Institution: Newcastle University

Unit of Assessment: UoA1

a. Context

The beneficiaries of our research include clinicians, companies, charities, interest groups, patients, healthcare organisations (providers and purchasers), government and other policy makers and the broader public. A key area of focus for us is the University's priority area of addressing the challenge of an ageing population, both in terms of reducing health burdens, including those associated with age-associated chronic disease, and improving the vitality and life quality of our older citizens. Our work has led to development of a varied portfolio of impact-related activities, reflected in the diverse nature of the impact case studies presented, and other, numerous, research activities which will, we predict, give rise to substantial impact in the future. There is a strong ethos to translate our research into clinical practice that has led to a very close relationship with our major NHS Trust partners (see www.ncl.ac.uk/biomedicine) manifest in a joint research strategy and research office and joint business executive and business office for translation into practice.

Patients & Public: As a medical unit of assessment in a translationally-focused organisation, it is natural that a major target for our impact activity should be the users of healthcare themselves, namely patients and other members of the public. Our research activity has a beneficial impact on patients via the obvious route of improved therapy for disease (in particular age-related chronic disease). We are also, however, committed to improving public and patient understanding and participation in both research and healthcare delivery; impacts which can improve disease management and patient perceived life quality through empowerment. Key routes to patient impact are through the development of individualised approaches to therapy which enable each patient to receive the optimal therapy for their clinical state/condition and the development and implementation of structured approaches to care delivery.

Government & NHS: Our principal route to external impact is via collaborative working with the NHS and through informing and influencing policy makers. 42% of the investigators returned in this UoA are active clinicians seeing patients in the NHS. A number of them are leaders in their fields with established track records of improving outcomes for patients both in the UK and world-wide in areas such as **liver disease**, **muscular dystrophy**, **immunodeficiency**, **mitochondrial disease**, **cancer** and **arthritis**. Impact through the NHS occurs in a number of ways. These include the development of new or improved drugs (examples include the work of ***Newell*** and colleagues in developing a new class of anti-cancer drugs (the PARP inhibitors) and the work of ***Rowan*** in developing a new class of agents potentially able to protect injured joints from the subsequent development of osteoarthritis (modifying the matriptase pathway)). Another approach is the informed repurposing of existing drugs (the work of ***Day*** identifying Losartan as a potential therapy for liver fibrosis, and the work of ***Jones*** identifying Rituximab as a potential therapy for fatigue in inflammatory liver disease; both agents under evaluation with MRC/NIHR EME trial funding). Other routes to impact through the NHS include the development and application of diagnostic and therapeutic technologies (the work of ***McNeil*** developing an integrated home monitoring and management system for liver disease patients), the development and implementation of physiological interventions (exercise (***Trenell***) and weight loss strategies (***Taylor***)) and the development of pathways for the delivery of clinical care in practice (the work of ***Bushby*** and colleagues in muscular dystrophy and ***Jones*** in autoimmune liver disease).

Industry: Whereas academic organisations can undertake discovery science which enables the development of novel treatments, the substantial costs of converting scientific discovery to evaluated and implemented treatment mean that collaboration with industrial partners is of critical importance for achieving impact. Such partnerships can arise either through the development of "spin-off" enterprises from university activity or through formal collaborative work with industrial partners. We undertake both forms of impact activity with a broad portfolio of national and international industrial partners ranging from multi-national companies (such as GSK, Novartis, Astex and Pfizer) to SMEs particularly in the biotechnology sector. A number of our international SME collaborators are new to working in the UK and have been attracted to do so by the unique opportunities offered by the translational and business-friendly environment we have created.

Benefits to all groups are linked, with patients as the ultimate beneficiaries. Improved working

within the NHS, and improved drugs and diagnostic tests developed in conjunction with industrial partners, will, if effective and implemented into practice (our work on structured care delivery in this context is key), necessarily feed through to improved patient outcomes. The University facilitates all these activities by providing readily-accessed professional support and expertise to facilitate engagement with industry, patients and the public. There is a well-developed clinical translational infrastructure of both people and facilities, and currently Newcastle Biomedicine is one of the leading organisations in the UK for accrual into NIHR portfolio clinical trials and other studies.

b. Approach to impact

Awareness of the importance of impact is embedded in our working structures and environment. We fully support investigators to undertake research which benefits end-users, thereby generating impact, and our approach is targeted to the needs of the potential users/beneficiaries.

Impact on Patients & Public: Direct patient impact (as opposed to patient benefit which occurs as a result of impact generated by collaboration with industry and the NHS) comes from a strong focus on positive engagement with patient groups and their active involvement in the research process. Critical to this is patient involvement in all stages of the research process from identification of the key research questions to protocol development and study implementation, superseding the traditional model of patients as merely recipients. We facilitate active involvement with national bodies such as **INVOLVE** and through the numerous local and frequently disease area-specific interactions initiated and promoted by our investigators. Examples of the approach include: the work of **VOICENorth** http://www.ncl.ac.uk/changingage/engagement/VOICENorth/, an innovative public engagement programme aimed at involving the people of the North-East in the design and delivery of our research in the area of ageing; and the work of ***Jones*** in the area of Primary Biliary Cirrhosis (PBC), with a 15 year programme of work in the specific area of fatigue in PBC being initiated following the identification, in conjunction with patient groups such as **LIVErNorth** and the **PBC Foundation**, of fatigue as the priority for research activity. The protocols for research studies have been developed in conjunction with these groups, research activity has typically been funded by research grants with patients/patient groups as co-applicants and studies then delivered using patient facilitators. The active involvement of patients in the work has led to a number of them taking more active roles in the research process through membership of ethics committees and lay panel membership for funders such as NIHR. Full patient involvement in the research process, and the resulting sense of ownership, has proved critical in successfully recruiting to studies. Other examples of active patient and public involvement include ***Bushby*** & ***Lochmuller*** working with patients and carers to develop structures to deliver optimal care in neuromuscular disease and ***Foster*** who works with patient groups to develop cutting edge educational media to support the training of young clinicians with the goal of improving clinical care nationally and internationally in juvenile arthritis. Successful engagement with patients and the public is facilitated by positive presentation of science by the media. We engage actively with the published and broadcast media and examples of the impact that this can have include the leading role we took in the debate on the ethics and acceptability of nuclear transfer as a therapy for mitochondrial genetic disorder (***Turnbull***), our work on the mechanisms and impacts of ageing (***Passos***, ***Kirkwood***) and the contribution of ***Taylor*** to awareness of the impact of diet in risk reduction in diabetes; strands of work which have had high profiles on the BBC (in the form of the "Hairy Dieters" BBC Television series in the context of the diabetes work) as well as front-page coverage in key newspapers.

An important local audience for our engagement activities are schools. We actively build relationships with schools in order to extend our impact to young people, and do so through delivering workshops and events such as the twice yearly "Science on a Plate" interactive event for year 9 school students which explores the links between nutrition and metabolism in an accessible and interesting way to encourage interest in science subjects when students are making key decisions about GCSE subjects. Vital to achieving our impact, especially in the areas of society and culture, is our full time External Liaison Coordinator (ELC) who supports staff in public engagement activities. Our ELC also works closely with the Faculty Press Officer to ensure timely impact to a wide audience.

Impact on the NHS & Government: NHS impact is achieved by the full and active involvement of Newcastle UoA1 investigators in clinical data derivation and evidence synthesis, implementation of

evidence-based therapy into clinical practice and the optimisation of clinical care delivery. Supported by a highly successful clinical trials unit, we are actively involved in clinical trial work funded both by industrial partners (a key element of our industrial interaction) and funding bodies. UoA1 returnees have been investigators on 79 clinical trials total value £38.1m (leading on 94% value £36.5m). Our NIHR funding portfolio is strong with 3 NIHR/MRC EME-funded and 4 HTA-funded trials led by UoA1 investigators, with UoA1 investigators being involved in a further 3 HTA funded trials. We have particular strength in EME, with our number of funded trials exceeding the total number for any other academic institution in the UK (by award value UoA1 in Newcastle is second only to Imperial College taken as a whole). Our trials portfolio ranges from evaluations of small molecule pharmaceuticals (for example the EME-funded *FELINE* exploring re-purposing of angiotensin receptor blockers for the treatment of fibrosis in Non-alcoholic Fatty Liver Disease (NAFLD) **(*Day*)** to innovative early phase and envelope-widening use of biological agents (for example the EME-funded *RitPBC* trial evaluating the use of Rituximab for the treatment of life-altering fatigue in PBC (***Jones***) and the pioneering work of ***Isaacs*** in immune joint disease under the auspices of the ARUK Experimental Arthritis Treatment Centre). Beyond pharmaceuticals our trial portfolio includes cell therapies (through the work of the ARUK Centre of Excellence for Tissue Engineering which is pioneering the use of cell therapies for the treatment of osteoarthritis and pioneering work at the whole organ level, including an HTA funded trial exploring techniques to improve lung transplantation through conversion of marginal donor lungs to ones which can be transplanted (***Fisher***)). In addition to the trials and other studies initiated by our own investigators, we are highly effective at recruitment into portfolio studies thereby supporting the research activity of investigators across the UK. In 2012-13, NUTH Trust, our partner trust, was top of the national league tables for the number of research studies opened (459) and 5th in the league table in relation to the number of patients recruited to research studies (13,795).

We also innovate and evaluate at the level of approaches to physiological assessment, with an HTA trial of management of falls in the community (***Parry***), and in physiological interventions which have the capacity to change the natural history of disease, including the work of ***Trenell*** (funded by an NIHR Senior Fellowship and the EU FP7 FLIP programme) on exercise interventions for people with diabetes or obesity-related liver disease which are suitable for everyday life (and thus actually used by people) and the ***Taylor*** strand on dietary intervention in type II diabetes. We have contributed to the development of stratified approaches to therapy through, for example, our work on paediatric pharmacology (***Veal***). Our strand on diagnostic and therapeutic technology is strong with an EME-funded trial in the area of foetal diagnosis using MRI (***Robson***). There has also been significant pull-through from underpinning science to the development of novel imaging markers of disease subsequently developed and utilised as trial outcome measures (for example *RitPBC*) and the development of novel clinical assessment tools, an example being our work with Becton Dickinson Biosciences in Ventilator-Acquired Pneumonia, funded by Wellcome/DH HICF (***Simpson***) where a bead based cytokine assay is being assessed with the aim of improving antibiotic stewardship in very high risk patients in the critical care setting.

NHS impact can also arise through the development of innovative evidence-based approaches to care delivery. Landmark examples include: the work of ***Bushby*** on developing a systematic approach to the management of Duchenne muscular dystrophy which has led to longer patient life and improved quality of life and has been adopted worldwide; and the work of ***Jones*** on structured care delivery in autoimmune liver disease, integrated into European treatment guidelines, which has resulted in improved patient satisfaction and clinical outcomes at the same time as significant cost-savings resulting from avoidance of un-necessary or duplicative clinical investigations and clinic visits. Structured approaches to care delivery have been informed by the development of simple predictive tools in areas such as fatty liver disease (***Day***) and PBC (***Jones***) which through utilisation of standard clinical information in patients allow pre-screening, at no additional cost, for the presence of advanced disease features, identifying low risk patients in whom costly and invasive investigations such as liver biopsy and endoscopy can be avoided without placing patients at risk of disease complications being missed.

Impact on Industry: A critical element of our industry-mediated impact is activity in the areas of drug development, improvement & application. Examples from this UoA include the development of PARP inhibitors, a new class of anti-cancer drug (***Newell***), the 5 year drug development programme with Astex and the work being undertaken by ***Mann*** in conjunction with GSK in the

context of the CRAFT programme with the goal of developing new treatments for fibrosis which will prevent the development of cirrhosis; the major cause of death in liver disease. The latter interaction includes a joint-funding model for a clinical academic post at Senior Lecturer level, with the post-holder facilitating novel interactions between GSK and Newcastle University, the joint funders of the post. This approach has already given rise to 2 novel trial opportunities which will involve significant new investment in the UK. Industrial impact can also arise through the development and commercialisation of technologies able to improve both diagnosis and monitoring of disease. Newcastle is the first and only UK centre to receive Pfizer INSPIRE (Investigator Networks, Site Partnerships and Infrastructure for Research Excellence programme) site status, one of 51 sites globally. At a national level the key network programmes led by Newcastle UoA1 investigators, including the UK-PBC MRC Stratified Medicine Programme (led by ***Jones***) and the MRC/ABPI RA-MAP consortium (led by ***Isaacs*** who also chairs the NIHR Translational Research Partnership in Joint and Related Inflammatory Diseases, one of only two such groupings) involve partnership with over 20 national and international companies.

Unusually for a medical school, we have also leveraged our industrial connections to host a number of KTP projects with diverse companies including Procter & Gamble, Boots and L'Oreal. We have also worked with commercial partners of our science and engineering schools on major collaborative cross-disciplinary projects such as the EPSRC-funded £2.5m joint Newcastle-Durham Knowledge Transfer Account, 'crossing the clinical boundaries', which enabled us to work with smaller regional medical device and diagnostic companies.

A total of 10 patents have been filed by UoA1 academics during the REF period, 5 of which have progressed to national phase. An example is our patent on Gene Signature for the Early Diagnosis of Seronegative Rheumatoid Arthritis (***Isaacs***) which is currently at national phase and is attracting significant commercial interest. Newgene, a University/NHS joint venture offering genetic testing which originated from within UoA1 has a turn-over of over £1m pa and is trading profitably. Our engagement with industry is also evidenced by the number of consultancy projects we have carried out. A total of 51 academics, 34% of the total entered in this unit of assessment, have carried out consultancy during the period, working with most of the major national and international pharma and biotechnology companies. Our commitment to effective working with industry is reflected in the increase in industry-linked income from £11.1m in 2011/2012 to £25.6m in 2012/13 (228%).

c. Strategy and plans

Effective delivery of impact within our model required establishment of an ***organisational culture*** which prioritises research translation and the impact which flows from it, the development of ***strategic and operational structures*** geared to impact generation (including through the systematic ***identification of novel opportunities***), and the establishment of the necessary ***infrastructure*** to enable the conversion of good ideas into practice. This infrastructure is both scientific (the physical structures necessary to generate impact) and intellectual (the academic support structures to assist investigators who may have scientific ideas and outputs which could generate substantial impact but who may themselves be inexperienced in the critical steps necessary to turn good ideas and good science into impact).

Impact Culture: Critical to our success has been development of a culture which values translational research and the impact that results from such activity. This is reflected in our institute structures, our operational and strategic planning and most of all in our interactions as an organisation with investigators, where impact generating activity is quantified and valued. Although organisational and infrastructure aspects are critical for impact generation neither of these would be nearly as successful if they didn't operate within a culture that highly values this approach.

Impact Opportunity Development: We have significant strengths resulting from our balanced portfolio of basic and clinical academics, our clinical cohorts (which in some areas such as NMD, PBC, mitochondrial disease and genetic immunodeficiency are world-leading), embedded translational ethos and strong patient and industry links. We will generate further opportunity through engaging basic-science focussed-groups, and linking them with translational investigators and support infrastructure to assist them to explore the translational opportunities arising from their work which will generate future impact, as well as linking our field-leading clinicians with an in depth awareness of need in their disease areas with basic science and translational researchers to facilitate development of novel programmes. The Diagnostic Evidence Cooperatives (DEC)

awarded to Newcastle 2013 (***Simpson***), with the aim of improving evaluation and clinical implementation of *in vitro* diagnostics will provide significant impact opportunities, in particular in the context of the validation of diagnostic and prognostic tests developed by or in conjunction with our industrial partners.

***Impact Strategy & Organisation*:** Our organisational structure has been established in order to facilitate impact generating activity. In terms of our interactions with the NHS, our corporate structure is one of an Institute-based unit of assessment within a Faculty which has strong links with the lead partner Trust (Newcastle upon Tyne Hospitals). We have a joint oversight organisation Newcastle Biomedicine which oversees research strategy at the interface and manages through a Joint Research Executive. Critically for impact generation there is also a Joint Business Executive optimising commercial activity across the Trust/Faculty interface; a major source of impact. Within the Faculty the organisation has been structured in such a way as to facilitate translation, with Research Institutes with a scientific remit to deliver impact and an underpinning organisational structure which facilitates it in terms of both underpinning services such as commercialisation activity and the physical infrastructure necessary to generate impact.

***Impact Infrastructure*:** Delivery of impact in relation to health is supported by outstanding clinical research infrastructure developed and managed jointly between the Faculty and NUTH. This level of integration allows seamless joint working with both NHS and industrial partners, particularly in the area of therapeutics development and evaluation. The Newcastle Clinical Trials Unit (http://www.ncl.ac.uk/nctu/) is a UKCRC-registered clinical trials unit which supports the development and delivery of high quality clinical trials supported both by grant funding (MRC, HTA, NIHR etc) and by commercial partners. Practical delivery of clinical trials and other impact generating activities is enhanced by availability of outstanding clinical research facilities, including specialist facilities in the areas of cancer trials (Sir Bobby Robson Cancer Trials Research Centre http://www.newcastle-hospitals.org.uk/services/cancer_services_sir-bobby-robson-cancer-trials-research-centre.aspx) and ageing (Clinical Ageing Research Unit, http://www.ncl.ac.uk/caru/) and the linked NIHR-funded CRESTA clinics (Clinics for Research and Service in Themed Assessment): a novel setting in which to undertake innovative work in clinical service development and delivery which is fully adapted to the needs of ageing patients. The work of the research facilities and the clinical trials unit is underpinned by outstanding imaging infrastructure in the form of the Newcastle Magnetic Resonance Centre (http://www.ncl.ac.uk/magres/research/) and a "state of the art" MHRA-licensed cell therapy manufacturing facility. Our significant investment in translational research infrastructure (supported by NIHR, Wellcome Trust and other funders) and joint approach to management provides a unique context in which to translate scientific discovery into patient benefit and commercial opportunity generating significant and sustained impact.

We have also invested significantly in the area of support for commercial activity. Our business development manager is part of a Faculty team and is available to advise staff on all aspects of opportunities (intellectual property, research contracts for services, consultancy, professional education, CASE studentships, Knowledge Transfer Partnerships and the route to market for translational research projects). We believe that this easy availability of commercial support has been a major factor in our significant increase in industry-linked research activity. Our facilities are available to industry (http://www.ncl.ac.uk/biomedicine/business/) and we provide incubation space for start-up companies. All staff are encouraged to develop skills in commercialisation through seminars by successful practitioners and through participation in our programme on entrepreneurship and enterprise (joint with the Business School). Our Career Pathway Scheme for early-career researchers emphasises the opportunities and value of a career outside academia. Our local lead for patient and public engagement works closely with the Faculty Engagement team and its co-ordinator, sharing ideas and good practice and participating in annual faculty-wide engagement events, and linking closely to **INVOLVE**, the national forum for patient participation in research. We work closely with the Medical Faculty press officers to publicise our research to a wide audience.

d. Relationship to case studies

Our case studies reflect our triple-track approach to impact generation, through partnership with patients, the NHS and industry.

Impact on Patients

One route to patient impact is through **Individualisation of Therapy. *De Soyza & Corris*** identified

that only one sub-species of a bacterium that commonly affects CF patients was a cause of death following lung transplant. This has allowed other patients, affected by other sub-species, to go forward for transplantation; an option which would have otherwise not have been open to them. ***Veal*** developed an approach to chemotherapy administration in children with cancer based on specific patient parameters, leading to increased drug efficacy and reduced toxicity. The approach is now in widespread use in treatment protocols across Europe for a wide range of tumour types. ***Bown*** identified the most common chromosomal abnormality of neuroblastoma, and the most powerful prognostic marker for this disease. This has resulted in assignation of treatment in a pan-European clinical trial. ***Daly*** was the first to demonstrate the link between genotype and the appropriate therapeutic dose of warfarin resulting in clinical trials and a new international standard algorithm for gene-guided dosing. **Bushby** developed a definitive technique for the diagnosis of limb girdle muscular dystrophy enabling targeted therapy for an important subgroup of patients. In the area of **Development of Novel Therapeutic Technologies & Approaches *Gibson & Bourke*** pioneered the use of non-invasive ventilation in patients with motor neurone disease, demonstrating that the approach can increase survival and quality of life. In the area of **Improving Diagnosis and Prognosis in Disease *Foster*** developed a new screening tool, pGALS, which allows simple and accurate diagnosis of paediatric musculoskeletal problems, thus ensuring that children receive timely therapy reducing long-term morbidity and impact on schooling. ***Turnbull*** and his group have developed a number of tests that allows the prevalence of mitochondrial genetic disease to be determined. These tests now form part of routine clinical practice worldwide, and the group has also contributed to raising awareness of mitochondrial disease.

Impact on the NHS

One important approach to generating impact via the NHS is through **Structuring the Delivery of Care. *Reynolds*** has innovated in the area of atopic eczema developing novel treatment paradigms which have been found to be effective and improve quality of life. His work has informed UK and European guidelines and demonstrated high uptake in clinical practice. ***Day*** developed a non-invasive, accurate and validated liver fibrosis scoring system which allows identification of patients with obesity-related liver disease (an important public health problem) who are at risk of developing cirrhosis. This has the dual advantage of allowing low risk patients to be identified and stratified for safe management in primary care without the need for liver biopsy, a costly and risk-associated procedure, and high risk patients to be identified for intensive risk reduction therapy through exercise and dietary intervention and risk monitoring. This group will also be suitable for future treatment with anti-fibrotic therapies under development by the ***Mann*** group in the context of our innovative public/private partnership with GSK. ***Bushby*** has undertaken a systematic approach to the management of Duchenne muscular dystrophy which has led to longer patient life and improved quality of life. Best practice guidelines have now been published and adopted worldwide. ***Gennery*** demonstrated that early bone transplantation was a cure for chronic granulomatous disease providing opportunity for life-saving therapy.

Impact on Industry

Our principle approach to impact in this area is through **Collaborative Working With Industrial Partners. *Newell*** developed a “first-in-class” PARP inhibitor which has progressed to clinical trials with more than ten compounds being used to treat hundreds of patients worldwide. A number of major pharmaceutical companies are now investing in this class of drugs which shows real clinical and commercial promise. ***Goodship*** discovered that two of the genes associated with atypical haemolytic uraemic syndrome (aHUS) encode molecules produced by the liver, making kidney/liver transplant a logical treatment. 25 such procedures have now taken place transforming the lives of patients. The molecules themselves regulate complement, a key part of the immune system, and as a result of Newcastle work a complement inhibitor has now been approved by the FDA and EMEA for aHUS treatment. ***Lunec*** undertook work which paved the way for licensing of the drug Pemetrexed. His group also recognised that the toxic effects can be significantly reduced with folic acid and B12 injections. This has been incorporated into worldwide guidelines. ***O’Brien*** discovered that the drug imatinib, a tyrosine kinase inhibitor, more than doubled the five year survival rate and significantly improved life quality for patients with chronic myeloid leukaemia.