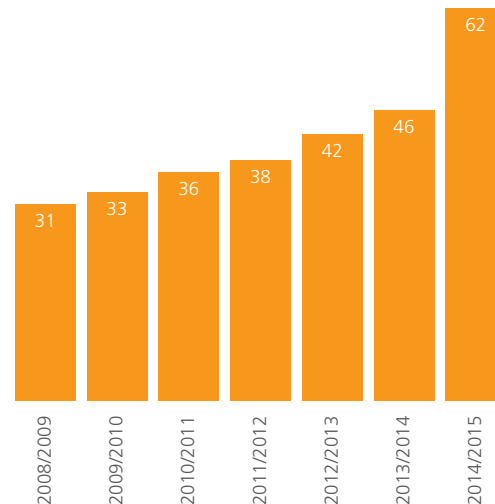
- Through its expert acute kidney injury service has supported a dedicated and innovative team of AKI nurses allowing prevention, recognition, education, treatment and audit of AKI patients;
- Through an exemplary peritoneal dialysis service, KCH has the highest percentage of peritoneal dialysis patients of any London unit and is widely recognised for innovation, e.g. nurse delivered local anaesthetic insertion of peritoneal dialysis catheters;
- A truly multi-disciplinary research team of nurses, physiotherapists, dieticians and doctors acting as principal investigators, with an output, in the last 5 years, of 152 research publications;
- A nationally acclaimed renal database allowing transparency of outcomes through excellent data returns together with a culture of audit and continuous improvement of service.

On the Guy's & St Thomas's Campus

- Having one of the largest kidney transplant programmes in Europe with the highest rate of live kidney donor programme in the country. From 2010 to 2014, 472 live donor transplants were performed at Guy's;
- Specialised transplant services for high risk kidney transplantation in antibody-incompatible patients;
- The second largest pancreas transplant centre in the UK (figures in transplant section);
- Prominent role in producing British Transplantation Society guidelines on transplantation;
- Extensive programme of home haemodialysis, which allows flexibility and better quality dialysis for a large number of patients;
- The first and only Medical Research Council Centre for Transplantation, which coordinates and leads medical advances through innovation in diagnostic, prognostic and immune monitoring tests and individualised patient care, across the CAG;
- National leadership in the ethics and regulation of transplantation and its research developments.

We have a growing number of home haemodialysis patients at Guys.

Figure 33 | Patients on home haemodialysis by year



In the next five years across KHP

- We will continue to build our specialist services including the highlighted joint clinics (renal/liver; renal/obstetric) and in Acute and Chronic kidney disease.
- We will develop better GP liaison services (and improved programmes of shared care), patient experience and patient education across the patch.
- Basic science focus will extend its translational research in renal fibrosis and regenerative medicine and optimising treatment for patients with chronic kidney disease.

Examples of excellence across KHP

- World renowned clinical renal anaemia research programme;
- Survival for patients on renal replacement therapy similar to the national average despite having one of the highest rates of patients with diabetes for any UK renal units;
- Internationally recognised renal palliative care service working in collaboration with Cicely Saunders Institute for palliative care;
- Increased number of patients receiving renal transplants by 100% over the last 8 years including significant improvements in our rates of pre-emptive transplantation at KCH;
- Large clinical trials activity out of local innovation in science.

Research and innovation around this speciality

Research at KCH has centred on anaemia based research including leadership of a number of pivotal and influential clinical trials in collaboration with industry. Another interest has been the mechanism of renal fibrosis including the application of novel approaches to therapy in basic research models. This activity including epidemiologically based research has resulted in 11 recent PhD awards and many first in man

and phase 3 commercial trials within the NIHR portfolio and in 152 publications and substantial research income over the last 5 years. Notable outputs of the research have included tools for measurement of patient experience, indicators of care in frail patients with chronic disease and expectation of outcomes for kidney patients who undergo exercise programmes or bariatric surgery for management of obesity. Awards have been given for the nurse led peritoneal dialysis insertion programme (Jane MacDonald leadership award) and for programmes of rehabilitation featuring exercise and dietary control.

Clinical science in renal transplantation has been the main focus at the Guy's campus. This has included optimisation of treatment in declining grafts using standard drugs. Clinical trials are also in progress for innovative methods such as cell based therapy that induce tolerance in experimental models, supported by biomarker studies to identify patients in whom these approaches are likely to be successful. We are also running trials of protein based therapies aimed at treatment of the donor organ in order to improve organ recovery after transplantation. Other research focuses on managing patients with a high risk of rejection due to antibodies and on reducing the general risk of immunosuppressive therapies such as viral infections, steroid complications and cardiac disease, and aligning these risks to biomarker studies. Quality of life studies and patient perception of risk taking, as well as the ethical and legal boundaries of research, mark out the holistic approach to improving transplantation though innovation at our centre.

Research on kidney disease at the Guy's campus has included participation in national studies on lupus nephritis and on minimisation of steroid treatment in other renal inflammatory conditions. We lead a national study on interventional radiology to salvage vascular access for dialysis patients. Research on the metabolic and cardiac consequences of renal disease is also a recognised strength of our centre. Since 2008, 12 successful PhD degrees have been awarded in clinically based areas, in addition to numerous basic science studentships at the Guy's campus, both in nephrology and transplantation.

The mental health of our patients has been an emphasis defined by KHP. We have looked at the effect of psychological interventions on the wellbeing of dialysis patients. As a participant in IMPARTS – an initiative funded by King's Health Partners to integrate mental and physical healthcare in research, training and clinical services at Guy's, St Thomas's and King's College Hospitals, as well as South London and Maudsley NHS Foundation Trust – we place value on the mental as well as physical wellbeing of the local population of kidney patients and provide national leadership on innovation in the standard of care in this group of patients.

What do the patients and staff think about the service

King's site

The renal service routinely monitors patient experience for every inpatient stay and outpatient visit.

In addition, patient stories are captured formally and informally across all of the service and reviewed at monthly management and governance meetings.

Complaints to the renal service are at the lowest level of any care group at KCH and together with adverse incidents are monitored and themes identified.

KCH have developed a questionnaire to look at patient experience in Acute Kidney Injury and have developed a dedicated counsellor service to these patients.

Patient representatives sit on our Renal Research Governance Board and a recently rejuvenated King's Kidney Patient Association is set to become more involved in decisions about service delivery.

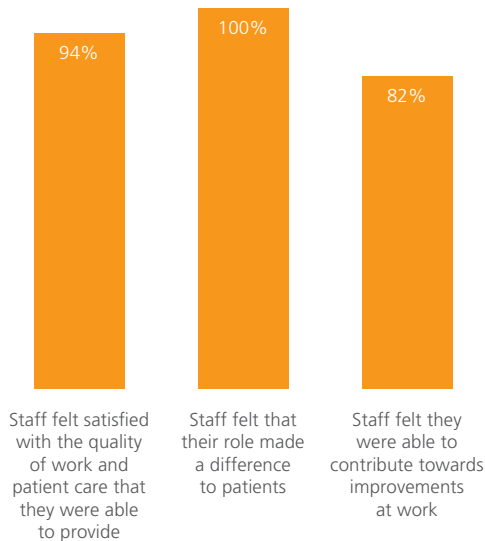
Patient feedback reflects high levels of satisfaction with the delivery of services close to home and tailor-made for particular conditions and decisions.

Our busy multi-disciplinary team focuses on patient involvement from the outset: 'On the night I came the doctor even called me to say that he was waiting for me for my treatment. The nurses welcomed me and took good care of me so they were excellent'.

Measurement of quality in our advanced kidney care clinic shows that patients are confident that they have been well supported to make difficult decisions about renal replacement therapy.

In most clinics, letters are written to patients (with a copy to the GP) and patients agree that this shows an approach which centres on their concerns.

Figure 34 | Staff satisfaction 2013/2014



A recent staff survey indicated very high levels of staff engagement in the renal department, despite acknowledging a high level of work pressure.

GSTT

The unit has regular patient satisfaction surveys for inpatients as well as patients on dialysis and some of the speciality clinics.

The unit strives to improve the service constantly. Within the past year patient satisfaction has been on average 88–92%.

Some of the patient's comments:

- 'Friendly courteous, polite, very helpful considering they are under pressure, best hospital in London'.
- 'I like the nurse that was dealing with my condition and I love the way the nurse on the ward dealt with me, Sandra is a very loving, caring nurse'.
- 'All staff and doctors always very helpful, treated like a person and not just a hospital number'.

The latest patient satisfaction survey from the annual review clinic showed 43 out of 47 patients who completed the survey were happy with the clinic.

Some of the comments are listed:

- Very thorough – prompt follow up of issues identified. Thank you all for looking after me so well. A welcome change.
- Yes I was happy to have the opportunity of talking over my concerns/worries with a trained professional, and listening to their comments.
- Again it was really good having conditions/ causes/treatments explained/discussed.
- I appreciate having time to talk over my problems with the nurse and the time she gave explaining simple answers to my questions.
- I found the AR beneficial and as always your team and Guy's were excellent.

Key clinical outcomes for this speciality

The number of patients starting Renal Replacement Therapy (RRT) continues to go up with 138 take on rate per million population (pmp) in 2013 compared to other renal units taking on approximately 120 pmp with a similar catchment population (Annual Report 2014 Table 1.4).

Exceptional standards of clinical care are evidenced by survival for patients on RRT that is similar to

the national average despite having one of the highest rates of patients with diabetes. King's has the 4th highest rate in England of patients starting on RRT who have diabetes, at 35.8%, however survival for patients on RRT is very similar to national average (89.8% vs. 91.0%).

Number of patients on home dialysis (haemodialysis and peritoneal dialysis) at King's site exceeds the NICE target of 15% at 18.3%, and is above the national average of 17.3%.

Catheter insertion

Figure 35 | Trends in methods of first PD catheter insertion in patients for general anaesthetic

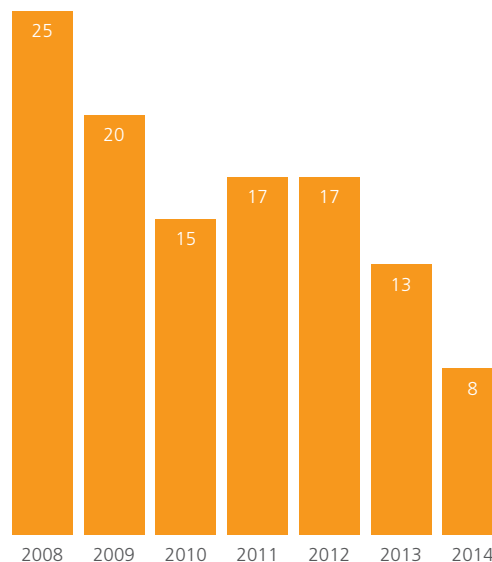
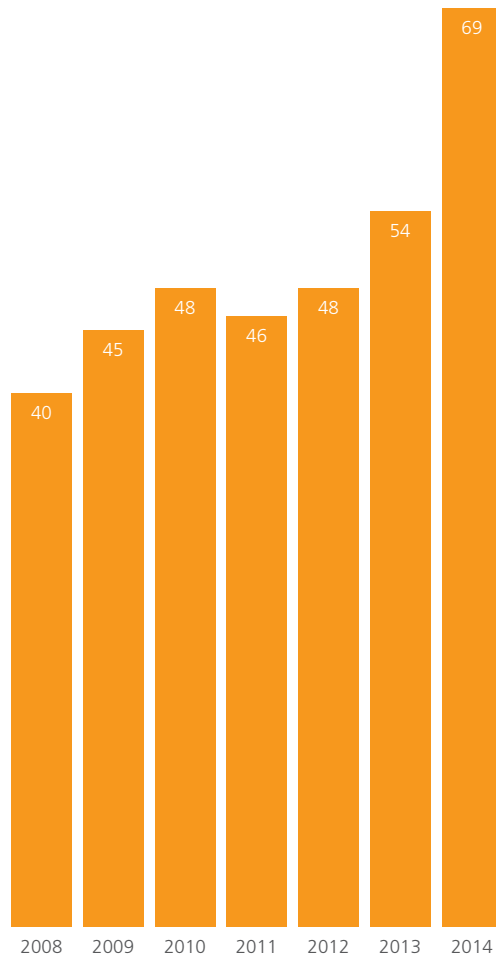


Figure 36 | Trends in methods of first PD catheter insertion in patients for local anaesthetic



Insertion of PD catheters under local anaesthetic reduces surgical workload and patient's length of stay.

Figure 37 | 90-day survival rates for a single year (2013) in newly diagnosed patients started on dialysis treatment

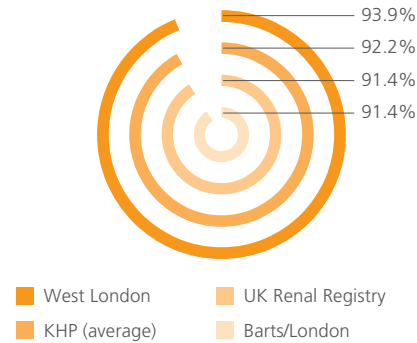
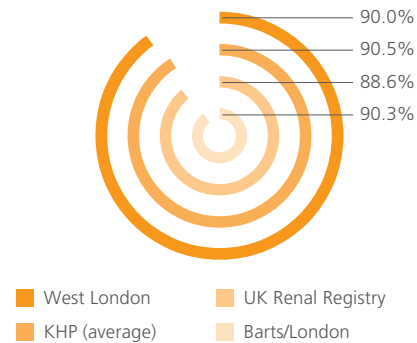


Figure 38 | One-year prevalent survival rates (adjusted to age 60) for patients on dialysis treatment (2013)



Prevalent cases are those whose disease developed or was diagnosed before they were identified for the study.

KHP averages 90.3% one-year prevalent survival rate, above the national average as recorded by the Renal Registry, and in line with other London centres.

Renal outcomes

The following outcomes were taken from the 2014 UK Renal Registry Report. This report is a resource for patients to know how well their care is being delivered and focuses on dialysis outcomes in the face of significant economic challenges and commissioning changes.

Figure 39 | Patients started on dialysis at KCH and GSTT combined

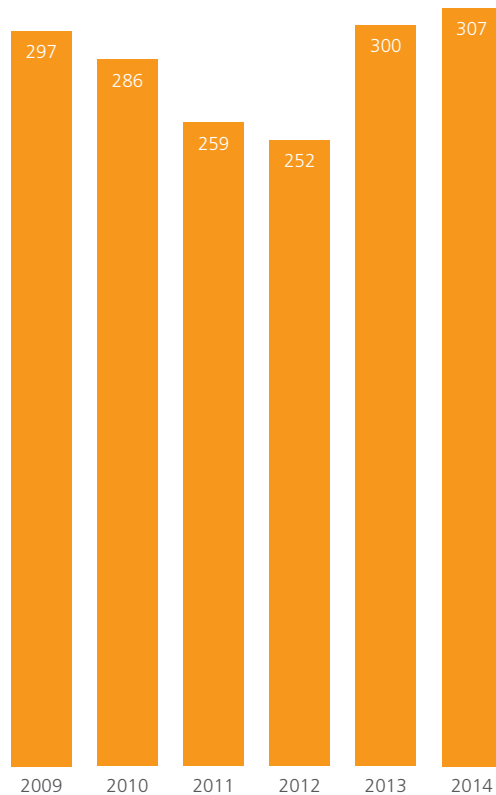


Figure 40 | Percentage status of patients 90 days after starting RRT 2013/2014

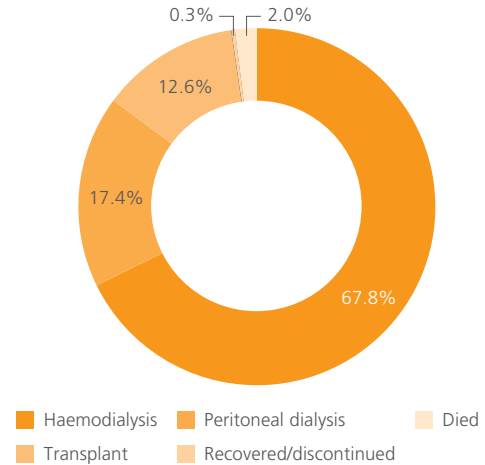
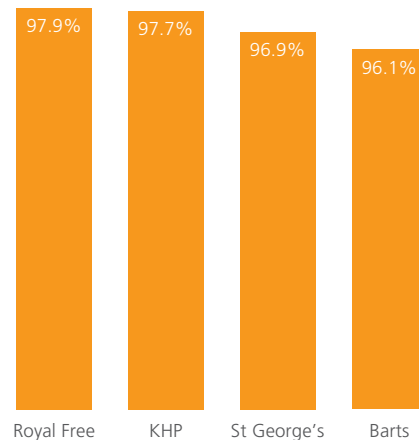


Figure 41 | 90 day incident survival (adjusted to age 60) 2013 (excludes hospitals with no recorded deaths in 90 days)



Other quality of care and performance measures

King's site

The KCH acute kidney injury (AKI) service provides renal ward based care alongside a consultant-led multidisciplinary outreach service. AKI admissions have gradually increased over the last 5 years (figure) with a much larger expansion of our outreach service, particularly in the last 12 months to deliver almost 800 AKI consults in 2014.

Figure 42 | AKI admissions to Renal Unit KINGS

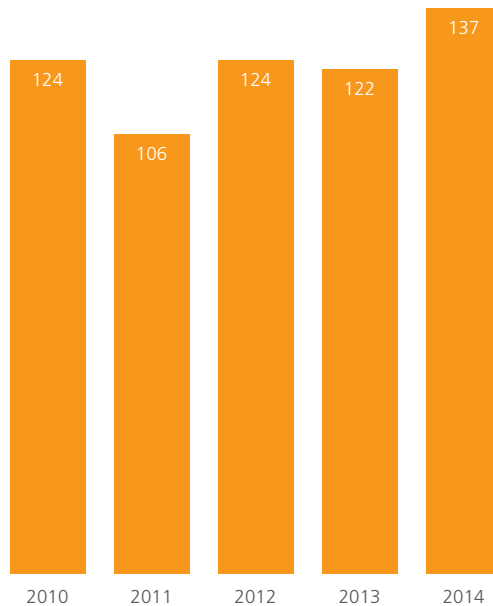
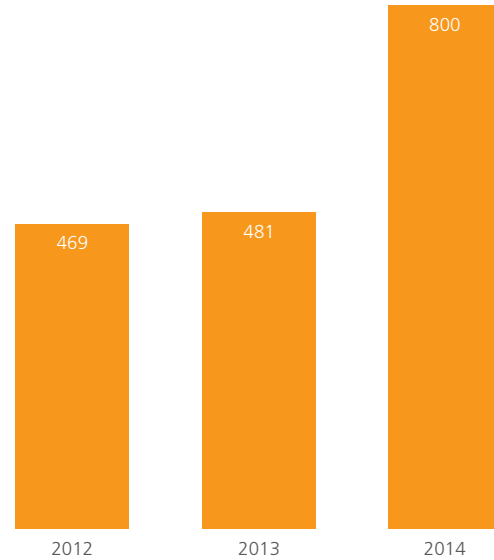


Figure 43 | KCH – number of AKI consults'



The high volume of acute kidney injury (AKI) at KHP is reflected in admission and inpatient referral data at KCH (figures 42 and 43). Data returns to the UK Renal registry Annual Reports (2011–2014) are 98–100% and are amongst the top 5 return rates in the UK, illustrating the fastidiousness level of reporting across KHP for this patient group.

Education and training

The renal units at KCH and Guy's & St Thomas' Hospitals have long been known for excellence in clinical training, including high quality training to renal specialist registrars. For example, junior doctor training at KCH were awarded top scores in the 2014 GMC trainee survey compared to the other lead education providers in London, in multiple indicators including overall satisfaction, induction, handover process, study leave and adequate clinical experience gained.

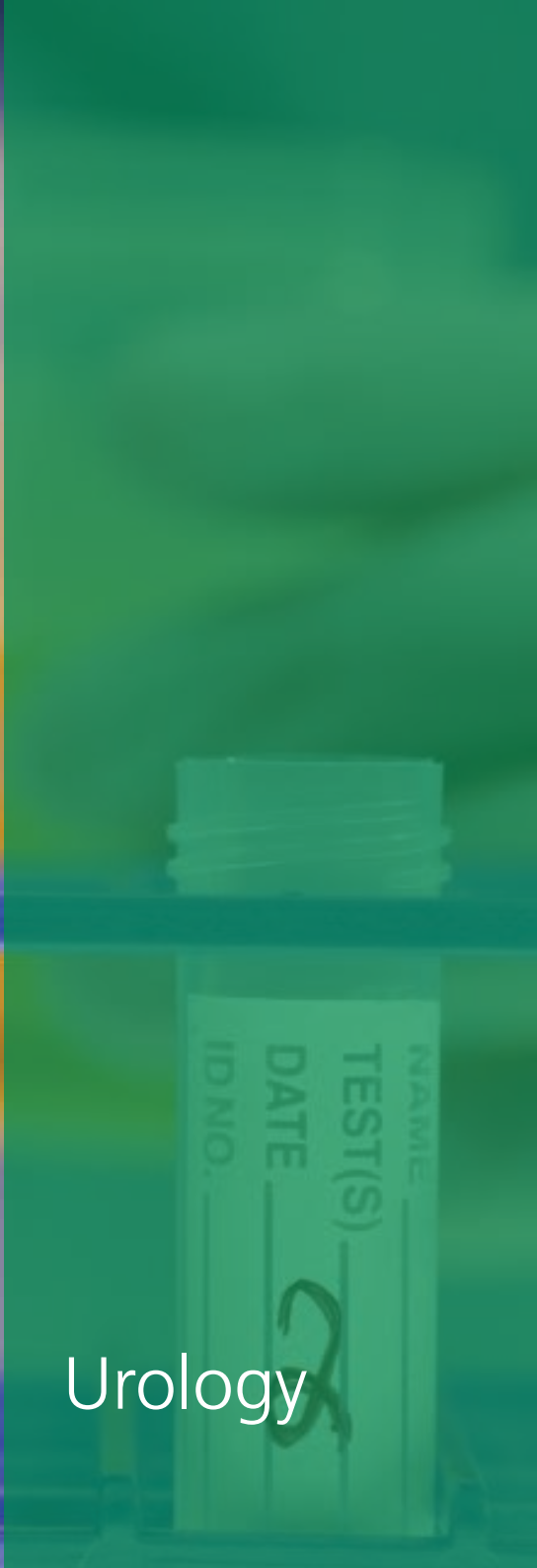
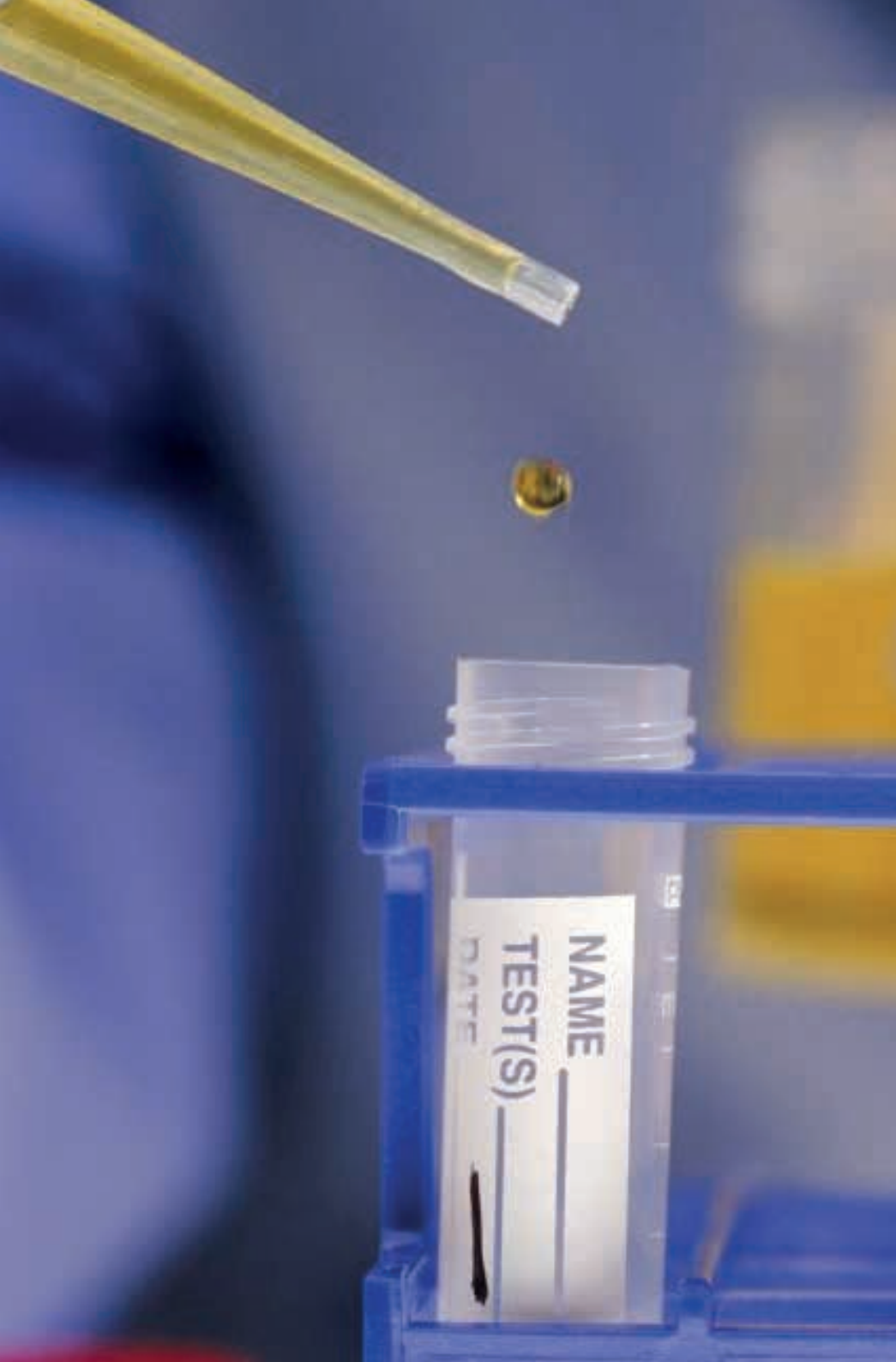
Since September 2012 KHP as part of MDECS (Medical & Dental Education Commissioning Scheme) process have been lead provider for renal medicine for South London for 40 trainees.

KCH and other providers have recently organised the London MRCP Nephrology Revision Course. The international reputation as training centres in renal and transplant medicine is reflected in the number of visiting fellows and observers from many countries including the USA, South America, Australia, China and Europe.

Training activities at KCH and Guy's Hospital include annual visiting professor programmes and training courses, with distinguished nephrologists, immunologists and transplant biologists contributing. KHP serves as the national base for Complement UK, a training and research programme with industry sponsored studentships and training days. In addition clinical teams from Australia, India, and Denmark have visited the KCH unit to learn from the supportive care programme.

Top grants awarded

Award details	Amount	Year
PIVOTAL (Macdougall) (Kidney Research UK)	£2,500,000	2013
PEDAL (Greenwood and Macdougall) (NIHR HTA)	£2,100,000	2013
eGFR-C (Sharpe) (NIHR HTA)	£2,100,000 (sponsored by Kent and Canterbury)	2013
Study of inhibition of T-type calcium channels as a potential renal therapy (Sharpe and Hendry) (Kidney Research UK)	£199,500	2015
European Collaboration on Chinese Herbal Medicine Research (Xu and Hendry) (European Research Council FP7)	€1,000,000	2009



Urology

Urology

A vibrant Professorial unit, Urology at King's Health Partners is based at two teaching hospitals – Guy's and King's and is designed around a custom-built £4m one-stop clinical hub The Urology Centre.

We are one of the largest urological cancer centres in the UK and the highest volume robotics institute. We have led numerous randomised trials comparing robotic surgery to open and laparoscopic surgery such as the LOPERA (robot assisted prostatectomy for prostate cancer), CORAL (outcomes of patients undergoing open radical cystectomy) and BOLERO (open versus minimal access cystectomy in patients with muscle invasive bladder cancer).

Our database manager prospectively reports to the British Association Urological Surgeons (BAUS) national audit where our kidney and prostate surgeons have performed excellently (https://www.baus.org.uk/patients/surgical_outcomes/). We were the first European centre to pioneer robotic cystectomy and one of the largest contributors to the International Robotic Cystectomy Consortium (IRCC). The national STUKA audit of bladder tumour resection was led by us and demonstrated reassuring outcomes. A randomised trial of blue versus white light bladder resection had its controversial

results highlighted on the front cover of the British Journal of Urology International (BJUI).

We also excel in benign diseases, being one of the largest European stone centres, pioneers in the management of the overactive bladder, leaders in the modern management of Benign Prostatic Hyperplasia with lasers and prostate artery embolisation and a tertiary centre for the management of retroperitoneal fibrosis.

Education and training

- We established the BAUS national simulation project to demonstrate the predictive validity of simulation in patient safety. This is supported by Health Education South London (HESL) and the School of Surgery. Amongst numerous sources of funding, we received program grants from The Urology Foundation and the Vattikuti Foundation for this important validation, of considerable interest to the National Patient Safety Agency;
- We led and published the first standardised international curriculum for training in robotic surgery and have employed NIHR

funded PhDs to implement and expand its role within the EU, otherwise known as the MARS project encompassing technical and non-technical skills;

- We have established a highly successful BSc module in Surgical Sciences at KCL;
- A number of SSC students have gone on to undertake further research into checklist development and igloo based simulation (immersive simulation);
- Our courses in Transperineal Template and Fusion biopsies (KISS) have been well attended;
- The national BAUS Chairman of the Office of Education is from Guy's;
- We have leadership roles within the BAUS Council, BAUS Academic Council, the Malcolm Coptcoat Charity, the EAU Robotic Urology Section (ERUS) and the Associated Parliamentary Committee for Surgical Services, House of Lords.

Key clinical outcomes for this speciality

Urology Centre Questionnaire: patient experience

Figure 44 | How likely are you to recommend our service to friends and family if they needed similar care or treatment?

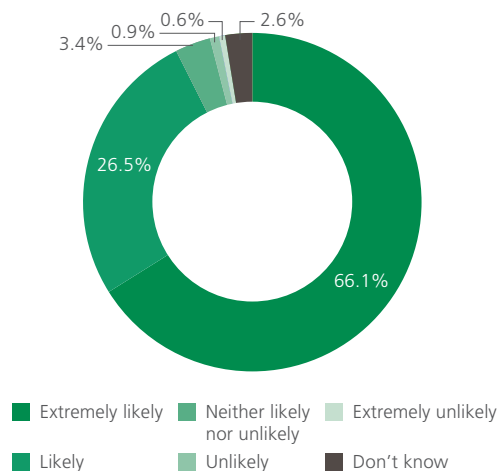
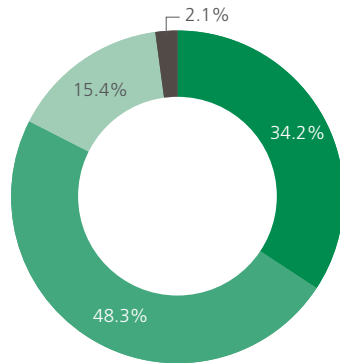
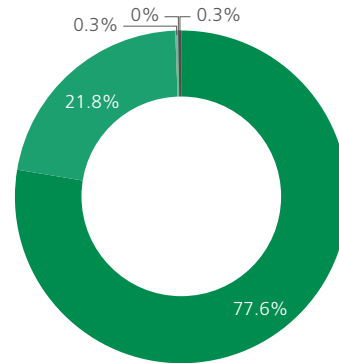


Figure 45 | Were you given a choice of appointment times?



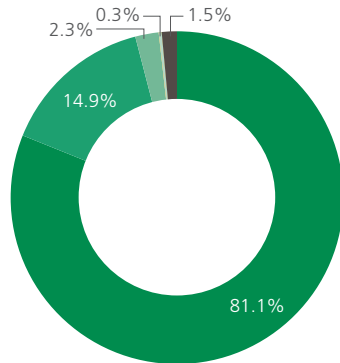
■ Yes
■ No, but I would have...
■ No, but I did not need, want...
■ Don't know

Figure 47 | In your opinion, how clean was the outpatient department?



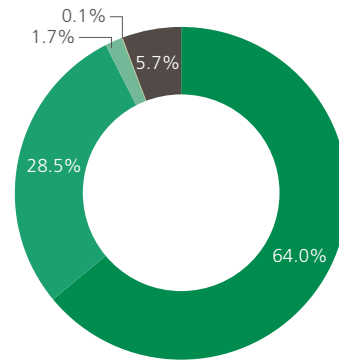
■ Very clean
■ Fairly clean
■ Not very clean
■ Not at all clean
■ Don't know

Figure 46 | Was your appointment date changed by the hospital?



■ No
■ Yes, once
■ Yes, two or three times
■ Yes, four times or more
■ Don't know

Figure 48 | In your opinion, how clean were the toilets and bathrooms that you used in the outpatient department?



■ Very clean
■ Fairly clean
■ Not very clean
■ Not at all clean
■ I did not use the toilets

Figure 49 | How long after the stated appointment time did your appointment start?

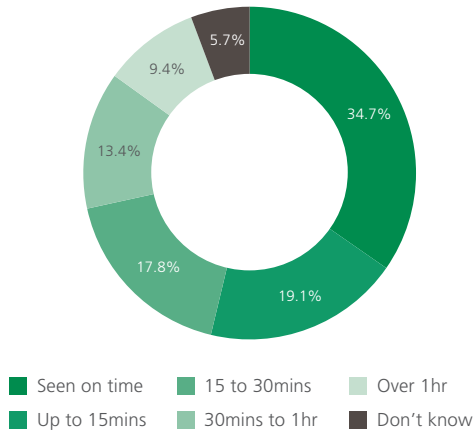


Figure 51 | During your visit were you treated with kindness and understanding?

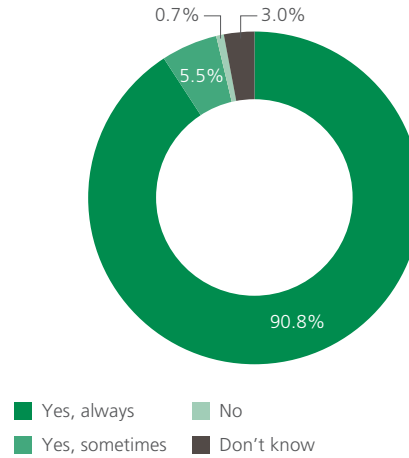


Figure 50 | Were you informed about how long you would have to wait?

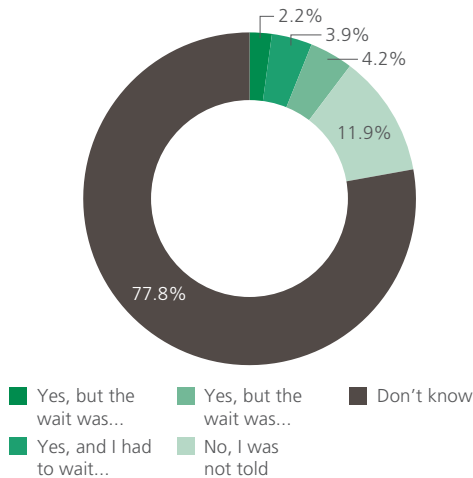


Figure 52 | Did you have confidence and trust in the staff treating you?

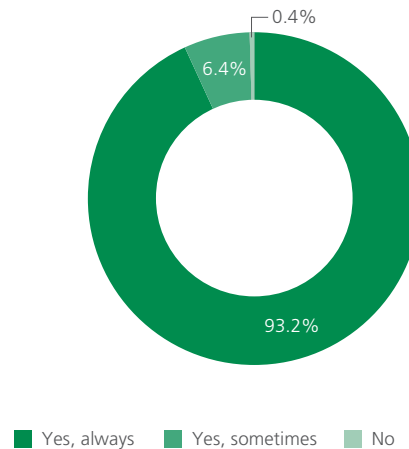


Figure 53 | If you ever needed to speak to a member of staff caring for you, did you get the opportunity to do so?

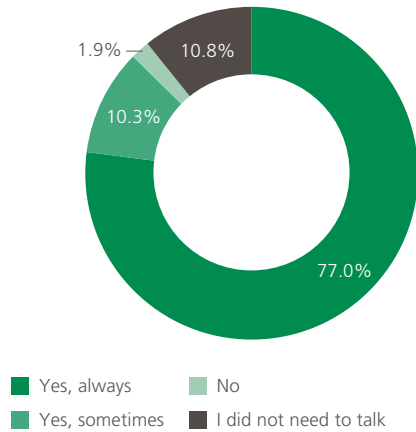


Figure 55 | Were you given enough privacy when discussing your condition or treatment?

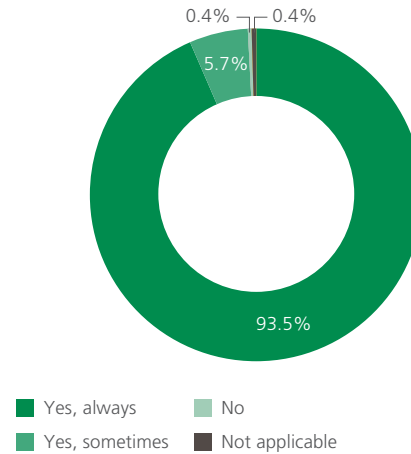


Figure 54 | Were you involved as much as you wanted to be in decisions about your care and treatment?

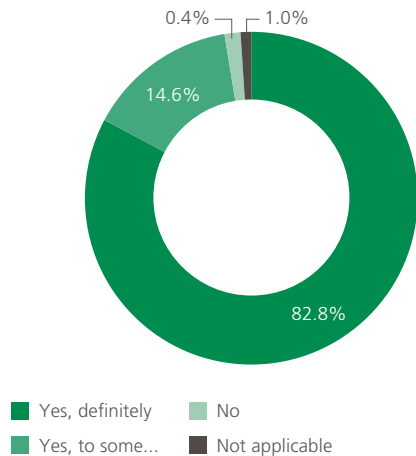


Figure 56 | How much information was given to you about your condition or treatment?

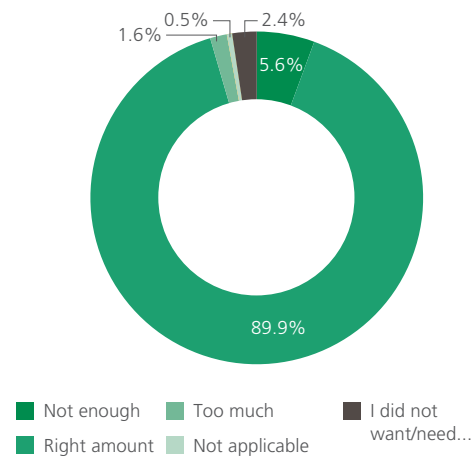


Figure 57 | Did hospital staff tell you who to contact if you were worried about your condition or treatment after you left hospital?

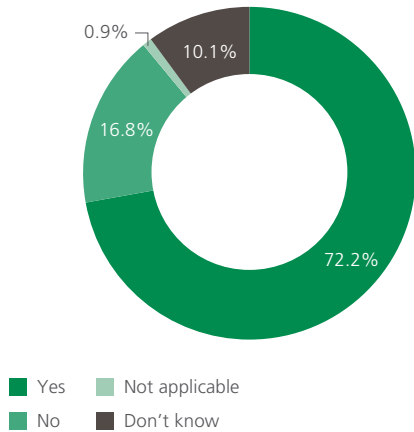


Figure 59 | Overall, did you feel you were treated with respect and dignity while you were at the hospital?

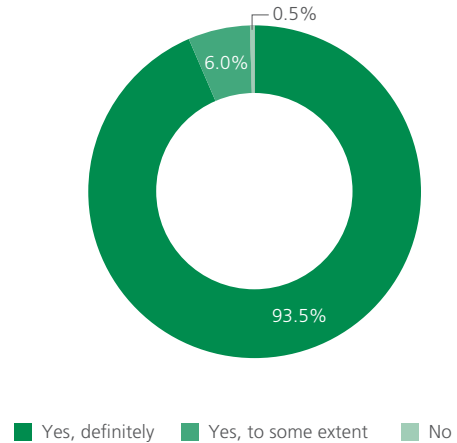


Figure 58 | Did your appointment help you to feel that you could better manage your condition or illness?

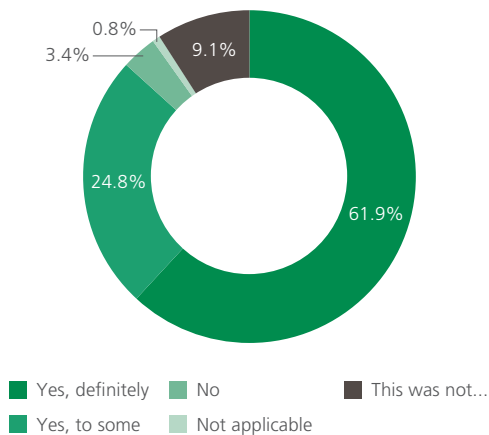
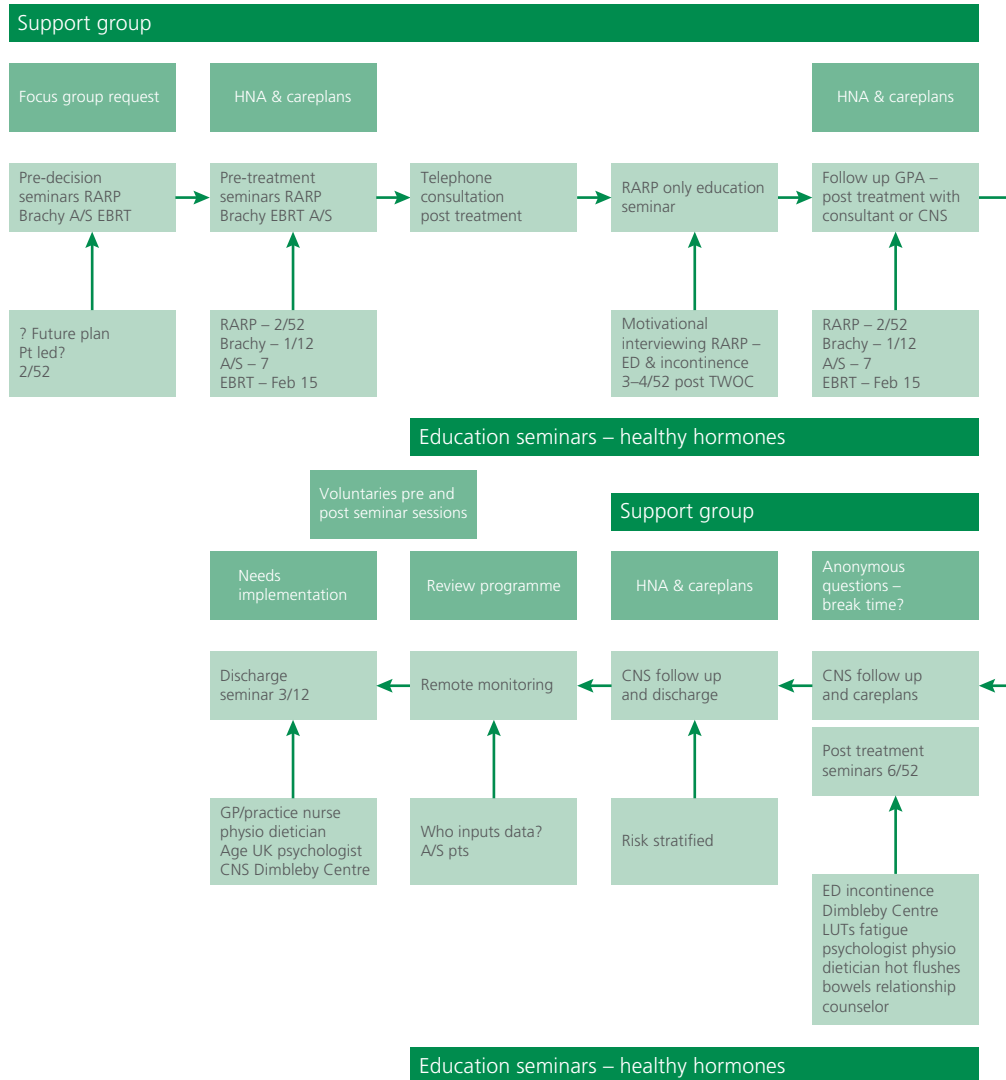


Figure 60 | Patient prostate survivorship pathway



Background

Robotic-assisted partial nephrectomy (RPN) is becoming the gold standard technique in surgical management of small renal masses.

RPN continued development 2010–2016.

With increasing experience and advances in technical skills more complex lesions are being considered as potentially suitable for RPN.

Maintenance of peri-operative and oncological outcomes is imperative with extending indications.

Objectives

To assess changes in tumour and patient characteristics during the evolution of RPN in a single tertiary referral hospital.

To assess intra-operative, post-operative and oncological outcomes within this period.

To compare outcomes with the British Association of Urological Surgeons (BAUS) national database reported outcomes.

Materials and Methods

Single-centre review between September 2010 and February 2016.

Prospective database of 230 patients with RPN – analysis of initial 200 cases, divided into four groups of 50 patients.

Assessment and comparison in relation to:

- Tumour size and complexity with aid of PADUA score;
- Patient outcomes including operative time (OT), warm ischaemia time (WIT) and length of stay (LOS);
- Intra-operative and post-operative complications;
- Oncological outcomes including incidence of positive surgical margin (PSM).

Results

Mean age: 55.8 years.

Approach: Trans-peritoneal 181, retro-peritoneal 19.

Four conversions to radical nephrectomy for oncological rather than technical factors.

No conversions to open surgery.

Complications:

- 1 transfusion;
- 5 positive margins;
- 3 Clavien III complications (1 stent, 2 embolisation).

Progressive increase in PADUA score and tumour size.

Criteria	Open	Lap	Robotic	R-GSTT
LOS	7	5	4	3.4
Positive margins	5.2	5.1	4.2	2%
Intraoperative complication	5.7	4.2	1.8	1%
Postoperative complications	17.8	14.5	13.9	8%
Transfusion	5.1	5.4	2.6	0.5%

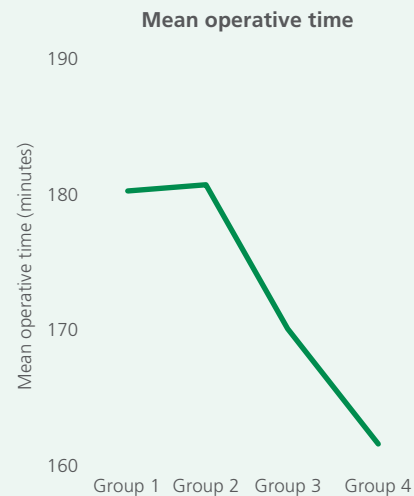
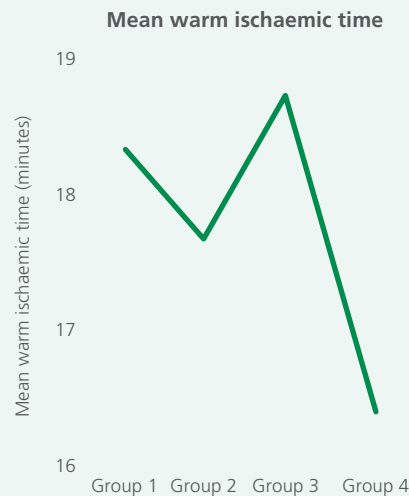
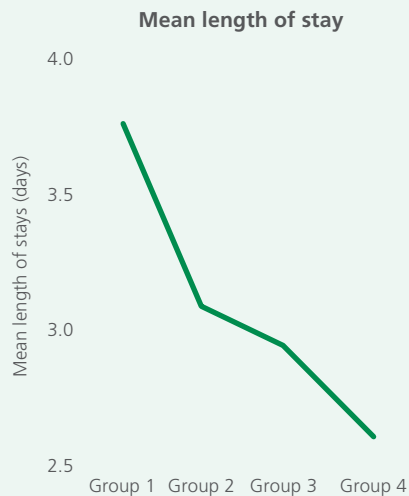
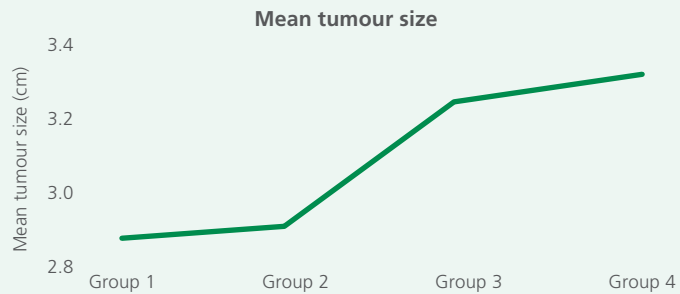
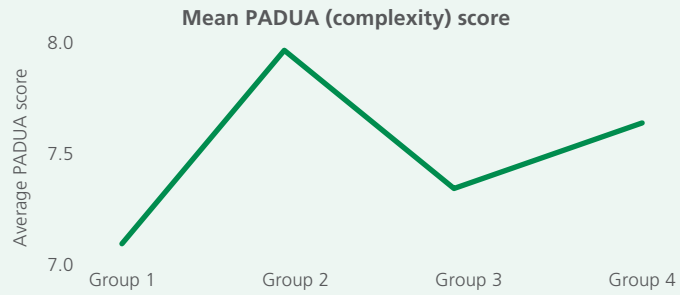
Comparison to *BAUS mandatory UK National Nephrectomy Audit 2012–2013*.

Compulsory national audit of all partial nephrectomies.

No consideration in audit of WIT or tumour complexity.

Overall favourable results for RPN.

Study results favourable despite likely higher complexity.



Discussion/Limitations

Single surgeon/single institution.
 Addition of training component with robotic fellow potentially confounding results in cases 110–200.
 Intraoperative US used in increasing complex endophytic lesions.
 Learning curve is somewhat expressed in case selection.
 No guidelines on achieving safe progression from simple to complex cases.

Conclusions

We report the largest RPN series in the UK.
 RPN can be performed with appropriate peri-operative and oncological outcomes and with suitable warm ischaemia time.
 More complex tumours and patients can be safely managed with RPN with increasing experience.

What the patients and staff think about the service

We invite patients to report PROMS in three main areas and have published these in the BJUI:

- Robotic and laparoscopic surgery – 97% satisfaction rate;
- Overactive bladders with the King's Health Questionnaire – higher satisfaction amongst those treated with Botox than placebo;
- Survivorship program in prostate cancer – patients counselled before treatment within a peer group (the Glee Club) have lesser regret as measured by Hospital Anxiety and Depression (HAD) scores.

Staff satisfaction

- Staff satisfaction, recruitment and retention levels are very high with many of the ward nurses taking up nurse specialist roles in cancer, benign diseases, andrology and functional urology within the Urology Centre;
- We have had fellows from UK, Australia, Belgium, USA, Italy, Greece, France, India, Pakistan, China and Egypt over the last 10 years with almost daily requests to visit and work at the Urology Centre. This is co-ordinated by the Directors of Fellowship and Education;
- We are a recognised and popular site for scholars from the European Urology Scholarship Program (EUSP) and The Urology Foundation (TUF) mentorship program with reported high satisfaction levels.

Performance measures

Figure 61 | Overall total referrals

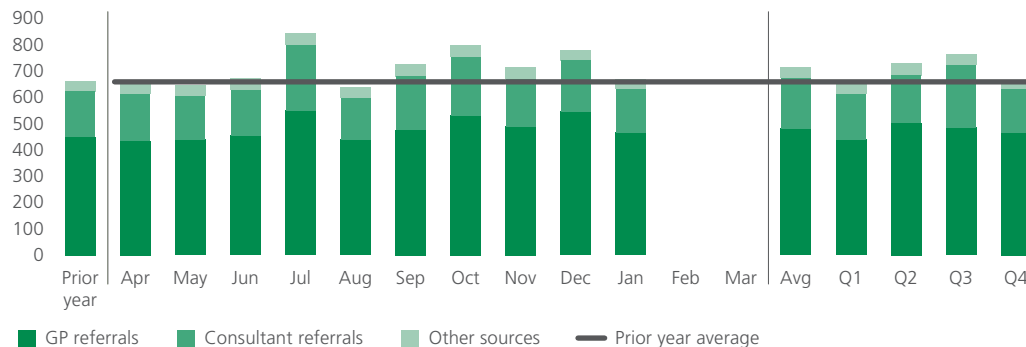


Figure 62 | New attendances seen by consultants

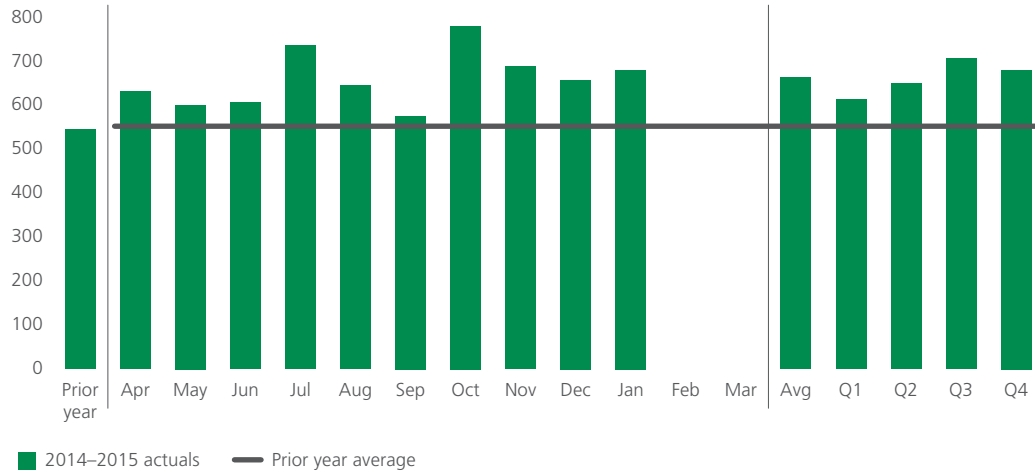
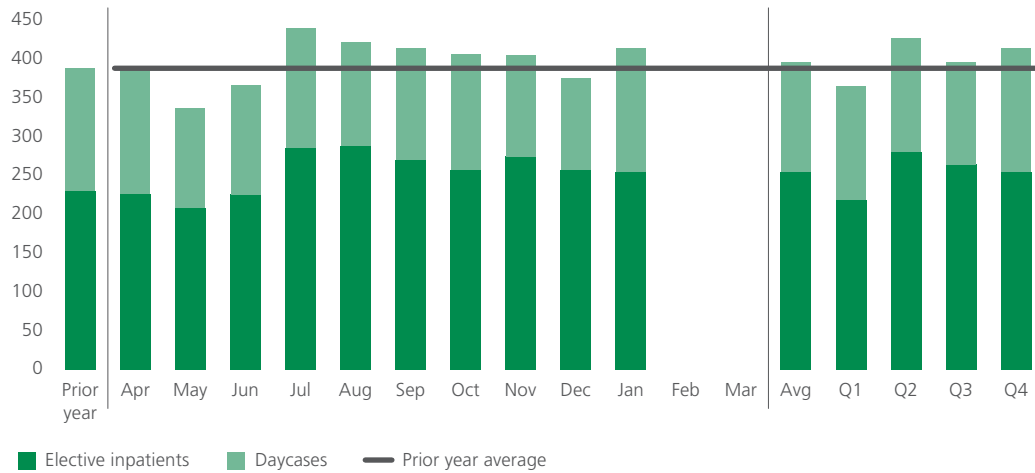


Figure 63 | Elective activity



- The Productive Operative Theatre (TPOT) project allowing for the seamless performance of three robotic assisted radical prostatectomies per day to cope with increasing demand;
- The development of a safety check list using Healthcare Failure Mode and Effectiveness Analysis (HFMEA).

Table 5 | Surgical safety checklist for robotic surgery

Anaesthetic room	Tick
1. Relevant history checked? Such as pre-medications, fasting time, drug/alcohol history or any obstructive airway conditions.	
2. Airway assessed? Check for dentures/crowns/bridges/loose tooth and any other obstructions.	
3. Equipment checked? Check anaesthetic/monitoring equipment for faults. Ensure all equipment is switched on.	
Operating theatre – before procedure	Tick
4. Operating table correctly adjusted?	
5. Patient correctly positioned/secured? Check that leg straps are not applied too tightly and that gel pads have been put in place.	
6. Surgical instruments counted?	
7. Equipment checked? Conform preliminary checks for robot have been completed. Check all equipment for faults.	
8. Correct marking site and insertion of ports?	
9. Robot docked and correctly positioned?	
10. Ports placed adequately to avoid arm collision?	
11. Effective communication between lead and assisting surgeon?	
Operating theatre – after procedure	Tick
12. Robot correctly de-docked?	
13. Specimen retrieval bags/other instruments removed? Such as needles, swabs, vascular clips, etc.	
14. Specimens correctly labelled?	
15. Surgical instruments counted?	

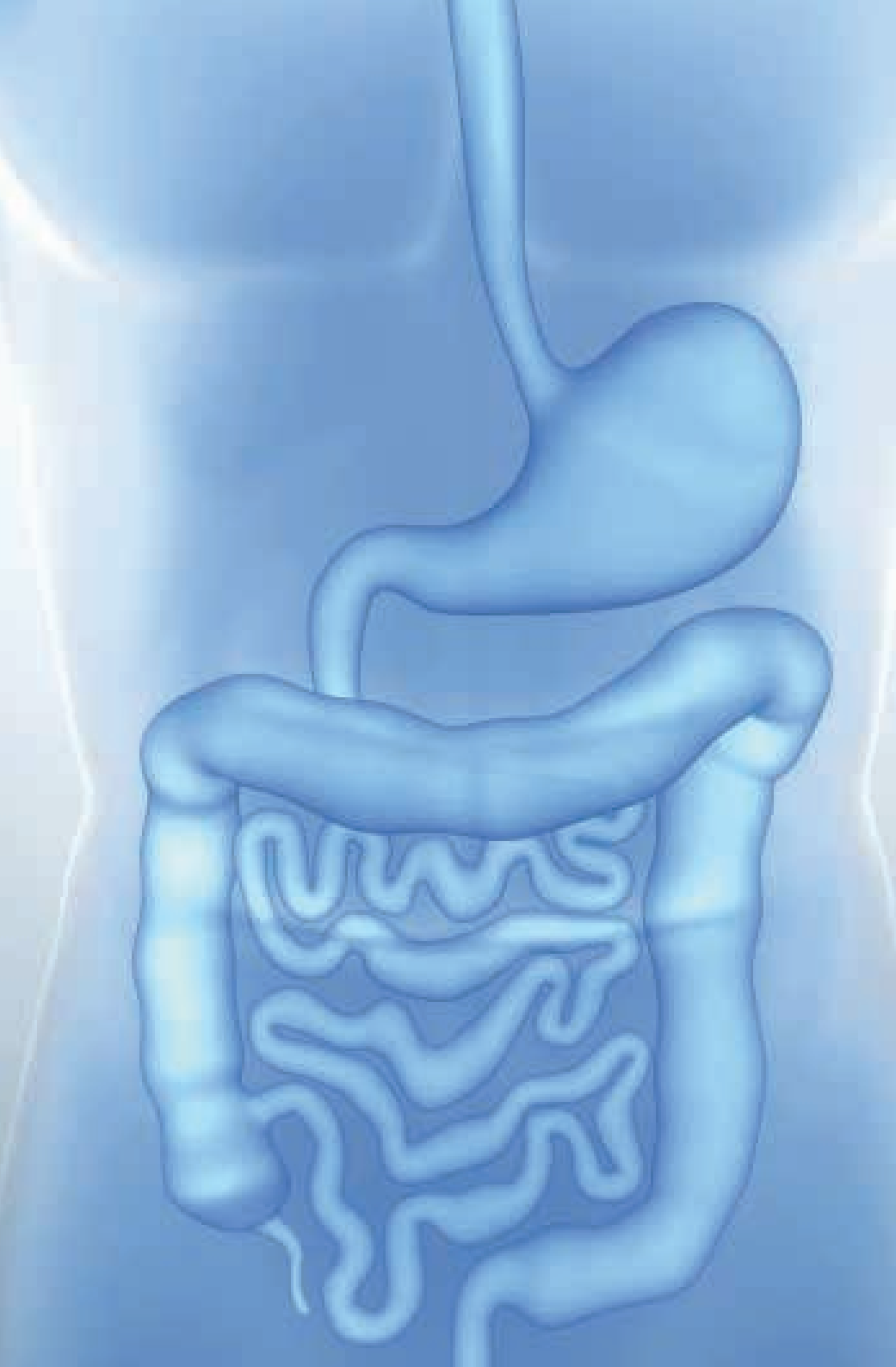
16. Equipment problems reported? Please make a formal report of any faults with the robot or any other equipment to be dealt with as soon as possible.	
17. Patient's chart updated?	
18. Anaesthetist present to monitor recovery?	
Handover to recovery	Tick
19. Accurate handover of details? Ensure that all patient and procedure details are passed on accurately to the recovery team.	
20. Recovery plans discussed? Ensure discussion of recover plans between surgical and recovery teams.	
21. Complications discussed?	

Top grants awarded

Award details	Amount	Year
The Prostate Cancer Research Centre	£2,100,000	2014
The STIFF-FLOP EU-FP7	£1,300,000	2011
The Vattikuti Foundation	\$600,000	2014
NIHR-TUF Research Fellowship for the BAUS-SIMULATE project	£108,000	2011
Technology Strategy Board	£54,000	2013
Prostate Cancer UK	£244,000	2006
Olympus Sim Centre plus equipment and personnel	£150,000	2011
The Guy's and St Thomas' Charity	£376,000	2010
The MS Society	£108,000	2013

Books authored by the group

Author	Title	Publisher
Dasgupta P, Kirby R	ABC of Prostate Cancer	BMJ (1996)
Dasgupta P, Ahmed K, Jaye P, Khan MS	Surgical Simulation	Anthem Press (January 2014)



Gastro-
intestinal –
upper GI

Gastrointestinal – upper GI

Introduction and headline about this speciality – upper GI

The incidence of adenocarcinoma of the oesophagus is higher in the United Kingdom than anywhere else in the world. The prognosis is poor due to the late detection of the disease. Efforts are being made to improve early detection and this year there is a national Oesophageal Awareness Campaign. Research is currently focusing on the genetic basis of the disease and identifying the most effective treatments.

Surgery is an important component of the treatment pathway. The unit performs one of the largest volumes of complex procedures in the country with excellent outcomes. Current aims are to minimise morbidity and psychological impact of surgery as well as identifying the patients who will benefit the most.

Combined, the Trusts handle a significant percentage of urgent cases, including GP referrals and emergency admissions. The number of urgent cases is above national averages in both instances.

Research and innovation around this speciality

The unit has a strong academic background running several clinical research projects aimed at improving outcomes in patients with oesophageal and gastric cancer.

Collaborations

Internally (King's College London and Guy's and St Thomas' NHS Foundation Trust), we collaborate with organisations looking at the genetics of squamous cell carcinoma of the oesophagus.

Externally, we have as a strong academic link with two research groups at the Karolinska Institute in Stockholm Sweden.

We also collaborate with the London Cancer Alliance partners in Upper Gastrointestinal surgery research. We collaborate with colleagues at the Royal Marsden and Imperial College London.

We are one of the largest contributors to the Oesophageal Cancer Clinical and Molecular Stratification (OCCAMS) collaboration. The organisation addresses the molecular targets for prediction of prognosis after surgery for oesophageal adenocarcinoma.

Education and training

The upper GI team focuses on the education and training of its trainees as well as providing education days for other specialists and allied professionals.

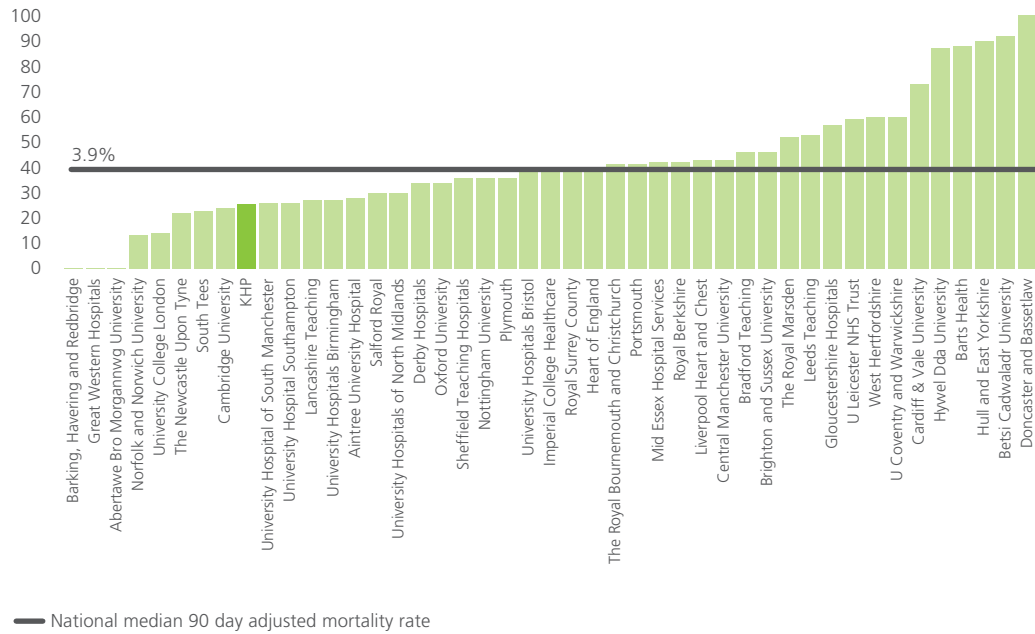
The unit works as part of the 'London Cancer Alliance' attending audit, pathway meetings and educational days aimed at improving patient outcome. We attract trainees from all over the world and take pride in the complex work performed in the unit.

Key clinical outcomes for this speciality

Oesophago-gastric cancers

Surgical mortality rates for Oesophago-gastric cancers for NHS Trusts in England and Wales.

Figure 64 | Percentage of patients that die within 90 days of operation 2012/2015 (adjusted mortality)



King's Health Partners showing lower than the national median in 2012/2015.



Gastro-
intestinal –
lower GI

Gastrointestinal – lower GI

Introduction and headline about this speciality – lower GI

In the past 2 years the King's College Hospital Colorectal Team have managed over 300 colorectal cancer patients with referrals from both tertiary and local sources.

The challenge of engaging ethnically diverse populations in health education and in accessing healthcare services is acknowledged by both Public Health England and the Department of Health; the socio-economic profile of Camberwell and Southwark is reflected in the colorectal service profile.

The King's College Hospital Colorectal Team has developed over the years to meet these challenges and has developed high quality specialist multi-disciplinary pathways and rapid access to specialist teams that has enabled the King's Colorectal cancer service to achieve a 2 year survival rate of over 85% (NBOCAP 2013) and

a 5 year survival rate of over 80%: currently the highest in Europe (Adams et al. 2013).

The Colorectal unit at GSTT has six surgeons with four of these doing colorectal cancer resections. It is also the regional anal cancer service for chemoradiotherapy and surgery. The Unit has particular interests in local advanced rectal cancer, recurrent rectal cancer and anal cancer surgery. This surgery is multidisciplinary with urology, plastics, vascular and gynae oncology specialists involved in the care of these complex cases. In 2017 these specialities formed The Pelvic Cancer Surgery service and run regular audits, operational meetings and monthly MDMs to deliver the best management to these complex surgical cases.

GSTT data from exenteration surgery has been submitted to the PELVEX collaboration, an international group set up to look at exenteration surgery in locally advanced rectal and recurrent rectal cancer surgery. The group results have been published in *The Annals of Surgery* (Ann Surg. 2017 Sep 21. Surgical and Survival Outcomes Following Pelvic Exenteration for Locally Advanced Primary Rectal Cancer: Results from an

International Collaboration), with a further paper in the *British Journal of Surgery*.

The unit continues to submit data to the National Bowel Cancer Project. The data from the NBOCAP 2016 is adjusted 90 mortality 4.8% with adjusted 2 year mortality of 21.7%.

The unit runs telephone clinics for TWW referrals and has run straight to test for many years. This has been designed to improve the time patients are on the cancer pathway.

The King's College Hospital Colorectal MDT

In October 2013 King's College Hospital acquired the Princess Royal University Hospital as part of the restructuring of NHS services across London. The Colorectal MDT formally became one in November 2013.

The King's College Hospital colorectal service provides secondary and tertiary service for both the local population of Southwark, Bromley and the Southeast managing all aspects of the colorectal cancer pathway from advanced diagnostic techniques (e.g. specialist endoscopic assessment), to the management of early colorectal cancer and complex colorectal cancer. As a support to its colorectal cancer services the King's College Hospital Colorectal Team also offer a service for pelvic floor dysfunction, treatment for benign polyps and benign lower gastrointestinal disease.

In the past 3 years the Colorectal MDT has developed to meet the needs of an ever changing patient profile; in particular the management of early colorectal cancer and an increasing number of patients with metastatic disease and those with complex hepatic related co-morbidity. The King's College Hospital Colorectal MDM is now structured to facilitate the management of these patients and improve communication and discussion between Multi-Disciplinary Team core and extended members for colorectal cancer. The meeting now has three sections: the joint Colorectal and HBP patients, Colorectal Cancer and Early Colorectal Cancers. We believe the range of speciality within the King's College Hospital Colorectal MDT and its robust patient pathways and service audit are reflected in its results.

The King's Colorectal MDT are proud that the results from the National Bowel Cancer Audit run by the ACPGI and published in 2013 demonstrates that significantly more patients treated at King's survive bowel cancer than the national average:

- Adjusted 90 day mortality – King's = 1.6% (national average is 4.5%)
- Adjusted 30-day mortality – King's = 0% (national average is 2.9%)
- Adjusted 2 year mortality – King's = 14.1% (national average is 24.5%)

A Two Week Wait Clinic for suspected colorectal cancer

Two week referrals have continued to increase and in 2013 referral rates increased by 35% compared to 2012.

The service includes Consultant pre-clinic triage of 2ww referrals, with the allocation of selected patients to “direct to test” flexible sigmoidoscopy (about 15% 2013–2014) and discharge from the Endoscopy Unit or to the clinical nurse specialist (CNS) 2ww clinic. The development of this 2ww specialist team also involves close work with the MDM co-ordinator, a secretary and a member of the management team.

This team runs a “multi-professional virtual clinic” weekly to review investigations and to discuss appropriate individual management plans. Patients with no identified pathology or who can be managed by primary care receive a call from the CNS advising them of results and discharging them back to the GP. This enables early patient discharge from the 2ww pathway and timely referral back to the GP reducing delays

to patients receiving results and a reduction in unnecessary outpatient appointments.

Establishing a virtual multi-professional clinic has enabled the colorectal team to manage their 2 week wait workload in a more efficient and cost effective way and has seen positive benefits for patients and the hospital.

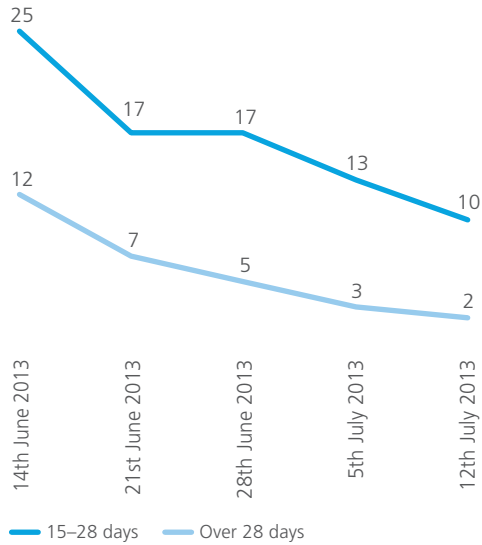
Positive benefits include:

- Clinic never cancelled as supported by 2 colorectal surgeons, 2 colorectal Clinical nurse specialist's, a secretary and an MDT co-ordinator – 1 hour per week;
- Reduced workload for cancer data team with less patients on tracking;
- Early reassurance for patients that they do not have cancer;
- Early fax communication with GP within 24 hours of removing patient from pathway;
- Reduction in follow up appointments.

Table 6 | Clinical referrals and case diagnosis from the 2ww colorectal clinic from 2009–2013

Financial years	Total referrals seen during the period	Total diagnosed with cancer	% diagnosed with cancer
2009	559	29	5.10%
2010	599	38	6.34%
2011	677	50	7.38%
2012	493	26	5.27%
2013	766	49	6.50%

Figure 65 | Impact of the virtual clinic on waiting times



TEMS Service for Early Rectal Cancer

The King's College Hospital Colorectal MDT continues to be a tertiary referral centre of excellence for TEMS (Transanal Endoscopic Micro Surgery) for rectal tumours as well as EMR/ESD (Endoscopic Mucosal Resection/Endoscopic Sub-mucosal Dissection) for colonic malignant polyps.

There is an Early Rectal Cancer MDM which was established in 2013 and receives referrals from South East London, Kent & Sussex.

Figure 66 | 2ww new to follow up appointments ratio before implementation of virtual clinic

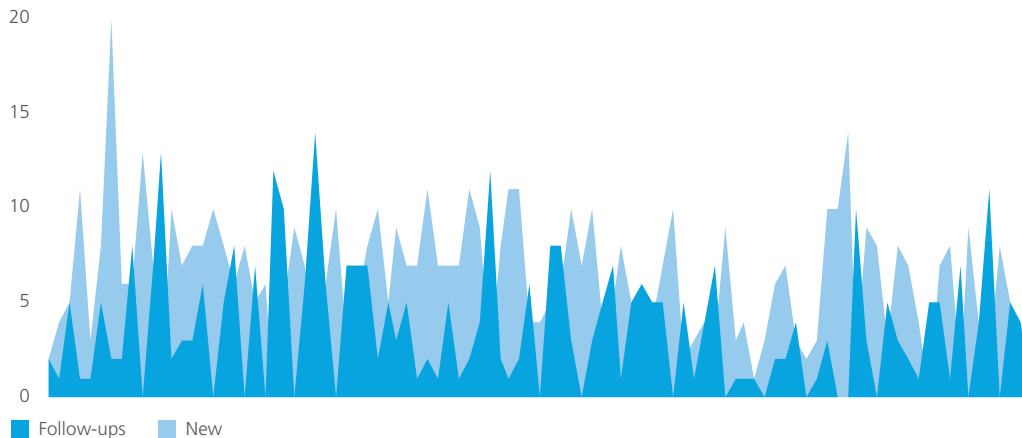
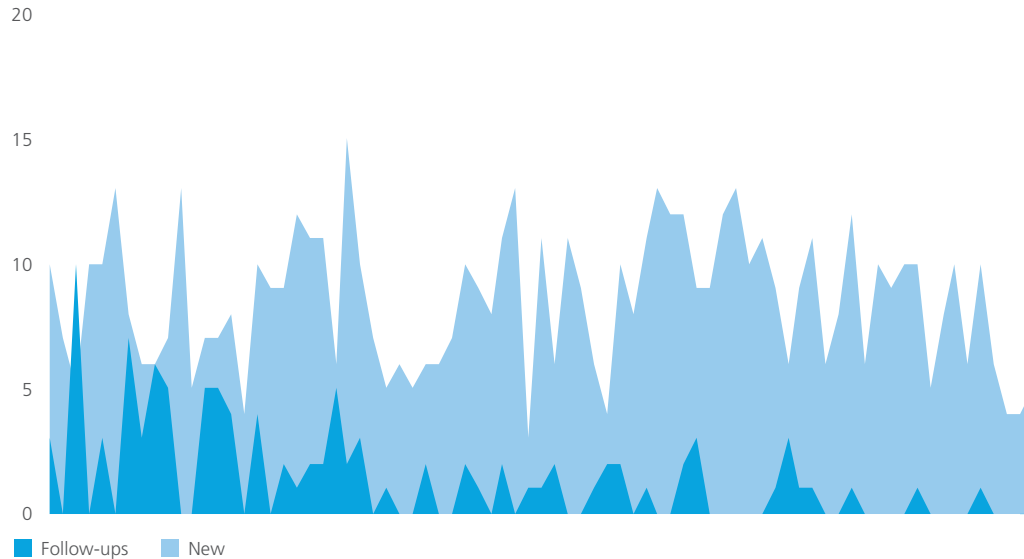


Figure 67 | Reductions in 2ww new to follow up appointments ratio after implementation of virtual clinic



King's Endo-surgery – Tertiary referral service for treatment of colorectal polyps

Endoscopic Mucosal Resection (EMR) has been performed at King's since early 2010. This service is unique in SE London and the SE coast. It prevents the need for a colectomy in a certain group of patients.

King's' now provides a tertiary referral service for patients identified to have large colorectal polyps for endoscopic treatment using techniques such as endoscopic mucosal resection (EMR) and

endoscopic sub-mucosal dissection (ESD). Traditionally, many of these patients would have undergone laparoscopic or open segment resection rather than endoscopic surgery.

The assessment of colorectal polyps is via 3 modalities prior to endoscopic treatment. Magnification colonoscopy is routinely used to assess these lesions determining the vascular pattern with Narrow Band Imaging and the pit pattern using magnification colonoscopy. In addition, the depth of invasion of the lesions is analysed using high frequency mini probe ultrasound with frequencies up to 25MHz.

On average we perform 125 EMR/ESD procedures a year with a mean polyp size of 5.5cm. On average 8% of patients will have early colorectal cancer invading the sub-mucosa.

Colonoscopic high frequency mini probe ultrasound is undertaken to locally stage colonic and rectal cancer, determine depth of invasion prior to endoscopic treatment and assess polyps with a focus of malignancy after endoscopic polypectomy.

Tertiary service for the treatment of recurrent and complex colorectal cancer

The Colorectal surgeons work in co-operation with the HPB team, the Department of Clinical and Medical Oncology, the palliative care team and interventional radiology team to provide specialist expertise in the management of colorectal metastases and high risk surgery patients such as those with colorectal cancer and complex liver co-morbidity e.g. alcohol related liver cirrhosis who are operated on in collaboration with the Liver Unit for peri-operative support.

Diverticular disease clinic

This is a specialist clinic receiving tertiary referrals from all of the UK. The clinic aims to rationalise the treatment of diverticular disease, identify the patients with appropriate criteria for surgical or medical treatment and avoid unnecessary or preventable surgery.

Anorectal physiology laboratory

Current uses of our pelvic floor laboratory

- Assessment of patients with faecal incontinence;
- Assessment of patients which chronic constipation to exclude obstructive defecation syndrome;
- Assessment of patients with endometriosis to excluded rectal involvement before surgery;
- Assessment of perianal fistula (Crohn's diseases related or crypto glandular in origin).

Our achievements

- Development of early colorectal cancer MDT and pathway for patients offering EMR, ESD and TEMS;
- Specialist rectal cancer service with dedicated radiology including MRI, 3D endorectal ultrasound and surgical techniques ranging from minimally invasive ESD and TEMS to advanced laparoscopic techniques. King's have developed a specialist practice for low rectal cancer with ultra low anterior resection, trans-anal Total mesorectal excision (TME) and extralevator abdominoperineal resection (APER);

- Amalgamation of colorectal services across Princess Royal University Hospital and Denmark Hill with joint operating policy;
- Annual postgraduate courses for colorectal disease and interventional endoscopy.

Over the next five years

- Further development of specialist rectal cancer surgery offering full range of techniques and research programmes to complement this;
- Expand the early colorectal cancer service with recruitment of specialist teams and nurses. Grant of £135k from Macmillan has already been awarded to support this;
- Complete amalgamation of all colorectal services on both Princess Royal University Hospital and Denmark Hill sites;
- Educational programmes for postgraduate education in Colorectal Surgery to be formalised with increased number of courses and conferences.

Research and innovation

Current research programmes in the department with supervision of 2 PhD students and 1 MD student along with 4 senior clinical fellows involved in regular research and audit:

1. Magnification endoscopy and high frequency mini probe ultrasound in assessment of early cancer and recurrence with evaluation of intensive surveillance

2. Molecular markers and assessment of colorectal cancer recurrence;
3. Medical and endoscopic treatment of symptomatic diverticular disease;
4. Novel treatments for anal fistula;
5. Diverticular Disease: Epidemiology, pathogenesis, serotonin, probiotics;
6. Artificial Neural Networks Risk for prevention of surgical complications.

Education and training lower GI

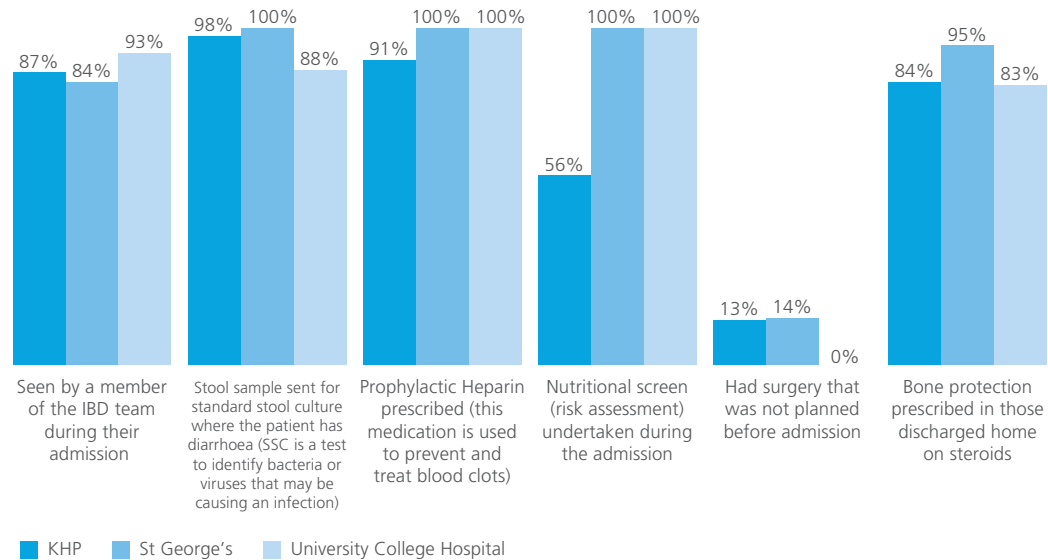
King's Colorectal have an extensive programme of both undergraduate and postgraduate education for King's College London in addition to courses offered externally.

These include

1. Basic and higher Surgical Skills for trainees;
2. Surgical skills for General Practitioners;
3. Laparoscopic inguinal hernia surgery;
4. Complex abdominal wall reconstruction and component separation;
5. Colonoscopic ultrasound and assessment of colorectal lesions;
6. Magnification endoscopy for assessment of gastrointestinal lesions;
7. Colorectal Controversies and Dilemmas;
8. King's Live – Interventional endoscopy.

Key clinical outcomes for this speciality lower GI

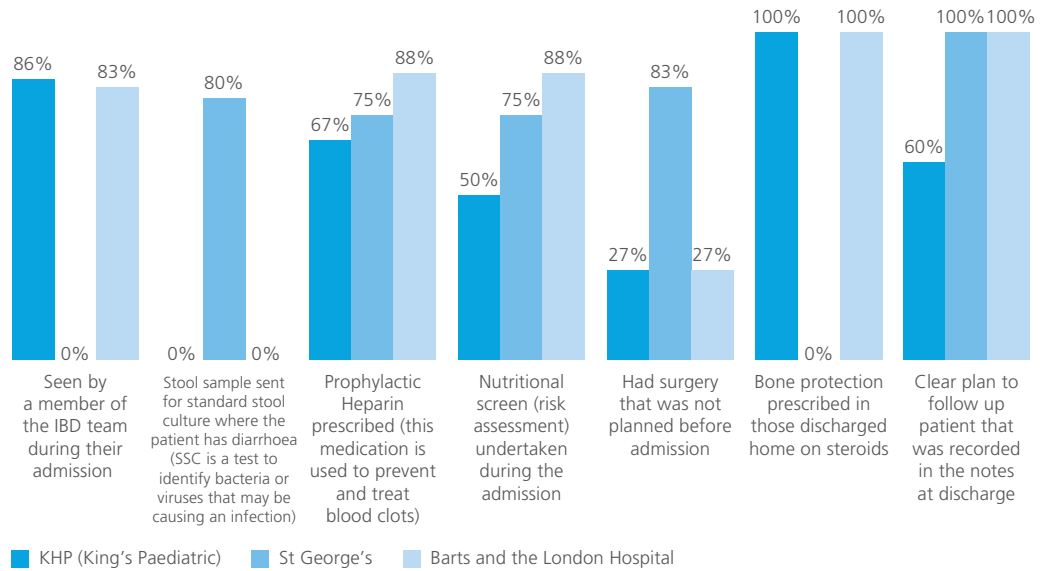
Figure 68 | Adults – quality of care provided to people admitted to hospital between January and December 2013



Please note that the percentage should be reviewed alongside the actual number of cases submitted to the audit:

- King's Health Partners (Kings, Guys and St Thomas and Princes Royal) = 91
- St George's Hospital = 25
- University College Hospital = 29

Figure 69 | Children – looking at the quality of care provided to people admitted to hospital between January and December 2013



Please note that the percentage should be reviewed alongside the actual number of cases submitted to the audit:

- King's Health Partners (King's) = 11
- St George's Hospital Paediatrics = 6
- Bart's and the London Children's Hospital = 15



Digestive
diseases –
endoscopy
services

Digestive diseases – endoscopy services

Endoscopy at King's College Hospital

The endoscopy department at Denmark Hill provides a comprehensive diagnostic and therapeutic service both.

The department has 4 endoscopy procedure rooms as well as a number of consultation rooms where pre-assessment and manometry procedures are undertaken. The service currently operates a 2-session per day model over 5 days. However, the service will soon be expanding to provide a 6-day service, eventually moving to a 7-day service.

The endoscopy service covers diagnostic and treatment services for all diseases of the digestive tract. In conjunction with the Liver unit the unit also undertakes endoscopic procedures for pancreatic and liver conditions.

Colorectal procedures and investigations of the small bowel are undertaken jointly between the surgical and gastroenterology specialties.

The department achieved Joint Advisory Group on Gastrointestinal Endoscopy (JAG) accreditation in 2013, and this was renewed following the submission of the annual report card in November 2014.

The department offers a wide range of diagnostic and therapeutic procedures including:

- Gastroscopy (OGD);
- Oesophageal, biliary and colonic dilatation & stenting;
- Colonoscopy;
- Flexible sigmoidoscopy;
- Endoscopic ultrasound (EUS);
- Endoscopic retrograde cholangio-pancreatography (ERCP);

- Endo-anal manometry;
 - Endoscopic mucosal resection (EMR);
 - Endoscopic submucosal dissection;
 - Peroral endoscopic myotomy for achalasia;
 - Video capsule endoscopy;
 - PEG & gastropexy;
 - Double balloon enteroscopy.
- Colonoscopy;
 - Flexible sigmoidoscopy;
 - Endoscopic retrograde cholangio-pancreatography (ERCP);
 - Video capsule endoscopy;
 - PEG & gastropexy;
 - Balloon enteroscopy;
 - Endoscopic mucosal resection (EMR).

Endoscopy at the Princess Royal University Hospital

The endoscopy department at Princess Royal University Hospital provides diagnostic and therapeutic services to the local population of Bromley and Lewisham. The department is a 2-roomed unit which operates 2-session working over 7 days.

The unit offers services to both inpatients and outpatients.

Although not currently JAG accredited, the unit will be applying for accreditation.

The following diagnostic and therapeutic procedures are offered in the unit:

- Gastroscopy (OGD);
- Oesophageal, biliary and colonic dilatation & stenting;

The endoscopy unit at Princess Royal University Hospital undertakes more than 8,000 procedures per year. Endoscopy procedures are undertaken by both Gastroenterology and Surgical clinical staff.

Our achievements

Introduction of tertiary referral service for management of colorectal polyps and early colorectal cancer

Magnification endoscopy is routinely used along with high frequency mini probe ultrasound to assess all colorectal lesions prior to endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Since 2010, the service has developed to serve South London and South East England with 120 endoscopic resections per year of lesions greater than 5cm.

Kings is also the tertiary referral centre for ESD for colorectal neuroendocrine tumours.

Tertiary referral interventional hepatobiliary for paediatric and adult post transplant population including ERCP and EUS

Accreditation with JAG as a training institution for upper and lower GI endoscopy in 2015

Endoscopic treatment of achalasia after successful mentorship with world experts established since 2013 and King's are currently the only centre in the United Kingdom to offer Peroral endoscopic myotomy (POEM) routinely.

Providing a local subspecialist service

We will, having previously agreed this with our colleagues at Guy's and St Thomas', develop a local service for Bravo (a test designed to assess acidity in the oesophagus) pH studies for subspecialist cohorts at Denmark Hill, such as patients with cystic fibrosis or GVHD that require investigation but cannot or will not travel to Guy's (as DNA rates for such cohorts is typically high when services are offered elsewhere).

We have also agreed on research strategies to make use of the expertise across the CAG (magnification and Bravo) to promote novel endoscopic imaging techniques. There is already good collaboration with the oesophageal lab at Guy's and research in patients with achalasia.

In the next five years, we will:

- Establish training courses for interventional hepatobiliary, endoscopic ultrasound, endoscopic resection in addition to basic upper and lower GI endoscopy. This will be in conjunction with establishment of National fellowships in interventional endoscopy;
- Establish as an independent bowel cancer screening centre and implementation of flexible sigmoidoscopy screening;
- Achieve JAG accreditation at Princess Royal University Hospital site to mirror practices currently at Denmark Hill;
- Increase capacity for endoscopy services with 2 additional rooms for endoscopy services across both sites allowing for a total of 8 procedure rooms;
- Continue to develop research programmes (MD, PhD) within interventional and magnification endoscopy with introduction of national fellowship schemes supported through industry, university and national grants.

Endoscopy at Guy's and St Thomas'

Introduction and headline

Endoscopy is a busy and very large service across King's Health Partners providing diagnostic and therapeutic endoscopy to patients from the local area, regionally and nationally. Over recent years, both Guy's and St Thomas' and King's College Hospital have worked hard to meet the highest standards determined by the GRS and JAG accreditation initiative. The successful achievement of this is a mark of excellence and a level not achieved by many centres in the UK. Whilst the routine diagnostic work is important, innovative specialist endoscopy is a key priority with several examples of this at Guy's and St Thomas'. In addition, there is a strong commitment to underpinning translational research at KCL facilitating the collection of gastrointestinal samples which make up an invaluable bioresource for KCL research.

Both sites offer unique tertiary clinical services, including novel procedures that we introduced to the UK (and remain among a small handful of centres offering these): endoscopic submucosal dissection for early gastrointestinal cancers and polyps; endoscopic myotomy for achalasia and gastroparesis; radiofrequency ablation for biliary

tumours; Endoscopic therapy for dysplasia and early cancer in Barrett's oesophagus; direct cholangioscopy; single and double balloon enteroscopy; high-frequency miniprobe ultrasound; the IntraGastric Balloon and Endobarrier™ for type 2 diabetes and obesity.

We have initiated a programme of teaching and training with Industry support: the continued success of the King's Live endoscopy symposium; being selected to be part of the prestigious Vista programme (Cook Medical Inc); holding JAG-accredited courses for UK endoscopy training; hands-on specialist procedures training with animal models in the Skills Lab at the Weston Education Centre.

The combination of working within regional networks and teaching courses attracts a significant number of referrals for high-tariff procedures to our centres from across the country.

Figure 70 | Number of endoscopy procedures carried out across King's Health Partners in 2014 (combined Kings, PRUH and Guy's and St Thomas')

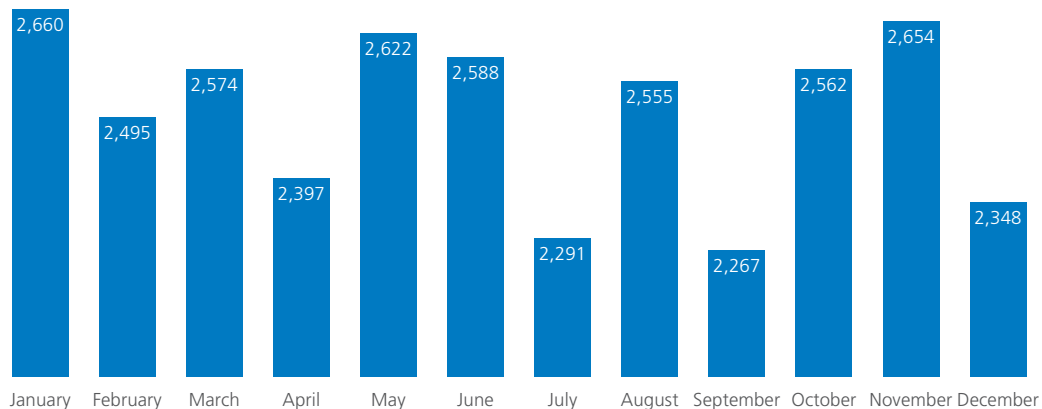


Table 7 | Increasing number of most specialist procedures

Total number of procedures	2014	2015	2016
	12,262	15,467	15,325
Total number of non-specialist procedures	2014	2015	2016
Colonoscopy	4,125	5,187	5,255
Flexible sigmoidoscopy	1,386	1,563	1,822
OGD	5,292	6,944	6,451
Total number of specialist procedures	2014	2015	2016
Push/single balloon enteroscopy	63	87	55
ERCP	277	306	306
EUS	441	537	535
Bravo	160	211	246
Halo	55	54	113
OGD EMR	35	72	92
OGD + dilatation	222	275	273
PEG insertion	65	76	102
IGB insertion	64	78	75

Research and innovation around this speciality

Endoscopy at King's

Apart from the obvious support for several research themes in providing patient samples, Endoscopy at DH has grown rapidly over the past two years to develop and deliver research as well as pioneering techniques and technology, often the first in the UK (and sometimes internationally) to do so. We hope to build on the success of Inflammatory Bowel disease (which is on a path to a truly cross-CAG model), to develop Endoscopy strategy and collaboration. The emphasis, we feel, should be on using expertise at either site to assist or develop in the spirit of King's Health Partners.

- **King's Live (KL)**

KL is an annual live endoscopy workshop run over a weekend. It is the largest endoscopy workshop of its kind in the UK, with an international faculty including the pioneers of modern endoscopy from Japan, Professors Shin-ei Kudo and Haru Inoue. We are regularly joined by European and US faculty as well as colleagues from the UK. Attendance last year topped 140 and feedback from Industry has always been that this is the most successful workshop in the UK. Indeed the aim has always been to strengthen links, not only with clinicians, but also with Industry – providing a platform to showcase new technology, equipment and

ideas as well as allowing the audience to observe and mingle with the leading names in Endoscopy. This year we also plan to emphasise teaching by running a workshop in diagnostic imaging the day before the main weekend.

- **Active research**

- **Fellowship in diagnostic imaging**

This is initially supported by an NIHR research for patient benefit project grant. The project is a feasibility and diagnostic accuracy study to study ultra-HD imaging and digital post-processing (FICE™) in the early detection of dysplasia in patients with colitis, during their routine surveillance colonoscopy. This is a randomised, time-delayed crossover design with involvement of the KCL Clinical Trials Unit and input from the London RDS. The intention is to support this post in future years with a combination of industry and Trust funds, but internal KCL funding would be very attractive to ensure security of the position;

- **Diverticular clipping**

We have a ground-breaking grant from Cook to support an open-label study to treat diverticular disease with endoscopic clips (ethical approval granted) in patients who have had one or more episodes of bleeding attributable to this condition. There is every expectation from anecdotal

reports that this will be a successful approach and, if borne out, will be the first report of the technique worldwide;

- **Diagnostic imaging in other diseases**

We hope to partner with Industry to provide funding to further this research across the CAG;

- **Molecular studies in early colorectal cancer and high grade dysplasia and identification of factors associated with recurrence;**

- **Patient related outcomes in early colorectal cancer.**

- **Pioneering techniques**

- **Magnification endoscopy**

We are one of three units in the UK that regularly employ magnification endoscopy (zoom) to diagnose and monitor patients. A longitudinal comparative study of magnification in the diagnosis of benign colorectal polyps and early colorectal cancer is planned;

- **Endoscopic resection of early cancer**

We have introduced this regional service and now have the largest case series in the UK of colorectal polyps removed with these techniques. We also offer a tertiary service for duodenal polyps at DH. We are the only unit in the country to include such patients within the cancer MDM and are very proud to have

pioneered the Early Cancer Specialist Nurse role. Endoscopic Submucosal dissection is a well established technique at DH and offered routinely to patients;

- **POEM (per-oral endoscopic myotomy) for achalasia**

This technique has gained worldwide acceptance as the treatment of choice for achalasia and we are part of an international collaborative group (with centres of excellence in Japan, Germany, Italy, Romania, US, China, Korea and India). We have performed 20 cases at Denmark Hill and were the first unit in the country to offer the technique. A particular strength is the use of expertise across the CAG, with the Oesophageal Physiology laboratory at Guy's offering world-leading diagnostics and follow-up for these patients;

- **Bariatric endoscopy**

We are pioneering endoscopic interventions for type 2 diabetes and obesity (such as the Endobarrier™ and the new Revita™). We are one of two centres in England to have participated in RCTs for this approach and collaborate with Prof Stephanie Amiel and Prof Francesco Rubino to deliver these groundbreaking techniques. Dr Bu Hayee has collaborated with Dr Jude Oben across the CAG to submit an NIHR-HTA grant application to study the Endobarrier as a potentially effective intervention in non-alcoholic fatty liver disease;

- **Robotic colonoscopy**

We are the first unit in the UK to offer robotic colonoscopy (www.endotics.com) for NHS patients. A completely painless procedure, the scope offers potential for development of novel tracking algorithms and IP within KCL.

- **Emphasis on cross-CAG collaboration**

Endoscopy at Guy's and St Thomas'

Research and innovation is a strong theme within endoscopy cutting across many disease areas and supporting numerous research groups within KCL.

- The unit has an excellent record in the recruitment of patients to research studies particularly in the collection of samples for mucosal research across KCL including immunology, genetics, infectious disease, oral and dental research and cancer;
- Innovation includes leading on the development of cutting edge endoscopy techniques such as Bravo wireless pH monitoring, Spyglass biliary imaging, therapeutic EUS, biliary lithotripsy, balloon enteroscopy and bariatric endoscopy;
- Diagnostic pathway research and innovation is also undertaken to enhance the patient journey and shorten waiting times especially for cancer.

Education and training

Endoscopy at King's

Medical student induction/visits to endoscopy

Medical students attend Endoscopy in pairs. We see under- and post-graduate teaching as an integral part of the service and we wish to create the best possible environment and opportunities for students. In order to gain the full range of experience outlined below a scheduled and sanctioned visit is highly recommended.

Two visits cover all aspects of Endoscopy as relevant to medical student teaching and experience. Including:

1. The layout of the Endoscopy Unit and patient flow;
2. If time is available, students can spend 30 minutes in Recovery attached to a nurse to see how the recovery and discharge process works;
3. Indications for upper and lower GI endoscopy;
4. Patient information leaflets;
5. Consent (although this will be covered in other parts of their curriculum-based teaching);
6. Patient experience and how it is assessed;
7. Talk to at least two patients for upper and lower GI endoscopy. This is not to take a full medical history, although a short conversation about what the patient

- understands as to the indication for their procedure, should form part of this interaction. The focus should be on the patients' ideas, concepts, concerns and expectations of the procedure;
8. Observe upper GI and colonoscopy – at least 2–3 cases each;
 9. This will include:
 - basics of endoscope function and cost;
 - medications used during procedures and risks/benefits of each;
 - perform a digital rectal examination – at least 2 procedures in 2 minutes.
 10. A short tour of the decontamination unit to gain a basic understanding of the principles of decontamination.

At the end of the two visits, students should attain the following personal learning objectives:

- Demonstrate an understanding of why patient flow is needed and how this applies to infection control and decontamination;
- Describe the basics of endoscope function, cost, decontamination, infection control;
- List the recognised indications for upper and lower GI endoscopy;
- Describe how patient experience is assessed during and after the procedure;
- Demonstrate an understanding of common ideas and concerns from a patient's perspective;

- Demonstrate/describe how to perform a digital rectal examination (and be signed-off);
- Explain in lay language what upper and lower GI endoscopy involves and the principles of consent (including risks of procedures).

Post graduate training

King's endoscopy are a JAG accredited training unit and provide 3 courses per year in basic upper and lower GI endoscopy skills providing training for specialty trainees in the United Kingdom.

Advanced courses for interventional endoscopy are run annually and include:

King's Colonoscopic Ultrasound Course

High frequency mini probe ultrasound to assess colorectal lesions prior to endoscopic resection, stage colorectal tumours and assess for residual disease after local resection of malignant polyps.

Interventional endoscopy course for nurses and first assistants

Practical tips for assisting in interventional hepatobiliary, upper and lower GI luminal endoscopy.

King's Live – www.kingslive.co.uk

Annual live endoscopy event featuring 20–25 live cases from 3–4 rooms over 2 days. This covers all aspects of interventional endoscopy including EMR, ESD, EUS, Magnification endoscopy, double balloon enteroscopy, POEM and colorectal stenting. 2015 was its 5th year with international faculty from Europe, USA and Japan performing live procedures.

Simulation training

This is available within the trust for trainees and shortens their learning curve for luminal endoscopy.

Endoscopists within the unit currently contribute to national and international educational programmes with faculty roles on many courses. Some of these include:

- UK ESD Users Group;
- Chair persons of International POEM Conference;
- Chair persons of International Magnification endoscopy group;
- Faculty of live courses include EndoSwiss Live, Zurich and Yokohama Live, Showa University, Japan.

Endoscopy at Guy's and St Thomas'

- Undergraduate education is an important activity with structured sign-ups available across all types of endoscopy. In addition, elective placements are encouraged and work experience for those considering entering medicine;
- The unit at Guy's and St Thomas' has a major commitment to postgraduate training at all levels and this is now supported by a state of the art Endoscopy Teaching Room with live interactive video feeds from each endoscopy room. Hence this has facilitated the development of a number of live endoscopy training courses, including the National Nurse Endoscopy Course and successful courses in Live ERCP and Live Upper GI Therapeutic Endoscopy;
- A number of Endoscopy Fellowships are provided to postgraduate trainees each year leading to higher degrees combining basic science research and endoscopy training (currently 4 fellows). There are also 2 visiting fellowships (EUS and Bariatric) and Guy's and St Thomas' has recently appointed to 2 dedicated training posts in Nurse Endoscopy.

Clinical outcomes

Bowel cancer screening at King's

Bowel cancer is the second most common cause of cancer deaths in the United Kingdom. The prognosis is related to the disease stage at diagnosis with an excellent outcome, if caught at an early stage. However, most patients are diagnosed at an advanced stage as they are often asymptomatic or are not aware of the symptoms of bowel cancer, or may not seek help because of embarrassment.

King's College Hospital, part of the SE London Bowel Cancer Screening Centre, has been providing a bowel cancer screening service to the populations of Lambeth and Southwark since 2008. The programme is aimed at 60–69 year old patients registered with a GP, and was recently extended in 2014 to include 70–74 year old patients. In 2015, we began to offer bowel scope (flexible sigmoidoscopy) screening to all patients aged 55 years and over. We also became an independent screening Centre in October 2016.

The initial screen is by the faecal occult blood test (FOBT) and this has been shown to reduce bowel cancer mortality in several large, controlled population studies and is highly cost-effective. The FOBT kit is sent directly to the patient by the London Screening Hub. This is completed by the patient and tested for the presence of blood. If this is positive, then the patient receives an appointment with a Specialist Screening Practitioner (SSP) at King's, to assess

their suitability for a colonoscopy. They are seen, assessed and offered a colonoscopy within a month of the positive FOBT test.

Every year, about 8,000 patients from Lambeth & Southwark complete their FOBT and all patients with positive results are offered a colonoscopy. Since its inception in 2008, over 1,500 patients have undergone a screening colonoscopy and about 100 patients have been diagnosed with bowel cancer. Most of these cancers were at an early stage with a good outcome. A small proportion of these patients also had polyp cancers, which were removed at the time of colonoscopy and needed no further treatment and avoided surgery. Furthermore, about 40% of patients were found to have polyps, which were removed and it is likely that this will protect them against future cancers as 95% of bowel cancers arise from polyps.

All patients are sent feedback questionnaires after the procedure and the overwhelming majority of the feedback has been positive but improvements have been made to the service, based on some of the comments.

The screening programme also funds staff and equipment for the Molecular Biology Laboratory, one of the first in the country to provide routine molecular markers for cancer, an invaluable research resource for the future.

Several promotion events have been held across Lambeth and Southwark to raise awareness of the screening programme and also of the symptoms of bowel cancer to try to improve

the uptake for bowel cancer screening. The King's Charity has donated a research grant

to investigate the reasons for the low uptake in SE London.

Table 8 | The endoscopy units on both sites report against the BSG Quality and Safety Indicators for Endoscopy

Colonoscopy	2014	2015	2016
Caecal intubation rate (QS>90%)	92	91.5	92
Adenoma detection rate (QS>15%)	17.5	17.5	19
Polyps retrieval rate (>90%)	96	92.5	92.5
Good quality of bowel prep (>90%)	87	89	90
ERCP	2014	2015	2016
Completion of intended therapeutic procedure rate (QS>80%)	89	93	
Decompression rate (>80%)	91	94	98
Cannulation rate (new standard since 2016) (QS>85%)	N/A	N/A	97
EUS	2014	2015	2016
Completion of diagnostic procedure (QS>90%)	95	96	94
Adequate FNA pancreas (>75%)	63	83	85
Adequate FNA other lesions (>90%)	80	68	72
Diagnostic UGI endoscopy	2014	2015	2016
Repeat OGD for gastric ulcer within 12 weeks (QS 100%)	85	79	82

What the patients and staff think about the service

Response from King's

- 96% of patients felt they had the opportunity to ask the nurses any questions they had before going into the endoscopy room;
- 100% of patients found the endoscopist undertaking the procedure courteous and considerate;
- 89% of patients said that based on the level of comfort they experienced, that they would have the procedure again if required;
- 93% of patients felt their privacy was respected as best it could have been;
- 86% of patients were happy they knew who to contact if any problems following the procedure.

Some patient comments from the survey:

'This was by far the most efficient and patient-centric endoscopy I have ever had to endure. The pre-procedure process focused on the administrative duties, removing the anxiety around the procedure itself. Rather than an area of improvement, this is an area insofar as I am concerned of best practice. Well done. Thank

you to the entire team for a slick, well managed process which removed the burden of anxiety. All staff were lovely, professional, empathetic and great ambassadors for King's'.

'I can't think of any improvement. Everyone was professional and very friendly and I could not wish for a better care than I received. In spite of having a procedure that is unpleasant, it was always bearable and the chance to watch on screen combined with the consultant information throughout made the experience very interesting. All the staff were very friendly to me and the experience provided many good laughs which were shared by me and all the staff along the way. I hope I don't have to have another procedure but if I do, I know that it will not be all bad but a lot of fun along the way to make it ok. Thanks to all who have helped me and looked after me so well. It could not be better than it was today. Keep up the good work and high standards'.

Response from GSTT

Patient and staff feedback is a part of Trust policy as well as a requirement for JAG accreditation. Feedback is reviewed regularly in the 2 monthly Endoscopy Users Group meetings and GI Medicine and Surgery Management board.

The patient feedback undertaken in 2014 was generally greater than 80% favourable across each domain with several high scoring aspects. Individuals comments were also very positive. For example:

'I have lived in the UK for 40 years and have never experienced such consistently high professionalism from nurses to consultant. Nurses were genuinely friendly, knowledgeable and it seemed even caring. Even the woman at endoscopy reception had a sense of concern and humour. My consultant was very reassuring because of his extensive knowledge, understanding, experience and sense of humour. This has been the very best treatment I have had in my 40 years in England. Thank you St Thomas' Hospital'.

Performance measures

Performance indicators at GSTT

The most important across each type of endoscopy are as follows (2014 GSTT scores in brackets):

- ERCP completion rate – (88% QS>80%)
- Caecal intubation – (92% QS>90%)
- Adenoma detection rate – (17% QS>10%)

Colonoscopy comfort scores

Comfort score 4 or above (Gloucester scale) = 1.9% (National average from Latest National Colonoscopy audit 9.8%).

For EUS, FNA adequacy will form the key performance metric.

Top grants awarded to GSTT

ABC of EUS, Meenan J; De Martino S.
 Vu C. Winner of 2014 ASGE AV-Award.
www.youtube.com/watch?v=nspw0I6R9AA

Performance indicators at King's

Figure 72 | Number of endoscopy procedures at King's from 2014–2017

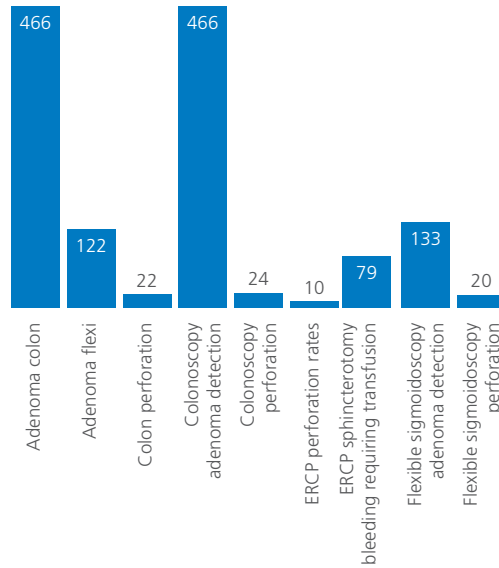
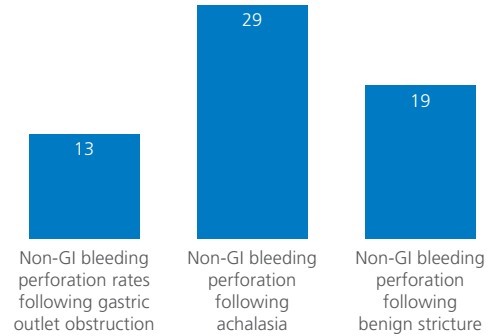
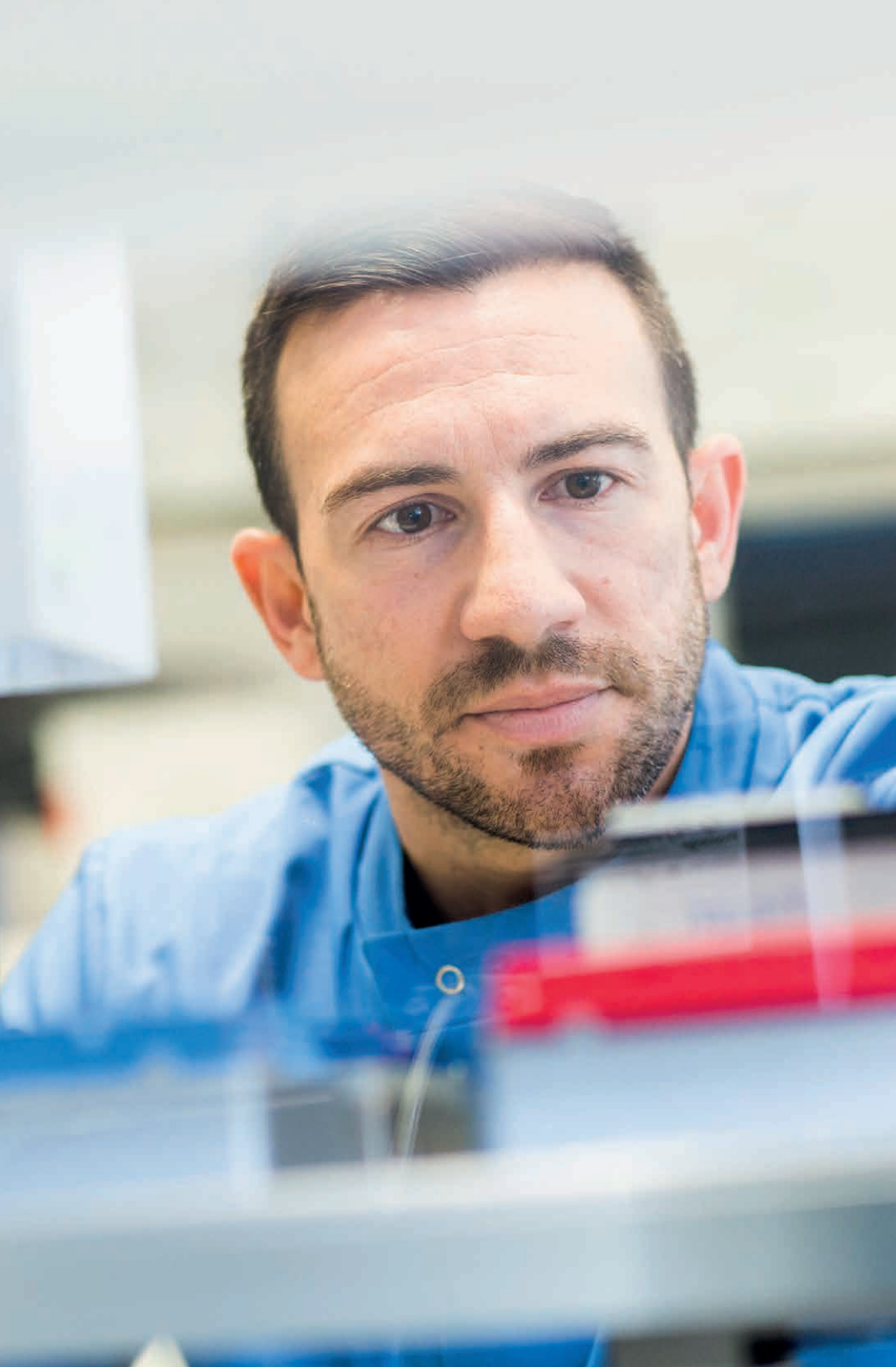


Figure 73 | Number of upper GI endoscopy procedures at King's from 2014–2017





Digestive
diseases –
gastroen-
terology

Digestive diseases – gastroenterology

Gastroenterology across King's Health Partners is a large speciality treating all aspects of Gastrointestinal disease and includes the provision of specialist Endoscopy and the Nutrition service. Luminal gastroenterology comprises mainly the treatment of inflammatory bowel disease (IBD) and the irritable bowel syndrome (IBS).

Key achievements

- The development of a highly renowned service for treating inflammatory bowel disease (IBD) receiving referrals from throughout the UK focussing strongly on personalised medicine;
- A high quality specialist endoscopy service across King's Health Partners undertaking cutting edge endoscopic diagnosis and therapy.

Aims and ambitions

- To develop an already renowned IBD service into a named King's Health Partners IBD Centre which will serve as a benchmark for excellence in the management of patients with Crohn's disease and ulcerative colitis;
- To strengthen further the track record of high quality translational IBD research at KCL across many themes within IBD with the ultimate aim of establishing IBD as a dedicated research theme at KCL and the BRC. In doing so, this will bring together key existing IBD focussed strengths in immunology, genetics, pharmacogenetics, metagenomics and dental research;
- To set up an International Training course in Personalised IBD Medicine;
- To further expand the set-up for IBD Clinical trials;

- To ultimately establish and physically house a named clinical IBD centre;
- To establish a Specialist IBS service across King's Health Partners focussed on the translation of gut microbiota research into enhanced therapy.
- A strong laboratory research output is also matched by top-scoring recruitment to clinical trials in IBD;
- The expansion of the Nutrition service over recent years has evolved the sites across King's Health Partners into an established Intestinal Failure unit likely to compete favourably for HIFNET bid to become a nominated IF centre.

The King's Health Partners Inflammatory Bowel Disease service

IBD is a major theme for clinical excellence across King's Health Partners with a focus on high quality individualised therapy and on broad-ranging clinical and basic science research. The service at each site attracts significant regional and national referrals and has a reputation for the application of personalised medicine to enhanced outcomes in therapy.

Research and innovation around this speciality

Examples of excellence

- The IBD service across King's Health Partners is a nationally renowned centre for the management of complex IBD combining high quality clinical care, excellent outcomes and underpinning successful high quality research;

Research and innovation in IBD

IBD research is a key strength across King's Health Partners and the BRC and a theme linking many collaborating groups including Immunology, Genetics, Pharmacogenetics, Hepatology, Twin research, the IMPARTS team and Dental research (metagenomics). Basic science research is supported by key engagement of the clinical IBD service in the recruitment of patients and collection of biological samples to underpin IBD research. In addition, there is an increasingly successful commitment to clinical trials. The success of IBD research can be measured in terms of outcomes such as publications, postgraduate degrees and research grants.

Examples of successful innovation and translation of KCL research include:

- Ratification of the commissioned IBD pathway. A year-long project involving patients, public and commissioners has led to the ratification of the UK's first fully commissioned IBD pathway. This

is a landmark achievement for the CAG – being a joint initiative between King's College Hospital and GSTT – and has already gained national recognition. In particular the use of high-cost biologics in patients at most need has been approved (subject to monitoring). The pathway is published on Lambeth CCG website. www.lambethccg.nhs.uk/news-and-publications/meeting-papers/south-east-london-area-prescribing-committee/Documents/Clinical%20guidelines/IBD%20pathways%20Jan%202015.pdf;

- Translation of a unique program of research at GSTT into Oral Crohn's disease into a novel dietary treatment protocol, rolled out across the UK and internationally through a dedicated KCL web portal and recognised as part of the KCL IMPACT initiative;
- Successful translation of the IBD pharmacogenetics and personalised medicine research programme into a UK wide service to measure thiopurine metabolite levels and anti-TNF drug and antibody levels;
- Establishing a successful program of investigator-led, CLRN portfolio and industry sponsored clinical trials in IBD (see details below);
- Development of an active patient care database. Operating within EPR, the database is also a stand-alone facility capable of being used 'remotely', eg. by community teams.

Key research themes and projects in IBD

This includes collaboration with the Department of Twin Research, Academic Department of Rheumatology, the IMPARTS team, Department of Cognitive Behavioural therapy and the Microbiome initiative.

Specialist IBD clinics

IBD across King's College Hospital and GSTT sites is managed in specialised multidisciplinary IBD clinics comprising Consultants, IBD fellows, IBD Clinical Nurse specialists, Dietitians and specialist Pharmacists. In addition, at King's College Hospital, a novel approach includes a specialist IBD psychologist and a one-stop approach to care. Each IBD clinic has a strong academic focus with undergraduate education, postgraduate training and the presence of clinical research Nurses to ensure recruitment to ongoing research studies and clinical trials.

Subspecialist clinics related to IBD

At Denmark Hill and GSTT, a number of important sub-specialist clinics are offered including the following:

- Hepatology (Primary Sclerosing Cholangitis);
- Colorectal surgery (Combined IBD management, virtual Perianal disease clinic);

- IBD: virtual biologics and immunosuppression clinic;
- Haematology (Graft versus host disease, Haemophilia);
- Combined oral medicine and Gastroenterology clinic (oral Crohn's disease);
- Transitional IBD clinics with Paediatrics.

In each of these clinics, there is a strong research emphasis with investigator-led initiatives, for example, GVHD in particular forming the basis of a nascent collaboration with the MRC centre for transplantation, personalised IBD research harnessed through the virtual IBD clinics. In combination with Endoscopy across sites, recruitment to research studies includes the expansion of several key IBD research cohorts as a bioresource for IBD research as follows:

- IBDGEN: approx. 5,000 DNA samples from patients with IBD (IBD genetics group at KCL plus collaborative link to UK IBD consortium and International IBD genetics consortium);
- Thiopurine and anti-TNF pharmacogenetics DNA cohort (1,500 patients);
- Crohn's disease fibrosis cohort (serum and mucosal biopsies);
- Oral Crohn's disease (approx. 300 patients);
- Primary sclerosing cholangitis.

Clinical trials in IBD

There is now a well-established set up for investigator led and commercial clinical trials supported by 3 clinical research nurses. Ongoing or recent multicentre CTIMP studies include:

- A Pilot Study of GWP42003 in the Symptomatic Treatment of Ulcerative Colitis (GWID10160); Over-recruited;
- A Multicenter Study to Evaluate the Impact of Adalimumab on Quality of Life, Health Care Utilization and Costs of Ulcerative Colitis Subjects in the Usual Clinical Practice Setting; Top recruiter in world;
- Efficacy, Safety and Pharmacokinetics of BI 655066 in Patients With Active, Moderate-to-severe Crohn's Disease; Recruiting;
- Golimumab Utilization and Impact on Ulcerative Colitis (MK-8259-032); Over-recruited;
- Phase iii, double blind, placebo-controlled, multicentre study of the efficacy and safety of etrolizumab during induction and maintenance in patients with moderate to severe active ulcerative colitis who are refractory to or intolerant of TNF inhibitors; Set up Jan 2015;
- Study Evaluating Ovasave, an Autologous Cell Therapy, in patients with active Crohn's Disease (CATS29); Set up Jan 2015.

There is also a strong commitment to participation in multicentre CLRN studies supported by the IBD clinical research nurses. Ongoing studies include:

- 5-ASA induced nephrotoxicity; Second top recruiter (>100 sites);
- Predicting serious drug Side effects in Gastroenterology (PRED4): Second top recruiter (>100 sites);
- Personalised anti-TNF therapy in Crohn's disease; Recruiting.

Education and training in IBD

The clinical and academic IBD groups across King's Health Partners provide numerous opportunities for training and education as follows:

- A strong commitment to undergraduate education through specialist clinics, study modules, lecture programs and elective placements;
- IBD education is represented strongly in a number of BSc and MSc programs within KCL;

- The IBD service across King's Health Partners has provided at least 3 registrar grade fellowships per annum in IBD over the last 3–5 years, mostly leading to a higher research degree. Likewise, grant funded MD and PhD fellowships in IBD research are regularly offered. Currently, across GSTT and King's College Hospital sites, there are 6 MD and 4 PhD students undertaking IBD research. In the last 5 years, 7 PhD's and 5 MD's have been awarded.

Key clinical outcomes for this speciality

Key performance and clinical outcome measures for IBD are not as well established as they are for Endoscopy within Gastroenterology. However, these will be given greater emphasis across sites in 2015–2016, with the help of the KCL IMPARTS team. This will be a central part of the strategy to report back to Commissioners (particularly for patients on high-cost drugs).

Furthermore, a Global Rating Scale (GRS) has now been developed for IBD and will be implemented in 2015 scoring performance in IBD against numerous agreed criteria. Similarly, criteria have been set out in the National IBD Audit to score the quality of management in acute severe UC.

What the patients and staff think about the service

A patient satisfaction and service development survey was conducted in late 2014 before many of the recent service developments were in place. There were 70 respondents over three clinics. 95% of patients rated the care they received as either "good", "very good" or "excellent" (with no respondents stating they received "poor" care). 74% of patients recorded these responses when asked how well co-ordinated they thought their care was between the IBD clinic and their

GP, and 75% between the IBD clinic and other specialists within the hospital. More than 60% of respondents stated they would like to see a dietitian and a psychologist in relation to their IBD – and we have been able to meet this demand. We expect to conduct this survey repeatedly to compare results.

At GSTT a patient survey was conducted regarding the IBD Nursing service in 2014. 98% of patients said they were extremely likely to recommend IBD nursing services to their friends and family. Some issues were identified for potential improvement, mainly related to booking appointments.

Top grants awarded

Award details	Amount	Year
Wellcome Trust (Intermediate Fellowship): Role of microRNA 142 in mucosal immunity	£1,008,622	2014–2018
NIHR BRC at GSTT and KCL, Bridging Fellowship, "Translational IBD"	£162,935	2013/2014
King's Health Partners Research and Development Challenge Fund. "A novel therapeutic to augment immunity in vaccination, cancer and infectious disease"	£76,567	2013/2014
Wellcome Trust (Clinical Research Training Fellowship): "The role of the transcription factor T – bet in intestinal inflammation"	£239,637	2009/2012
Crohn's and Colitis UK. Hughes L, Irving P, Moss-Morris R. Development and pilot testing of a self-administered intervention to target psychological distress in IBD	£101,917	2014
For Crohn's. Optimising surgery in Crohn's disease. Patel K, Sanderson J, Irving P	£25,000	2014
For Crohn's. Anti-TNF drug levels in Crohn's disease. Irving P	£15,000	2014
NIHR Clinical Doctoral Fellowship Investigating the impact of dietary interventions for irritable bowel syndrome on luminal microbiota symptoms, nutrient intake and quality of life. Staudacher H, Lomer MC, Irving P, Whelan K	£298,003	2013
Industry grant. Genentech. Investigating the role of alpha E Bets7 T cells in IBD. Hayday A, Gibbons D, Irving P	£100,000	2012



Bariatric
surgery

Bariatric surgery

Introduction

Bariatric surgery (from the greek term “baros” = weight) has been practiced worldwide since the 1950s for the treatment of severe obesity. In addition to causing major and sustained weight reduction, bariatric surgery induces substantial health benefits including dramatic improvements of several metabolic conditions, most notably type 2 diabetes, reduction of overall cardiovascular risk, heart attacks and stroke.

Experimental studies pioneered by members of our Faculty (Prof F. Rubino) provided evidence that some of the modifications of gastrointestinal anatomy used in bariatric surgery can directly improve glucose metabolism by weight-independent mechanisms. This discovery contributed to transforming bariatric surgery from a mere weight loss therapy into a novel surgical discipline aimed at treating diabetes and metabolic illnesses (“metabolic surgery”).

Remarkable clinical efficacy, improved safety due to the widespread use of minimally invasive techniques and a constantly growing interest over the fascinating mechanisms of action of such surgery have made this discipline one of the fastest growing fields of 21st century medicine.

Our bariatric and metabolic surgery service is one of the largest programmes in this specialty in the UK. Pre-and post-operative patient care is based at both King's and Guy's and St Thomas' hospital sites while inpatient services and surgical procedures are based at King's College Hospital and Princess Royal. Services involve a dedicated multidisciplinary team that includes surgeons, endocrinologists, dieticians/nutritionists, psychologists, psychiatrists, gastroenterologists, anaesthetists and specialised nurses.

We offer all types of surgical procedures including gastric bypass, sleeve gastrectomy, gastric banding, biliopancreatic diversion, revisional bariatric surgery for failed weight loss and novel endoluminal interventions. All procedures are performed through a laparoscopic, minimally invasive approach, allowing for fast-track recovery and reduced postoperative pain.

In 2013 we established the first university chair in Metabolic and Bariatric Surgery in the UK and in the world. Our programme is internationally recognized as one of the leading international academic centres for surgical treatment of type 2 diabetes, performing cutting-edge clinical and translational research and engaged in important educational initiatives.

Research and innovation around this speciality

Attesting to our international reputation, in 2015 we hosted the 3rd world congress on interventional therapies for type 2 diabetes bringing together multidisciplinary diabetes experts from over 50 countries. The congress was jointly held with the 2nd Diabetes Surgery Summit (DSS-II), a historical international consensus conference that for the first time recognized gastrointestinal surgery as a standard-of-care treatment option for type 2 diabetes. The guidelines from the DSS-II were published in *Diabetes Care* in June 2016 with the endorsement of 47 international scientific societies, including the American Diabetes Association, the International Diabetes Federation, Diabetes UK, and many national diabetes, gastroenterological and surgical organizations from around the world. Accompanying editorials in prestigious scientific journals such as *Nature*, as well as in the general media, highlighted how the introduction of surgery as a standard treatment for diabetes represents one of the most significant changes in the management of the disease since the discovery of insulin.

The new guidelines advise that metabolic surgery be considered specifically for the treatment of diabetes in people who have not adequately controlled their blood- sugar levels through other means, and whose BMI is greater than 30 (or 27.5 for people of Asian descent).

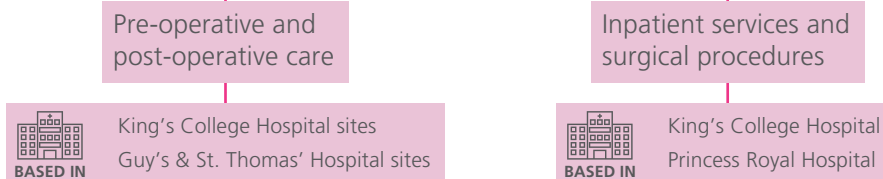
The effectiveness of Metabolic Surgery on diabetes and the mechanisms behind its clinical effects point to the gastrointestinal tract as an important metabolic organ and a suitable target for anti-diabetes interventions. Novel, device-based endoluminal interventions have been recently developed to mimic at least in part the mechanisms of metabolic surgery and some of them are currently available for routine clinical use in UK and Europe or are being tested in phase II and III clinical trials. Our Institution is involved in multicentre and international trials testing these new technologies and approaches to type 2 diabetes.

We are also exploring the effects of gastrointestinal interventions on non-alcoholic steatohepatitis (NASH) and the mechanisms that may reduce or prevent metabolic liver disease.

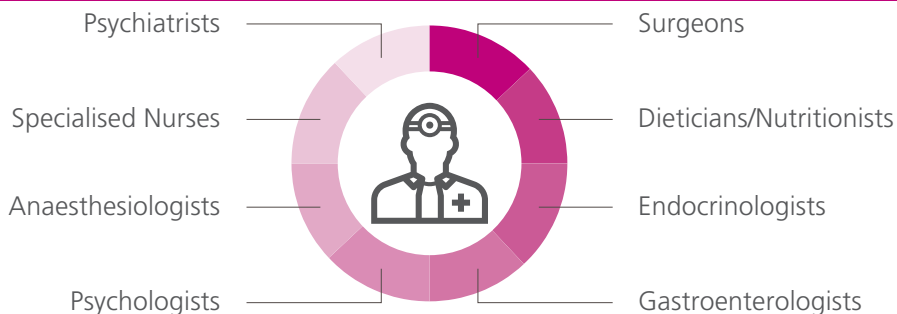
Education and training

Our metabolic and bariatric surgery program is committed to education. In partnership with the Royal College of surgeons KCH has recently established a program for international clinical/research fellowships in metabolic surgery. We offer two clinical/research fellowships every year to surgeons in training or to practicing surgeons wishing to acquire specialised expertise in surgical treatment of obesity and diabetes. Our programme also hosts research fellows from UK and from abroad, offering training in translational research within the metabolic surgery laboratory at the James Black Centre. We are also hosting students from around Europe as part of the Erasmus programme.

Bariatric and Metabolic Surgery Service

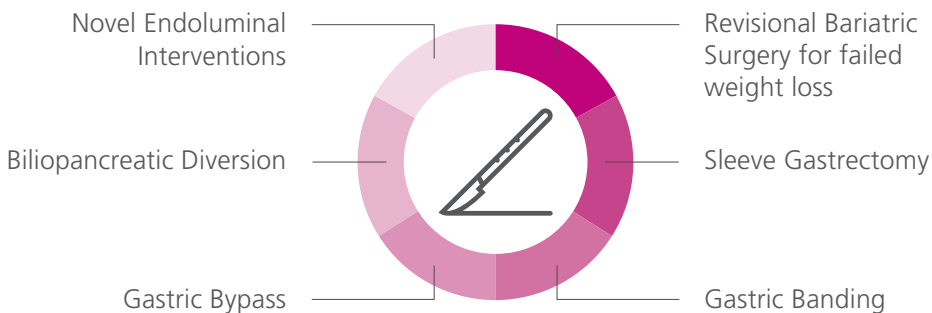


Dedicated Multidisciplinary Team



Surgical Procedures

All procedures are performed through a laproscopic – minimally invasive approach. Allowing for fast-track recovery and reduced postoperative pain.



Key clinical outcomes for this speciality

In a recent randomized clinical trial performed by our team in collaboration with the Università Cattolica of Rome, Italy up to 80% of subjects with obese type 2 diabetes were either in remission (= normal glycemia without need for diabetes medications) or had excellent control of blood-sugar levels using reduced medication or just a calorie-controlled diet at 5 year after metabolic surgery. These findings are consistent with those of non-randomized trials in which rates of sustained diabetes remission range between 30 and 60% at 5 years.

Despite the safety of these surgical procedures having dramatically improved in the last two decades as a result of the advent of minimally invasive approaches, bariatric surgery is still widely perceived as high-risk surgery. To investigate the relative safety of bariatric and metabolic surgery compared to other commonly performed elective procedures, we recently compared rates of major complications and health care utilization

across 8 different elective surgical specialties at KCH. The findings show that safety outcomes of bariatric/metabolic surgery compare favourably with those of gallbladder surgery, anti-reflux surgery and colorectal surgery. Overall, reported rate of major complications in centres of excellence are 4% or less with mortality rates of 0.2–0.3%, similar to hysterectomy, gallbladder surgery or hip replacement.

Performance measures

We perform between 350 and 500 bariatric/metabolic procedures per year between our KCH campus and the PRUH. All standard-of-care procedures are offered at our centre, including laparoscopic Roux-en-y gastric bypass, sleeve gastrectomy, gastric banding and biliopancreatic diversion duodenal switch. We also offer revisional bariatric surgery for patients with weight regain or diabetes relapse after primary bariatric surgery. Novel endoluminal, device-based procedures for weight loss or diabetes control (e.g. endobarrier, duodenal mucosa resurfacing) are also offered across KHP.

Top grants awarded

Award details	Amount	Year
National Institute of Health Research (NIHR), Efficacy and Mechanism Evaluation (EME). Are gut hormone changes why the long-limb gastric bypass is more effective than the standard-limb gastric bypass in improving type 2 diabetes mellitus?", National Institute of Health Research, Efficacy and Mechanism Evaluation; (multicenter study in partnership with Imperial College, Prof Steve Bloom)	£795,285.32	02/2015–08/2018



Nursing
prowess

Nursing prowess

Service profile

Liver and Renal Care Groups employs over six hundred nursing staff across its departments and specialties. Within the Care Groups there are a variety of sub speciality services for patients with liver, kidney and gastro intestinal diseases.

Renal

Renal Care Group provides care to patients who have acute and chronic kidney disease. There is also a proactive living donation programme which works jointly with GSTT in transplantation. Services are delivered through several departments. There is a dedicated acute renal ward incorporating a HDU, and acute dialysis team, along with a dialysis services, and an outpatient department.

Sub specialties

- Anaemia;
- Peritoneal dialysis;
- Living donation;

- Palliative care;
- End stage renal failure;
- Dialysis.

Ward and departments

- Fisk and Cheere ward – 30 bedded acute renal ward with 4 bedded HDU and acute dialysis service;
- Main Unit Dialysis – 20 stations;
- Renal outpatients.

Satellite units

- Dartford – 12 stations;
- Bromley – 17 stations;
- Queen Elizabeth Woolwich – 10 stations;
- Dulwich – 12 stations;
- Sydenham – 18 stations.

Nurse Specialist, Counselling and Social Work teams

There are a number of specialist teams which contribute to the patient pathway and service.

Anaemia team

The anaemia team comprises a band 7 and band 6 nurse and part time band 3 admin assistant. They provide clinical anaemia expertise to the King's College Hospital Renal Unit. This includes practical support such as giving IV iron and Erythropoiesis stimulating agent (ESAs), teaching patients to self-administer and resolving anaemia issues at King's College Hospital and the satellite dialysis units. They have expanded the service to include outreach clinics at Darent Valley and Queen Elizabeth Hospitals, and provide anaemia support to other divisions in the Trust such as the Heart Failure team. They also provide a strong link to community services who administer ESAs for some patients.

PD

The provision of peritoneal dialysis (PD) at King's College Hospital is predominantly delivered by a specialist nursing team. The PD team, consisting of in-house and community nursing staff facilitate and care for the patients receiving PD therapy. The nursing team are supported by a doctor's clinic one morning per week, the rest of clinic schedule is provided by a dedicated nurse-led service.

Low clearance clinic

Low Clearance & Transplant team – One band 7 and 3.6 band 6 nurses support these two distinct patient groups, totalling nearly 700 patients. Low Clearance patients require significant education and support to learn to self-manage their kidney disease and prepare for their preferred form of renal replacement therapy. Transplanted patients are helped to adapt to life with a new kidney and monitored for complications such as infection and rejection. The team have recently expanded their role to provide day-case procedures including transplant biopsies, transfusions, and administration of intravenous medications. They also provide patient education support to patients on the renal ward and in other departments.

Access team

Co-ordinates all activities for all ESRD patients needing vascular access for renal replacement therapies, and consists of 1 in-house vascular surgeon, 3 transplant surgeons and 1 band 7 senior sister and a junior sister. It is a growing service.

Research Nursing team

This comprises a band 7 research co-ordinator, two band 6 research nurses and a band 4 data manager. The team are currently recruiting to 8 commercial studies and 1 NIHR funded non-commercial study. A further 8 studies are in follow-up and data collection phases. The team are international leaders in the field of

anaemia research and are the first centre in the world to recruit patients to a Phase 1 study investigating an oral ESA type drug that could revolutionise anaemia management. The team have expertise in the full range of the research process including study assessment, ethical and R&D approval, patient recruitment and consent, sample collection, processing and storing, and data collection and transcription.

Counselling & Social Work teams

Provide support and advice to patients during the treatment pathways.

Liver services

The Liver Care Group contains the largest liver transplant service in the UK with an international reputation for surgical and medical intervention. The specialities are outlined below and are delivered through a number of departments. These include dedicated outpatient, ITU theatre and liver wards. The Care Group provides a service to the local population and is also a tertiary referral centre.

Sub specialities

- Hepatology;
- Hepatitis;
- Hepatobiliary and pancreatic surgery;
- Interventional endoscopy;

- Liver intensive care;
- Hepatocellular cancer;
- Liver transplantation.

Wards and departments

- Todd Ward – 21 pre- and post-Liver Transplant beds;
- Dawson Ward – 21 Hepatobiliary Surgical beds;
- Howard Ward – 15 General Hepatology beds;
- Liver ITU – 15 beds;
- Surgical Step Down Unit – 4 beds;
- Liver Out Patients;
- Endoscopy units at Kings College Hospital and Princess Royal University Hospital Bromley;
- Liver Theatres – providing 24 hour Liver Transplant and retrieval service;
- HPB theatres.

Nurse Specialist teams

There are a number of specialist teams which contribute to the patient pathways and services.

Hepatitis team

The Viral Hepatitis Service at King's College Hospital is the largest clinical viral hepatitis service in the UK and accounts for 40% of the Liver Outpatients activity. The viral hepatitis clinical nurse specialist's (VHCNS) provide an extensive range of services which includes the provision of specialist care via 11 weekly nurse led clinics. These include assessment and antiviral treatment clinics for patients with hepatitis C virus (HCV), hepatitis B virus (HBV) and associated co-infections. There are also clinics to monitor low infectivity HBV patients, a nurse prescribing service for HBV patients requiring nucleos(t)ide analogues and a renal monitoring service for HBV patients receiving Tenofovir. There are three trained nurse fibroscanners within the team who sit within two weekly multi-disciplinary clinics to provide a one stop consultation for patients. The nurse led fibroscanning service feeds into a national project evaluating fibroscanning (1 of 3 UK centres). The VHCNS team also provide antiviral treatment for complex patients within the multidisciplinary setting.

HPB team

Provides expert, specialised, holistic care for people with liver, pancreatic and biliary disorders: Primary and Secondary Liver Cancer, Pancreatic and Biliary Cancer and Neuroendocrine Tumours (NETs).

They are responsible for the care and clinical coordination of all patients referred into the HPB

service: repatriating patients where appropriate to their clinical need and providing continuing care and support for those who require longer term involvement i.e. dual pathology, rare disease and complex case management.

Transplant co-ordinators

Oversees the management of both adult and paediatric patients through the transplant programme.

Irritable Bowel Disease Nurse

Supports patients through the care pathway.

Nurse Endoscopists

Perform upper and lower GI endoscopy, dyspepsia outpatient clinics and co-ordinate the percutaneous endoscopic gastrostomy service.

Research Nursing Team

Supports the delivering of the clinical trials programmes within the Care Group.

Management and Leadership Capacity

The Head of Nursing provides leadership and management to the nursing teams across the Care Groups. Matrons have professional and line management responsibility for wards and departments. The Consultant Nurse in Nephrology manages the Anaemia and Research

Teams, runs nurse led clinics and provides professional and research support. There are also a number of nurse specialists which manages their teams.

Nursing achievements

Liver research

We are currently conducting 41 studies (Hepatitis, HCC, Surgery, Transplant, PNET and general hepatology) per year within the liver research team. The team has generated £840,140 (Table 1, the highest income from the commercial trials within King's Health Partners) income from the commercial study and received £206,724 from CRN funds in 2014.

Not only have the team generated outstanding income, but also have saved NHS cost (broader health economy) approximately £5,500,000 over the last 6 years. Our team has grown significantly, now consisting of a research manager, a research fellow, 7 research nurses, a study coordinator, a data manager, a research assistant and an admin post, hence is able to undertake more studies and deliver them at a high standard.

In addition, the team is able to support other service areas, such as Renal and Gastroenterology research.

Table 9 | Liver clinical trials activities since 2009

Year	Number of trials			Number of patients enrolled			Generated income (£)	Broader health economy (£)	
	Hepatitis	HCC	Others	Hepatitis	HCC	Others		Drug saving (HCV)	Clinic visits (HCV)
2009	6	5	6	12	10	4	82,805	180,000	24,000
2010	9	6	6	17	15	9	112,701	255,000	48,000
2011	12	7	7	38	11	12	206,106	570,000	76,000
2012	17	7	7	45	14	28	730,729	675,880	90,000
2013	23	9	8	77	12	14	868,723	2,695,000	154,000
2014	21	11	10	54	45	29	840,140	810,000	108,000
Total	88	45	44	243	107	96	2,841,204	5,185,000	500,000

Key aims for the next 5 years

- Recognition from MHRA as a centre of excellence;
- Expand the service to GSTT within hepatology;
- Share the expertise with other departments and other hospitals;
- Continue to grow.

Examples of excellence

- Achieving top recruitment for two studies globally, and 6 top recruitment in the UK;
- Requests from other hospitals to observe what we are doing;
- Good feedback from the sponsors, hence they come back with new studies;
- Training and personal development for all staff including the medical team.

Patient experience

Patient feedback is good with excellent patient retention (<5% attrition) and with 97% of participants returning to the trial clinic for the Registry follow up studies.

"I had a final appointment last July and have been discharged. I have been meaning to send you this for ages but just never quite got round to it, for which I am sorry. I just wanted to say thank you very much for everything you and your team have done for me. I feel very lucky and very grateful that the trial was a success. I have never felt so well and healthy. Please pass on my thanks to everybody. You all made it so easy for me and you all treated me with utmost kindness and respect. Thank you very much".

"Julie and I would like to thank you and the team for all the support we received during the trial. It is great news that the virus has gone and big relief for me. All the help we received from you made a big difference to us. Wishing you have as much success with the rest of the trial. Many thanks".

"Just a few lines to say thank you for looking after me during my trial at Kings. I can hardly believe that this virus is now dead, I can now be of use to my grandchildren, and I am feeling better than I have for years. As for all the worried people coming through the clinical trial door, they could not be in better hands. Kindest regards to you all and Thank you".

Research and innovation around this speciality

Service development

- Integrated pathway being written;
- New information leaflets produced to improve donor access to health care providers;
- Setting up a formal living donor MDM;
- Participation in national consultation process to develop Liver Living Donation Policy.

Virtual clinic

The purpose of the clinic is to improve the patient experience within the first three months post discharge, to follow up outstanding issues, symptom management and to identify patients that would benefit from entry into the health promotion programme. All post-transplant patients will be entered into the virtual clinic.

Our aim is to:

- To improve patient accessibility with health care providers;
- To increase patient confidence on discharge by improving psycho-social support;
- To increase patient education and understanding, improving self-management;

- To identify patients that have cardiovascular or lifestyle associated risk factors early;
- To identify patients that are low in mood have increased anxiety and refer appropriately, particularly within the Acute Liver Failure (ALF) population;
- To maximise the benefit/need of the Health Promotion Clinic (HPC) by assessing the patients readiness to engage and make behavioural/lifestyle changes;
- The clinic will aim to focus on the patients current and immediate post-transplant issues first, before exploring long term health promotion strategies.

Health promotion clinic

The virtual clinic will identify patients who would benefit from the health promotion clinic and providing that their post-transplant recovery is on the correct trajectory and patients are willing to engage they will be invited to attend the clinic.

Our aim is to:

- To provide education and information to patients to increase their level of knowledge regarding the long term side effects of immunosuppressant therapy, including cardiovascular risk factors and to raise understanding of how these can be self-managed;

- To optimise attendance at liver follow up appointments and concordance with the therapeutic regime;
- To provide continued support to post transplant patients;
- To assess the feasibility of such a service and to obtain data to evaluate the impact of the health promotion clinic on health behaviours and longer term health outcomes;
- To develop and strengthen links between primary and secondary care;
- To develop the role and strengthen the contribution of the recipient transplant coordinator in the long term care of these patients.

Transition service

The adult transplant coordinator and the social worker are part of the Transition team. Due to the nature of the MDT some of the roles and responsibilities may overlap. However, the advantage is that it ensures communication channels remain open at all times and that seamless transition care is provided to the young person and their families.

The roles and responsibilities of the adult transplant coordinator consist primarily to educate and support the young person, overseeing the transition process and linking with paediatric services to provide a seamless transition. Education

includes understanding of the disease, rationale of therapy, identification of symptoms to recognize deterioration and taking appropriate action on how to seek help from health care professionals including primary and emergency care.

Other tasks include teaching the young person to take responsibility for their medication, promote their skills in communication, decision-making, assertiveness and self-care; providing information about adult services and helping them through transition; developing a sense of control and independence; providing support for parents/care givers through the process; provide shared care with GP's for bloods; liaising with other hospitals; working with the MDT and refer to appropriate resources; provide education through the transplant assessment and following up whilst on the list for transplantation.

The social worker's role is to complete psychosocial risk screening of the young people, including addressing any safeguarding concerns which may arise; optimize educational and early employment opportunities; liaising with local community services to optimize support for the young person during the transition process; provide welfare rights advice, assistance with housing matters and financial assistance through charitable applications where appropriate; promoting the rights, interest and independence of the young person, providing information, advice and counselling as well as screening and promoting the emotional well-being of the young person and where necessary liaising with the MDT and external resources ensuring services are provided in the best interest of the young person.

Education – Patients and families

The transplant coordinators aim to provide patients and their families with a comprehensive individualised education throughout the transplant continuum. A variety of media are used: written, verbal, computer programmes, and interactions with post-transplant patients. Web based access to educational material is currently in development.

Assessment phase

Tailored education to individual patient's symptoms and their management within the context of their liver disease. Emphasis on health promotion issues; smoking, weight, mobility, alcohol use.

Pre listing education

All patients (and their families) prior to listing for transplant are invited to an education session. In cases where patients are unable to attend due to the severity of their medical condition or require an interpreter one to one sessions will be undertaken. This education session is also part of the consent process for transplantation.

Our education programme is currently undergoing a review taking into account responses from a patient questionnaire.

Waiting list

During the waiting time on the transplant list patients will be seen in clinic at least every 12 weeks or more frequently as their clinical condition dictates. This provides an opportunity to reinforce educational information provided previously and to address any concerns.

Every interaction with waiting list patients whether face to face or over the telephone is used as an opportunity to inform, reinforce and gather feedback.

Post-transplant

All post-transplant patients are provided with one to one teaching as part of the self – medication process and discharge education to ensure their safety on discharge home.

Further advice is provided through the virtual clinic, patients are called on day 1 post discharge, week 6 and week 12. Post-transplant coordinators are available to speak to patients in the post-transplant clinics on Tuesday and Thursday afternoons.

Education and training

Renal Nursing

Feedback from new nurses to the area on why they chose to work in Renal

- As a renal nurse, I will be able to learn more about nephrology and there is a lot of opportunity to specialise. Dialysis/renal nurses work harmoniously with professionals from many disciplines, and this speciality has a wide inter professional collaboration for the care of patients at all times and this will in turn develop my knowledge and skills. The autonomous role enables me to engage with patients in their own care. I find the analytical skills inherent in this specialty extremely rewarding. I feel the work load is manageable, and there is less stress and tension during work. The opportunities for career development are vast in renal nursing and there are always chances to learn new things, which is what interests me most.
- I am fascinated with renal function and I want to learn more about it in detail. I had the opportunity to work in cardiothoracic surgery before, caring for a number of patients with heart failure. However, I found that those 2 disciplines are connected with each other. Particularly, I find the principle of haemodialysis amazing because a synthetic kidney can replace the loss of function of the patient's kidney and prolonged patient's lives, thereby maintaining their quality of life. I feel professionally satisfied knowing I am

developing as a renal nurse. I look forward to expanding my knowledge and experience and to translated acquired skills into practice in order to deliver a higher quality care to renal patients. I feel supported by my mentors.

Training programmes in Liver Intensive Care

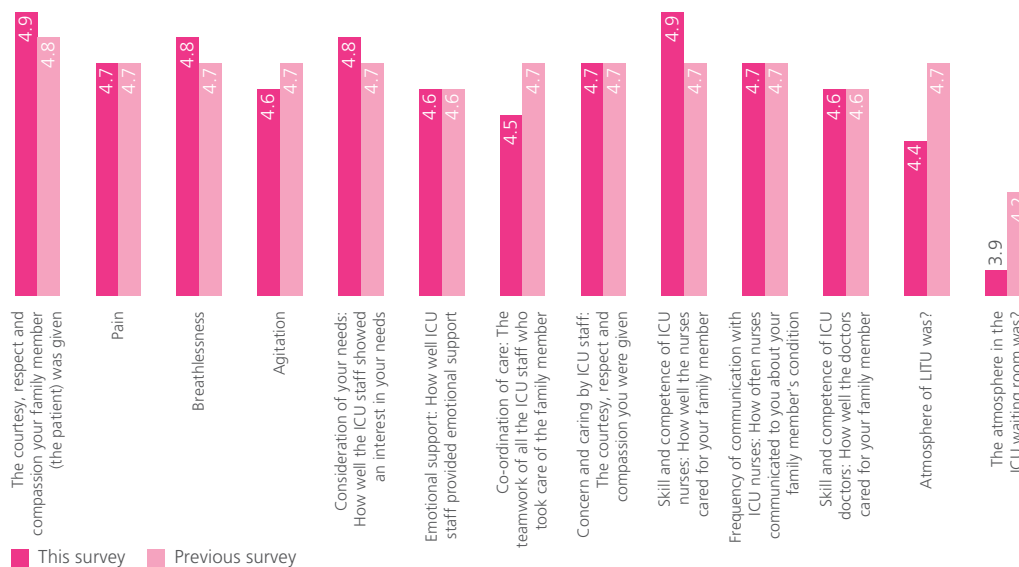
- We have digitised the Introduction to Critical Care course run in conjunction with GSTT, using the King's Health Partners learning hub. The course is now putting through close to 300 nurses new to critical care per year. We plan to extend this to the in-house liver staff development programme, as well as potentially opening this up as a learning opportunity for other trusts.
- We have introduced a senior staff development programme, filling a gap in clinical teaching for those nurses who have already undertaken the university based ICU & Liver courses. Through this we hope to develop a core base of highly clinically specialised Liver ITU nurses who also have the management skills required for further career progression.

Feedback from students nurses on the support they receive from their mentors

I had a nursing placement on Dawson ward last October. After the placement and having had a placement since, I have come to realise how high the standard of mentorship was from Jessica and I feel no mentor will ever come close to the support she offered me.

What the patients think about the service

Figure 74 | Satisfaction with care

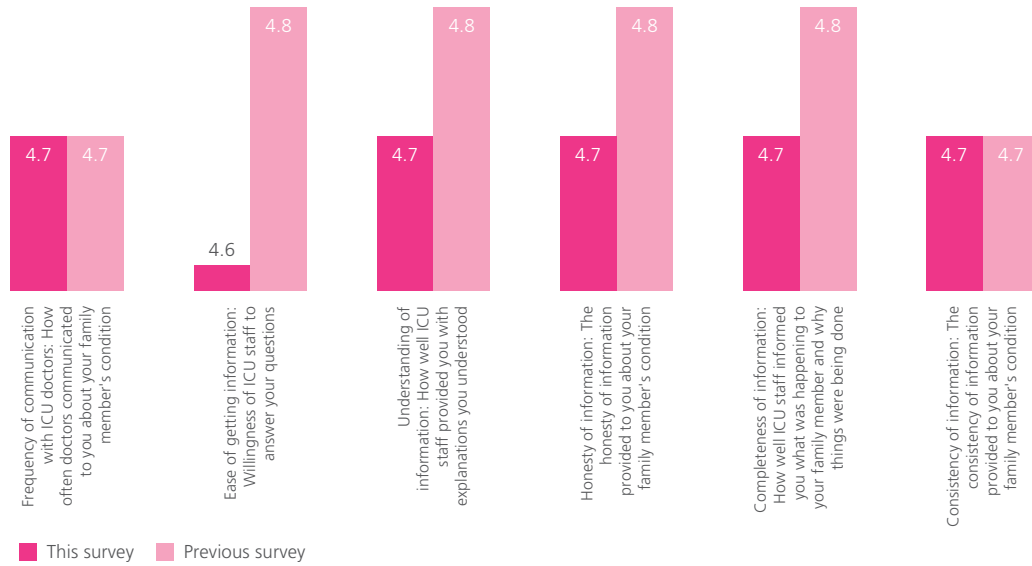


5=excellent, 4=very good, 3=good, 2=fair, 1=poor.

Patient comments about their care on the liver transplant ward

- All staff are very friendly and knowledgeable;
- Good care and very nice staff;
- I could not fault the care I received. The staff were polite, the cubicle was spacious as well as airy and the meals were great;
- I have had the best of guidance and care before and after my transplant;
- Nurses are fully qualified, very friendly, caring and when you need them they are always around;
- Staff were very helpful, friendly and welcoming. They accommodated to our every need. Thank you so much for your help.

Figure 75 | Family satisfaction with decision-making around care of critically ill patients



5=excellent, 4=very good, 3=good, 2=fair, 1=poor.



Research
in focus

Research in focus

Since the CAG's establishment personnel from across the partnership have collaborated with both national and international researchers. Since 2010 the CAG has published over 1,900 peer reviewed articles, reviews and papers. Their work has been substantially viewed by the scientific community amassing over 60,000 citations. The relevance of these publications goes to the very core of the CAG's mission and has helped us understand more about how the body works both in health and in disease, informing clinical guidelines, best practice and facilitating the development of new solutions to revolutionise our clinical care.

In this section, we provide a selection of abstracts from the groups research endeavours grouped into respective themes.

Transplantation and Regenerative Medicine

Liver transplantation and adolescence: The role of mental health, *Liver Transplantation*, 2016

Hames, A., Matcham, F., Joshi, D., Heneghan, M.A., Dhawan, A., Heaton, N., Samyn, M.

Young people (YP) with chronic illness have higher rates of mental health problems than the general population, with psychosocial complexity associated with nonadherence and poorer health outcomes. This study aimed to describe the prevalence of anxiety and depression in YP after liver transplantation, with autoimmune liver disease and other chronic liver diseases, identify the factors YP attribute their distress to and the relationship between anxiety/depression, and describe YP's beliefs about their illness and treatment. An electronically administered questionnaire battery was given routinely to YP attending an outpatient liver transition clinic;

187 YP participated, of which 17.7% screened positive for anxiety or depression. There were no significant differences between disease groups. This is significantly higher than the prevalence of common mental health problems in the general adolescent population. Patients most frequently attributed their distress to fatigue, sleep difficulties, financial concerns, problems at work/school, worry, and low self-esteem. Higher levels of depression and anxiety were significantly associated with specific illness and treatment beliefs but not with perceived understanding of illness or treatment control. In conclusion, the increased prevalence of mental health problems in YP and the intertwined nature of these with their physical health outcomes provide evidence that holistic care should be delivered as standard for this age group.

The role of complement in the early immune response to transplantation, *Nature Reviews Immunology*, 2012

Sacks, S.H., Zhou, W.

The complement system is a key element of the innate immune system, and the production of complement components can be divided into central (hepatic) and peripheral compartments. Essential complement components such as C3 are produced in both of these compartments, but until recently the functional relevance of the peripheral synthesis of complement was unclear. Here, we review recent findings showing

that local peripheral synthesis of complement in a transplanted organ is required for the immediate response of the donor organ to tissue stress and for priming alloreactive T cells that can mediate transplant rejection. We also discuss recent insights into the role of complement in antibody-mediated rejection, and we examine how new treatment strategies that take into account the separation of central and peripheral production of complement are expected to make a difference to transplant outcome.

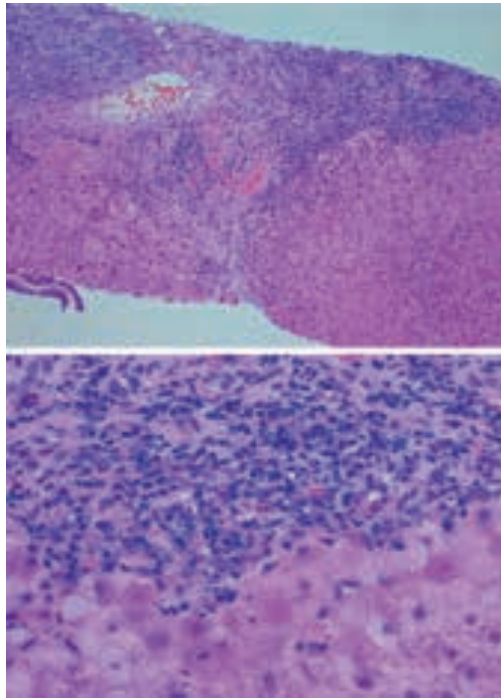
Autoimmune Hepatitis after Liver Transplantation, *Clinical Gastroenterology and Hepatology*, 2012

Liberal, R., Longhi, M.S., Grant, C.R., Mieli-Vergani, G., Vergani, D.

Liver transplantation is an effective treatment for patients with end-stage acute and chronic autoimmune hepatitis. However, despite the good outcomes reported, disease recurrence is relatively common in the allograft. In addition, autoimmunity and autoimmune liver disease can arise de novo after transplantation for non-autoimmune liver disorders. Little is known about the mechanisms by which autoimmune diseases develop after liver transplantation, but genetic factors, molecular mimicry, impaired regulatory T-cell responses, and exposures to new alloantigens might be involved. Regardless of the pathogenic mechanisms, it is important to remain aware of the existence of

recurrent and de novo autoimmune hepatitis after liver transplantation; these disorders are similar to classic autoimmune hepatitis and are therefore not treated with standard antirejection strategies.

Figure 76 | The portal tract is densely infiltrated by mononuclear cells, with a clear presence of plasma cells, that invade the parenchyma, disrupting the limiting plate. Reproduced from *Clinical Gastroenterology and Hepatology*.



Impact of tacrolimus compared with cyclosporin on the incidence of acute allograft rejection in human immunodeficiency virus-positive kidney transplant recipients, *Transplantation*, 2016

Gathogo, E., Harber, M., Bhagani, S., Levy, J., Jones, R., Hilton, R., Davies, G., Post, F.A.

Kidney transplantation (KT) of human immunodeficiency virus (HIV)-positive patients has transformed the management of end-stage kidney disease in this population. Although favourable outcomes have been reported, patients experience high rates of acute allograft rejection (AR). We examined factors associated with AR in the first year after KT, with particular emphasis on the choice of calcineurin inhibitor (CNI) immunosuppressive therapy.

We conducted a national observational cohort study of HIV/KT in the United Kingdom. Patients were included if HIV positive at KT, transplanted in the United Kingdom between January 2005 and December 2013, and did not experience primary graft failure. Kaplan-Meier methods were used to estimate host/graft survival and cumulative incidence of biopsy proven AR. Logrank tests were used to compare survival, and Cox proportional hazard models to examine factors associated with AR.

Our study analyzed the incidence of AR in the first year after KT in 78 HIV-positive patients of whom 31 initiated cyclosporin (CsA) and 47 tacrolimus (Tac) based immunosuppression. AR was observed in 28 patients (36%) after a median of 2.6 (interquartile range, 0.5–5.9) months. The cumulative incidence of AR at 1 year was 58% and 21% among patients on CsA and Tac, respectively ($p = 0.003$). Choice of CNI was the only factor significantly associated with AR (hazard ratio for Tac vs CsA 0.25 [95% confidence interval, 0.11–0.57], $p = 0.001$). Subtherapeutic CNI concentrations were common in the first 12 weeks after KT.

Our data suggest that Tac may be the preferred CNI for use in KT in people living with HIV.

Rituximab in renal transplantation, *Transplant International*, 2013

Barnett, A.N.R., Hadjianastassiou, V.G., Mamode, N.

Rituximab is a chimeric anti-CD20 monoclonal antibody that leads to B cell depletion. It is not licensed for use in renal transplantation but is in widespread use in ABO blood group incompatible transplantation. It is an effective treatment for post-transplant lymphoproliferative disorder, and is also used in both HLA antibody incompatible renal transplantation and the treatment of acute rejection. Recent evidence suggests rituximab may prevent the development of chronic

antibody mediated rejection. The mechanisms underlying its effects are likely to relate both to long-term effects on plasma cell development and to the impact on B cell modulation of T cell responses. Rituximab (in multiple doses or in combination with other monoclonal antibodies and/or other immunosuppressants) may lead to an increase in infectious complications, although the evidence is not clear. Rarely, the drug can cause a cytokine release syndrome, thrombocytopenia and neutropenia. It has been related to an increased risk of progressive multifocal leucoencephalopathy and, recently, deaths from cardiovascular causes. Trials examining the effects of rituximab in induction therapy for compatible renal transplantation and the treatment of chronic antibody mediated rejection are ongoing. These trials should aid greater understanding of the role of B-cells in the alloresponse to renal transplantation.

Collectin-11 detects stress-induced L-fucose pattern to trigger renal epithelial injury, *Journal of Clinical Investigation*, 2016

Farrar, C.A., Tran, D., Li, K., Wu, W., Peng, Q., Schwaeble, W., Zhou, W., Sacks, S.H.

Physiochemical stress induces tissue injury as a result of the detection of abnormal molecular patterns by sensory molecules of the innate immune system. Here, we have described how

the recently discovered C-type lectin collectin-11 (CL-11, also known as CL-K1 and encoded by COLEC11) recognizes an abnormal pattern of L-fucose on postischemic renal tubule cells and activates a destructive inflammatory response. We found that intrarenal expression of CL-11 rapidly increases in the postischemic period and colocalizes with complement deposited along the basolateral surface of the proximal renal tubule in association with L-fucose, the potential binding ligand for CL-11. Mice with either generalized or kidney-specific deficiency of CL-11 were strongly protected against loss of renal function and tubule injury due to reduced complement deposition. Ex vivo renal tubule cells showed a marked capacity for CL-11 binding that was induced by cell stress under hypoxic or hypothermic conditions and prevented by specific removal of L-fucose. Further analysis revealed that cell-bound CL-11 required the lectin complement pathway-associated protease MASP-2 to trigger complement deposition. Given these results, we conclude that lectin complement pathway activation triggered by ligand-CL-11 interaction in postischemic tissue is a potent source of acute kidney injury and is amenable to sugar-specific blockade.

Liver

High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial, *Journal of Hepatology*, 2016

Larsen, F.S., Schmidt, L.E., Bernsmeier, C., Rasmussen, A., Isoniemi, H., Patel, V.C., Triantafyllou, E., Bernal, W., Auzinger, G., Shawcross, D., Eefsen, M., Bjerring, P.N., Clemmesen, J.O., Hockerstedt, K., Frederiksen, H.-J., Hansen, B.A., Antoniades, C.G., Wendon, J.

Acute liver failure (ALF) often results in cardiovascular instability, renal failure, brain oedema and death either due to irreversible shock, cerebral herniation or development of multiple organ failure. High-volume plasma exchange (HVP), defined as exchange of 8–12 or 15% of ideal body weight with fresh frozen plasma in case series improves systemic, cerebral and splanchnic parameters.

In this prospective, randomised, controlled, multicentre trial we randomly assigned 182 patients with ALF to receive either standard medical therapy (SMT; 90 patients) or SMT plus HVP for three days (92 patients). The baseline characteristics of the groups were similar. The primary endpoint was liver transplantation-free survival during hospital stay. Secondary-endpoints included survival after liver transplantation with or without HVP with

intention-to-treat analysis. A proof-of-principle study evaluating the effect of HVP on the immune cell function was also undertaken.

For the entire patient population, overall hospital survival was 58.7% for patients treated with HVP vs. 47.8% for the control group (hazard ratio (HR), with stratification for liver transplantation: 0.56; 95% confidence interval (CI), 0.36-0.86; $p = 0.0083$). HVP prior to transplantation did not improve survival compared with patients who received SMT alone (CI 0.37 to 3.98; $p = 0.75$). The incidence of severe adverse events was similar in the two groups. Systemic inflammatory response syndrome (SIRS) and sequential organ failure assessment (SOFA) scores fell in the treated group compared to control group, over the study period ($p < 0.001$).

Treatment with HVP improves outcome in patients with ALF by increasing liver transplant-free survival. This is attributable to attenuation of innate immune activation and amelioration of multi-organ dysfunction.

ABT-450/r-ombitasvir and dasabuvir with ribavirin for hepatitis C with cirrhosis, *New England Journal of Medicine*, 2014

Poordad, F., Hezode, C., Trinh, R., Kowdley, K.V., Zeuzem, S., Agarwal, K., Shiffman, M.L., Wedemeyer, H., Berg, T., Yoshida, E.M., Forns, X., Lovell, S.S., Da Silva-Tillmann, B., Collins, C.A., Campbell, A.L., Podsadecki, T., Bernstein, B.

Interferon-containing regimens for the treatment of hepatitis C virus (HCV) infection are associated with increased toxic effects in patients who also have cirrhosis. We evaluated the interferon-free combination of the protease inhibitor ABT-450 with ritonavir (ABT-450/r), the NS5A inhibitor ombitasvir (ABT-267), the nonnucleoside polymerase inhibitor dasabuvir (ABT-333), and ribavirin in an open-label phase 3 trial involving previously untreated and previously treated adults with HCV genotype 1 infection and compensated cirrhosis.

We randomly assigned 380 patients with Child-Pugh class A cirrhosis to receive either 12 or 24 weeks of treatment with ABT-450/r-ombitasvir (at a once-daily dose of 150 mg of ABT-450, 100 mg of ritonavir, and 25 mg of ombitasvir), dasabuvir (250 mg twice daily), and ribavirin administered according to body weight. The primary efficacy end point was a sustained virologic response 12 weeks after the end of treatment. The rate of sustained virologic

response in each group was compared with the estimated rate with a telaprevir-based regimen (47%; 95% confidence interval [CI], 41 to 54). A noninferiority margin of 10.5 percentage points established 43% as the noninferiority threshold; the superiority threshold was 54%.

A total of 191 of 208 patients who received 12 weeks of treatment had a sustained virologic response at post-treatment week 12, for a rate of 91.8% (97.5% CI, 87.6 to 96.1). A total of 165 of 172 patients who received 24 weeks of treatment had a sustained virologic response at post-treatment week 12, for a rate of 95.9% (97.5% CI, 92.6 to 99.3). These rates were superior to the historical control rate. The three most common adverse events were fatigue (in 32.7% of patients in the 12-week group and 46.5% of patients in the 24-week group), headache (in 27.9% and 30.8%, respectively), and nausea (in 17.8% and 20.3%, respectively). The hemoglobin level was less than 10 g per deciliter in 7.2% and 11.0% of patients in the respective groups. Overall, 2.1% of patients discontinued treatment owing to adverse events.

In this phase 3 trial of an oral, interferon-free regimen evaluated exclusively in patients with HCV genotype 1 infection and cirrhosis, multitargeted therapy with the use of three new antiviral agents and ribavirin resulted in high rates of sustained virologic response. Drug discontinuations due to adverse events were infrequent.

Increased Survival for Patients With Cirrhosis and Organ Failure in Liver Intensive Care and Validation of the Chronic Liver Failure-Sequential Organ Failure Scoring System, *Clinical Gastroenterology and Hepatology*, 2015

McPhail, M.J.W., Shawcross, D.L., Abeles, R.D., Chang, A., Patel, V., Lee, G.-H., Abdulla, M., Sizer, E., Willars, C., Auzinger, G., Bernal, W., Wendon, J.A.

During the past decade, survival has increased among patients admitted to general intensive care units, but it is not clear if it has increased for patients admitted with cirrhosis and organ failure. The chronic liver failure-sequential organ failure assessment (CLIF-SOFA) recently was developed as an adaptation to the SOFA to predict outcomes of patients, but requires validation. We investigated changes in outcomes of patients with cirrhosis and organ failure since 2000, compared the abilities of SOFA and CLIF-SOFA to predict patient survival, and validated the CLIF-SOFA system.

In a retrospective study, we collected data from 971 patients (median age, 52 y; age range, 16–90 y; 62% male) with cirrhosis (54% alcohol associated, 12% viral, and 34% other causes). The patients were admitted under emergency conditions from January 1, 2000,

to December 31, 2010, to a liver intensive therapy unit in the United Kingdom. Patient survival while in the hospital was compared with measures of illness severity, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, model for end-stage liver disease (MELD) scores, SOFA scores, and CLIF-SOFA scores.

Patients had a median APACHE II score of 21 (range, 5–50) and a median MELD score of 23 (range, 6–40). The median APACHE II score at admission decreased from 23 to 22 over the study period ($p < 0.001$), whereas the median MELD score at admission decreased from 23 to 18 ($p < 0.001$). Overall survival until hospital discharge was 51%; this value increased from 40% in 2000 to 63% in 2010 ($p < 0.001$). The unadjusted odds ratio for change in mortality/year was 0.87 (95% confidence interval, 0.83–0.91; $p < 0.001$). The APACHE II score adjusted odds ratio for mortality was 0.89 (95% confidence interval, 0.84–0.93; $p < 0.001$). The etiology of cirrhosis was not associated with a significant difference in survival. CLIF-SOFA and SOFA scores at the time of admission predicted patient survival with area under the receiver operating curve (AUROC) values of 0.813 and 0.799, respectively; the scores at 48 hours after admission predicted survival with AUROC values of 0.853 and 0.840, and scores after 1 week predicted survival with AUROC values of 0.842 and 0.844, respectively. These AUROC values were higher than those obtained from APACHE II or MELD scores.

The proportion of patients with cirrhosis who survived after admission to intensive care increased from 2000 to 2010. SOFA and CLIF-SOFA scores during the first week of critical care appear to have similar abilities to predict patient survival.

Hepatobiliary

Phase 1 dose-escalation study of S-222611, an oral reversible dual tyrosine kinase inhibitor of EGFR and HER2, in patients with solid tumours, *European Journal of Cancer*, 2015

Spicer, J., Baird, R., Suder, A., Cresti, N., Corbacho, J.G., Hogarth, L., Frenkel, E., Matsumoto, S., Kawabata, I., Donaldson, K., Posner, J., Sarker, D., Jodrell, D., Plummer, R.

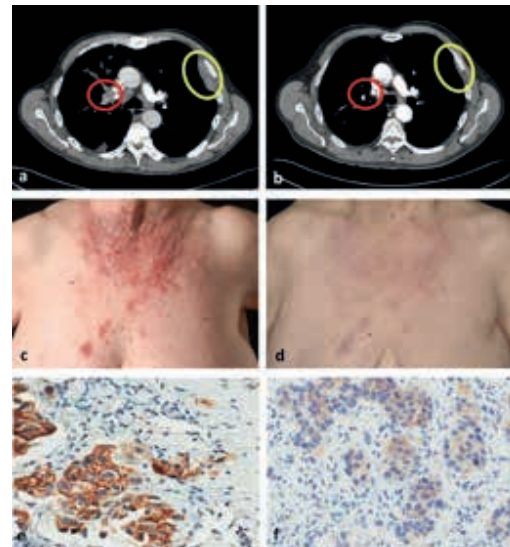
S-222611 is a reversible inhibitor of EGFR, HER2 and HER4 with preclinical activity in models expressing these proteins. We have performed a Phase 1 study to determine safety, maximum tolerated dose (MTD), pharmacokinetic profile (PK) and efficacy in patients with solid tumours expressing EGFR or HER2.

Subjects had advanced tumours not suitable for standard treatment, expressing EGFR or HER2, and/or with amplified HER2. Daily oral doses of S-222611 were escalated from 100 mg to 1,600 mg. Full plasma concentration profiles for drug and metabolites were obtained.

33 patients received S-222611. It was well tolerated, and the most common toxicities, almost all mild (grade 1 or 2), were diarrhoea, fatigue, rash and nausea. Only two dose-limiting toxicities occurred (diarrhoea and rash), which resolved on interruption. MTD was not reached. Plasma exposure increased with dose up to 800 mg, exceeding levels eliciting pre-clinical responses. The plasma terminal half-life was more than 24 h, supporting once daily dosing. Responses were seen over a wide range of doses in oesophageal, breast and renal tumours, including a complete clinical response in a patient with HER2-positive breast carcinoma previously treated with lapatinib and trastuzumab. Four patients have remained on treatment for more than 12 months. Downregulation of pHER3 was seen in paired tumour biopsies from a responding patient.

Continuous daily oral S-222611 is well tolerated, modulates oncogenic signalling, and has significant antitumour activity. The recommended Phase 2 dose, based on PK and efficacy, is 800 mg/day.

Figure 77 | Pre- (a) and post-treatment (b) CT scans showing hilar lymphadenopathy (red circle) and pleural metastases (yellow circle) in a patient with renal cell carcinoma expressing EGFR, which had previously progressed on sunitinib and everolimus. Pre- (c) and post-treatment (d) appearance of cutaneous disease in a female with HER2-positive breast cancer who had previously failed treatment with trastuzumab and lapatinib; baseline (e) and post-cycle 1 (f) tumour biopsies from the same patient showing downregulation of pHER3. Reproduced from *European Journal of Cancer*.



Efficacy and safety of sorafenib in patients with advanced hepatocellular carcinoma: Age is not a problem, *European Journal of Gastroenterology and Hepatology*, 2017

Ziogas, D.C., Papadatos-Pastos, D., Thillai, K., Korantzis, I., Chowdhury, R., Suddle, A., O'Grady, J., Al-Khadimi, G., Allen, N., Heaton, N., Ross, P.J., Sarker, D.

Sorafenib is the standard of care for patients with advanced hepatocellular carcinoma (HCC), but data on its use in the elderly are inconclusive.

All consecutive HCC patients who were treated in our institution with sorafenib since its licensing were included in the analysis. Patients were divided into two groups: (A) up to 75 and (B) older than 75 years old. Our endpoints were overall survival (OS) and time to treatment failure (TTF) because of disease progression or toxicity. Safety parameters and the prognostic effect of HCC characteristics were also investigated.

Data from 190 patients (157 men), median age 66 (26–87) years, were studied (A = 151 and B = 39). No significant difference in OS and TTF was detected between the two groups [7.1 (5.5–8.7) vs. 10.4 (6.5–14.3) months, $p = 0.360$ and 4.2 (2.3–6.2) vs. 5.6 (3.1–8.1) months, $p = 0.369$, respectively]. Incidence of toxicities at all grades and dose reductions were comparable between groups A and B. In

a multivariate setting, patients with Child-Pugh B score at baseline were associated with a higher risk of death (adjusted hazard ratio = 2.17, 95% confidence interval: 1.24–3.79, $p = 0.007$) and treatment failure (adjusted hazard ratio = 4.64, 95% confidence interval: 2.55–8.42, $p = 0.001$) and had shorter OS and TTF compared with patients with a Child-Pugh A ($p = 0.004$ and $p < 0.001$, respectively).

Elderly patients with advanced HCC, when treated with sorafenib, have an equivalent clinical outcome with similar toxicity rates as their younger counterparts. Age alone should not be a discriminating factor for the management of advanced HCC with sorafenib.

Renal

Peginesatide for anemia in patients with chronic kidney disease not receiving dialysis, *New England Journal of Medicine*, 2013

Macdougall, I.C., Provenzano, R., Sharma, A., Spinowitz, B.S., Schmidt, R.J., Pergola, P.E., Zabaneh, R.I., Tong-Starksen, S., Mayo, M.R., Tang, H., Polu, K.R., Duliege, A.-M., Fishbane, S.

Peginesatide is a peptide-based erythropoiesis-stimulating agent (ESA) that may have therapeutic potential for anemia in patients with advanced

chronic kidney disease. We evaluated the safety and efficacy of peginesatide, as compared with another ESA, darbepoetin, in 983 such patients who were not undergoing dialysis.

In two randomized, controlled, open-label studies (PEARL 1 and 2), patients received peginesatide once a month, at a starting dose of 0.025 mg or 0.04 mg per kilogram of body weight, or darbepoetin once every 2 weeks, at a starting dose of 0.75 µg per kilogram. Doses of both drugs were adjusted to achieve and maintain hemoglobin levels between 11.0 and 12.0 g per deciliter for 52 weeks or more. The primary efficacy end point was the mean change from the baseline hemoglobin level to the mean level during the evaluation period; noninferiority was established if the lower limit of the two-sided 97.5% confidence interval was -1.0 g per deciliter or higher. Cardiovascular safety was evaluated on the basis of an adjudicated composite end point.

In both studies and at both starting doses, peginesatide was noninferior to darbepoetin in increasing and maintaining hemoglobin levels. The mean differences in the hemoglobin level with peginesatide as compared with darbepoetin in PEARL 1 were 0.03 g per deciliter (97.5% confidence interval [CI], -0.19 to 0.26) for the lower starting dose of peginesatide and 0.26 g per deciliter (97.5% CI, 0.04 to 0.48) for the higher starting dose, and in PEARL 2 they were 0.14 g per deciliter (97.5% CI, -0.09 to 0.36) and 0.31 g per deciliter (97.5% CI, 0.08 to 0.54), respectively. The hazard ratio for the cardiovascular safety end point was 1.32 (95% CI, 0.97 to 1.81) for peginesatide

relative to darbepoetin, with higher incidences of death, unstable angina, and arrhythmia with peginesatide.

The efficacy of peginesatide (administered monthly) was similar to that of darbepoetin (administered every 2 weeks) in increasing and maintaining hemoglobin levels. However, cardiovascular events and mortality were increased with peginesatide in patients with chronic kidney disease who were not undergoing dialysis.

Increased prevalence of renal cysts in patients with sickle cell disease, *BMC Nephrology*, 2017

Meeks, D., Navaratnarajah, A., Drasar, E., Jaffer, O., Wilkins, C.J., Thein, S.L., Sharpe, C.C.

Early detection and interventions have enabled patients with sickle cell disease (SCD) to live well into adulthood. Consequently, the chronicity of SCD allows for the insidious manifestation of multisystem complications, including renal damage. Cystic renal lesions are commonly incidentally discovered on ultrasound and computerised tomography (CT) imaging of the abdomen. Most are benign simple cysts, however, difficulties may be encountered if infection, rupture, haemorrhage or cancerous changes develop. We aimed to determine whether patients with SCD have a higher prevalence of simple renal cysts compared to non-SCD individuals.

Data for a group of 223 patients with SCD who had undergone an ultrasound and/or CT imaging of the abdomen were extracted for comparison with 180 control patients (haemoglobin genotype unknown), matched for age and ethnicity. Scans were evaluated for 198 SCD patients and 180 controls.

Renal cysts were found in 58% of the SCD group and 20% of the controls (OR 5.4 (CI 2.6–11.0), RR 2.8 (CI 1.9–4.2)). Bilateral renal cysts were found in 28% of the SCD participants in comparison with 5% of the control group. In those who had one or more cysts identified, the average number of cysts was 3.76 for the SCD group and 1.94 for the controls. Men with SCD were more likely to develop cysts than women (66% vs 53%), as were men without SCD (22% vs 17%).

Simple renal cysts occur more frequently, are more abundant and develop at a younger age in patients with SCD than ethnically-matched controls. Further study of the mechanism underlying cyst formation may shed light on both sickle cell nephropathy and other cystic renal diseases.

Antiretrovirals and the kidney in current clinical practice: Renal pharmacokinetics, alterations of renal function and renal toxicity, *AIDS*, 2014

Yombi, J.C., Pozniak, A., Boffito, M., Jones, R., Khoo, S., Levy, J., Post, F.A.

Assessment of renal function in HIV-positive patients is of increasing importance in the context of ageing and associated comorbidities. Exposure to nephrotoxic medications is widespread, and several commonly used antiretroviral drugs have nephrotoxic potential. Moreover, specific antiretrovirals inhibit renal tubular transporters resulting in the potential for drug-drug interactions as well as increases in serum creatinine concentrations, which affect estimates of glomerular filtration rate in the absence of changes in actual glomerular filtration rate. This review explores the effects of antiretroviral therapy on the kidney and offers an understanding of mechanisms that lead to apparent and real changes in renal function.

Bone: A new endocrine organ at the heart of chronic kidney disease and mineral and bone disorders, *The Lancet Diabetes and Endocrinology*, 2014

Vervloet, M.G., Massy, Z.A., Brandenburg, V.M., Mazzaferro, S., Cozzolino, M., Ureña-Torres, P., Bover, J., Goldsmith, D.

Recent reports of several bone-derived substances, some of which have hormonal properties, have shed new light on the bone-cardiovascular axis. Deranged concentrations of humoral factors are not only epidemiologically connected to cardiovascular morbidity and mortality, but can also be causally implicated, especially in chronic kidney disease. FGF23 rises exponentially with advancing chronic kidney disease, seems to reach maladaptive concentrations, and then induces left ventricular hypertrophy, and is possibly implicated in the process of vessel calcification. Sclerostin and DKK1, both secreted mainly by osteocytes, are important Wnt inhibitors and as such can interfere with systems for biological signalling that operate in the vessel wall. Osteocalcin, produced by osteoblasts or released from mineralised bone, interferes with insulin concentrations and sensitivity, and its metabolism is disturbed in kidney disease. These bone-derived humoral factors might place the bone at the centre of cardiovascular disease associated with chronic kidney disease. Most importantly, factors that dictate the regulation

of these substances in bone and subsequent secretion into the circulation have not been researched, and could provide entirely new avenues for therapeutic intervention.

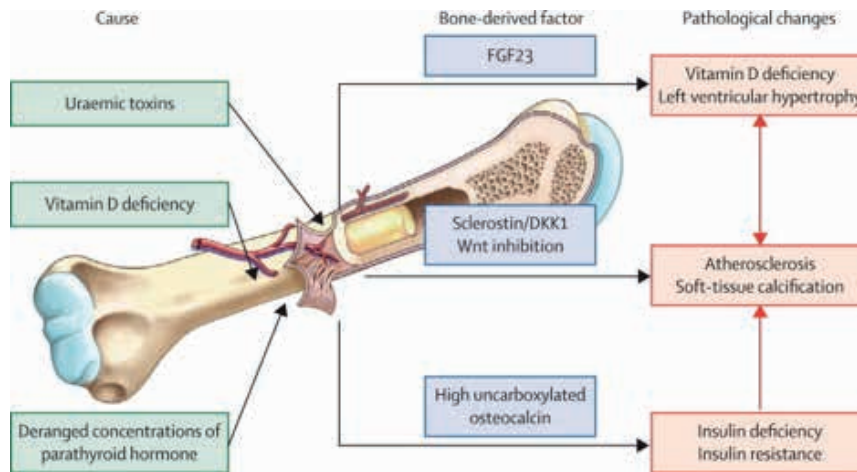
Urology

Simulation-based training and assessment in urological surgery, *Nature Reviews Urology*, 2016

Aydin, A., Raison, N., Khan, M.S., Dasgupta, P., Ahmed, K.

Simulation has become widely accepted as a supplementary method of training. Within urology, the greatest number of procedure-specific models and subsequent validation studies have been carried out in the field of endourology. Many generic-skills simulators have been created for laparoscopic and robot-assisted surgery, but only a limited number of procedure-specific models are available. By contrast, open urological simulation has only seen a handful of validated models. Of the available modalities, virtual reality (VR) simulators are most commonly used for endourology and robotic surgery training, the former also employing many high-fidelity bench models. Smaller dry-lab and ex vivo animal models have been used for laparoscopic and robotic training, whereas live animals and human cadavers are widely used for full

Figure 78 | The possible role of bone in CKD-MBD. Hormonal changes associated with CKD or poorly defined uraemic toxins (green boxes) induce changes in bone metabolism, leading to a maladaptive increase of several humoral factors (blue boxes) from bone into the circulation. These circulating factors directly induce pathological changes (red boxes). The red arrows show the amplifying effects of pathological changes induced by diseased bone. (CKD = chronic kidney disease. MBD = mineral bone disorders). Reproduced from *Nature Reviews Urology*.



procedural training. Newer concepts such as augmented-reality (AR) models and patient-specific simulators have also been introduced. Several curricula, including one recommended within, have been produced, incorporating various different training modalities and nontechnical skills training techniques. Such curricula and validated models should be used in a structured fashion to supplement operating room training.

King's Health Partners' Prostate Cancer Biobank (KHP PCaBB), *BMC Cancer*, 2017

Saifuddin, S.R., Devlies, W., Santaolalla, A., Cahill, F., George, G., Enting, D., Rudman, S., Cathcart, P., Challacombe, B., Dasgupta, P., Galustian, C., Chandra, A., Chowdhury, S., Gillett, C., Van Hemelrijck, M.

The KHP PCaBB was established in 2013 and recruits donors from the Urology or Oncology Departments at Guy's Hospital in London (UK). Prostate cancer patients may be approached to give their consent for biobanking at any point in their treatment pathway, which allows residual material from their earlier diagnosis to be transferred and used by the Biobank. Currently, patients are specifically asked to donate samples of blood and surplus prostate tissue as well as permitting access to their clinical and pathological data that continues to be added throughout the course of their disease. Between 2013 and 2015, 549 prostate cancer patients

gave their consent to the biobank and, the tissue repository collected 489 blood samples, 120 frozen prostate tissue samples and 1,064 formalin fixed paraffin embedded diagnostic blocks. Prostate cancer has become a chronic disease in a large proportion of men, with many men receiving multiple subsequent treatments, and their treatment trajectory often spanning over decades. Therefore, this resource aims to provide an ideal research platform to explore potential variations in treatment response as well as disease markers in the different risk categories for prostate cancer. A recent audit of the KHP PCaBB revealed that between 2013 and 2015, 1,796 patients were diagnosed with prostate cancer at King's Health Partners (KHP), out of which 549 (30.6%) gave their consent to KHP PCaBB. Comparisons between demographic and clinical characteristics of patients who had consented compared to the total patient population revealed that the KHP PCaBB is demographically representative of the total prostate cancer patient population seen in Guy's and St Thomas' NHS Foundation Trust (GSTT). We observed no differences in distribution of ethnicity ($p = 0.507$) and socioeconomic status ($p = 0.097$). Some differences were observed in clinical characteristics, specifically with treatment type - which differed significantly between the patients who had given consent and total patient population. The KHP PCaBB has thereby amassed a rich data and tissue repository that is largely reflective of both the demographic and clinical diversity within the total prostate cancer patient population seen at KHP, making it an ideal platform for prostate cancer research.

A single-centre early phase randomised controlled three-arm trial of open, Robotic, and Laparoscopic Radical Cystectomy (CORAL), *European Urology*, 2016

Khan, M.S., Gan, C., Ahmed, K., Ismail, A.F., Watkins, J., Summers, J.A., Peacock, J.L., Rimington, P., Dasgupta, P.

Laparoscopic radical cystectomy (LRC) and robot-assisted radical cystectomy (RARC) are increasingly popular, but high-level evidence for these techniques remains lacking. To compare the outcomes of patients undergoing open radical cystectomy (ORC), RARC, and LRC.

From March 2009 to July 2012, 164 patients requiring radical cystectomy for muscle-invasive bladder cancer or high-risk non-muscle-invasive bladder cancer were invited to participate, with an aim of recruiting 47 patients into each arm. Overall, 93 were suitable for trial inclusion; 60 (65%) agreed and 33 (35%) declined. Intervention ORC, RARC, or LRC with extracorporeal urinary diversion. Outcome measurements and statistical analysis Primary end points were 30- and 90-d complication rates. Secondary end points were perioperative clinical, pathologic, and oncologic outcomes, and quality of life (QoL). The Fisher exact test and analysis of variance were used for statistical analyses.

The 30-d complication rates (classified by the Clavien-Dindo system) varied significantly between the three arms (ORC: 70%; RARC: 55%; LRC: 26%; $p = 0.024$). ORC complication rates were significantly higher than LRC ($p < 0.01$). The 90-d complication rates did not differ significantly between the three arms (ORC: 70%; RARC: 55%; LRC 32%; $p = 0.068$). Mean operative time was significantly longer in RARC compared with ORC or LRC. ORC resulted in a slower return to oral solids than RARC or LRC. There were no significant differences in QoL measures. Major limitations are the small sample size and potential surgeon bias.

The 30-d complication rates varied by type of surgery and were significantly higher in the ORC arm than the LRC arm. There was no significant difference in 90-d Clavien-graded complication rates between the three arms. Patient summary We compared patients having open, robotic, or laparoscopic bladder removal surgery for bladder cancer and found no difference in Clavien-graded complication rates at 90 d.

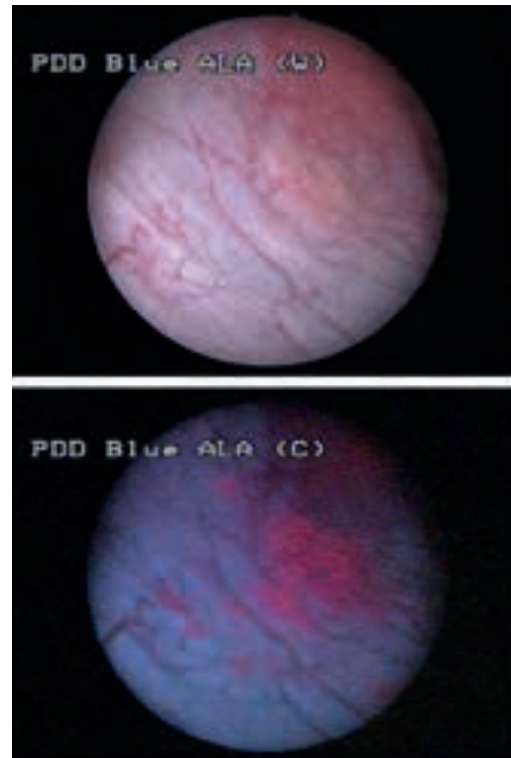
Recent advances in the diagnosis and treatment of bladder cancer, *BMC Medicine*, 2013

Cheung, G., Sahai, A., Billia, M., Dasgupta, P., Khan, M.S.

Bladder cancer is the commonest malignancy of the urinary tract. In this review, we look at the latest developments in the diagnosis and

management of this condition. Cystoscopy and urine cytology are the most important tools in the diagnosis and follow-up of bladder cancer. Various alternatives have been investigated, either to reduce the frequency of cystoscopy, or improve its sensitivity for detection of tumors. These include urine-based markers and point-of-care tests. Narrow-band imaging and photodynamic diagnosis/blue-light cystoscopy have shown promise in improving detection and reducing recurrence of bladder tumors, by improving the completion of bladder resection when compared with standard resection in white light. The majority of patients with a new diagnosis of bladder cancer have non-muscle-invasive bladder cancer, which requires adjuvant intravesical chemotherapy and/or immunotherapy. Recent developments in post-resection intravesical regimens are discussed. For patients with muscle-invasive bladder cancer, both laparoscopic radical cystectomy and robot-assisted radical cystectomy have been shown to reduce peri-operative morbidity, while being oncologically equivalent to open radical cystectomy in the medium term. Bladder-preserving strategies entail resection and chemoradiation, and in selected patients give equivalent results to surgery. The development, advantages, and disadvantages of these newer approaches are also discussed.

Figure 79 | Top – White-light and bottom – blue-light endoscopic image of flat lesions adjacent to a small papillary tumor. Reproduced from *BMC medicine* article.



Upper gastrointestinal

Extent of lymphadenectomy and prognosis after esophageal cancer surgery, *JAMA Surgery*, 2016

Lagergren, J., Mattsson, F., Zylstra, J., Chang, F., Gossage, J., Mason, R., Lagergren, P., Davies, A.

The prognostic role of the extent of lymphadenectomy during surgery for esophageal cancer is uncertain and requires clarification. **OBJECTIVE** To clarify whether the number of removed lymph nodes influences mortality following surgery for esophageal cancer.

Conducted from January 1, 2000, to January 31, 2014, this was a cohort study of patients who underwent esophagectomy for cancer in 2000–2012 at a high-volume hospital for esophageal cancer surgery, with follow-up until 2014. **EXPOSURES** The main exposure was the number of resected lymph nodes. Secondary exposures were the number of metastatic lymph nodes and positive to negative lymph node ratio.

The independent role of the extent of lymphadenectomy in relation to all-cause and disease-specific 5-year mortality was analyzed using Cox proportional hazard regression models, providing hazard ratios (HRs) with 95% CIs. The HRs were adjusted for age, pathological T category, tumor differentiation, margin status, calendar period of surgery, and response to preoperative chemotherapy.

Among 606 included patients, 506 (83.5%) had adenocarcinoma of the esophagus, 323 (53%) died within 5 years of surgery, and 235 (39%) died of tumor recurrence. The extent of lymphadenectomy was not statistically significantly associated with all-cause or disease-specific mortality, independent of the categorization of lymphadenectomy or stratification for T category, calendar period, or chemotherapy. Patients in the fourth quartile of the number of removed nodes (21–52 nodes) did not demonstrate a statistically significant reduction in all-cause 5-year mortality compared with those in the lowest quartile (0–10 nodes) (HR, 0.86; 95%CI, 0.63–1.17), particularly not in the most recent calendar period (HR, 0.98; 95%CI, 0.57–1.66 for years 2007–2012). A greater number of metastatic nodes and a higher positive to negative node ratio was associated with increased mortality rates, and these associations showed dose-response associations.

This study indicated that the extent of lymphadenectomy during surgery for esophageal cancer might not influence 5-year all-cause or disease-specific survival. These results challenge current clinical guidelines.

Surgical prevention of reflux after esophagectomy for cancer, *Annals of Surgical Oncology*, 2013

van der Schaaf M, Johar A, Lagergren P, Rouvelas I, Gossage J, Mason R, Lagergren J.

Reflux frequently occurs after a gastric conduit has replaced the resected esophagus. In this Swedish population-based cohort study, the potential antireflux effects of using cervical anastomosis, intrathoracic antireflux anastomosis, or pyloric drainage, and a risk of dysphagia due to cervical anastomosis and intrathoracic antireflux anastomosis were studied.

Patients undergoing esophagectomy with gastric conduit reconstruction in 2001–2005 were included. Reflux symptoms and dysphagia were assessed 6 months and 3 years postoperatively using a validated questionnaire (EORTC QLQ-OES18). The study exposures were cervical anastomosis, antireflux anastomosis, and pyloric drainage procedure. Multivariable logistic regression and propensity-adjusted analyses based on multinomial logistic regression estimated odds ratios (OR) with 95% confidence intervals (CI), adjusted for potential confounding.

A total of 304 patients were included in the study. Adjusted ORs for reflux symptoms were 0.9 (95% CI 0.3–2.2) for patients with a cervical anastomosis compared to patients with an intrathoracic anastomosis, 0.9 (95% CI 0.4–2.0)

for patients with an antireflux anastomosis versus patients with a conventional anastomosis, and 1.5 (95% CI 0.9–2.6) for patients after pyloric drainage versus patients without such a pyloric drainage procedure. Dysphagia was not statistically significantly increased after cervical anastomosis or antireflux anastomosis. ORs were virtually similar 3 years after surgery. No interactions were identified. The propensity analyses rendered similar results as the logistic regression models, except for a possibly increased dysphagia with a cervical anastomosis.

Cervical anastomosis, antireflux anastomosis, and pyloric drainage do not seem to prevent reflux symptoms 6 months or 3 years after esophagectomy for cancer with a gastric conduit.

Tumor stage after neoadjuvant chemotherapy determines survival after surgery for adenocarcinoma of the esophagus and esophagogastric junction, *Journal of Clinical Oncology*, 2014

Davies AR, Gossage JA, Zylstra J, Mattsson F, Lagergren J, Maisey N, Smyth EC, Cunningham D, Allum WH, Mason RC

Neoadjuvant chemotherapy is established in the management of most resectable esophageal and esophagogastric junction adenocarcinomas. However, assessing the downstaging effects

of chemotherapy and predicting response to treatment remain challenging, and the relative importance of tumor stage before and after chemotherapy is debatable.

We analysed consecutive resections for esophageal or esophagogastric junction adenocarcinomas performed at two high-volume cancer centres in London between 2000 and 2010. After standard investigations and multidisciplinary team consensus, all patients were allocated a clinical tumor stage before treatment, which was compared with pathologic stage after surgical resection. Survival analysis was conducted using Kaplan-Meier analysis and Cox regression analysis.

Among 584 included patients, 400 patients (68%) received neoadjuvant chemotherapy. Patients with downstaged tumors after neoadjuvant chemotherapy experienced improved survival compared with patients without response ($p < 0.001$), and such downstaging (hazard ratio, 0.43; 95% CI, 0.31–0.59) was the strongest independent predictor of survival after adjusting for patient age, tumor grade, clinical tumor stage, lymphovascular invasion, resection margin status, and surgical resection type. Patients downstaged by chemotherapy, compared with patients with no response, experienced lower rates of local recurrence (6% v 13%, respectively; $p = 0.030$) and systemic recurrence (19% v 29%, respectively; $p = 0.027$) and improved Mandard tumor regression scores ($p < 0.001$). Survival was strongly dictated by stage after neoadjuvant chemotherapy, rather than clinical stage at presentation.

The stage of esophageal or esophagogastric junction adenocarcinoma after neoadjuvant chemotherapy determines prognosis rather than the clinical stage before neoadjuvant chemotherapy, indicating the importance of focusing on postchemotherapy staging to more accurately predict outcome and eligibility for surgery. Patients who are downstaged by neoadjuvant chemotherapy benefit from reduced rates of local and systemic recurrence.

Lifestyle Intervention in Gastroesophageal Reflux Disease, *Clinical Gastroenterology and Hepatology*, 2016

Ness-Jensen, E., Hveem, K., El-Serag, H., Lagergren, J.

Gastroesophageal reflux disease (GERD) affects up to 30% of adults in Western populations and is increasing in prevalence. GERD is associated with lifestyle factors, particularly obesity and tobacco smoking, which also threatens the patient's general health. GERD carries the risk of several adverse outcomes and there is widespread use of potent acid-inhibitors, which are associated with long-term adverse effects. The aim of this systematic review was to assess the role of lifestyle intervention in the treatment of GERD.

Literature searches were performed in PubMed (from 1946), EMBASE (from 1980), and the Cochrane Library (no start date) to October 1, 2014. Meta-analyses, systematic reviews,

randomized clinical trials (RCTs), and prospective observational studies were included.

Weight loss was followed by decreased time with esophageal acid exposure in 2 RCTs (from 5.6% to 3.7% and from 8.0% to 5.5%), and reduced reflux symptoms in prospective observational studies. Tobacco smoking cessation reduced reflux symptoms in normal-weight individuals in a large prospective cohort study (odds ratio, 5.67). In RCTs, late evening meals increased time with supine acid exposure compared with early meals (5.2% point change), and head-of-the-bed elevation decreased time with supine acid exposure compared with a flat position (from 21% to 15%).

Weight loss and tobacco smoking cessation should be recommended to GERD patients who are obese and smoke, respectively. Avoiding late evening meals and head-of-the-bed elevation is effective in nocturnal GERD.

Lower gastrointestinal

Elderly patients have more infectious complications following laparoscopic colorectal cancer surgery, *Colorectal Disease*, 2016

Kvasnovsky, C.L., Adams, K., Sideris, M., Laycock, J., Haji, A.K., Haq, A., Nunoo-Mensah, J., Papagrigroriadis, S.

Elderly patients may be at higher risk of postoperative complications, particularly infective, than younger patients.

We prospectively followed 163 consecutive patients undergoing elective laparoscopic resection for cancer. We compared patients <65, 65–80 and >80 years of age at the time of surgery.

Seventy (42.9%) patients had no complication; 93 (57.1%) had at least one complication following surgery and in 20 (12.3%) this was major. There was no difference in major complications between the groups ($p = 0.47$). Patients over 65 years of age were more likely to have a complication of any severity [<65 years, 39.3%; 65–80 years, 69.3%; and >80 years, 63.0% ($p = 0.002$)]. The frequency of gastrointestinal complications (30.1%) was similar in the groups ($p = 0.29$), as was wound infection (25.2%) ($p = 0.65$). There was an increase in the frequency of infectious complications, especially chest infection, with age, from 14.8% in patients <65 years, to 22.7% in patients 65–80 years, to 44.4% in patients >80 years ($p = 0.01$). Multivariate analysis showed no increase in overall complications in elderly patients, but Stage II or Stage III cancer (OR = 2.59, $p = 0.04$) and increasing body mass index (BMI) (OR = 1.07 for each unit increase in BMI, $p = 0.04$) were related to complications. Age remained the only predictor of an infective complication on multivariate analysis. Patients >80 years of age had 4.21 times the OR of an infective complication ($p = 0.03$).

Older patients are more susceptible to infective complications postoperatively, particularly chest complications. Surgeons should alter their practice to reduce morbidity, such as adopting protocols requiring early physiotherapy.

Use of Confocal Laser Endomicroscopy to Assess the Adequacy of Endoscopic Treatment of Gastrointestinal Neoplasia: A Systematic Review and Meta-Analysis, *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*, 2015

Ypsilantis E, Pissas D, Papagrigroriadis S, Haji A.

Evaluation of the adequacy of endoscopic mucosal resection (EMR) of gastrointestinal lesions remains challenging by use of conventional endoscopy. Confocal laser endomicroscopy (CLE) is a novel imaging technique, designed to provide in vivo histology, and facilitate diagnosis with real-time intervention. We undertook a systematic review of the available literature, exploring the role of CLE in assuring completeness of EMR of gastrointestinal lesions. The number of pertinent studies is very limited, including only 1 randomized controlled study and 2 prospective comparative case series. Per-lesion meta-analysis showed that the sensitivity of CLE for detection of residual neoplasia was 91% (95% confidence interval, 82.5–96%) with specificity of 69% (95% confidence interval,

61–77%), with significant heterogeneity noted in all outcomes. In conclusion, the evidence underpinning the usefulness of CLE in ensuring adequate EMR of gastrointestinal neoplasia is currently very weak, with limited promising results related to gastric and colorectal polyp resections.

A randomized double-blind placebo-controlled trial of a multi-strain probiotic in treatment of symptomatic uncomplicated diverticular disease, *Inflammopharmacology*, 2017

Kvasnovsky, C.L., Bjarnason, I., Donaldson, A.N., Sherwood, R.A., Papagrigroriadis, S.

Diverticular disease is a significant burden on healthcare systems that is managed, surgically or medically, mainly as an emergency or acute condition. There are no standardized treatment recommendations for symptomatic uncomplicated disease. We hypothesized that a probiotic would reduce abdominal pain in such patients.

We conducted a single-center, double-blind, placebo-controlled trial of probiotic treatment (Symprove) in adult patients with moderate-to-severe chronic, non-acute symptomatic diverticular disease. 143 patients were randomized to receive 1 mL/kg/day of probiotic liquid (n = 72) or placebo (n = 71) daily for 3 months. The primary endpoint

was abdominal pain severity. Secondary endpoints consisted of the change in the frequency of eight abdominal symptoms and the level of intestinal inflammation (fecal calprotectin).

120 patients completed the trial. Abdominal pain score, the primary end point, decreased in both groups, but no significant difference between the groups was found ($p = 0.11$). In relation to placebo, the probiotic significantly decreased the frequency of four of the eight secondary endpoints: constipation, diarrhea, mucorrhea, and back pain ($p < 0.04$). No significant differences were found in frequency of abdominal pain, PR bleeding, dysuria, and bloating.

Multi-strain liquid probiotic did not improve abdominal pain scores significantly, but significantly improved the frequency of four other symptoms associated with chronic, non-acute symptomatic diverticular disease.

Stapled transanal rectal resection (STARR) for obstructive defaecation syndrome: patients with previous pelvic floor surgery have poorer long-term outcome, *Colorectal Disease*, 2013

Adams K, Papagrigroriadis S.

Stapled transanal rectal resection (STARR) is used for patients with obstructive defaecation syndrome (ODS) not responding to conservative management.

Reports indicate mixed results and there are no studies publishing the long-term outcome.

Following full investigation, 37 patients with ODS underwent a STARR procedure by one of the authors (SP) between 2005 and 2010.

The median (range) patient age was 53.0 (28–79) years and all were female. Median (range) follow up was 13 (0–57) months, and nine (24.3%) patients were followed for longer than 24 months. Eighteen patients had undergone at least one (and often multiple) previous gynaecological procedures, including hysterectomy ($n = 14$), colposuspension ($n = 3$), vaginal rectocele repair ($n = 4$) and pelvic floor repair ($n = 5$). Four patients had had at least one previous rectal operation [stapled anopexy ($n = 3$) and Delorme's procedure ($n = 2$)]. One patient did not attend for postoperative follow up. Of the remaining 36 patients, 18 had resolution of obstructive symptoms. Of the 18 with residual symptoms, 17 eventually reported the same level of symptoms as before the STARR procedure. There was a significant correlation between the presence of residual symptoms and long-term ODS recurrence ($p < 0.0005$). For those with residual symptoms, the mean (95% CI) time to symptom recurrence was 3 (2.86–11.81) months. Twenty (56%) patients were satisfied with the outcome from the STARR procedure.

Residual symptoms are a strong indicator of long-term failure. STARR was effective for symptom resolution in 50% of patients. Those who had undergone pelvic floor or rectal prolapse surgery were significantly more likely to experience recurrent symptoms.

High frequency mini probe ultrasound as a useful adjunct in the management of patients with malignant colorectal polyps, *Colorectal Disease*, 2013

Haji A, Ryan S, Bjarnason I, Papagrigroriadis

Colorectal polyps with a focus of malignancy, identified postpolypectomy, pose a management challenge of whether endoscopic treatment is adequate or whether further surgical resection is required. This study assessed 12- and 20-MHz colonoscopic ultrasound to evaluate the presence of residual disease and local lymph nodes.

Consecutive cases of all colorectal polyps with a focus of malignancy were included. Colonoscopic high-frequency ultrasound was performed (20-MHz mini-probes for residual polyps and 12-MHz ultrasound for local lymph nodes) in the region of previous polypectomy. Biopsies were taken of the polypectomy site if any abnormalities were seen.

Twenty-one malignant polyps (sigmoid, n = 10; rectum, n = 8; transverse colon, n = 1; ascending colon, n = 1; and caecum, n = 1) were identified. All were invasive adenocarcinomas; 12 were intramucosal and nine were submucosal (seven sm1 lesions in the upper third of the submucosa; and two sm2 lesions in the middle third of the submucosa). Excision was histologically complete in 12 patients, four had involved margins and histology was uncertain in five owing to diathermy artefacts. Further colonoscopy revealed

a residual abnormality in eight patients. The 12- and 20-MHz ultrasound imaging revealed mucosal irregularity with normal bowel-wall layers and no lymph-node involvement, with normal histology. High-frequency ultrasound was normal in the remaining 13 patients. At the time of writing, 15 (72%) of the 21 patients were disease free without further surgery. Six of the 21 patients underwent surgery, despite normal high-frequency ultrasound findings, because of submucosal invasion (sm1 or sm2) and uncertain completeness of resection. The specimens were free of cancer in all six patients.

High-frequency ultrasound is feasible for the assessment of colorectal malignant polyps.

Gastroenterology

A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial, *Gastroenterology*, 2017

Staudacher, H.M., Lomer, M.C.E., Farquharson, F.M., Louis, P., Fava, F., Franciosi, E., Scholz, M., Tuohy, K.M., Lindsay, J.O., Irving, P.M., Whelan, K.

Dietary restriction of fermentable carbohydrates (a low FODMAP diet) has been reported to reduce symptoms in some patients with irritable bowel syndrome (IBS). We performed a randomized, placebo-controlled study to determine its effects on symptoms and the fecal microbiota in patients with IBS.

We performed a 2x2 factorial trial of 104 patients with IBS (18–65 years old), based on the Rome III criteria, at 2 hospitals in the United Kingdom. Patients were randomly assigned (blinded) to groups given counselling to follow a sham diet or diet low in FODMAPs for 4 weeks, along with a placebo or multistrain probiotic formulation, resulting in 4 groups (27 receiving sham diet/placebo, 26 receiving sham diet/probiotic, 24 receiving low FODMAP diet /placebo, and 27 receiving low FODMAP diet/probiotic). The sham diet restricted a similar number of staple and non-staple foods as the low FODMAP diet; the diets had similar degrees of difficulty to follow. Dietary counselling was given to patients in all groups and data on foods eaten and compliance were collected. The incidence and severity of 15 gastrointestinal symptoms and overall symptoms were measured daily for 7 days before the study period; along with stool frequency and consistency. At baseline, global and individual symptoms were measured, along with generic and disease-specific health-related quality of life, using standard scoring systems. All data were collected again at 4 weeks, and patients answered questions about adequate symptom relief. Fecal samples were collected at baseline and after 4 weeks and analyzed by quantitative PCR and 16S rRNA sequencing. The co-primary

endpoints were adequate relief of symptoms and stool Bifidobacterium species abundance at 4 weeks.

There was no significant interaction between the interventions in adequate relief of symptoms ($p = 0.52$) or Bifidobacterium species ($p = 0.68$). In the intention-to-treat analysis, a higher proportion of patients in the low FODMAP diet had adequate symptom relief (57%) than in the sham diet group (38%), although the difference was not statistically significant ($p = 0.051$). In the per-protocol analysis, a significantly higher proportion of patients on the low FODMAP diet had adequate symptom relief (61%) than in the sham diet group (39%) ($p = 0.042$). Total mean IBS-Severity Scoring System score was significantly lower for patients on the low FODMAP diet (173 ± 95) than the sham diet (224 ± 89) ($p = 0.001$), but not different between those given probiotic (207 ± 98) or placebo (192 ± 93) ($p = 0.721$). Abundance of Bifidobacterium species was lower in fecal samples from patients on the low FODMAP diet (8.8 rRNA genes/g) than patients on the sham diet (9.2 rRNA genes/g) ($p = 0.008$), but higher in patients given probiotic (9.1 rRNA genes/g) than patients given placebo (8.8 rRNA genes/g) ($p = 0.019$). There was no effect of the low FODMAP diet on microbiota diversity in fecal samples.

In a placebo-controlled study of patients with IBS, a low FODMAP diet associates with adequate symptom relief and significantly reduced symptom scores compared with placebo. It is not clear whether changes resulted from collective FODMAP restriction or removal of a single component, such as lactose. Co-administration of the multistrain

probiotic increased numbers of Bifidobacterium species, compared with placebo, and might be given to restore these bacteria to patients on a low FODMAP diet.

Researchers in the group have also contributed to the development of several international multi-centre papers including features in the prestigious *Nature* journal.

Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease, *Nature*, 2012

Jostins, L., Ripke, S., Weersma, R. K., Duerr, R. H., McGovern, D. P., Hui, K. Y., ... Cho, J. H.

Crohn's disease and ulcerative colitis, the two common forms of inflammatory bowel disease (IBD), affect over 2.5 million people of European ancestry, with rising prevalence in other populations. Genome-wide association studies and subsequent meta-analyses of these two diseases as separate phenotypes have implicated previously unsuspected mechanisms, such as autophagy, in their pathogenesis and showed that some IBD loci are shared with other inflammatory diseases. Here we expand on the knowledge of relevant pathways by undertaking a meta-analysis of Crohn's disease and ulcerative colitis genome-wide association scans, followed by extensive validation of significant findings, with a combined

total of more than 75,000 cases and controls. We identify 71 new associations, for a total of 163 IBD loci, that meet genome-wide significance thresholds. Most loci contribute to both phenotypes, and both directional (consistently favouring one allele over the course of human history) and balancing (favouring the retention of both alleles within populations) selection effects are evident. Many IBD loci are also implicated in other immune-mediated disorders, most notably with ankylosing spondylitis and psoriasis. We also observe considerable overlap between susceptibility loci for IBD and mycobacterial infection. Gene co-expression network analysis emphasizes this relationship, with pathways shared between host responses to mycobacteria and those predisposing to IBD.

Bariatric surgery

Metabolic surgery for the treatment of type 2 diabetes in obese individuals, *Diabetologia*, 2018

Cummings, D.E., Rubino, F.

Several bariatric operations originally designed to promote weight loss have been found to powerfully treat type 2 diabetes, causing remission in most cases, through diverse mechanisms additional to the secondary consequences of weight loss. These observations have prompted consideration of such operations as 'metabolic

surgery', used expressly to treat diabetes, including among patients who are only mildly obese or merely overweight. Large, long-term observational studies consistently demonstrate that bariatric/metabolic surgery is associated with reductions in all cardiovascular risk factors, actual cardiovascular events, microvascular diabetes complications, cancer and death. Numerous recent randomised clinical trials, directly comparing various surgical vs non-surgical interventions for diabetes, uniformly demonstrate the former to be superior for improvements in all glycaemic variables, as well as other metabolic endpoints. These benefits are similar among individuals with type 2 diabetes and a preoperative BMI of 30–35 kg/m² compared with traditional bariatric surgery patients with a BMI >35 kg/m². The safety profiles of modern laparoscopic bariatric/metabolic operations are similar to those of elective laparoscopic hysterectomy and knee arthroplasty. However, more evidence regarding the risks, benefits and costs of surgery is needed from very long-term (>5 year) randomised clinical trials powered to observe 'hard' clinical endpoints following the operations most commonly used today. Given the efficacy, safety and cost-effectiveness of metabolic surgery, the second Diabetes Surgery Summit (DSS-II) consensus conference recently placed surgery squarely within the overall diabetes treatment algorithm, recommending consideration of this approach for patients with inadequately controlled diabetes and a BMI as low as 30 kg/m², or 27.5 kg/m² for Asian individuals. These new guidelines have been formally ratified by 53 leading diabetes and surgery societies worldwide. Given this broad level of endorsement, we feel that the DSS-II recommendations should now replace

the outdated National Institutes of Health (NIH) suggestions that have governed bariatric surgery practice and insurance compensation worldwide since 1991.

The Effect of Bariatric Surgery on Intestinal Absorption and Transit Time, *Obesity Surgery*, 2014

Carswell, K. A., Vincent, R., Belgaumkar, A. P., Sherwood, R., Amiel, S. A., Patel, A., le Roux, C. W.

Bariatric surgical procedures are classified by their presumed mechanisms of action: restrictive, malabsorptive or a combination of both. However, this dogma is questionable and remains unproven. We investigated post-operative changes in nutrient absorption and transit time following bariatric surgery.

Participants were recruited into four groups: obese controls (body mass index (BMI) >30 kg/m²), n = 7), adjustable gastric banding (n = 6), Roux-en-Y gastric bypass (RYGB, n = 7) and biliopancreatic diversion with duodenal switch (DS, n = 5). Participants underwent sulphasalazine/sulphapyridine tests (oro-caecal transit time); fasting plasma citrulline (functional enterocyte mass); 3 days faecal collection for faecal elastase 1 (FE-1); calprotectin (FCp); faecal fatty acids (pancreatic exocrine function, gut inflammation and fat excretion, respectively); and 5 h d-xylose, l-rhamnose and lactulose test (intestinal absorption and permeability).

Age and gender were not different but BMI differed between groups ($p = 0.001$). No difference in oro-caecal transit time ($p = 0.935$) or functional enterocyte mass ($p = 0.819$) was detected. FCp was elevated post-RYGB vs obese ($p = 0.016$) and FE-1 was reduced post-RYGB vs obese ($p = 0.002$). Faecal fat concentrations were increased post-DS vs obese ($p = 0.038$) and RYGB ($p = 0.024$) and were also higher post-RYGB vs obese ($p = 0.033$). Urinary excretion of d-xylose and l-rhamnose was not different between the groups; however, lactulose/rhamnose ratio was elevated post-DS vs other groups (all $p < 0.02$), suggesting increased intestinal permeability.

Following RYGB, there are surprisingly few abnormalities or indications of severe malabsorption of fats or sugars. Small bowel adaptation after bariatric surgery may be key to understanding the mechanisms responsible for the beneficial metabolic effects of these operations.

Acknowledgements

In addition to the teams at King's Health Partners and the Health Innovation Network, the CAG would like to thank the following for contributing to the development of this outcomes book:

- Alberto Sanchez Fueyo
- Francesco Rubino
- Mark George
- Aryn Haji
- Iain MacDougall
- Mike Heneghan
- Andreas Prachialis
- Ivan de Mello
- Nick Powell
- Andy Williams
- Jacky Sinclair
- Nigel Heaton
- Bu Hayee
- James Gossage
- Paula Allchorne
- Ceri Freeman
- Jeremy Sanderson
- Prokar Dasgupta
- Chris Callaghan
- John Jeffords
- Raj Srirajaskathan
- David Hardy
- Kate Childs
- Sabina Demartino
- Debbie Shawcross
- Katie Vinen
- Shamim Khan
- Ellie Asgari
- Kosh Agarwal
- Steven Sacks

King's Health Partners
Ground Floor
Counting House
Guy's Hospital
London SE1 9RT

Tel: 44 (0)20 7188 4058

Email: kingshealthpartners@kcl.ac.uk

Website: www.kingshealthpartners.org

Twitter: @kingshealth



Guy's and St Thomas' 
NHS Foundation Trust

King's College Hospital 
NHS Foundation Trust

South London and Maudsley 
NHS Foundation Trust