

Institution: University of Sheffield

Unit of Assessment: A-01 Clinical Medicine

1. Unit context and structure, research and impact strategy

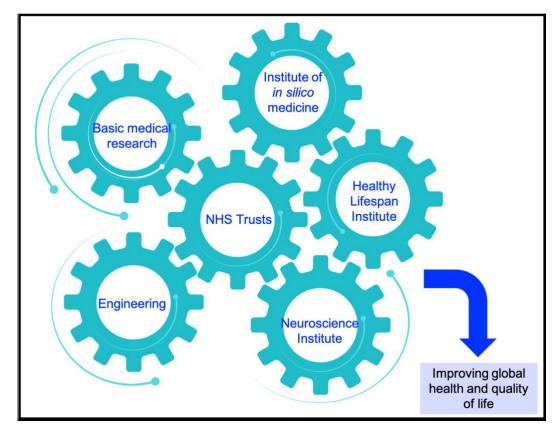
1.1 Unit Context

Sheffield's Medical School integrates discovery biology, clinical science, healthcare, engineering, and computing to create an exciting research environment. The formation of two new University Flagship Research Institutes exemplifies this cross-faculty interdisciplinary environment. The **Neuroscience Institute** and **Healthy Lifespan Institute**, both led by staff within our unit, were established to tackle key issues facing humanity by harnessing interdisciplinary and translational research to deliver real-world solutions.

Our aims are to:

- Translate discovery science into clinical impact that improves lives and healthcare.
- Grow interdisciplinary partnerships across engineering, imaging, computational modelling and disease models to deliver novel healthcare solutions.
- Provide an agile response to urgent healthcare needs, such as emerging global infections.

Fig 1: Sheffield clinical medicine - integrating discovery medical research, clinical science, healthcare, engineering, in silico medicine, Health Lifespan Institute, Neuroscience Institute to deliver improved health and quality of life.





Over this assessment period, we grew our research income by 50% (from £71.7M to £107.4M) with total research funding of £139M including philanthropic donations and royalties, and PGR student registrations by 21% (from 163 to 197). We delivered our REF2014 research and impact strategy to publish ~3,700 open access papers including >80 in *Lancet, NEJM, Nature, Cell, EMBO J* and *Science* from 116 submitted staff. We successfully retained our Athena SWAN Silver Award, as part of our actions to promote an equal, diverse and inclusive environment. Building on this we have developed an ambitious and interconnected research and impact strategy.

1.2 Unit structure

This unit sits in the Faculty of Medicine, Dentistry and Health where our research *encompasses* discovery to translational and clinical studies. Our research maps onto seven themes (Fig 2) with the Neuroscience and Healthy Lifespan Institutes spanning multiple themes. This is coordinated by Directors of Research & Innovation, Impact and Knowledge Exchange who meet regularly at a Faculty Research and Innovation Committee.

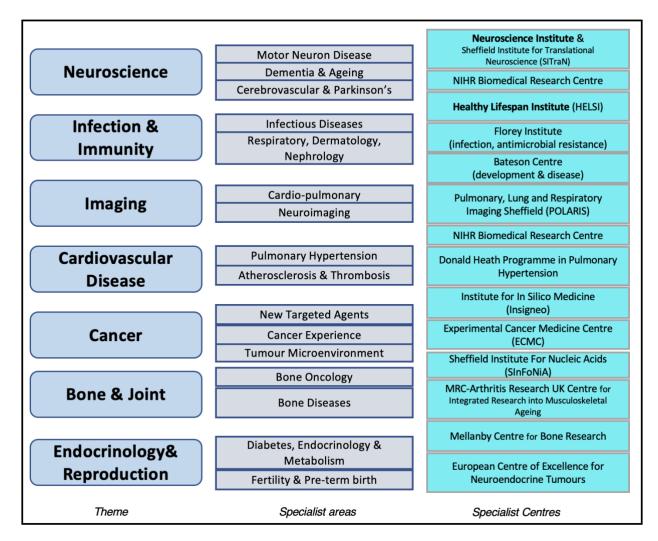


Fig 2: Unit structure: themes and expertise in clinical medicine

1.3 Research themes, progress against objectives, and future strategy

Neuroscience

Sheffield is an international centre for pre-clinical, translational, and clinical research in neurodegenerative diseases particularly motor neuron disease (MND), spinal muscular atrophy

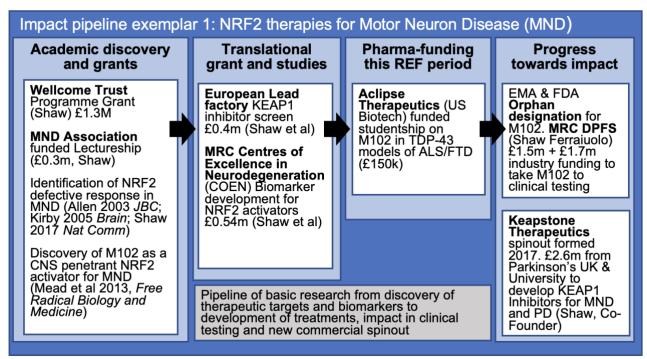
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(SMA), Parkinson's disease, multiple sclerosis (MS), Alzheimer's disease and dementia. Grant awards exceed £23M from funders including MRC, NIHR, ERC and industry. We were awarded a **Neuroscience NIHR Biomedical Research Centre** (BRC) (£4M, 2018) to translate our neuroscience research into patient benefit. The **flagship Neuroscience Institute** led from the

purpose-built *Sheffield Institute for Translational Neuroscience (SITraN),* focuses the expertise of over 120 translational, sensory, developmental and systems neuroscience researchers from the Engineering, Science and Medical faculties to improve prevention, diagnosis and treatment of degenerative, sensory and developmental neurological disorders.

Our strategy over this assessment period focussed on increasing translation in neurodegenerative diseases, recognised in 2019 by a **Queen's Anniversary Prize for Innovation** for improving patient outcomes, and the **National Future NHS Parliamentary Award** for our autologous <u>stem</u> <u>cell treatment of multiple sclerosis</u> (see **MIST** impact case). Our NIHR BRC delivered this break-through treatment of MS, a new genomics hub for Yorkshire, a new PET-MRI facility and improved stratification of Parkinson's disease (<u>Bandmann</u>: 2020). We are an international centre for the Tofersen Phase III Biogen Trial in MND, and the **only UK site** to complete an intra-thecal antisense oligonucleotide Phase I/II trial for MND patients with *SOD1* mutations (Shaw/McDermott: NEJM 2020), with a Phase III currently completing. We lead a **€25.5M** Innovative Medicines Initiative award (Azzouz/Shaw/Ferraiuolo/Majid 2020-25) with 23 institutions and 11 pharma companies to accelerate research and innovation of advanced therapies. We have therapies in development built on our discovery that NRF2 is defective in MND (see impact exemplar 1). Our preclinical neuroprotective viral therapies (Azzouz: 2018) are now in phase 1-2 clinical trials.

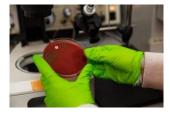


We have delivered supportive care and assistive technologies for MND, exemplified in our two case studies, where we shaped global clinical policy and safeguarded MND patients treated with diaphragm pacing (**DIPALS**) and commercialised a bespoke collar to support neck weakness in MND patients, with thousands sold worldwide (<u>HeadUp</u>, <u>Talarmade</u>). We expanded our critical mass by key appointments at professorial (Li Su) and career track fellowship levels (Twelvetrees, West, Livesey, Mortiboys) contributing expertise relevant to our future research strategy such as PET-MRI, super-resolution imaging, *Drosophila* disease models and neurogenetics.



Future strategy: To enhance patient outcomes for people living with neurodegenerative diseases and facilitate translation we are establishing a **Gene Therapy Innovation and Manufacturing Centre** which includes a state-of-the-art Good Manufacturing Practice clinical grade vector manufacturing facility (£9.45M funding, including £6.45M from MRC and LifeArc, led by Azzouz). This will circumvent viral vector manufacturing bottlenecks, accelerate translation of gene therapy approaches and address the skills-shortage in this landscape. We will conduct clinical trials and identify new therapeutic targets and biomarkers of disease progression. We will build on the University's investment in the interdisciplinary flagship **Neuroscience Institute**, for example to use advanced imaging modalities, transcriptomics, and computational modelling to improve disease stratification, prognosis, treatment, and quality-of-life in neurodegenerative diseases. We will renew our BRC and continue to develop our neurotherapeutic pipeline building on existing partnerships with industry (e.g. GSK, AstraZeneca, Pfizer, Benevolent AI).

Infection and Immunity



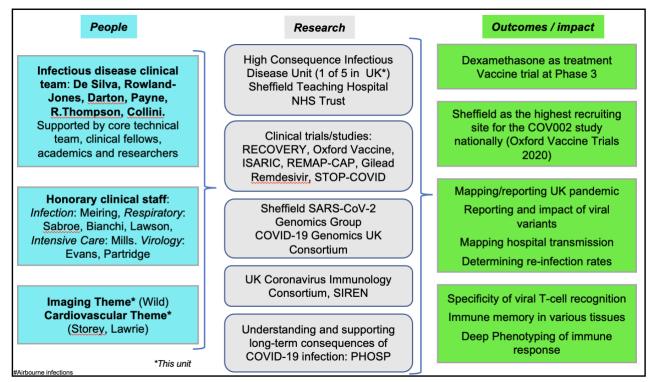
We possess expertise in infectious diseases, host immunity, antimicrobial resistance, emerging infections and global health. Rowland-Jones coleads the interdisciplinary <u>Florey Institute</u>, which studies the host/pathogen responses including immunity (I.Evans *PLOS Pathogens*, 2017; Preston, *Amer J Resp Crit Care Med*, 2019). This combines cell and developmental biology, stem cell biology, mechanobiology, imaging

and mathematical modelling with translational biomedicine working with colleagues from biology (UOA-5) and engineering (UOA-12). The Florey Institute won a NIHR infrastructure award (£1.4M) in 2019 and £3.5M in 2016 for the <u>SHIELD</u> consortium to combat antimicrobial resistance.

In this assessment period we have recruited researchers in virology, vaccines and global infections including Rowland-Jones, De-Silva, Darton and Payne from Oxford. Their backgrounds in HIV (Ajaykumar *Clin Infect.Dis* 2020; Yindom, *Clin Infect.Dis*, 2019), Ebola vaccines (Ewer, *NEJM*, 2016) and typhoid pathogenesis (Blohmke, *J.Exp.Med*, 2016) allowed our rapid response to COVID-19 (Fig 3). Our COVID-19 research integrates experts from immunity and infection, thrombosis, genomics, cardiovascular disease, pulmonary, vascular, and functional imaging with the Sheffield Teaching Hospitals NHS Foundation Trust's Laboratory Medicine and Infectious Diseases Directorates in a cohesive and collaborative effort. By example, we were the **largest national recruiter to the Oxford COVID-19 vaccine trials** in 2020 (<u>Darton, Lancet 2020</u>).



Fig 3: Infection and Immunity: key players in an agile response to combat the COVID-19 pandemic



The Bateson Centre (led by Renshaw) pioneers non-mammalian models of infection and immunity. Work includes using zebrafish to identify mechanisms of *S.aureus* infection (Hepburn, *Science*, 2014; Boldock, *Nature Microbiology*, 2018) and novel anti-inflammatory lead compounds (Robertson, *Sci. Translational Med*, 2014). We use Drosophila, zebrafish, and murine models to examine how macrophages regulate inflammation (Weavers, *Cell*, 2016; Roddie, *PLOS Biology*, 2019; Li, *PNAS*, 2019; Johnston, *Science Advances*, 2019). Kiss-Toth led an EU-network (TRAIN 2015-20) exploring links between immunity, metabolism, and cancer. We commercialised our infection research receiving >£1.4M of venture-capital, Innovate UK and DoHSC MRC, Novartis, GSK and Pharming funding to combat infection and treat immune deficiency syndromes.

Future strategy: Our flagship **Healthy Lifespan Institute** will investigate ageing-related immune dysfunction in interdisciplinary consortium efforts. In our forthcoming NIHR BRC renewal we will apply for an additional theme in 'Infection & Immunity' to provide a step-change in our experimental medicine and in the large-scale consortia combatting COVID-19. We will perform clinical studies using novel antimicrobials developed by our spinout company to treat *N.gonorrhoeae* infections. Our goal is to improve outcomes from infection, reduce antibiotic usage, combat antimicrobial resistance and increase global vaccination against COVID-19 and other communicable diseases.

Imaging



Imaging is central to the Sheffield **Institute for** *in silico* **Medicine** (<u>Insigneo</u>, led by Wild), Europe's largest research institute dedicated to the development, validation, and use of biomedical modelling, imaging and informatics in healthcare. Insigneo comprises >150 staff from 28 departments across medicine, engineering, and science, attracting £54M of research income. Imaging and Insigneo interact closely with our Neuroscience, Infection and Immunity and Cardiovascular Disease themes, providing novel diagnostic tools coupled to functional disease measures

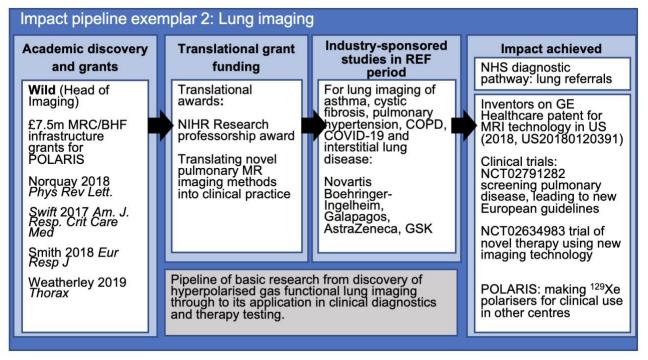
while informing discovery research.



Our strategy has been to translate imaging research for patient benefit and build interdisciplinary research. Our VIRTUheart programme received £1.16M in translational awards (BHF, NIHR, Wellcome Trust, NIHR sequentially) to develop computational models from coronary angiography (Morris, *JACC*, 2017; Sciola, Eurointervention 2018) now used in Sheffield hospitals as a clinical research tool to inform clinical decision-making. The strategic importance of imaging across the University was supported by chair appointments of Sourbron (from Leeds) and Su (from Cambridge) and several externally funded career development fellowships for our future imaging leaders (Morris, Wellcome).

Sheffield <u>medical imaging facilities</u> provide a pipeline from new technology development, preclinical to clinical imaging. Our preclinical MRI facilities include a 7T animal scanner and a 9.4T microscopy scanner. We have two whole-body 1.5T research scanners for pulmonary, cardiac, and *in-utero* imaging, a 3T whole-body system for neuroimaging, cutting-edge hyperpolarisation labs and a new 3T PET-MRI scanner. We pioneered technology development with world-class MRI physics and engineering, leading to partnerships with GE Healthcare (GE innovate UK industry scholarship) and hardware contracts with other centres (MSKCC, UCL-BRC, Columbia University, Kiel University purchased our ¹²⁹Xe polarisers and RF coils). We established neonatal and *in-utero* MRI scanning to accurately predict risk of pre-term delivery up to three months in advance.

Through <u>POLARIS</u> Sheffield pioneered the use of hyperpolarised gas and proton lung MRI for early diagnosis and functional assessment of lung diseases including asthma, cystic fibrosis, chronic obstructive pulmonary disease, pulmonary fibrosis, and pulmonary hypertension. Over this assessment period, we received £7.5M funding from MRC/BHF, established an MHRA manufacturing specialist licence to produce hyperpolarised gas for clinical indications, and a world-first NHS diagnostic pathway for clinical lung MRI imaging (see impact exemplar 2).

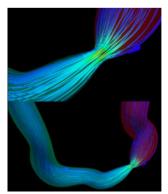


Future strategy: Imaging will represent a cross-cutting theme in our NIHR BRC renewal application. We will further grow our internationally competitive imaging with our recent investment (£11.4M including £2M University investment) in **PET-MRI**, the only such scanner in Yorkshire and one of only eight in the UK. This enables new translational projects across multiple areas including neuroscience, oncology, paediatrics, cardiology, and respiratory medicine in collaboration with the NHS. New MRI technologies such as hyperpolarised gas MRI will be integrated into analysis of pulmonary and vascular function. This will be expanded in respiratory diseases, prognostic



evaluation of pulmonary hypertension and infection, including assessment of lung disease and recovery in the <u>PHOSP-COVID</u> study. Our POLARIS team will develop hyperpolarised gas MRI technology to offer low-cost MRI hardware and bespoke image engineering for healthcare providers internationally, expanding industrial partnerships enabling widespread clinical application. Insigneo's integration of computational medicine, imaging, modelling, and simulation technologies contributes directly to prevention, assessment, diagnosis, prognostic tools, treatment planning, delivery and management of disease. Over the next five years we will build on the excellence in these allied fields of healthcare technology in Sheffield to expand and enhance **digital healthcare**.

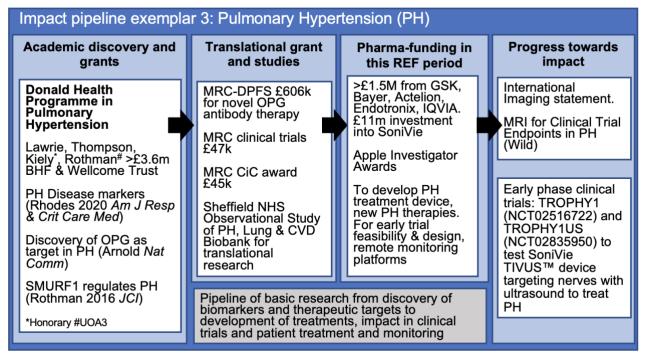
Cardiovascular Disease



Research in this theme improves prediction, diagnosis, treatment, and monitoring of a range of cardiovascular diseases and interacts closely with the Imaging, Neuroscience, Infection and Immunity themes. This extends to stroke and dementia through partnerships with the NIHR Biomedical Research Centre in Translational Neuroscience and aims to understand why cardiovascular risk increases with ageing and frailty in partnership with the flagship **Healthy Lifespan Institute**.

We achieved our strategy to translate and commercialise our research for patient benefit and wider impact. In 2017 we launched the **Donald**

Heath research programme in **pulmonary hypertension** (PH) led by Lawrie bringing together clinical experts from the **largest pulmonary hypertension treatment centre in Europe** (referral population 15 million) with excellent discovery science, preclinical and patient-facing research. We identified new biomarkers of PH severity and therapeutic targets which have been developed into translational pipelines, industrial investment and early-stage clinical trials (see impact exemplar 3).



Our antiplatelet research led to new treatments such as **Ticagrelor** (impact case study) to reduce risk of further heart attack, stroke, or death, following PLATO and PEGASUS clinical trials led by Sheffield (Storey) in partnership with AstraZeneca. We led the first clinical study of a novel antiplatelet drug developed by Idorsia Pharmaceuticals (Storey, *European Heart Journal* 2019) and therapeutically

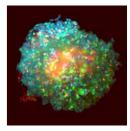


targeted IL-1 as a driver of arterial inflammation (ILA-HEART) leading to the CANTOS clinical trial using Canakinumab (Francis, Gunn).

Over the assessment period, we grew mechanobiology in atherosclerosis (P.Evans, BHF Programme grants, 2015 and 2020). With experts from engineering, physics, and mathematical modelling within Insigneo we developed computational tools to model blood flow and support clinical decision-making; our software for blood flow modelling has been developed in an industrial partnership with Ansys (Gunn, Morris). Our multinational **Digital Healthcare consortium** (ECHOES) builds on Insigneo modelling to incorporate real-world symptom, activity, physiological and imaging data into a "Cardiovascular Digital Twin" to predict, diagnose, treat, and monitor cardiovascular diseases; this is one of four teams shortlisted for the £30M British Heart Foundation "Big Beat" Challenge (Chico, UK Co-ordinator).

Future strategy: Our future NIHR BRC renewal application we will request an additional theme in 'Cardiovascular Diseases' to support experimental and translational medicine research. We will apply novel informatics-based diagnostics that identify risk of PH (Lawrie: European Respiratory Journal) to other cardiovascular diseases. We will continue to develop and trial new devices such as pulmonary artery pressure monitors, novel therapeutics such as pulmonary denervation for PH, anti-thrombotics and anti-inflammatories for acute coronary syndromes and cerebrovascular disease. We will exploit our discovery, clinical and imaging strengths to understand the **cardiovascular effects of COVID-19**. We will expand our **digital healthcare** and computational technology studies including the ECHOES consortium to aid remote healthcare during COVID-19 and in other settings where direct healthcare access is challenging.

Cancer



We specialise in bone oncology (including bone metastasis, and bone loss due to cancer treatment) and the tumour microenvironment; new targeted approaches; and cancer experience, with significant research programmes in breast, thoracic, urological, and haematological cancers. Basic research is complemented by drug discovery, target and biomarker identification and *in vitro* and *in vivo* models that translate towards patient benefit. We work across disciplines through the **Sheffield Institute for Nucleic Acids (SInFoNiA)**,

connecting with the University's genome stability and gene expression expertise from biological sciences and engineering.

We achieved our REF2014 aim of expanding translation of cancer research into clinical trials. In 2014 we launched the Yorkshire Cancer Research Early Phase Trials Network, providing infrastructure for early phase oncology research, and in 2015 commissioned a purpose-built, Cancer Early Clinical Trials Unit. In 2017 we received £1M from DoHSC and Cancer Research UK as an Experimental Cancer Medicine Centre (ECMC), in recognition of our outstanding translational interface research. In 2018 Helleday was recruited back to Sheffield and in 2019 received the Nation's Lifesaver Award for making a life-changing difference to health by his discovery and development of Lynparza ('personalised therapy' case study), recommended in 2018 by NICE as first line therapy in BRCA-mutated ovarian, Fallopian, and peritoneal cancer. Lynparza was the second highest-earning oncology drug for AstraZeneca in 2018, generating \$847M sales revenues per year. In 2017 we established the Yorkshire Cancer Research Catalyst for Innovation in Cancer Care and Treatment in Sheffield (YCR CONNECTS) and invested £5M to recruit Hussain, Helleday, Gad, Toseland and Rantala. We led the AZURE trial resulting in introduction of **bisphosphonate** treatment into routine clinical practice to prevent breast cancer metastasis (impact case study), and the BRAVO trial (2017) to identify risk and benefits of bladder cancer treatments. We used basic science modelling to change



recommendations on PSA screening for prostate cancer to prevent harm caused by biopsy and development of alternative diagnostic modalities (**PROBE**, impact case study).

Our strategy has been to commercialise our research for wider impact and patient benefit. Our spinout company, Modulus Oncology Ltd. incorporated in July 2020, resulting from a £5M Wellcome Trust Seeding Drug Discovery award to identify adrenomedullin receptor antagonists to treat pancreatic cancer (see impact exemplar 4). We are currently determining the feasibility of targeting and improving patient stratification for the rare disease, Sezary syndrome, supported from the University IP Development and Commercialisation fund (£150k) and the CCF Northern Triangle Initiative (£100k). Our new spinout company, Modulus Oncology, plans to raise £6.5M in seed-funding.

Impact pipeline exemplar 4: Adrenomedullin receptor as anticancer target			
Academic discovery and grants	Translational grants	Seed-funding in REF period	Progress to impact
RAMPs modify Adrenomedullin (AM) receptor signalling: BBSRC 2007 £300k; Prostate Cancer 2013 £50k	Richards: development of novel therapeutics: BBSRC/RSE enterprise fellowship 2006, £80K	University of Sheffield IPDaC award £146.7k (2019) NTI-CCF	Modulus Oncology Ltd incorporated July 2020
AM Receptor in disease modulation: Rosetrees Trust 2018 £125k + £125k HEIF Disrupting AM signalling in skeletal abnormalities & cancer: Kadmiel 2011 <i>Mol</i> <i>Endocrinol</i> ; Weston 2015	Skerry, Richards, Harrity: AM Receptor 2 as an anticancer target, £5m Wellcome Trust Seeding Discovery Awards (2015 & 2017) AM1R inhibition assay European Lead Factory	award £110k (2019)	Underpinning IP: Pending AM2R inhibitor patent applications: WO2018/211275
J.Bio. Chem; Prakash 2019 Gene X. Small molecule AM2 antagonists inhibit cancers. Avgoustou 2020 ACS Pharmacol. Transl. Sci.	(£0.4m, 2019). Pipeline of basic research fr anti-cancer targets to develo molecule therapies, to impac pending and spin-out toward	WO2020/099885 WO2020/099882	

Future strategy: In partnership with the NHS we will re-develop the Weston Park Cancer Centre to **accelerate our pipeline of translational research**. Whilst this will initially focus on our existing strengths in bone oncology, primary breast, and prostate cancer, we will expand our expertise in urological cancers (e.g. bladder) following Catto's recent receipt of an **NIHR Research Professorship** and the appointment of Hussain, an expert in clinical trials and early drug development in urological cancers. The recent appointment of Gad and Toseland (mechanical properties of cancer cells) will strengthen our links with engineering. We are investing £791k in the EVIDENT (Ex VIvo DEtermiNed cancer Therapy) project to **personalise treatment** using *ex vivo* drug response screening from patient biopsies (Rantala).

Bone and Joint



Successes in this theme have built on the creation of the Mellanby Centre for Bone Research in 2010. We were awarded one of two UK MRC-Arthritis Research UK **Centres for Integrated Research into Musculoskeletal Ageing** (CIMA), in partnership with Liverpool and Newcastle in 2012, renewed in 2017. This theme brings together experts in osteoporosis, osteoarthritis, osteogenesis imperfecta and bone metastasis. We work closely within the flagship **Healthy Lifespan Institute** on multiple age-related diseases, in preventing or reversing

ageing of stem cells and diseases of the musculoskeletal system. We have identified new treatments for osteoporosis (<u>Eastell</u>, *NEJM* 2020), and in 2019 we organised an international conference in Sheffield celebrating 50 years of bisphosphonates.

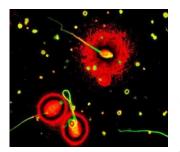
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Our strategy has been to expand our external and industrial partnerships including Alexion, Amgen and Roche to improve prevention and treatment of bone diseases. We achieved this through funding renewal and expansion of CIMA, working with other institutions to increase our research impact. In collaboration with London and Manchester Universities, we led clinical trials resulting in new recommendations for treatment to reduce bone-loss in women at risk of breast cancer (Sestak, Lancet, 2014). Our Wellcome Trust funded small molecule drug discovery programme (£4.95M: Skerry, Richards), and work with the European Lead Factory, has been built on proof-of-concept discovery of a drug target and antibody development of bone tumour inhibitors.

We achieved our REF2014 aims to translate research for patient benefit, including generating **SCOOP-FRAX** (impact case study), an online fracture risk assessment tool (used in 64 countries) to direct treatment and reduce fracture incidences in the elderly (McCloskey). In 2020, we launched jointCalc, an on-line tool already used by 15,000 people from 110 countries to assist in making an informed decision about joint replacement surgery (Wilkinson). Eastell led development of guidelines for treatment of osteoporosis by the Endocrine Society and we are part of Fidelio, the EU Horizon 2020 innovative training network on **diabetes and bone**, working with 10 European centres. We improved patient identification for osteoporosis in collaboration with the our School of Health and Related Research (ScHaRR) and University of California, San Francisco. With the University of California, LA we are co-investigators on an NIH-funded study of bone turnover markers women across the menopause. Osteolytica has been developed as a powerful research tool to detect and quantify cancer induced bone destruction using micro-CT (Chantry). We are developing a novel computational model of myeloma bone disease in collaboration with Sheffield's Automated Systems and Insigneo, using deep learning artificial intelligence algorithms.

Future strategy: In collaboration with Insigneo, we will expand our Skeletal Analysis Laboratories (<u>Skelet.AL</u>) set up to deliver new innovations and customised solutions for the analysis of the skeleton. These tools will improve methods to assess animal models and patients with bone diseases and in ageing as a focus of our **Healthy Lifespan Institute**. We will translate these to treatments in children's bone fragility and the diagnosis of rare bone disorders such as hypophosphatasia. Following our participation in the FNIH Bone Quality project to establish bone mineral density as a surrogate for drug development in osteoporosis and in 2020/21 we will complete our Final Qualification Plan submission to the Food and Drug Administration and then apply to the European Medicines Agency.

Endocrinology and Reproduction



This theme exploits Sheffield's unique strengths and access to important patient populations to perform world-leading research in diabetes, adrenal disease, neuroendocrine tumours, fertility, neonatal imaging, pre-term labour and complications of pregnancy.

We achieved our REF2014 aim to translate research and to commercialise diagnostics and therapies for wider patient benefit. **Alkindi** (impact case study, Ross) was developed and marketed as a

treatment for paediatric adrenal insufficiency, the commonest inherited endocrine disorder. Ross is founder and Chief Scientific Officer of **Diurnal** Group PLC, receiving £12M in private investment and £40M from flotation on AIM in 2015, as well as co-directing Asterion, a company that engineers novel therapies based on its innovative ProFuse[™] technology. We were awarded £2.4M (MRC-DPFS) for development of a hormone antagonist to treat acromegaly (Ross). We are a European Centre of Excellence for Neuroendocrine Tumours with strengths in adrenal disease and neuroendocrine tumours.



Our diabetes research focuses on hypoglycaemia (Heller, Selvarajah), in particular its cardiovascular effects (Zoungas, *NEJM*, 2014; Chow, *Diabetes*, 2014), patient self-management, and central nervous system effects. We produced a patient training programme for Type 1 diabetes "Dose Adjustment for Normal Eating" (<u>DAFNE</u>, Heller) which has been included in NICE Guidance since 2015. Subsequent funding from DAFNE led to the **REPOSE trial** to test effectiveness of pump treatment in Type 1 diabetes.

In reproductive medicine, our andrology (male fertility) research was ranked second in the UK to Cambridge for highly cited papers in the most recent 2015 <u>NIHR RAND</u> 10-year report. Using our imaging expertise (above), we continue to develop improved diagnostic methods of sperm and semen quality (Reynolds, *Mol. Hum.Reprod*, 2017) and *in-utero* MRI scanning of the foetus to prevent premature birth by accurately predicting the chances of pre-term delivery, up to three months in advance (Griffiths, *Lancet*, 2016). In 2020 EveryBaby Ltd. (Anumba) was licenced to market a novel device to predict premature birth and improve maternal care. We lead a major **Global Challenge initiative** (<u>PRIME Global Health</u>) to improve the lives of women and babies around the world, with awards of over £6M in the last three years alone and partners in Dhaka, Bangladesh and Cape Town, South Africa.

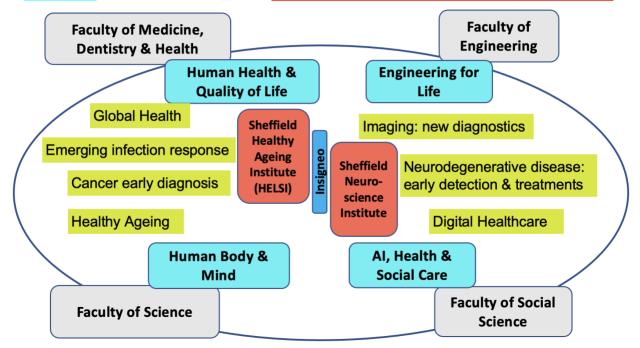
Future strategy: In reproduction we will strengthen our response to global challenges by expanding PRIME Global Health to include researchers in Nigeria and India. We will also establish a new programme with <u>MRC Gambia</u> investigating fertility care in low-income countries. We aspire to become a centre for reproductive biology and health, and in partnership with the Royal College of Obstetricians and Gynaecologists and the University of Bristol will become part of the <u>Tommy's National Centre for Maternity Improvement</u>. In endocrinology we will continue to translate research into clinical studies and trials, and to expand commercial partnerships, thereby increasing our impact in improving patient treatments and care.

1.4 Support for interdisciplinary research

Our highly interdisciplinary research themes include researchers from four of the five University faculties (Medicine, Dentistry and Health; Science; Engineering; Social Sciences). Our investment of £20M over four years in the flagship Neuroscience and Healthy Lifespan Institutes (alongside Insigneo) will further such interdisciplinarity through joint programmes, seminar series, pump-priming seed funding and other ventures.

Fig 4:

Interdisciplinary Research: Healthcare intervention cuts across University Faculties & Four Pillars where we lead Sheffield's <mark>Flagship Neuroscience and Healthy Ageing Institutes</mark>

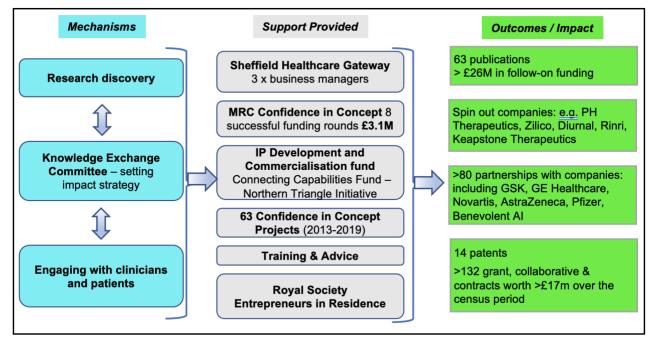


1.5 Impact strategy

Evidence of our REF2014 strategy to achieve impact from our research is described for each theme above (section 1.3). We are committed to maximising patient benefit translated from our medical research, achieving global reach and delivering solutions to health challenges. The University has supported us by investing substantially into developing and maintaining relationships between our researchers and external partners, and providing an environment to accelerate translation, promote innovation and generate impact (REF5a). IP Development and Commercialisation Fund (IPDaC) investment was £437k and patent expenditure £371k to our unit over this assessment period. The <u>Sheffield Healthcare Gateway</u> (SHG) provides a single point of access for business to our healthcare facilities and expertise (section 3.3), facilitating collaboration with >2,000 organisations, generating >£17M since 2014. We support staff in time allocation to develop impact from research and reward its achievement through promotion (section 2.2).



Fig 5: Enabling impact in clinical medicine



We exploit our extensive NHS links to achieve clinical impact. All research themes rely on close partnerships between discovery and clinical scientists to drive discovery-to-clinical-to-discovery research. Our clinical research facility (section 3), NIHR Biomedical Research Centre and clinical trials centres, alongside support of trial design through ScHARR (UOA-2), support translating research into clinical trials and treatments. We have over 40 Patient and Public Involvement groups in Sheffield Teaching Hospitals NHS Foundation Trust, allowing exchange of expertise and experience between researchers, patients and families. We measure the impact of our research through initiatives including VICTOR (Section 1.6).

Relationship of impact cases to our approach to developing impact

Our impact case studies are the result of NHS partnerships, clinical trials, intellectual property, and commercial partnerships enabled via dedicated support.

Case study	Mechanisms enabling impact	Impact
Ticagrelor: New drug saves lives following heart attack	University supported partnership with AstraZeneca to run PLATO and PEGASUS clinical trials in our clinical research facility. SHG and commercial team helped secure IP value.	Reduction in risk of further heart attack, stroke, or death in patients on treatment
DiPALS: Evidence to inform guidance on Diaphragm Pacing for MND patients	NIHR funding to clinically assess the NeuRx/4 Diaphragm Pacing in patients with MND with help from SHG	Shaped global clinical policy and safeguarded MND patients
MIST: Autologous haematopoietic stem cell treatment for relapsing remitting multiple sclerosis (MS)	Active funding of work through NHS. Phase II and III trials led through our NIHR Biomedical Research Centre	Offers the most effective treatment for this group of MS patients. New health guidance.

Table 1: Summary of impact case studies



Alkindi: Treatment for children with adrenal insufficiency	SHG facilitated the formation of the Diurnal Group spinout company in 2015 to support commercialisation of treatments for adrenal insufficiency such as Alkindi	Preventing patient death from adrenal crisis. £12M private investment, £40M flotation. Prescriptions >£350k in 2018.
Personalised Therapy: Novel tailored therapy for BRCA-mutated cancers	IP registered in 2003 and licenced to KuDOS Pharmaceuticals (purchased by AstraZeneca in 2005) ensuring commercial development	Recommended by NICE as first line therapy in BRCA-mutated ovarian, fallopian & peritoneal cancer
Adjuvant Bisphosphonates into routine practice for breast cancer	Clinical trials and experimental cancer centres to support AZURE trials with NIHR, underpinning new treatment	Prevents metastases in breast cancer
FRAX: the internationally applicable fracture risk calculator	FRAX online fracture prediction tool is incorporated into over 120 clinical guidelines worldwide	Reduces hip fracture incidents

Pipeline of future impact

We will ensure future impact through strategic investment and research support and have built a strong impact pipeline (section 4.3). For example, Heller, Francis, and Storey are influencing clinical recommendations based on their research showing that hypoglycaemia is associated with adverse cardiovascular events in Type 2 diabetes. McDermott & Shaw are improving nutritional management for patients with MND, Ross is developing hormone antagonists to treat acromegaly, Skerry is developing bone tumour inhibitors and Anumba was recently granted a licence to EveryBaby Ltd. to market a novel device to detect the likelihood of premature birth.

1.6 Progress towards an open research environment

The University promotes a culture of open research and has an Open Research Advisory Group, comprising experienced academics and expert professional colleagues, that reports directly to the University's top-level Research and Innovation Committee. Within this unit open research policy is scrutinised and updated regularly at our Faculty Research and Innovation Committee, supported by our <u>Research Practice Lead</u>. We are implementing electronic lab notebooks and mirrored electronic data storage for 10 years in line with UKRI requirements.

We regularly host seminars and workshops on open data, sharing practices, research communications and OA. In 2014 we introduced training in OA, research design and reproducibility, data management, thesis completion and careers for our PGRs to embed the principles of open research early in academic careers. 18 of our staff are editors for 22 OA journals.

To ensure maximum discoverability of our research, we aim to put all outputs in White Rose Research Online, our shared repository with Leeds and York (green route). The 4,246 outputs deposited over this assessment period were downloaded >235,000 times. This is our preferred route, ensuring equity in publishing opportunities regardless of available funding; we also publish outputs in fully OA journals, or hybrid where required for funder compliance. In addition, staff increasingly submit papers to preprint services such as <u>medRxiv</u> or <u>bioRxiv</u> to ensure timely dissemination of research findings.



Appropriate data are shared in national or international data centres or repositories, e.g. Gene Expression Omnibus (<u>GEO</u>). Large-scale research data is deposited to the University's data repository (<u>ORDA</u>) provided by *figshare* to enable it to be preserved, discovered, and accessed.

Accessible Databases: Research within the NHS can lead to significant changes within the organisation itself, including potential impacts on skills and knowledge, service delivery, patient and carer experience, as well as economic benefits. To capture and share these effects, <u>VICTOR</u> (Visible ImpaCT Of Research) was launched in 2019, a tool that we have implemented in our research capacity development, to make the impact of delivering research visible within the NHS organisation itself and into the community.

Clinical trials data: In accordance with current guidelines, we ensure that any research involving patients that is considered a trial, is registered in a suitably accessible database. Many of our larger projects, managed by NIHR-funded Clinical Trials Research Units, have study specific websites and/or Twitter accounts, which also help with the recruitment of participants and disseminating study outcomes. Our policy is to publish findings of all clinical trials regardless of outcome.

1.7 Promoting a culture of research integrity

We strive to support robust, reliable, and reproducible research. The University is a founder member of the UK Reproducibility Network, a peer-led consortium which aims to improve the quality of UK research output, and in 2019 created a new academic Research Practice Lead position to scrutinise our processes used across the whole lifecycle of research to identify and share best practice (see REF5a). All recruits to our unit undertake online training. Every PGR receives compulsory training in **research integrity**, agrees and signs a **Research Data Management Plan**, appraised over the project. We engage closely with the National Centre for the Replacement, Refinement and Reduction of Animals in Research (<u>NC3Rs</u>, where P.Evans is board member); we host regular seminars from their representatives facilitating researchers to design optimal experiments so methods and findings are <u>robust and reproducible</u>.

All research requiring research governance is automatically flagged at costing/application stage. Post-award, funds are released only when research licencing and ethics governance is agreed and in place. Sheffield Teaching Hospitals' Clinical Research & Innovation Office is responsible for research involving human patient samples. Ethical approval applications for human interventional studies and clinical trials are supported by our Medical School <u>Research Ethics</u> team. Our flow <u>chart tool</u> helps researchers identify the appropriate governance requirements for each study. Human volunteer studies not requiring NHS ethics approval require ethical approval from our Medical School Research Ethics Committee, chaired by an academic who sits on the University Research Governance sub-committee. Towards the **study end** the ethics office flags the biorepository and the investigator with reminders on sample storage requirements (destroy, extend, transfer) governed by the agreed ethics. We perform an **annual audit** of all project-leads to confirm that all **samples are held in accordance with the Human Tissue Act** or under active ethics approval. All PGRs take research ethics training and detail ethics proposals within their Data Management Plan. We view maintaining strong integrity as essential to conducting impactful research that is transparent and reproducible.

REF2021

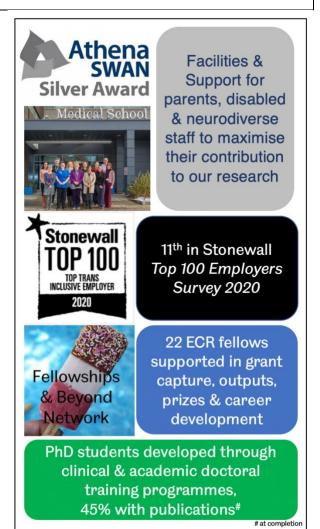
2. People

We foster a supportive and collegiate environment and a community where research excellence and career progression can be achieved. Our recruitment strategy, mentorship, support networks and career development schemes aim to attract, nurture, and grow diverse and successful researchers. We aim to uphold the principles and implement the Concordat to Support the Career Development of Researchers, of which we are a signatory. We are the only University to feature in the Sunday Times '*Top 100 best not-for-profit organisations to work for*' three years running.

The University is a truly civic university, founded through the aspirations and financial support of the people of Sheffield. We are a signatory (2019) to the Civic University Agreement, where our medical research and our people align to the priorities of the city and the local region. Our place in the wider community, together with a supportive workplace, underpin the reasons why our staff choose us as a place to work.

2.1 Staffing and recruitment

Our approach to staffing reflects an overarching mission to support the research excellence of our



themes. The unit comprises 116 clinical and non-clinical academic staff over a balanced age group (see Table 2) and we have submitted 100% of Category A staff. Our research and impact activities are supported by 84 technical and 33 professional staff, funded both internally and externally.

Table 2: Number of staff across grades
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	All staff	Clinical	Non-clinical
Independent research fellows	23	5	18
Lecturer/Senior Lecturer	49	27	22
Professorial	42	24	18
Professorial Fellow	2	0	2
Total	116	56	60

Our recruitment has centred around a strategy to complement and enhance our research themes. For example, the Infection and Immunity theme recruited experts to expand our expertise in host and adaptive immunity, complementing existing staff who work on pathogen biology and innate immunity. We appointed Sourbron (from Leeds) in 2019 and Su (Cambridge) in 2020 to expand our imaging strengths. In 2018 Helleday was appointed Chair of Translational Oncology (from the Karolinska Institute) and our subsequent investment in cancer allowed recruitment of Hussain,



Toseland, Gad and Rantala. Our strategy is also to recruit and support independent fellows to improve sustainability and invest in the future.

Over the assessment period we recruited 17 independent fellows and one professorial fellow (Su), while five staff from within our unit have obtained externally funded fellowships (R.Thompson, Morris, Reynolds, Twelvetrees, Fragiadaki) and one a professorial fellowship (Lawrie). These fellows are given protected research time and have published a number of strong outputs in *Cell* (I.Evans), *Circulation* (Lawrie), *Nature* journals (Lawrie), *eLife* (R.Thompson, Twelvetrees), *PNAS* and *Neuron* (Twelvetrees). Several of our recruits are former PGRs who returned at later stages of their career, testament to their positive experience of our environment: in 2014 Ferraiuolo returned to Neuroscience as a fellow (*PNAS* 2016, *Nat.Med*.2016); Darton, De Silva, Roger Thompson and Morris began their careers in Sheffield clinical training programmes and are now independent fellows each with research funding \geq £1M. Elks, Ruth Thompson, Lawrie and Kemp have been supported into independent fellowships from within Sheffield.

Our career succession planning strategy led to 40 promotions since 2014. Recruitment policies are subject to positive selection criteria emphasising Athena SWAN-promoting gender equality. As expected for any institution with a healthy turnover, not all staff choose to stay. Former colleagues have made prestigious career progressions since leaving us during this assessment period: Walmsley is now Chair of Respiratory Medicine (Edinburgh) and Whyte is Head of Medicine, University of Edinburgh; Hellewell is now Vice Provost and Dean, Brunel University.

We recognise the importance for our research of support from skilled and experienced technical staff. In the last assessment period we introduced a **technician apprenticeship scheme**, recruiting and retaining new staff with excellent potential.

2.2 Staff development and support for ECRs

Mentoring

We have a strong commitment to mentoring staff at all career stages, from both clinical and nonclinical backgrounds. Formal mentoring focuses on ECRs, but mentored staff appraisal and career development meetings are offered to all staff, with several having progressed to permanent posts under the mentorship of senior colleagues (Ferraiuolo, Morris, Weatherley, Mortiboys). The University's researcher-led Think Ahead scheme (see REF5a) is open to all research staff including PDRAs, using established mentoring and coaching techniques. After induction and mentoring skills training, each mentee is matched with a mentor from outside their department for six months (extended by mutual agreement). Mentors support research staff at all career stages and into their next position within and beyond academia. Our unit has 33 trained mentors; >100 ECRs have been mentored in the past 6 years (59% female). This mentoring programme helps staff enhance skills, maximise potential and develop their careers.

Appraisal

Staff of all grades and contract types (from academic to professional services) are provided with a tailored induction on arrival. Staff are mentored through an annual appraisal (the *Staff Review and Development Scheme, SRDS*), which provides an important opportunity for individuals to reflect on their previous year's work, including the most and least satisfying aspects, and consider career aspirations and how to achieve these. Reviews are performed with a designated reviewer, designed to support staff who wish to apply for promotion, by building a portfolio of achievements. Objectives align with both personal and organisational goals and opportunities for staff to achieve



reward and recognition including promotion following the Academic Career Pathway Framework (ACP, see REF5a).

Training

Continuous staff development is also achieved through training programmes, which are discussed and planned at SRDS. A Learning Management System provides a portal for staff to access >170 courses in all areas of development from data management, academic writing to leadership training. The Sheffield Leader programme (designed to enable individuals to develop the foundations, practical skills and behaviours required to succeed in their leadership and management roles) benefitted 32 staff members with 17 subsequently progressing to leadership positions. Staff have compulsory and additional options for research integrity training (section 1.7).

Early career researchers (ECRs)

To recruit ECRs with strong potential, we provide a supportive environment with opportunities for career progression. In line with the Concordat to Support the Career Development of Researchers, our 'Inspire' and 'Aspire' framework has been adopted as a University-wide charter. We have developed a **Faculty Early Career Group** whose representatives champion the researcher career agenda and steer the Think Ahead programme, a blend of training workshops, career mentoring, and carefully selected work-based opportunities, designed and developed originally for the Medical School using a research-led approach. In addition, there is a well-established mentoring and Integrated Academic Training (IAT) programme for academic clinical fellows and lecturers, who are mentored by senior clinical academics from other departments. The IAT programme interfaces with other innovative PGR training schemes (below). By sharing best practice across the clinical/non-clinical interface we have improved the quality of the training programme offered to both.

Regular research seminars are given by external and internal speakers, averaging twice weekly. Early career and trainee researchers are encouraged to attend; their involvement is enriched with interactive follow-up Q&A discussions involving the invited speaker. The session is intended to give ECRs and PGRs the opportunity to discuss topics such as mentoring, career options and work-life balance. We hold regular 'Bitesize' sessions on career and skills development (e.g. conference presentations, data presentation) and an annual Medical School Research Day with dedicated sessions for ECR presentations.

We actively support ECRs into fellowship programmes, with many successes: Darton, De Silva, Roger Thompson and Morris began their careers in Sheffield academic clinical training programmes and are now independent fellows each with research funding \geq £1M. Elks, Ruth Thompson, Lawrie and Kemp have been supported into independent fellowships from within Sheffield, whilst we have recruited several independent fellows from external institutions. We instigated the <u>Fellowships and Beyond</u> (FAB) network (I.Evans), providing peer support and practical help to staff looking to move towards independence in their research career. We participate in the Wellcome Trust **Café Culture** initiative for staff to reflect on and propose solutions to improve research culture.

Promoting collaboration

Our interdisciplinary institutes and structures promote collaboration via workshops, grant aim review sessions and internal/external seminars. We provide Learned Society funding to support staff travel for conference attendance and to establish new collaborations, recognising this benefits our staff by broadening experience and strengthening impact (section 4.1).



Supporting, recognising, and rewarding impact

Impact is firmly embedded as part of our institutional research culture. We engage researchers in impact-related activities in a variety of ways throughout their careers. The new Academic Career Pathways explicitly recognises impact in the promotion process and in workload allocation (REF5a). Staff have access to HEIF and public engagement funds to facilitate activities that build impact (sections 1.5, 3.3). We offer public engagement masterclasses and host two Faculty Royal Society *Entrepreneurs in Residence* to provide mentoring and commercialisation training. A joint University/Sheffield Teaching Hospital Clinical Research & Innovation Office provides co-ordinated administrative support for clinical studies (section 4.1 on outcomes from this support). The Northern Health Science Alliance connects companies with the NHS/University, generating opportunities to work with external partners and create healthcare partnerships and collaborations with service providers and pharmaceutical, clinical, life science and biomedical companies. Each department has an Impact Lead. These meet monthly at the Knowledge Exchange Committee to influence impact strategy and disseminate University policy and opportunities.

2.3 Postgraduate researchers (PGRs)

We have a thriving community of 197 PGRs, aligned to strategic research priorities. PGRs are funded through a number of doctoral training partnerships (DTPs), including the BBSRC DTP in Mechanistic Biology and its Strategic Applications (Leeds, York, Sheffield), the MRC Versus Arthritis Centre for Integrated research into Musculoskeletal Ageing (CIMA; Newcastle, Liverpool, Sheffield) and the MRC Discovery Medicine North (DiMeN) DTP (Leeds, Liverpool, Newcastle, Sheffield), which awards 30 fully-funded studentships (includes 6 iCASE) each year, focussing on genetic influences on health, ageing and disease, bioinformatics and personalised medicine. The Wellcome Trust 4Ward North Clinical PhD Academy (Sheffield, Manchester, Newcastle, Leeds) supports doctoral training for clinical candidates, incorporating the opportunity to compete for our Leading Scholars Programme in collaboration with the Crick Institute offering 12-month's research support post-PhD to pump-prime career development applications.

PGRs are also supported via NIHR training fellowships, EU-ITN training programmes, MRC standard and iCASE Studentships, MRC National Productivity Investment Funds; BBSRC iCASE awards, DTP CASE Conversion, EPSRC Standard and iCASE Studentships, our joint PhD programme with Tongji University Medical School, the A*STAR-Sheffield Research Attachment Programme with Singapore, clinical and non-clinical training fellowships from the BHF, Heart Research UK, Chernajovsky Foundation, Rosetrees Trust and several Royal Colleges. 45% of PGRs complete their PhD with publications. We recruit a diverse cohort of PGRs: 30% international, 13% EU, 57% UK, and set aside faculty funds to support progression of our top-ranking masters graduates onto PGR programmes, guaranteeing interviews for those candidates meeting widening participation criteria. We recruited 77 academic clinical fellows and 30 academic clinical lecturer posts over this assessment period. Our clinical fellows frequently progress to higher degrees: 55% obtained a clinical PhD fellowship/MD. Eight staff started their research careers via NIHR clinical academic training in Sheffield, including Darton, De Silva and Morris.

Monitoring and support: PhD training is organised by Faculty and Departmental PGR committees, which ensure engagement of PGRs with the University's Doctoral Development Programme, monitor progress, and ensure high standards of supervision, mentoring and pastoral care. All PGRs are assigned two supervisors and one/two impartial advisors/mentors. **Supervisors** are expected to attend an annual supervisor update session to **share best practice** in PGR provision and in bimonthly supervisor support sessions. Monthly records of formal supervisory meetings are submitted and checked centrally. Issues with progress are flagged and promptly



acted upon. Early in this assessment period, we took steps to improve our 70% on-time submission rate. A culture-change encouraging PGRs to develop academic writing skills from the outset, increased support for writing, submission review planning and flexible study leave arrangements have resulted in **94% in-time thesis submission** for PGRs entering in 2014/2015.

PGRs use peer mentoring and are encouraged to use Vitae's Researcher Development Framework to plan their development and attend sessions on open access, research design, reproducibility, data management, thesis mentoring and career planning. Online data management plans, CV builder and thesis planning tools are reviewed at key checkpoints including confirmation review and final thesis submission. In the 2019 **Postgraduate Research Experience Survey**, 99% of our PGRs felt their methodological skills had developed, 95% that their critical analysis skills had improved and 93% that their understanding of 'research integrity' (e.g. rigour, ethics, transparency, attributing the contribution of others) had developed during their programme.

All PGRs participate in the Faculty Postgraduate Induction Course in their first week. Designed to support the transition to a research environment, this provides opportunities for networking and cohort building alongside training, information on health and safety, ethics and integrity, unfair means and managing the supervisor-student relationship. New PGRs are offered trained peer mentors from the same department. We offer non-clinical PGRs a PhD Intensive Clinical Experience (PhD-ICE) to support understanding of clinical problems linked to their research projects. Sharing best practice across the clinical/non-clinical interface improved the quality of the training programme offered to both. Our PGRs are embedded into our research; they develop presentation skills in weekly theme research meetings, annual Medical School research away days and are required to give at least two oral and one poster presentations during their PhD. We organise journal clubs, research reproducibility and integrity seminars to facilitate an understanding of journal and grant review processes. PGRs organise departmental PhD societies, which provide peer support, organise departmental seminars and social events.

2.4 Equality, diversity, and inclusion (EDI)

The University aims to be a leader in driving excellence through inclusion, providing an environment in which researchers thrive and achieve their full potential. We were ranked 11th in the Stonewall Top 100 Employers 2020, our seventh year in the top 100, reflecting the emphasis the University places on EDI, matching our own ambitions. We recognise the importance of an inclusive, diverse, and high-performing culture which leads to richer, more creative, and innovative research. We have altered our structures over this assessment period to ensure that **EDI is considered in all decision-making processes**, with EDI Directors in each department and a Faculty EDI Director sitting on the Faculty Executive Board (the highest faculty management structure).

Strategies to support EDI

Athena SWAN and gender equality

We achieved an Athena SWAN <u>silver award</u> for promoting gender equality in 2010 and are seeking renewal in 2020. Female staff in our unit play key leadership roles: P.Shaw was Pro-Vice Chancellor and Vice-President of our Faculty (2015-19); Francis was Head of a Department (2015-18), Cox is current Deputy Head of a Department and Kirby is PGT Director. We were cited by the Universities and Colleges Employers' Association (UCEA) as a good practice example in our work on the gender pay gap.



Females comprise 31% of submitted staff (27% of professors). We have introduced several structural changes to improve this balance. We promote gender equality in recruitment by removing gender bias from job descriptors, providing unconscious bias training for all selectors and independent scoring of candidates against job criteria. We instigated the "Dame Pamela Shaw Awards" in 2018 to give PGRs and staff the opportunity to apply for small awards aligning with the goals of Athena SWAN, including bursaries of up to £1,000 for conference attendance or projects to develop and explore equality issues. Staff on parental leave can access the "Whyte payment" contributing to childcare expenses on keep-in-touch days. The academic pathway for female surgical trainees has been shortened by focusing on competency rather than time-dependent progression. T&Cs for trainees moving between University and Hospital posts have been harmonised. An Athena SWAN Breastfeeding Room and facilities have been provided by the Medical School since 2014.

The University's flagship **Women Academic Returners' Programme** provides financial support to women to mitigate the impact of maternity/adoption leave on research progression. These offer funding for additional posts or research. Over this assessment period 10 WARP awards have been provided to staff in our unit, 86% of whom achieved subsequent external funding. This was cited by UCEA as another example of good practice. The University has a **flexible working** policy with all applications so far approved; 13% of submitted staff of all genders work part-time.

We established a University-wide **Futures Mentoring** Programme for senior female academics where Faculty Vice-Presidents mentor senior female academics enabling discussions on career progression from outside their own faculty. Our Athena SWAN Champions meet three times per year to share best practice/learning and celebrate achievements.

Improving diversity

This assessment period the University instigated an action plan to address under-representation, progression and attainment of minority ethnic students and staff, who constitute 19% of our submitted staff and 18% of professors. We aim to create a diverse and inclusive community and reduce the gap in pay, attainment, and representation. Offiah chairs the **BAME Staff Network**, set up to address the needs, priorities, and concerns of staff from diverse non-White groups. In recruitment we use targeted adverts, job descriptions and de-biasing of selection processes. All staff on boards and committees undertake training in implicit bias and addressing diversity. We are actively involving ourselves in the recently established <u>Sheffield's Race Equality Commission</u>, which held its first hearing focussed on health equality in 2020. We aim to improve diversity from the ground-up, building and progressing minority ethnic talent from PGR and ECR stages using mentoring and support networks, with senior role models as advocates.

Support for LGBTQ+ staff

Sheffield's commitment to promoting diversity and eliminating discrimination includes strong support for our LGBTQ+ staff and students. We were ranked 11th in the Stonewall Top 100 Employers 2020 survey and a "Top Trans Inclusive Employer", testament to the importance we place on LGBTQ+ inclusion, reflected in our own unit's inclusion policies and community. The EDI Medical School Committee supports LGBTQ+ via EDI leads and LGBTQ+ champions in departments, by improving signposting and designing improved mandatory staff training on how to support other LGBTQ+ staff.



Support for disabilities and neurodiversity

We value diversity and include and support staff or students with disabilities. Our unit has the third highest proportion of staff with disabilities in the Russell Group. J.Brown co-chairs the University Disabled Network, which allows staff to gain or offer support, participate in social activities, and share experiences. We support staff to manage their health/fitness/disabilities by providing leave for staff adjustment, treatment, assessment or rehabilitation, which includes managing mental health and wellbeing concerns. Our disability liaison officer (Staton) represents needs and supports individuals in our unit. Neurodiverse staff are supported with flexible working arrangements and task management to capitalise on strengths; we value the positive contribution diversity brings to our unit.

Preparation for REF2021

In preparation for REF2021, all members of the REF Committee undertook institutional REFfocussed EDI training to mitigate against unconscious bias. Our REF team is representative in gender and as inclusive as possible, with output selection performed by a range of academic staff with a breadth of expertise. We selected papers in rank order. It is not possible to maintain anonymity for authors of submitted outputs, therefore we ensured that where there was an excess outputs at the cut-off, an appropriate career-stage and gender-balanced selection was submitted. The unit staffing strategy, including recruitment, development, and support, is assessed and updated by our EDI Committees, consistent with institutional strategy. This includes a commitment that there should be no detriment to staff in the number of outputs submitted and that REF submission data is not used during review or promotion.

3. Income, infrastructure and facilities

3.1 Income

Our strategic aims to translate discovery science to clinical impact, to grow partnerships with engineering and computing for digital healthcare, and to respond to global challenges in healthcare, was underpinned by a **50% growth in funding** since REF2014, from £71.7M to £107.4M over this assessment period (£1.0M per FTE). This growth is across all career stages and linked to our research priorities.

Enabling our research priorities: Over this assessment period we sought to diversify our funding sources, reflecting our strategy to grow commercial partnerships to widen our impact for patient benefit. We received 35% of our income from charities, 23% from UKRI and 15% from NIHR.



Grants (108) totalling £3.4M were awarded to fund clinical trials to translate our work. A variety of



clinical studies received charity support. For example, Yorkshire Cancer Research Catalyst for Innovation in Cancer Care and Treatment in Sheffield received £2.7M to improve outcomes in bladder cancer.

To strengthen *translating discovery science* into developing new clinical treatments and diagnostics, we increased the number of our commercial partnerships, with a **187% increase in industry spend** over this assessment period (12% of our income). For example, Neuroscience received £5.5M funds from Pfizer, Biogen, Forma Therapeutics, Celgene, Cure Fund, New Zealand Pharmaceuticals, GSK, AstraZeneca, and Benevolent AI to assess neurotoxicity and genetics in motor neuron disease and to accelerate novel treatments for Parkinson's, Alzheimer's, and ALS. Our **cancer drug discovery programme** was supported by £2.8M Wellcome Trust Seeding Drug Discovery funds (Skerry). Therapy development for targets we identified for pulmonary hypertension treatment received >£1.5M support from Pharma including GSK, Bayer, Actelion, Endotronix and Novartis (Lawrie, Thompson). A number of our commercial projects were developed from HEIF IAA funded support (£5.9M). Licence income from Lynparza provided £63M over the assessment period.

We have targeted specific funding to grow areas of strength. In **Imaging**, we grew our Pulmonary, Lung and Respiratory Imaging Sheffield (POLARIS) infrastructure with £7.5M from MRC and BHF to provide new equipment with the capacity to generate novel technological solutions for hyperpolarised gas imaging, with further £6.7M in research programme funds to advance research in this area (Wild). The University invested £11.4M including £2M from donations and alumni to build a new PET-MRI facility and scanner to deliver advanced imaging and powerful new diagnostics. The £4M NIHR-BRC **Neuroscience** investment has driven expansion of new collaborative neurodegenerative disease research initiatives. Global challenges in **infection** have been supported by the Bill and Melinda Gates Foundation (£836k, Darton) for early infection diagnosis, by the MRC (£3.5M to a consortia) and £11.4M capital fund (cross-faculty, Florey Institute) to support antimicrobial resistance research. We received rapid-response funds to support our response to the COVID-19 challenge in multiple trials and studies, enabling Sheffield to become the largest recruiting centre for the Oxford vaccine trials (section 1.3). **Digital healthcare** research has been underpinned by several EU Commission programmes, e.g. £4.9M to EurValve to optimise patient-specific intervention in Valvular Heart Disease (Hose).

Our strategy to nurture and develop ECRs into fellowships and successful research careers is evidenced by **£12.4M in fellowship awards** to 24 individuals over this assessment period. **Half** of our successful junior fellows are **female**, promoting our aims to improve gender balance and invest in the future. Our fellows are supported by a diversity of funders including Dorothy Hodgkin (Ruth Thompson), Kidney Research UK & UKRI (Fragiadaki), EU (Hamilton), MRC and BHF (Lawrie, Thompson), Yorkshire Cancer Research (Mayland), Versus Arthritis (Ismail) and Wellcome Trust (Morris, Elks, I.Evans, Henriques, Twelvetrees, Gurevic). A number of our fellows have gone on to attract significant additional funding (e.g. Roger Thompson £158k BHF, Morris £295k BHF, Fragiadaki £227k BHF and £1.1M UKRI, Ruth Thompson £136k Royal Society, Henriques £77k Dunhill Medical Trust).

3.2 Organisational infrastructure and facilities

We expanded our infrastructure to create a research environment with state-of-the-art facilities to drive our strategic research priorities.

We have dedicated support for **translational and drug discovery** programmes, including two <u>NIHR Clinical Research Facilities</u> to support clinical research from first-in-man to late phase; since 2014 supporting 871 studies, recruiting 26,085 participants. Over this assessment period, trials

including PLATO and PEGASUS (Storey, 2016, JACC), leading to the Tigacrelor impact case study, were conducted via these facilities. Sheffield Institute for Translational Neuroscience received major philanthropic donations to provide a new building (£20m), housing under the same roof interdisciplinary teams of neuroscientists and clinicians with state-of-the-art equipment to increase understanding of disease mechanisms, identify new therapeutic targets and translate these insights into effective therapies and outcomes for patients in the clinical care setting. Sheffield's Experimental Cancer Medicine Centre will make more new treatments available to patients in early trials, help develop new anticancer treatments and develop predictive biomarkers for personalised treatment planning. The Centre has facilities for imaging, flow cytometry, DNA sequencing and histopathology, Biobanks (Breast Cancer Now), and trials unit. This centre has led AZURE and BRAVO trials in this assessment period, resulting in new cancer treatments for patients (section 1.3). Our drug discovery laboratory provides optimised storage of test drugs and compounds in a fully automated system using dry nitrogen. Neuroscience and Cancer programmes benefit from high-throughput liquid dispensing systems for rapid large-scale screening experiments. We host and manage the Sheffield Biorepository, a Human Tissue Authoritycompliant facility for storage of human tissues and cell samples, used in multiple studies over this assessment period.

Sheffield houses advanced **pre-clinical imaging** facilities including our MRI facility, the Wolfson Light Microscopy and Electron Microscopy services. We are developing technologies allowing us to image the same subject across a range of spatial scales and time, enabling assessment of normal function and disease, capturing better-quality data from fewer subjects. Over this assessment period, our Pulmonary MRI facility received major capital investment to add five polarisers, a radio frequency lab dedicated to creating and building new technology scanners and a pulmonary function test (PFT) lab to couple functional breath testing to imaging. Our human brain imaging facilities are



expanding and currently include 1.5T MR scanners, FIREFLY-Neonatal 3T Brain Imaging Scanner, a 3T Phillips Ingenia MR Scanner and EEG systems. Our £11.4M investment in a ground-breaking PET-MRI facility in 2020 will transform our understanding of diseases and the way we treat them in the future. These facilities, alongside recruiting experts in advanced imaging, supports our strategy to continue to lead in cutting-edge imaging and diagnostic research.

We use **high performance computing** (HPC) in our research in biomechanics, fluid dynamics, bioinformatics (below) as well as in imaging for gas exchange modelling simulations, parallel computing image processing and image registration workflows. Through Insigneo and POLARIS we have benefited from HPC infrastructure and have invested heavily in this in liaison with central University workgroups. For example, £350k was allocated from the MRC POLARIS award for <u>SHARC</u> computing infrastructure and staff (section 3.3).

Neuroscience is part of the Adaptive Behaviour Research Group, housing our Active Touch Lab facility. Over this assessment period these facilities expanded to include **robotics**, computational modelling and methods in animal behaviour, neuroethology, and human psychophysics to investigate tactile sensing in animals, people and intelligent machines. The group boasts one of the largest UKRI/EU-funded robotics research programmes in the UK, with specialist laboratories and facilities for electrophysiology, motion capture, neurophysiology, human psychophysiology, transcranial stimulation, and optical imaging, building into our **digital healthcare** strategy. **Translational neuroscience** incorporates a drug discovery laboratory (above), neuropathology & histology, neurogenetics functional genomics, RNA and molecular biology laboratories and a computational biology team. Our genomics and sequencing (including HiScan SQ) infrastructure is



supported by a bioinformatics core, with expertise to support cutting-edge research across all themes. Most recently, our **bioinformatics** core performed sequencing and analysis for the **COVID-19 Genomics consortium**.

We invested in **healthy ageing** research by continuing to build our infrastructure. *The Bateson Centre* houses one of the largest and best-equipped **zebrafish facilities** in Europe, holding a globally important collection of >750 mutant and transgenic lines and accommodating a behavioural analysis suite, advanced microscopy, microinjection facility, programmable light boxes and light cycle incubators and cryogenic storage for IVF. Staffed by



experienced fish husbandry technicians, the facility offers a genotyping service for all facility users and sorting of fish for breeding. In **ageing**, **immunity**, and **infection** research we study mechanisms of change throughout life, including growth, remodelling, degeneration, and repair to improve maintaining health, fighting pathogens and treating diseases of ageing. **Cellular imaging** forms an important part of this study, where we are fortunate to access the University's superb *Imagine* facilities. These provide state-of-the-art imaging techniques from molecular structures to whole organisms, including electron microscopy and the Wolfson Light Microscopy Facility which includes confocal, multiphoton, widefield imaging, super resolution and light sheet fluorescence microscopy.

3.3 Infrastructure support

We built a team of dedicated support staff to manage our facilities, provide staff training and strategic support over this assessment period. An objective in the last five years has been to increase grant funding. We established a **Research Support Hub** to improve pre-award application support and coordinate peer grant review, consisting of two support officers and four hub managers responsible for supporting grant submission, disseminating information from the Faculty Research and Innovation Committee, contractual support and internal grant review. This has been effective, evidenced by growth in grant applications and funding.

Our research facilities benefit from dedicated managers and expert technicians. We are a sector leader in our support for research technicians (see REF5a and section 2.1) who play a critical role in maintaining facilities and training staff in their use, ensuring our research benefits from access to the latest technologies. Staff in our **Bioinformatics Core** provide advice and training on experimental design, high-throughput next generation sequencing (NGS) analysis and offer clinical bioinformatics services and consulting.

Sheffield is a sector-leader in **digital infrastructure** support, software engineering and highperformance computing and storage through its <u>SHARC</u> facility (see REF5a). Research in our unit, particularly in **imaging**, **bioinformatics** and **digital healthcare**, has dramatically expanded its use of high-performance computing over this assessment period. We have invested in central facilities (as above), and benefit from support staff who develop software and support our intensive computing and storage requirements. This is central to our strategy to lead in research programmes using advanced imaging, bioinformatics and in data-intensive projects such as VIRTU-Heart and the ECHOES consortium.

The <u>Sheffield Healthcare Gateway</u> provides a single point of access for business to our healthcare facilities and expertise. They promote and support academic knowledge and commercialisation by: securing external funding such as MRC CiC; placing Entrepreneurs in Residence; capturing and progressing IP including directing patent applications; assisting with the



development of the exploitation pathway and IP strategies, that are also required for the planning and compiling of translational funding bids from a variety of sources (e.g. NIHR, Wellcome Trust, MRC DPFS, BHF); facilitating agreements/contracts for collaborative and/or contract research so they meet the needs of all parties; and/or negotiating licences with external partners and working to set up spinout companies. Over this assessment period the Healthcare Gateway facilitated collaboration with >2,000 organisations to harness expertise, technology and insights from our research teams. This supported our strategy to increase our research impact (section 1.5).

Support staff administer our **research ethics and governance** processes, facilitating review of all research involving human participants under University NHS ethics processes as appropriate, under strict **data security**. Projects required to comply with data security and cyber security are supported by the University **information governance group** for policy implementation, and all staff must undergo annual information security training.

4. Collaboration and contribution to the research base, economy and society

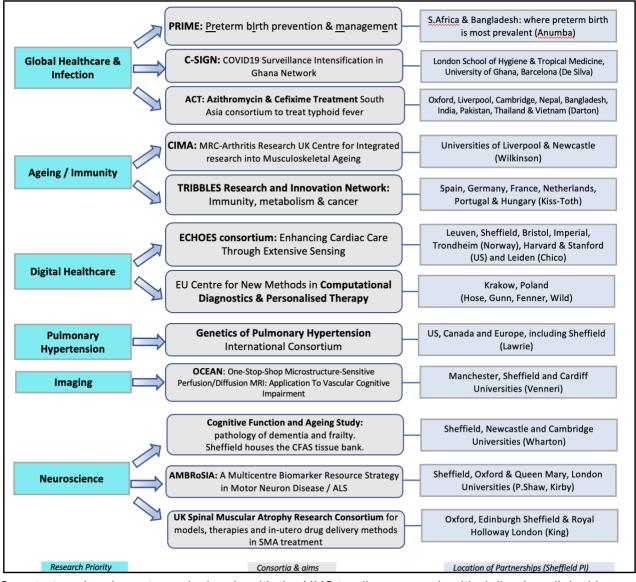
4.1 Research collaborations

Our mission to improve global health requires an interdisciplinary, collaborative, and international approach. The mechanisms and funding to support staff are outlined in sections 2 and 3. We provide our staff with the support and time to build collaborative initiatives to make significant research advances and to achieve impact.

Our unit has formed a number of strategic national and international collaborations that strengthen our research and its clinical impact. As examples: we developed global healthcare and infection research through a number of collaborative initiatives and consortia. We led and formed significant partnerships across Europe in our digital healthcare programmes, immunity, and ageing research programmes, while pulmonary hypertension has expanded its clinical impact to join with European and international centres (see Fig 6). As a result, 46% of our submitted outputs represent international collaborations.

Fig 6: Exemplar collaborations driving our strategic research priorities





Our strategy has been to work closely with the NHS to align research with delivering clinical impact and improving healthcare. We have actively built our research and institutes to complement our clinical strengths: Sheffield Teaching Hospitals NHS Foundation Trust includes national specialist healthcare centres in neuroscience, pulmonary hypertension, infectious diseases, and imaging. Our collaboration with Sheffield NHS partners is key to developing impact and enriching our research environment. Submitted staff in this unit work closely with >70 honorary staff; 41 honorary clinical staff co-supervise PGRs. Their involvement provides research programmes with improved opportunities to involve patients, collect patient samples, perform studies and trials within clinical settings and to integrate research to real clinical challenges. In this period, as a result of our NHS partnerships, the unit has been directly involved in >700 clinical trials and influenced 317 policies (see Table 3) with 75k Altmetric Attention Score.



Table 3: Summary of policymakers citing our research

	No. papers cited	No. policies
NIH and Care Excellence	100	73
UK Government (gov.uk)	70	31
World Health Organization	65	57
Other worldwide policy commissions	194	156
Total	429	317

In Neuroscience, our honorary staff member, Sharrack, is director of the Sheffield Multiple Sclerosis Research Clinic, Chair of the Sheffield Research Ethics Committee and Member of the EBMT Autoimmune Diseases Working Party. He plays a leading UK role in MS clinical trials including **MIST** (impact case study), the first cell therapy trial at the Sheffield Teaching Hospitals NHS Foundation Trust and the first phase III autologous haematopoietic stem cell transplantation treatment in MS. **Sourbron** leads image analysis and quality assurance in a 10-year longitudinal cohort study in 500 patients with chronic kidney disease, partnering with NHS nephrologists. **Kurien** and **Aziz** work closely with Sanders (Chair of the Coeliac UK Health Advisory Council) and colleagues in the Unit of Gastroenterology, a leading centre in coeliac disease and the <u>NHS</u> <u>England National Centre for Refractory Coeliac Disease</u>. Kiely is honorary professor in the <u>Sheffield Pulmonary Vascular Disease Unit</u>, one of the largest pulmonary hypertension centres in Europe, who works closely with Lawrie and R.Thompson to support translational research.

Sheffield is one of five UK High Consequence Infectious Disease units that respond to pandemic/epidemic respiratory infections. Rowland-Jones, De Silva and Darton work closely with NHS colleagues Sabroe, Lawson and Bianchi (respiratory), Mills (critical care, surge planning lead for COVID-19) and Meiring (infection). This group has been dynamic in supporting COVID-19 trials and rapid-response research including the <u>UK Coronavirus Immunology Consortium</u>.

In addition to collaborations with academic institutions and the NHS, we **expanded our commercial partnerships** to increase our impact by delivering clinical solutions to health problems. As outlined in section 3, the unit's income from commercial sources has grown markedly over this assessment period. This is underpinned by a breadth of industrial partnerships. For example, imaging work with GE Healthcare, Siemens, Philips, Novartis Sanofi and Bayer (amongst others) supports development of hardware, imaging markers and artificial intelligence technologies (Wild, Sourbron). Boehringer Ingelheim funded the NEO-BLADE trial to treat bladder cancer (Hussain); Artios Pharma and Domainex support cancer therapy research (Collis); Novartis, Philips, Siemens and Ixico support brain vascular MR imaging (Venneri); NZP UK Ltd., Celgene, Cypralis, Khondrion, MitoBiopharm and Keapstone Therapeutics support Alzheimer's research programmes (Mortiboys); while Pfizer, AstraZeneca, GlaxoSmithKline, Takeda, Celgene, BenevolentAl, Verge Genomics SoseiHeptares, Aclipse Therapeutics have funded projects to identify new therapies in neurodegenerative diseases (Ferraiuolo, P.Shaw, McDermott).

4.2 Relationships with key research users, beneficiaries, and audiences

Staff within the unit contribute nationally and internationally to public engagement and dissemination of research and research principles. A significant body of our research involves **users beyond academia** including the NHS, Department of Health and Social Care, NICE, patients, the public and industry. End-users of research are involved in project and programme steering groups, patient groups and participation of co-investigators in research planning, delivery and dissemination. We work with a proactive media team to ensure research findings are



disseminated to the wider research community and the public, using platforms ranging from University website news articles, social media, press and broadcasting. We engage the local Sheffield community in disseminating our discoveries and healthcare initiatives through local media, <u>community relations</u> and public events.

Our unit actively **engages patients with our research**. The Clinical Research Facility works with the Sheffield Teaching Hospitals-University of Sheffield Clinical Research and Innovation Office to support Patient Public Involvement and Engagement (PPIE) activities. We involve and engage patients and members of the public to promote learning and sharing of healthcare knowledge using examples of best practice. **Patients participate** in patient panels, focus groups and events in every stage of the research process, adding value to both the patient experience and to study development and impact. Examples of our clinical trials that embedded PPIE from ideas development to design, delivery and dissemination of the trial are HeadUp, ProGAS, DIPALS (McDermott) and DAFNE (Heller).

Our staff support a wide range of patient involvement activities, including: International Clinical Trials Days (Elks); advisory groups to patients and carers with MND (West, Kirby); MND patient community (Ramesh); nutritional approaches to support healthy ageing (Protein for Life project, Williams); MRC patient day (Eastell); invited patient seminar at Polycystic Kidney Disease Foundation, Australia (Ong) and contributing to "Living with Dementia" magazine (West).

We **engage with diverse communities** and the public to improve public awareness of health and science and to inspire the next generation of researchers. Our staff delivered events for the Festival of Science, Festival of the Mind, the Virtual Life Science Project in partnership with community schools, Researchers Night, and "Pint of Science"; and have given interviews, documentaries and phone-ins on national and local TV/radio, and lectures at the Cheltenham Science Festival, the largest such event world-wide. University engagement teams provide masterclasses, practical advice, activity marketing, evaluation, funding support, partner finding and online resources to support these activities. Since 2018, 20 of our staff were included in 2,774 pieces of new media coverage, averaging 139 media pieces per individual in under two years. Altmetrics show that we received 92,801 mentions for 5,492 outputs, including 7,851 in news, 79,936 in Twitter and 224 in policies.

Our staff also contribute to **wider society** in a range of activities. McDermott is a specialist advisor who has developed NICE guidelines for MND; Lawrie is an advisor to UK Government Office for Life Sciences on the use of artificial intelligence; Payne is a member of the SuppoRTT working group in Health Education England; Chico took part in the EU Scientist-MEP pairing scheme (2019) to gain an understanding of EU research funding, legislation, and lobbying. Fenner is a registered clinical scientist with the Health and Care Professions Council; Darton is external clinical reviewer for the Pasteur Institute, Paris, sits on the Scientific Advisory Board for MRC Leishmaniasis Human Challenge Model project in York and has served on the Data and Safety Monitoring Boards for Typhoid Challenge and COV001 COVID-19 vaccine studies in Oxford. Kirby supports Ethics for the Health & Safety Executive and Offiah has served on the Yorkshire and Humber Sheffield Research Ethics Committee.

4.3 Wider contributions: impact beyond our case studies

As detailed in section 1.5, we instigated a number of mechanisms to increase our research impact. We received £5.9M in HEIF and IAA funds (BBSRC/EPSRC), made >132 non-academic partnerships or work agreements, 75 patents were filed and 14 granted, securing >£17M in commercial funding. The strategy and pipelines we used to enable impact over this assessment period are outlined below.



We have undertaken a variety of activities leading to impact. Examples beyond our impact case studies include "**BresDex**", an online tool used by >12,500 patients to improve choice in breast cancer treatment, developed following our research showing there were wide variations in surgery provided to patients (Coleman). **POLARIS** builds, designs, and sells the world's highest performance MHRA approved ¹²⁹Xe polarisers for lung imaging, sponsored by Novartis, AstraZeneca, Boehringer-Ingelheim and Galapagos (Wild). We led the European **Haemophilia Safety Surveillance** website to report adverse events and regular surveillance of people with inherited bleeding disorders (Makris). New guidance was implemented for the way infants' skin is treated from birth, to **prevent allergy and dermatitis**, following our research showing wash products damage the skin barrier (Danby). **VIRTUheartTM** is an innovative clinical tool using computational fluid dynamics (CFD) to calculate coronary blood flow, guiding decision-making by clinicians (Gunn, Morris). We developed a dedicated orthopaedic and neonatal magnetic resonance (MR) imaging system to safely scan neonates, leading to global commercialisation of a **neonatal MR system** and transport incubator, fundamentally changing neonatal MR imaging (Paley).

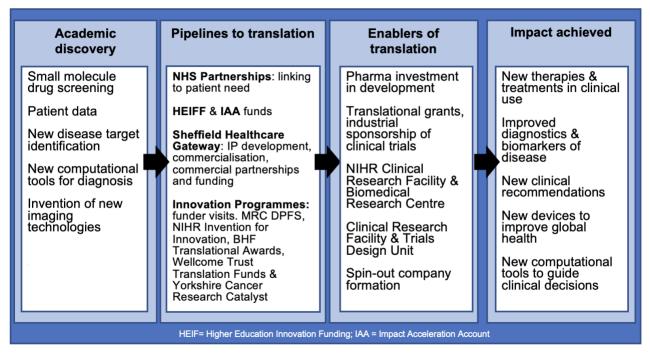


Fig 7: Mechanisms: strategy to enable impact from research

4.4 Contributions to the discipline

We recognise that contributing to the discipline also provides opportunities for staff development and promotes new research partnerships. We support staff and students to develop presentation skills in weekly theme research meetings, annual Medical School research away days with ECR oral presentation sessions. PGR students are required to give at least two oral and one poster presentation. We organise journal clubs, research reproducibility and integrity seminars to facilitate an understanding of journal and grant review processes. These provide our researchers with skills to disseminate research at invited talks, review funding applications and research articles for journals, thereby contributing to our fields of expertise.

Staff from this unit support leading **peer reviewed journals** through their roles as editors and reviewers. Over the assessment period staff from this unit have been members of the editorial boards of >90 key journals in their fields including 24 staff who have been editors. All our staff have reviewed papers and the majority have reviewed grants for funding bodies. 36 staff work closely



with national and international funders with membership on the following panels: MRC Clinical Training and Career Development, MRC Neuroscience and Mental Health, MRC DPFS, UKRI Future Leader Fellowships, British Heart Foundation Project Grants and Fellowships Committee, NC3R Project Grants NIHR EME, MND Association Health Research Board, Heart Research UK, Alzheimer's Research UK, EPSRC, Cancer Research UK, Hong Kong Research Council, French and German National Research Agencies, Academy of Medical Sciences New Lecturers.

We support our staff to make broader contributions to the discipline. These include **chairing of regional, national, or international panels**, such as NIHR National Speciality Lead for Early Phase Cancer Trials (Danson), NCMM Research Council of Norway Evaluation Committee (Azzouz); Future Neuro Ireland Board (Shaw), Lister Institute Board of Governors (Shaw), Research Council of Norway Infection and Immunity Panel (Rowland-Jones); ASBMR Rising Star Awards Committee Co-chair (Eastell). We have significant roles in advisory boards to improve healthcare, including North West Cancer Research Scientific Advisory Committee (Cox), Breast Cancer Campaign Scientific Advisory Board (N.Brown), EPSRC Strategic Advisory Team for Healthcare (Hose) and Wellcome Trust Vaccines Advisory Board (De Silva).

Our unit has 36 members of **strategic panels or learned societies** including President of the British Orthopaedic Research Society, Chairs of the European Society for Cardiology Working Groups, Board of Directors, Zebrafish Disease Models Society, and the Lister Institute Board of Governors. Staff of all grades, including ECRs and PGRs, have been invited to give notable international lectures on their research. We have given 43 keynotes or invited lectures at national and international conferences.

A number of our staff have been recognised for their research contributions to clinical medicine over this assessment period, some of which we highlight. In 2014 Pamela Shaw was made a Dame Commander of the Order of the British Empire for services to neuroscience, Catto won the BAUS Karl Storz Golden Telescope, Wilkinson received the Hip Society (USA) Otto Aufranc Award, Orthopaedic Research Society William Harris Award and the Orthopaedic Research Society Research Translation Award and Eastell received the Frederick C Bartter Award of the American Society for Bone and Mineral Research for excellence in clinical research (only previously awarded to two UK clinicians) and the Translational Cancer Research Prize from Cancer Research UK for work in the prevention of breast cancer. In 2015 Offiah received group awards: BIR/Bayer Make it Better Award; Winner and BMJ Awards Highly Commended Imaging Team. In 2017 Whitby received the British Institute of Radiology medal for distinguished service and Tahir was awarded Institute of Physics and Engineering in Medicine Academic Early Career Prize for significant contribution to the advancement of academic practice and research in medical physics within 12 years of their career. In 2018 Wilkinson received the British Hip Society President's Prize. In 2019 P.Shaw was awarded the Association of British Neurologists medal, while Venneri received the Italian Women Physicians career achievement award; the Sheffield Institute for Translational Neuroscience (SITraN) was awarded the Queen's Anniversary Prize for research that has improved patient outcomes for people living with some of the most devastating neurodegenerative diseases.

Conclusion

Our staff are a dedicated and highly effective research community committed to improving global health and quality of life. This is frequently achieved across disciplines and in partnership with the NHS and industry to find solutions to clinical problems. We have invested in and strategically developed our research base to maximise our responsiveness to emerging health challenges. The impacts from our research and professional activities extend far beyond academia, bringing about



new therapies, medical devices, diagnostics, industrial innovation, and competitiveness, and ultimately improved global healthcare.