Prioritisation of Topics for Future Specialised Services Research 2018
Contents

Introduction ................................................................................................................. 3

1 Internal Medicine ................................................................................................. 4
   Specialised Respiratory (A01) ................................................................................. 4
   Hepatobiliary & Pancreas (A02) .............................................................................. 4
   Specialised Endocrinology (A03) ............................................................................ 4
   Specialised Vascular (A04) ..................................................................................... 4
   Cardiothoracic Services (A05) ................................................................................ 4
   Renal Services (A06) .............................................................................................. 4
   Specialised Rheumatology (A09) ............................................................................ 5

2 Cancer ................................................................................................................. 6
   Radiotherapy (B01) ................................................................................................. 6
   Cancer Surgery (B03) ............................................................................................. 7
   Cancer Diagnostics (B04) ....................................................................................... 7
   Children & Young People (B05) .............................................................................. 7

3 Mental Health ...................................................................................................... 8
   Specialised Mental Health (C01) ............................................................................. 8
   Adult Secure (C02) ................................................................................................. 8
   Child and Adolescent Mental Health Services (CAMHS) (C03) .............................. 8
   Perinatal Mental Health (C04) ................................................................................. 9

4 Trauma .............................................................................................................. 10
   Rehabilitation & Disability (D01) ........................................................................... 10
   Major Trauma & Burns (D02) ................................................................................ 10
   Spinal Services (D03) ........................................................................................... 10
   Neurosciences (D04) ............................................................................................ 10
   Adult Critical Care (D05) ....................................................................................... 11
   Ears and Ophthalmology (D06) ............................................................................. 11
   Specialised Pain (D07) .......................................................................................... 11
   Hyperbaric Oxygen Therapy (HBOT) .................................................................... 12

5 Women and Children ......................................................................................... 12
   Medical Genetics (E01) ......................................................................................... 12
   Paediatric Medicine (E03) ..................................................................................... 12
   Congenital Heart Services (E05) ........................................................................... 12
   Metabolic Disorders (E06) .................................................................................... 13

6 Blood and Infection ............................................................................................. 13
   Blood & Marrow Transplant (F01) ......................................................................... 13
   HIV (F03) .............................................................................................................. 13
   Infectious Diseases (F04) ..................................................................................... 13
   Haemoglobinopathies (F05) ................................................................................. 13
   Immunology & Allergy (F06) ................................................................................ 13
Introduction

As the single commissioner (funder) of NHS specialised services in England, NHS England is in a unique position to influence the future focus of research into specialised care. We can do this both by sharing our understanding of current research priorities with research funding partners (for example by highlighting areas of current and future NHS specialised clinical practice in which the clinical evidence may currently be incomplete) and by making decisions around which studies we provide funding for as part of our responsibilities to consider ‘excess treatment costs’ for non-commercial research studies (excess treatment costs or ‘ETCs’ are the additional costs of care provided in line with a study’s protocol over and above the costs of routinely funded NHS clinical practice).

This document lists suggested current priorities for future research as identified by our Clinical Reference Groups.
1 Internal Medicine

Specialised Respiratory (A01)

1. Pulmonary Hypertension: Exercise Training (Pulmonary Rehabilitation) in Pulmonary Hypertension.
2. Severe Asthma: Understanding the impact of Severe Asthma on health care utilisation and outcomes - the development of a national registry.
3. Interstitial lung disease: Improving our understanding of the impact of pulmonary hypertension on outcomes in interstitial lung disease.
4. Cystic Fibrosis: A systematic review of research priorities has been identified by work performed in partnership with the James Lind Alliance http://www.jla.nihr.ac.uk/priority-setting-partnerships/cystic-fibrosis/

Hepatobiliary & Pancreas (A02)

2. Preoperative (neoadjuvant) therapy versus standard postoperative therapy for resectable pancreatic cancer.
3. Radiofrequency ablation (RFA) versus irreversible electroporation (IRE) for centrally located hepatocellular carcinoma (HCC) up to 3cm.
4. Transjugular intrahepatic porto–systemic shunt (TIPS) for variceal haemorrhage.

Specialised Endocrinology (A03)

1. Adrenal surgery for adrenal incidentaloma in patients with incidentally found adrenal cortex tumours (10% of the population aged 70y) with excess cortisol secretion (30-50% of these) – 3-5% of the ageing population.

Specialised Vascular (A04)

1. Claudication
2. Deep vein intervention
3. Aortic Aneurysm Repair

Cardiothoracic Services (A05)

1. Outcomes (PROMS and maintenance of sinus rhythm maintenance) following atrial fibrillation ablation.
2. Outcomes (PROMS and frequency of appropriate and inappropriate defibrillation) following Implantable Cardioverter Defibrillator implantation.
3. Outcomes (mortality, readmissions, PROMS) following transcatheter aortic valve implantation.

Renal Services (A06)

1. Address health inequalities in access to dialysis and transplantation, especially for ethnic minorities.
2. Establish a national biobank for transplant recipients.
3. Develop an infrastructure to collect QOL and PROMS data on all dialysis and transplant patients, so that these outcomes are available for all trials.

**Specialised Rheumatology (A09)**

   
   **Inclusion criteria:**
   
   i. Patients aged between 18 and 75 years
   
   ii. Patients with four or more criteria for SLE according to the American College of Rheumatology (ACR) 1997 criteria or SLICC 2012 Criteria or biopsy proven lupus nephritis with one additional supportive test on at least two occasions (positive ANA, anti-dsDNA antibodies or anti-Sm antibodies)
   
   iii. Patients with Hb levels at screening below 120 g/l.
   
   iv. Patients with significant fatigue measured by the Fatigue Severity Score-FSS (defined as a score above 36).
   
   v. Patients with platelets levels at screening above 100 x10^9/l.
   
   vi. Ability to provide informed consent

   As no previous studies of iron therapy in patients with lupus are available, we opted for an early phase study design powered on changes in the haemoglobin (Hb) levels, using a cut-off value (ΔHb) of 8 g/l, which was associated with benefits in fatigue levels in patients with cardiac disease was achieved in the majority of patients after a single dose iron infusion.

   We propose to recruit 60 SLE patients (>18 years), and randomise 30 patients to receive a single dose iron infusion and standard of care and 30 patients to receive placebo and standard of care (randomisation 1:1).

   The patient and treating physician/nurse will be blinded to the study medication. The sample size was calculated at 80% power and 5% significance level, assuming a 10% drop-out rate. We also took into account and an additional 20% severe SLE flare related drop-out rate.

2. Rituximab for idiopathic inflammatory myopathy.

   Idiopathic inflammatory myopathies (IIM) are heterogeneous autoimmune disorders of considerable health impact. IIM are thought to be complex genetic diseases, initiated by immune activation following specific environmental events in genetically predisposed individuals. IIM are characterized by inflammation of muscle tissue, leading to weakness, fatigue and associated disability with associated comorbidities such as cancer and interstitial lung disease. Overall, IIM sufferers are often left permanently disabled from irreversible muscle and organ damage, due to delays in diagnosis and poorly targeted existing therapeutic treatments. Currently, preventative strategies don’t exist to identify those patients who may be at risk of developing IIM or those that will respond well to specific treatments.

   The cornerstone of IIM treatment is control of inflammation with immunosuppressive therapy. In patients with severe refractive disease, a B cell depleting agent such as Rituximab (RTX) may be used. Identifying clinical and cellular biomarkers for severe and refractive
disease, and poor responders to RTX, would minimise continuing muscle and organ damage and exposure to side effects as well as increasing our understanding of the pathogenesis of IIM. We propose to include adult-onset IIM patients, with active inflammatory disease, about to start rituximab (RTX). Subgroups of patients would include patients with particular extra-muscular manifestations including predominantly lung disease (interstitial lung disease, ILD) or skin involvement (dermatomyositis, DM).

NHS England estimate that 60 patients per year with IIM will be commencing RTX and entered on to the MYOACT registry. We would aim to capture patients being recruited into an existing research study, MYOPROSP. We estimate that 30 IIM patients per year starting RTX could be recruited into MYOPROSP (over the last 14 months, 30 such RTX starters have already been recruited).

3. Rituximab retreatment according to B cell numbers for systemic lupus erythematosus.

4. Tocilizumab for severe resistant giant cell arteritis.

## 2 Cancer

### Radiotherapy (B01)

1. Stereotactic ablative radiotherapy (SABR) for hepatocellular carcinoma (HCC). HCC usually arises in people with liver cirrhosis, the common causes of which include alcohol consumption, metabolic syndrome, and chronic viral infections. Patients who are eligible are offered liver transplant; the remainder are usually treated with RFA and/or TACE2. Disease recurrence and progression after these treatments is common. These patients are offered palliative systemic therapy if performance status is permissive. A proportion of patients with HCC are not suitable for invasive ablation procedures or palliative systemic therapy due to co-morbid illnesses, despite retaining a good performance status. Patients with progressive disease after RFA/TACE, or those who are not suitable, with good performance status and acceptable liver function, are the target group for the proposed study. This is closely aligned with the existing criteria for SABR within the CtE programme.

A one-sided log rank test with an overall sample size of 150 subjects (75 in the control group and 75 in the SABR group) would achieve an 80.2% power at a 20% significance level to detect a hazard ratio of 0.74 (equivalent to an improvement of median overall survival from 8.5 months in the control group to 11.5 months in the SABR group). The trial would recruit over 36 months with a minimum one-year follow-up (of the last patient). Given the rate of accrual to date within the CtE programme, we believe that a rate of accrual of 50 patients/year across the same centres is feasible. Please note that this statistical analysis is provisional.

2. Using big data to improve radiotherapy outcomes.
3. Utilising MR to improve radiotherapy delivery.

**Cancer Surgery (B03)**

1. Device evaluation (indications and outcomes associated with) including but not confined to robotic surgery.
2. The impact of increased case volume arising from centralisation.
3. Outcomes associated with specialist care models for less common cancers.
4. The value associated with national MDT panels for rare conditions.
5. The meaning of precision medicine to cancer surgery.

**Cancer Diagnostics (B04)**

1. FDG PET CT - Assessment of PET-MRI in paediatric oncology as an alternative to PET-CT.
   Paediatric patients currently undergo PET-CT and MRI staging in a number of tumour subgroups including lymphoma and neuroblastoma. A combined PET-MRI scan could offer a one stop shop that limits the number of appointments patients must attend reducing time in hospitals, sedation/anaesthetics (if required) and reducing radiation dose.
2. FDG PET CT - Assessment of patients with osteosarcoma and Ewing’s sarcoma.
   Patients with Osteosarcoma (OS) and Ewing’s sarcoma (ES) which are the most common paediatric bone tumours. It is anticipated that a population of more than 50 patients with Ewings sarcoma and more than 50 patients with Osteosarcoma will need to be included.
3. PET CT - Assessment and comparison of FDG metabolic activity on PET-CT and Diffusion Weighted Imaging (DWI) on MRI in treatment response assessment (broad pathway proposal).
   For patients with tumours undergoing chemotherapy or radiotherapy that would normally have FDG PET-CT as part of their staging and response assessment. Measure the ability of DWI to assess treatment response in comparison to FDG PET-CT. Subgroups would include Myeloma and lymphoma. Analysis could be performed on PET-MRI scanners or standalone PET-CT scanners and MRI scanners. Large scale multisite study to ensure adequate power. Long term follow up to ensure response assessment is accurate.

**Children & Young People (B05)**

1. Impact of treatment on quality of life/ future health in children and young people (life course) and efficacy of interventions to mitigate.
3. Provision of psychosocial support to patients and families with a cancer diagnosis (could be chronic disease).
4. Evaluation of interventions to mitigate the Impact of current treatments on children and young people with brain tumours.
3 Mental Health

Specialised Mental Health (C01)

1. Systematic review of treatment across the age ranges to address disparities between evidence and NICE guidelines for treatment of eating disorders.
2. Treatment of self harm for young people with personality disorder.

Adult Secure (C02)

1. Tiered services for personality disorder (persistent, problematic and pervasive interpersonal difficulties, and harm to self and others).

Child and Adolescent Mental Health Services (CAMHS) (C03)

1. Genetic investigation of severe mental illness to discover the rates of atypically presenting Mendelian genetic disorders in child psychiatric inpatients.
   
   For children aged 12 years or under who have been admitted for residential treatment of a severe and complex psychiatric illness to include psychosis, eating disorders, affective disorders, developmental disorders (including autism, ADHD and tic disorders), obsessive compulsive disorders, anxiety and emotional disorders, self-harm and emotional regulation disorders, primary diagnosis of a mental illness with co-morbid learning difficulties and somatising disorders.
   
   For children aged 13, 14 or 15 who have been admitted for residential treatment of psychosis.
   
   For children aged 13, 14, or 15 who have been admitted for residential treatment of severe and complex psychiatric illness who have:
   - a first-or second degree relative with psychosis, autism, epilepsy, developmental delay/intellectual disability (DD/ID)), OR
   - related parents (e.g. parents are first/ second cousins), OR
   - neurological signs (such as ataxia or another movement disorder that pre-dates drug treatment), seizures or MRI abnormalities, OR
   - other clinical features suggesting a genomic cause (e.g. narcolepsy, severe cardiac/cardiomopathy, autoimmune disorders, skeletal abnormalities, deafness, dysmorphic features).

   By focusing on the unusually early-onset, most severely affected individuals (as evidenced by the necessity of in-patient or residential treatment), we maximally enrich the cohort for those with rare identifiable Mendelian causes.

2. Analysis of patient-staff interactions in adolescent psychiatric units and relation to outcome.
There are no systematic analyses of patient-staff interactions in adolescent psychiatric units which can inform overall therapeutic processes and how, these in turn, relate to patient outcomes. For non-psychotic adolescents admitted to Tier 4 facilities, this would be a pilot for feasibility and estimate of effect sizes, N = 60. We will carry out this study on the Highfield Unit in Oxford and at 4 further units, with whom we have close links.

3. Psychiatric and economic evaluation of admissions to distant adolescent psychiatric units
   Admission to distant (over 50 miles from home base) adolescent units is thought to be associated with adverse psychiatric outcomes and increased family hardship. Over a one-year period, it is proposed to quantify the number of such cases nationally, and to determine the effects of such displacement upon adolescent mental health outcomes and the families. For all adolescents admitted to general psychiatric units and eating disorder units – either adolescent or adult - nationally within a year period 2018- 2019.

4. Evaluation of ‘far away’ admissions to adolescent psychiatric units over 50 miles from home base to determine the number of ‘far away’ admissions with a one-year period and the effects of such displacement upon adolescent mental health outcomes and the effects upon the families. For all adolescents admitted to a psychiatric unit –either adolescent or adult - in 3 English regions within a year period 2018- 2019.

5. Investigation of staff-patient interactions as determinants of outcomes of adolescents with borderline personality disorder (A-BPD) admitted to adolescent inpatient psychiatric units to assess the wide variation in outcomes and negative effects of admission for patients with A-BPD.

6. A Tier 4 CAMHS (Child and Adolescent Mental Health Service) reorganisation in Greater Manchester: evaluation over 12 months pre and post reorganisation to evaluate the health service outcomes and costs of this service re-organisation. For all patients (under 18 years) referred to the Single point of entry into the Greater Manchester Tier 4 provider network (child and general adolescent/PICU referrals).

Perinatal Mental Health (C04)

1. Evaluation of routine clinical outcomes measurement (RCOMS) on an inpatient mother and baby unit for severe mental illness in the perinatal period.
2. Admission to a Mother and Baby Unit for severe mental illness in the perinatal period of women from a range of diverse backgrounds including BAME and LGBT.
3. Admission to a Mother and Baby Unit for severe mental illness in the perinatal period of women under the care of in reach/outreach teams and inpatients of the MBUs.
4 Trauma

Rehabilitation & Disability (D01)


2. Systematic assessment and follow-up through establishment of a national clinical registry for prolonged disorders of consciousness to provide critical data on frequency, prognosis and costs to support planning and delivery of services and improve patient care for this vulnerable group. For patients in prolonged disorders of consciousness (PDOC) following sudden onset severe brain injury. Approximately 500 per year in the first instance but rising over time once the database is established.

3. Provision of microprocessor prosthetic knees to limited mobility walkers. The population group will be transfemoral or knee disarticulation amputees, categorised as K2 activity level. Based on previous literature and expert opinion in the field, this group will subdivided into K2a (higher mobility) and K2b (lower mobility). The intervention will be MPK vs mechanical knee. There will be an MPK group and a non-MPK group for each K2a and K2b. We will aim for 30 participants in each group, giving a total of 120 participants.

Major Trauma & Burns (D02)

1. Core Outcome Set for burn care. Standardise research trials in order to allow evidence synthesis currently impossible in burn care.

2. Look at the psychological needs of patients - and carers of patients - who have functional limitations and/or changes in appearance as a result of major trauma or burns but are not flagged by routine screening processes.

3. What & how rehabilitation should be delivered for people with predominantly MSK injuries, or injuries with MSK consequences (such as abdominal & chest trauma) once patients leave hospital.

Spinal Services (D03)

1. Treatment strategies for reducing or preventing a scoliosis from deteriorating to avoid need for surgery.

2. Vertebral body tethering (VBT) in idiopathic scoliosis for progressive idiopathic scoliosis in a child 8 years and above with skeletal growth potential.


Neurosciences (D04)

1. Deep brain stimulation for epilepsy.

2. Deep brain stimulation for Tourette’s.

3. Service delivery evaluation of care pathway for functional neurological disorder (FND) to establish evidence for a service delivery model for the diagnosis and management of FND in order to inform future service delivery and commissioning of care.
Adult Critical Care (D05)

2. Is critical care outreach effective? How can we use big data analysis in physiological observations and review of deteriorating patients and prognostication?
3. ECMO for cardiac arrest: evaluation for efficacy.
4. Sport for recovery post critical care.
5. Psychology of decision making and consistent care over seven days with decision support systems (electronic systems).

Ears and Ophthalmology (D06)

1. Interventions (drugs, devices, biomaterials, dressings) for reducing long-term effects of scar formation in patients presenting with immunobullous diseases or significant skin and mucous membrane loss.
2. Risk stratification of corneal transplantation to improve outcome of corneal transplantation. For patients undergoing corneal transplantation for Fuchs endothelial corneal dystrophy and pseudophakic bullous keratopathy. Of the 3000 corneal transplants are undertaken in the UK each year approximately 1500 (50%) of these are for FECD and PBK.
3. Gender risk stratification of corneal transplantation to improve outcome of corneal transplantation according to gender matching. For patients undergoing corneal transplantation – approximately 3000 corneal transplants are undertaken in the UK each year. Patients and donors to be stratified according to gender. To determine the benefit, a two year study inclusion with a two year follow-up is needed. Therefore in total a five year study assuming a one year recruitment.
4. Utilising genetics/genomics to develop preventative therapy and personalised treatment for inherited disease for Mendelian genetic disorders and multifactorial common disease with partial genetic aetiology.
5. Development of a patient reported outcome measures to properly assess the impact of costly interventions on patients’ quality of life for patient led design of specialist services.
6. The provision of cochlear implant[s] for severe or profound deafness, as specified in NICE TA 166.
7. Dry eye disease; improving societal burden.
8. Mental health and cataract surgery.

Specialised Pain (D07)

1. High frequency spinal cord stimulation for adults with chronic neuropathic pain of failed back surgery syndrome.
2. Radiofrequency denervation for low back pain of facet joint origin.
4. Intrathecal drug delivery for adults with chronic non-malignant pain.
Hyperbaric Oxygen Therapy (HBOT)

1. Evaluation of hyperbaric oxygen therapy for mandibular osteoradionecrosis.
2. Evaluation of hyperbaric oxygen therapy for diabetic foot wounds.
4. Evaluation of hyperbaric oxygen therapy for malignant otitis externa.

5 Women and Children
Medical Genetics (E01)

1. The impact of whole genome and whole exome sequencing on the patient pathway—a health economic and health outcomes analysis of severe early onset paediatric neurological disease.
2. Towards a molecular re-classification of disease—impact of molecular testing on defining the natural history, surveillance, health care needs and patient outcomes in inherited rare cancer syndromes.
3. Development of a comprehensive free fetal DNA testing strategy-application to non-invasive prenatal testing for Mendelian diseases.

Paediatric Medicine (E03)

1. Assessing the indications and outcomes of paediatric endoscopy (and patient perception of endoscopy) for paediatric gastroenterology.
   Retrospective patient outcome data of 1000 patients in England recruited over a 3 month period obtained from 4-6 regional paediatric endoscopy units, each handling 1000-1200 procedures a year. Follow up data obtained for one-year post procedure.
2. Cost effectiveness of a managed model of transitional care for young people with chronic disorders.
   Cohorts of Young people age 14-24 years with IBD recruited into:
   - Prospective study recruiting large representative sample of 100 young people from specialised IBD centres using standardised instruments.
   - Longitudinal study to measure the long-term impact of transition programme and age appropriate health care on the cost effectiveness of the programme.

Congenital Heart Services (E05)

1. Variation in practice: surgical closure of arterial duct in preterm neonates to reduce variation in practice, reduce unnecessary procedures.
2. Identify demographic variations in the incidence of congenital heart disease in England through targeted surveillance and healthcare resource.
3. Nitric oxide administration during cardiopulmonary bypass in neonates undergoing Arterial Switch Operation for repair of transposition of the great arteries to improve outcomes after open heart surgery in children (United Kingdom branch of the study).
For patients with antenatal and postnatal diagnosis of TGA, undergoing Arterial Switch Operation. The study will last 2 years, and each UK centre will enrol, if they would like to participate, approximately 10 to 20 cases per centre per year.

**Metabolic Disorders (E06)**

1. Stem cell transplantation for specific inherited metabolic disorders with neurological with no effective therapy for neurological involvement.
2. Newborn screening for MPS I (iduronidase deficiency) for mucopolysaccharidosis type I.
3. Dietary therapy for phenylketonuria.

**6 Blood and Infection**

**Blood & Marrow Transplant (F01)**

1. Autologous haematopoietic stem cell transplantation (aHSCT) for highly active relapsing remitting multiple sclerosis (RRMS).
2. Stem cell transplantation for sickle cell disease for adults with severe sickle cell disease.
3. BK specific T-cells for post-transplant haemorrhagic cystitis.
4. Long term effects of hydroxyurea in sickle cell disease.

**HIV (F03)**

1. Peer support programmes for the treatment and care of HIV positive patients.
2. Integrated care model for HIV treatment and care and sexual health services.

**Infectious Diseases (F04)**

1. Outcomes for people treated for MDR TB in England to assess efficacy of drug regimens and delivery, with particular reference to delamanid and bedaquiline. For patients being treated for laboratory confirmed tuberculosis resistant to rifampicin and isoniazid.
2. Point of care hepatitis C testing in needle exchange pharmacies. Estimating potential number of patients with HCV who are not aware of their infection, and are not in touch with health or drug services.
3. Open/unlinked testing of entrants to English local prisons for HCV. ‘Opt out’ testing in prisons is only covering about 20% of entrants. It is not known what proportion of those not being tested are likely to be HCV+.

**Haemoglobinopathies (F05)**

1. Bone marrow transplant for sickle cell disease.

**Immunology & Allergy (F06)**

1. A novel computerised decision support system (CDSS) for rapid and safe de-labelling of penicillin allergy by a non-specialist. For rapid and safe de-labelling
of ‘low risk’ inpatients with a diagnostic label of penicillin allergy. Study to include adult patients (≥18 years) undergoing PenA tests in allergy specialist clinics and requires 800 patients.