Institution: University of East Anglia

Unit of Assessment: 1 – Clinical Medicine

a. Overview

This is the first return by the Norwich Medical School (NMS) to a hospital-based research unit of assessment, with 12 of the 16 academics being returned having joined UEA since 2010. Our clinical medicine research has been published in the world's top ranked biomedical journals including 4 papers in the New England Journal of Medicine, 6 in the Lancet, 1 in Science, 1 in Nature and 3 in Nature Genetics. Total grant funding held within NMS over the REF period is £71M of which £22.3M is attributable to those being returned in UOA 1.

Founded in 2002, NMS has grown significantly since 2008 building on existing strengths in health services and public health research, and in nutrition. The School has established ambitious new areas of research reflecting the strengths of the Norwich Research Park (NRP), invested in important catalysing infrastructure, expanded academic clinical medicine, and actively engaged with the NIHR Integrated Clinical Academic Training programme and the NHS to help build capacity within the School. The NRP is a unique cluster of high quality life science and bio-medical researchers located within six partner institutions: UEA; three BBSRC-funded research institutes (Institute of Food Research, John Innes Centre, Genome Analysis Centre); the Sainsbury Laboratory; and the Norfolk and Norwich University Hospitals Foundation Trust (NNUH).

For REF 2014, NMS is making a highly selective return, reflecting the constraints of the REF impact case study rules on newly established departments, with 50 researchers being submitted, principally across UOAs 1, 2 and 6. Staff submitted to UOA 1 are drawn from the Department of Clinical Medicine which is one of 4 research active departments in NMS. NMS itself sits within the Faculty of Medicine and Health Sciences at UEA.

Our research in clinical medicine is focused on gastroenterology, medical microbiology, musculoskeletal science and cardiovascular medicine. These areas have been identified and developed explicitly to take advantage of the NRP environment. Our new senior academic appointments will further develop these groupings by building strong translational research on an excellent BBSRC base.

b. Research strategy

The overarching goal of the Norwich Medical School research strategy in clinical medicine has been to establish a highly innovative and competitive translational medicine research programme linking the excellent fundamental biological science in the University and NRP with improvements in patient care, validated by large, phase 3, randomised studies of cost effectiveness and further downstream implementation research.

To achieve this goal we have:

- Appointed 21 new senior academic research staff (across UOAs 1, 2, 3 and 6) since 2008; 11 professors, 2 senior lecturers, 4 clinical lecturers and 4 non-clinical lecturers.
- Established 4 new clinical medicine research groups in microbiology, gastroenterology, musculoskeletal medicine and cardiovascular medicine.
- Aligned the research themes and goals of the School with those of the University and the NRP, and the priorities of key funding bodies.
- Started construction of a new medical research building (£19M) adjacent to the University hospital.
- Established a UK Clinical Research Collaboration (CRC) fully registered Clinical Trials Unit with full statistical and health economic support as well as a 6 bedded Clinical Research Facility (CRF).
- Installed a 3T Magnetic Resonance Scanner for clinical research.
- Established a state-of-the-art animal unit including a germ-free facility.
- Established an NIHR Integrated Academic Training programme.
- Reorganised the management structure of the School to prioritise and promote research.

Organisation and structure: The development of a vibrant and sustainable programme of hospital-based research has been facilitated through the development of key relationships within the University and with neighbouring institutions; and the establishment of appropriate management structures to drive the research strategy forward. In 2011, the newly appointed Head of School (Crossman) consolidated NMS into 4 research active departments. In conjunction with the Deputy Head of School (Research) (Watson), he is responsible for the development of research strategy within NMS. School research activity is overseen by the School Research Committee (Chair Watson), and a joint research committee with the NNUH (Chair Flather). The joint research committee within the hospital reports to the Trust executive of which Crossman and Flather are members. The UEA Vice Chancellor is a member of the NNUH Trust Board.

Development of research strategy: The research strategy for NMS has been developed using the expertise of newly recruited senior academics along with the advice of an external Scientific Advisory Board. A guiding principle has been to develop the School in alignment with existing scientific excellence within UEA and the NRP. This has resulted in the School concentrating activity primarily in the areas of Nutrition, Gastroenterology, Medical Microbiology, Musculoskeletal Science and Cardiovascular Medicine while continuing to build Public Health and Health Services Research relevant to these and other areas.

Research strategy and the Norwich Research Park: The NRP is one of 6 BBSRC-designated Research and Innovation Campuses. The partner institutions are within easy reach of each other, facilitating close working relationships and cross-fertilisation of research ideas. Crossman and Watson represent the NMS on the NRP Science Strategy Board. The outstanding potential of the NRP to make a major contribution to the Government's growth agenda, particularly the biomedical economy, has been recognised through a £26M investment by the Department of Business, Innovation and Skills, announced in March 2011. This is funding a range of scientific infrastructure including a large biorepository facility within the new Norwich Medical Research Building.

The NMS strategy builds upon the NRP as a science discovery engine, driving clinical translational research through the partnership, and using the techniques of health services research to study patient outcomes and disseminate cost-effective interventions. Examples of close working with Norwich Research Park partners are given below.

- The Institute of Food Research is a world leader in research in gastrointestinal science, particularly mucosal immunology, food safety and the emerging field of gut microbiota. It comprises 26 senior scientists, and links research in the areas of GI science, diet and health. The Institute is extensively integrated with NMS. The Director (Boxer) and Deputy Director (Carding) are both members of the medical school. The current institutional programme grant has 5 of its 25 principal investigators based in NMS.
- The John Innes Centre is an international centre of excellence in plant science and microbiology. A number of league tables place it as the top plant laboratory in the world. One of the Centre's major research themes is therapeutic chemicals produced by plants including fruit and vegetables. There is an active antibiotic development research programme, involving McArthur, Watson and Livermore from NMS, supported by collaborative funding from NMS.
- The Genome Analysis Centre is a national genomics and bioinformatics centre specialising in genomics technology, high throughput data analysis and advanced bioinformatics. Watson, Hall and Wain (NMS) hold joint projects with Caccamo (TGAC).
- The Norwich Research Park hosts 56 principal investigators in microbiology, 11 of whom are NMS staff (http://www.micron.ac.uk).

Joint research strategy with the Norfolk and Norwich University Hospital Foundation Trust: The NNUH has been a joint funder and strategic ally in the development of academic medicine within NMS. A recent initiative funded jointly between the Medical School and the hospital to recruit new clinical academics has appointed 5 senior academics (Fraser, Livermore, Wain, Johnson, Swart) with 6 additional Professors appointed from other funds. In addition UEA and the NNUH have co-funded the development of a 3T MR scanner for research purposes. Other joint initiatives include the establishment of a joint research office led by a senior administrator from UEA, the appointment of a jointly funded R&D director (Flather) and the funding of academic sessions for research-active NHS consultants e.g. Sampson (diabetes) & Donell (orthopaedics).

Clinical trials: Evaluation of health interventions using techniques of research synthesis and phase 1, 2 & 3 clinical trials, forms an area of NMS excellence in its own right and involves all the clinical research groups. There are strong health economics and medical statistics groups within the School (staff returned in UOA 2). The Norwich Clinical Trials Unit is led by a newly appointed director (Swart, with extensive experience at the MRC CTU) and has full UK CRC registration. Within this REF period, investigators from the School have completed and published 35 RCTs, 8 of which have been led by researchers returned to this UOA.

Norwich Medical School future research strategy: Over the next 5 years we will further strengthen our core activities. Specifically we will:

- Continue to recruit additional Clinical Academics using NHS and university funds. There is secured funding to establish senior academic posts in Gastroenterology, Urology, Infectious Disease, Clinical Imaging and Old Age Psychiatry.
- Increase the flow through the translational pathway of science developed on the Norwich Research Park into clinical practice.
- Open the Norwich Medical Research Building in September 2014 and establish this as the centre of translational medicine on the Norwich Research Park.
- Bring together CRF activity onto one site on the Norwich Research Park.
- Continue to develop aetiological epidemiology (using established links with major cohorts e.g. European Prospective Investigation into Cancer and Nutrition (EPIC) and health services research in the key priority areas of the Norwich Medical School (Nutrition, Gastroenterology, Medical Microbiology, Musculoskeletal and Cardiovascular disease).
- Collaborate in securing funding for a new £50M Centre of Food, Health and the Gut, to which BBSRC has committed a project manager. This will rehouse the existing BBSRC Institute of Food Research and also include relevant UEA gastroenterology, nutrition and microbiology laboratories together with outpatient endoscopy services for NNUH. The co-location of a BBSRC research institute with clinical gastroenterology services will create outstanding new opportunities for translational research.

Research groups - strategy and achievements: Within the overarching strategy of the Norwich Medical School detailed above, the four research groups within clinical medicine each develop their own research strategies as set out below.

Gastroenterology: The development and growth of gastroenterology was prioritised because of existing excellence on the NRP in nutrition, microbiology and normal (non-diseased) gut biology. Established in 2008, with the appointment of a mucosal gastrointestinal immunologist (Carding), the group developed further with the appointment of PIs Watson (clinical gastroenterology, epithelial biology), Hall (mucosal immunology and microbiology), and Schuller (gastroenteritis). The gastroenterology group works closely with the nutrition group (UOA 6) through Hart who researches dietary risk factors for gastrointestinal disease using the EPIC Norfolk cohort. Gastroenterology research is closely integrated with the IFR, with Watson, Hall and Schuller having laboratory space in the IFR building. Carding is the lead PI on IFR's £27M Institute Strategic Programme grant 'Gut Health and Food Safety' with Watson and Wileman as Co-PIs. This group addresses the MRC priorities of *Natural Protection*, and *Lifestyles Affecting Health*, and the BBSRC priorities of *Healthy and Safe Food,* and *Lifelong Health and Wellbeing*. Key achievements include:

- Identification of the mechanism of maintenance of barrier function during epithelial cell shedding and its relationship to prognosis of inflammatory bowel disease (Watson).
- The development of genetically engineered *Bacteroides ovatus* as a delivery platform for bioactive peptides for the treatment of inflammatory bowel disease (Carding).
- The discovery that dietary n-6 polyunsaturated fatty acids are a risk factor for the development of ulcerative colitis (Hart).

A priority for the future includes the appointment of a senior academic to lead clinical trials in gastrointestinal disease.

Medical Microbiology: The NRP is one of the UK's premier sites for microbiology, with over 30 groups and 56 principal investigators. NMS is taking advantage of this superb environment to develop medical microbiology research. Since 2011, 4 professors of microbiology have been

appointed (Livermore, Wain, Gray and Dong) to join Professor Hunter (UOA 2) who joined the Medical School in 2002. Livermore and Wain have been appointed by the Medical School to provide a focus of expertise in multi-drug resistant pathogens and novel drug discovery. Dong works on structural and functional studies of the pathogenesis of viral disease. Key achievements include:

- Demonstration that a combination of aztreonam with avibactam overcame the mechanism of resistance to carbapenem-resistant members of the *Enterobacteriaceae* and encouragement from AstraZeneca to pursue this into phase I (Livermore).
- The discovery of a novel immune suppression mechanism by Lassa fever virus nucleoprotein (Dong).
- The development of dense transposon insertion libraries for the identification of antibiotic resistance and susceptibility pathways (Wain).

This group addresses the urgent call from the Chief Medical Officer during the 2013 G8 summit to develop new antibiotics and measures to combat antibiotic resistance. Infectious disease is a priority area for the Wellcome Trust, MRC and BBSRC, particularly the emergence of new pathogens and drug resistance. A major goal for NMS is the development of a translational pipeline for the development of new antibiotics.

Musculoskeletal Science: The Musculoskeletal Science Group currently includes basic researchers from UEA's School of Biological Sciences and clinical researchers from NMS (Fraser, Macgregor (UOA 6), and Watts). They are examining bone, tendon, cartilage and skeletal muscle with the specific aim to improve musculoskeletal health in patients, the frail elderly, pregnant women and individuals subject to tissue injury. These are major expanding patient groups in the UK and worldwide. The ARUK Centre of Excellence in Arthritis Epidemiology was recently awarded jointly to UEA and Manchester recognising the outstanding epidemiological and biochemical (Fraser) expertise at UEA. This 5 year research programme will be facilitated by the ability to exploit unique patient and population cohorts in Norfolk such as the Norfolk Arthritis Register (NOAR) and EPIC. Key achievements include:

- The demonstration that there is no association between maternal vitamin D status in pregnancy and offspring bone mineral density in late childhood. This discovery has profound implications for the management of normal pregnancy (Fraser).
- The discovery that proteinase 3 ANCA-associated vasculitis and myeloperoxidase ANCA-associated vasculitis are distinct autoimmune syndromes with a strong genetic component (Watts).

This group is addressing the priority areas defined by Arthritis Research, MRC, and NIHR of degenerative diseases and ageing. Research centres on the causes and treatment of osteoporosis, Paget´s Disease, osteoarthritis and osteomalacia using novel technologies. Moving forward, the appointment of a Professor in Clinical Imaging to complement the recent appointment of a Professor of Medical Physics (Johnson) will enhance the expertise in MRI investigation of muscle, bone and joint disease. The appointment of an additional senior investigator in this area is a high strategic priority to build our capacity for clinical studies.

Cardiovascular Medicine: In the NMS return to RAE 2008, Potter was the sole cardiovascular investigator. Since that time, Crossman and Flather have joined. This develops research both in the basic mechanisms of, and clinical trials in, cardiovascular disease. Potter's work on the management of hypertension at the time of stroke is submitted as one of this UOA's impact case studies and its quality is reflected in the recent further award of a BHF Programme Grant. Flather has a well-established reputation in influential phase 3 cardiovascular clinical trials. Crossman has worked in the area of vascular biology applied to atherosclerosis and pulmonary vascular disease and now collaborates with the School of Biological Sciences. He was previously Director of a Cardiovascular BRU in Sheffield. Cardiovascular phenotyping is a strength of the group, in collaboration with the nutrition group researchers returned to UOA 6. Key achievements are:

- Establishment of IL-1 as a target for intervention in atherosclerosis through the use of several experimental model systems (Crossman).
- Proven lack of benefit of Irbesartan in atrial fibrillation (Flather).
- First trial directly comparing different anti-hypertensive agents in BP reduction post stroke

against placebo, showing overall mortality was reduced at 3 months in those treated (Potter).

This group leads research in key priority areas including stroke and the MRC Priority theme 2: *Living a long and healthy life*. It is a future priority to appoint additional senior investigators in this area to consolidate clinical trials.

c. People:

To develop our new translational medicine programme we have made the following appointments since 2008:

Gastroenterology: Carding and Watson (Professors); Hart (Clinical Senior Lecturer); Chan (Clinical Lecturer); Hall and Schuller (Lecturers).
Medical Microbiology: Dong, Gray, Livermore and Wain (Professors); O'Grady (Lecturer).
Cancer Biology: Cooper (Professor; returned to UOA 5) and Kim (Clinical Lecturer).
Radiology: Johnson (Professor).
Musculoskeletal Science: Fraser (Professor); Watts (Lecturer).
Cardiovascular Medicine and Clinical Trials: Crossman, Flather and Swart (Professors); Philpott (Senior Lecturer); Rechel (Clinical Lecturer); Sankaran (Lecturer).

i. Staffing strategy and staff development

The University appoints academic staff to either Academic Teaching and Research (ATR) posts that have a strong research focus or Academic Teaching and Scholarship (ATS) posts, which have an emphasis on teaching and enterprise. Only ATR post holders are returned to the REF. Staff research performance is monitored through completion of an annual personal Research Plan and reinforced by annual appraisal.

Implementation of the Concordat to support career development of researchers: UEA is committed to supporting the personal, professional and career development of contract research staff. A Research Staff Working Group, chaired by PVC for research, oversees implementation of the *Concordat to Support the Career Development of Researchers*. Departmental 'Research Staff Coordinators' act as points of contact and mentors for research staff. In September 2012, UEA was awarded the *HR Excellence in Research Award* from the European Commission.

Evidence of support for equality and diversity: UEA's Single Equality Action Plan sets out equality and diversity policies. These are implemented proactively by the Equality and Diversity Committee. Information on relevant characteristics of staff and student populations is provided by an Equality and Diversity Officer and helps to ensure that equality and diversity considerations are taken into account in decision making. The University has achieved Athena Swan Bronze status.

ii. Research students

UEA has a thriving community of postgraduate research (PGR) students who are integrated into research programmes. PGR student recruitment to NMS is managed by the Faculty of Medicine and Health Sciences Graduate School. The Graduate School offers a credit-bearing programme designed to equip students with the generic and transferrable skills required for their research careers. Student progress is monitored through a web-based system of reporting. The Graduate School also delivers compulsory supervisor training. Doctoral research students initially register for MPhil and following a year of study transfer to PhD if a transition panel judges transfer to be appropriate. Progress is then assessed annually. MPhil and PhD candidates are encouraged to take appropriate modules from taught Masters courses provided by the Faculty. There is a Faculty seminar programme on students' research in progress, and an annual PGR conference where students present and discuss their work.

In 2010 the Norwich Academic Training Office (Director: Watson) was established to organise the Integrated Academic Training Programme. This coordinates the management of the trainees across the University, the East of England multi-professional Deanery and the partner NHS Trusts. (http://www.uea.ac.uk/health/academic-clinical-training/home). Only specialties that are consistent with the School's research plan are selected for formula NIHR ACF and ACL posts. Similarly competitive bids are made only for disciplines that are adequately supported within the Medical School's research plan. From 2008 to 2013 the School was allocated 3 formula ACFs and 1 ACL annually. From 2013 onwards the School has been allocated 2 formula ACFs posts and 1 ACL position. Since inception of the Office there has been 100% completion of the MSc in Health

Research with 3 progressing to higher degrees.

The Medical School also supports clinical academic trainees with a grant scheme which covers consumables and other expenses for projects that the trainees are developing into fellowship applications. To develop academic training further, the school is working with the University of Cambridge to provide more Academic Foundation posts. The school is also developing more locally funded ACF posts in partnership with local NHS Trusts.

The Dean's lecture series, the most important in the medical school calendar, highlights the research achievements of UEA and NNUH to the medical students. To complement this, joint UEA/ NNUH Research Seminars are held on a monthly basis at NNUH. UEA has invested heavily in PGR studentships and hosts a BBSRC Doctoral Training Centre.

d. Income, infrastructure and facilities

Income: Members of UOA 1 currently hold £11.4M of grant funding. This is an increase of 50% from that held in 2008. To maximise grant success, applications from researchers in the school go through extensive internal review. UEA has established committees to review applications to the UK Research Councils and to the NIHR, with a resultant increase in success rates.

New Medical School Building: A major new joint initiative with the NNUH is the construction of a new £19M, 4400 m^2 research building which will be situated immediately between the NNUH and TGAC. This building will also enhance collaborations in translational biomedical research with the School of Biological Sciences. Additionally, the Wolfson Foundation has recently awarded a grant of £0.5M towards construction costs.

Research Facilities: A framework for sharing core research facilities across the NRP has been established. The Biomedical Research Centre on the UEA campus houses our current wet laboratory facilities, including the Wellcome Trust SRIF-funded 4000 cage Disease Modelling Unit where all animal work is conducted (see below). The Henry Wellcome Cell Imaging facility houses confocal and 2-photon microscopes.

Clinical trials facilities: UEA and the Norfolk and Norwich University Hospital manage the Clinical Trials Unit and the Clinical Research Facility, with facilities in the Medical School and at the NNUH. Medical School academics have leadership roles in the Clinical Trials Unit, supporting the Director (Swart), with Flather (Professor of Clinical Trials), Shepstone (medical statistician, UOA 2) and Barton (health economist, UOA 2) as management committee members. Most of our UK-based RCTs are run though the CTU, which provides services for study design, remote electronic data capture for patient registration, randomisation, and data management. Quality assurance is regulated by comprehensive Good Clinical Practice regulations and Standard Operating Procedures. The NNUH Research and Development Office is co-managed by UEA's Research and Enterprise Services. A long-term goal is to bring the facilities in the university and the hospital together on a single site. NNUH was recently appointed to host the NIHR Clinical Research Network (Eastern) which will cover the whole of East Anglia including Cambridge.

Laboratory facilities: All wet laboratory, cell culture and human sample analytical equipment is housed in the Biomedical Research Centre, a £16.5M investment at UEA, which provides facilities for 200 researchers. Core facilities across the institutions of the NRP now have common management including web-based booking and shared costing templates. Facilities include cellular imaging, FACS analysis, DNA sequencing, mass spectroscopy, protein and carbohydrate chemistry, 3T MR and an animal research facility.

Animal facilities: All animal studies are conducted in The Wellcome Trust SRIF-funded Disease Modelling Unit, a 4,000 cage facility for housing wild-type, transgenic and gene knockout models. Within the animal unit there is one of very few germ-free animal facilities in UK HEIs.

e. Collaboration or contribution to the discipline or research base

Collaborations: Researchers within the School collaborate widely with other academics, with industrial partners and with government. These collaborations are actively encouraged by the School's positive grant winning and project management culture, by strategic decisions made

within the School and by our internal management processes.

Collaborations with academic partners: Over the REF period, UOA 1 researchers have participated in 51 collaborative projects. Examples where we have played a *leading role* are:

- The BBSRC funded *Gut Health and Food Safety Programme* together with the Institute of Food Research (Carding and Watson).
- The analysis of Vitamin D for the major MRC-funded Avon Longitudinal Study of Parents and Children (ALSPAC) run from the University of Bristol. Vitamin D data from this study have been acknowledged to be of the highest quality (Fraser).
- A Wellcome Trust funded collaboration, *NF-kB and cell shedding in Inflammatory Bowel Disease*, with Liverpool, Erlangen (Germany) and University of Southern California (Watson).
- An ARUK *Centre of Excellence in Arthritis Epidemiology* awarded to UEA and University of Manchester.
- A BHF Programme grant for stroke and hypertension with Universities of Oxford and Leicester (Potter).

Collaborations with industry, government and other research users: The School takes a proactive approach to its collaborations with research users so that its research tackles questions relevant to them. We also interact closely with the Department of Health and the Ministry of Defence. Examples include:

- The Public Health England (HPA) funded project *Epidemiology of antibiotic resistance and public health* involving 5 partners (Livermore).
- Responding to a call from the Ministry of Defence (ARTD) for research into vitamin D and prevention of stress fractures.
- Contributing extensively to chapter 5 on antibiotic resistance in the CMO's Annual Report 2011 (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/138331/CMO_Annual_Report_Volume_2_2011.pdf).
- Evidence to the Parliamentary Science and Technology Committee (House of Commons) on Probiotics and their commercial development (Carding).

Fellowships: UEA has strongly supported several successful Fellowship applications with matched funding. Our researchers have held 5 fellowships in the REF period including an NIHR fellowship (Alexandre) and a British Heart Foundation fellowship (Fenech). A new blood HEFCE post has been created in Medical Microbiology (Schelenz). Hall has been awarded a Wellcome Trust New Investigator award (£1.2M) and Dong has a Wellcome Trust Career Development Fellowship.

Responsiveness to national and international priorities: Much of our research addresses the priority areas identified by key funders such as MRC and NIHR. For example:

- MRC priority areas: *Natural Protection* e.g. gut immunology, intestinal barrier function & microbiology (Carding, Dong, Livermore, McArthur, O'Grady, Wain, Watson); *Tissue Disease and Degeneration* (Crossman, Flather, Fraser, Watts).
- NIHR Efficacy and Mechanism Evaluation Programme (Flather, Swart).
- BBSRC priority area: *Healthy and Safe Food* (Livermore, O'Grady, Wain and researchers submitted to UOA 6).
- Wellcome Trust priority: *Combating Infectious Disease* (Dong, Hall, Wain).

Contribution to the wider discipline: Many of our researchers participate in activities which contribute to the broader research base. For example:

- Editor for *International Journal of Antimicrobial Agents* (Livermore).
- Deputy editor of GUT until March 2008 (Watson).
- Editorial Board for *Antimicrobial Agents & Chemotherapy* (Livermore).
- Member of the MRC/ NIHR EME Board (Crossman).
- Chair of the BSR Guideline working group on systemic vasculitis (Watts).
- Member of the advisory panel to WHO on vaccine development (Carding).