NHS Lothian Research and Development
Research Strategy Overview
(2022-2027)

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Final draft completion date: 21st June 2022
Review period: July 2022
Launch date: 1st August 2022
Review date: 31st July 2023

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Introduction

The recently published UK-wide vision for the future of clinical research delivery has the ambition to make every patient interaction a research opportunity and every clinical service research active with the aim of improving clinical outcomes for patients in the NHS (Saving and Improving Lives: The Future of UK Clinical Research Delivery, 2021).[1] A partner publication aims to support improvements in health care in parallel to supporting economic recovery by harnessing the growth and capabilities of the health life science sector.[2] To deliver this vision, active engagement in this process and journey will be essential for anyone thinking about being involved in health research, those who sponsor or support research, and most importantly, everyone working in the NHS.

The UK Research and Development implementation plan highlights the importance of creating opportunities for people to develop their skills and experience to address the lack of clinical research capacity amongst healthcare staff. The National Institute of Health and Care Excellence (NICE) 5-year strategy complements this by including plans on how to drive the future research agenda, to make sure it addresses priority questions for NICE and patients. These endeavours align with the Chief Scientist Office's research vision for Scotland and associated work packages, the first being around the development of a digitally enabled trials system in Scotland. Other professional bodies, including the GMC are recognising the necessity to embed clinically focussed research in everyday clinical care, with its recently published "Normalising research – Promoting research for all doctors". This sets out how all doctors should be research active and research aware.

The benefits of research are frequently demonstrated at individual, local and national level. Economic benefits to the life science sector are significant underpinned by the unique institutional framework provided by the NHS, alongside significant public, industry and third sector investment in health life sciences. For example, for every £1 spent on R&D by the National Institute of Health Research, over £19 is generated in total economic return – the highest return on investment for any public service.[3] Research provides both organisational and staff benefits not just through supporting system improvement and efficiency but by creating thousands of high-value jobs across the UK - 47,000 full-time equivalents from 2016 – 2019.[3] In Scotland, the 2022 published report by the Fraser of Allander Institute details the incredible impact of charity supported clinical research on the broader Scottish economy: 7475 jobs, £470 million output and £320 million gross value added (GVA). This report also estimated the multipliers for charity funded research compared with 97 sectors in the Scottish economy. For every million pounds spent on research there was £1.98 million of output (23rd highest multiplier of 97 sectors); £1.33 million GVA (4th highest of 97 sectors); and 31 jobs (6th highest multiplier of 97 sectors).

Impactful research is reliant on health service staff translating their day-to-day clinical experiences into research designs that will deliver improvements to healthcare processes, performance and patient care. Engagement from healthcare professionals can enhance job satisfaction, prospects and professional confidence, with improved staff recruitment and retention helping to build and retain clinical expertise and improve patient care. Supporting research also makes an invaluable contribution to the health of future patients across the UK and wider world.

Patients are clearly the key beneficiaries of research, and not just those who participate in research. Evidence suggests that patients in highly research active healthcare settings have significantly better outcomes across their services, even if the individual patients are not part of research.[4-6] The Covid-19 pandemic has unequivocally demonstrated the clear link between clinical research embedded in clinical care and improved outcomes, clinical research has never been so publicly recognised or high profile. Moreover, it provided the opportunity to "trial" novel platform trial design, research network driven study prioritisation, large scale genomics studies, and streamlined ethics and governance processes.

Major barriers still prevent maximum engagement with research by clinical teams and NHS organisations. Some of these have been identified in reports from the UK Government, Academy of Medical Sciences, and Cancer Research UK.[7,8] The pandemic has highlighted health inequalities and workforce pressures, but as recovery begins following the pandemic, clinical research can offer a vital opportunity to address these and build back better to improve patient care, boost future health resilience, and stimulate economic growth.

This Research and Development 5-year research strategy sets out how NHS Lothian plans to support, to grow and to develop research opportunities for all our patients, enable research to be embedded into routine clinical care, communicate the value of clinical research to all and ultimately improve the quality, processes of care and clinical outcomes of patients in NHS Lothian. This will be delivered by embedding research into the core conversation, culture and ethos of NHS Lothian.

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2. Life Sciences Vision. Build back better: our plan for growth. (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1013597/life-sciences-vision-2021.pdf).
3. NIHR (2019) Impact and value of the NIHR clinical research network. (https://www.nihr.ac.uk/news/new-report-highlights-how-nihr-support-for-clinical-research-benefits-the-uk-economy-and-nhs/22489).
4. Jonker L, Fisher SJ. The correlation between National Health Service trusts' clinical trial activity and both mortality rates and care quality commission ratings: a retrospective cross-sectional study. Public Health. 2018 Apr;157:1-6.
5. Ozdemir BA, Karthikesalingam A, Sinha S, et al. Research activity and the association with mortality. PLoS One. 2015 Feb 26;10(2):e0118253.
6. Downing A, Morris EJ, Corrigan N, et al. High hospital research participation and improved colorectal cancer survival outcomes: a population-based study. Gut. 2017 Jan;66(1):89-96.
7. Academy of Medical Sciences (2020) Transforming health through innovation: Integrating the NHS and academia London. (https://acmedsci.ac.uk/file-download/23932583).
8. Cancer Research UK (2021) Creating time for research: Identifying and improving the capacity for healthcare staff to conduct research (https://www.cancerresearchuk.org/sites/default/files/creating_time_for_research_february_2021_-_full_report-v2.pdf).

Vision

The 5-year vision for NHS Lothian Research, in collaboration with key partners, is to embed clinical research across NHS Lothian, by improving research efficiency, capacity and resilience, and creating a research-positive culture in which all NHS staff are supported and expected to participate in research, and every patient has the potential for a research opportunity that will enhance their care.

Strategic objectives

- Develop a skilled and educated, resilient and retained research workforce with clear career pathways to support efficient, clinically embedded research delivered across all clinical areas of NHS Lothian.

- Research embedded within clinical services and management systems as part of routine. This would be in conjunction with quality, service improvement and innovation to improve clinical care and outcomes. It would be enabled by closer collaboration between research and strategic planning and service re-design and underpinned by strong representation of research activity and value by NHS Lothian Board and senior executive team .

- Work in collaboration with patients and public to ensure that patients are central to all aspects of clinical research from application, delivery and dissemination with the aim that NHS Lothian is participating in research that is important to patients in Lothian and Scotland.

- Develop a communication system, relating to all aspects of clinical research in NHS Lothian, to ensure that all parties are aware of what research is being delivered, enable all patients and staff to understand the true value of being a research active organisation and ensure research findings and success are disseminated widely and celebrated.

- Build and develop our research and information governance systems so that NHS Lothian continues to be seen as an exemplar site and system for delivering safe and efficient research across all research designs.

- Build collaboration with partner organisations, in particular the University of Edinburgh, industry and third sector, to enhance the opportunities for NHS Lothian patients, so that research is offered as part of routine clinical care whenever possible.

Current NHS Lothian research portfolio and infrastructure

Established in 2006, the Academic and Clinical Central Office for Research and Development (ACCORD) is a joint office comprising clinical research management staff from the University of Edinburgh (UoE) and NHS Lothian Board (NHSL). There is a long-standing, close and well developed partnership between the UoE and NHSL, and our joint research office offers a single point of access to the world class clinical research infrastructure and expertise of both institutions.

ACCORD supports approximately 900 projects every year (Figure 1) recruiting ~10,000 participants (Figure 2), ranging from single centre proof of concept studies to complex interventional investigations and multicentre international trials (40% UoE / NHSL Co-Sponsored, 60% Hosted). We work closely with industry to deliver a growing portfolio of commercial and investigator-led studies across a broad spectrum of disease, and we provide advanced infrastructure to enable the development and execution of increasingly complicated and innovative projects. We work in close partnership with our colleagues in Edinburgh's Clinical Research Facilities (CRFs), Edinburgh Imaging (EI), Edinburgh Clinical Trials Unit (ECTU) and NHS Lothian's NRS Biorepository to deliver this portfolio. Funding allocations from NHS Research Scotland (NRS) have remained stable and are allocated across a range of services and activities to support key infrastructure, clinical support and researchers (Figures 3 and 4).

NHS Lothian Research Exemplar – Information Summary 1
Research Governance

ACCORD provides a single point of entry for researchers throughout the lifecycle of their research. Role is to ensure that investigators and institutions meet research governance and regulatory requirements, fulfilling legal, ethical and scientific obligations.

First joint Research Framework Agreement in Scotland between University of Edinburgh and NHS Lothian. Benefits include:

- Complementary indemnity provisions offered by the institutions: the UoE holds clinical trials insurance and NHSL is a member of the Clinical Negligence and Other Risks Indemnity Scheme (CNORIS).
- Single Quality Management System (QMS) and regulatory inspection model, saving time, resource and fees.

Edinburgh Clinical Research Facility (CRF) became the first non-commercial clinical research facility in the UK to be awarded Phase I Accreditation with the MHRA. Accreditation now includes our Children's Clinical Research Facility (CCRF).

In 2019, Medicines and Healthcare products Regulatory Agency (MHRA) inspection revealed no critical or major findings – an outstanding achievement.

See Appendix for more details

Figure 1: Number of Studies Undertaken by Year

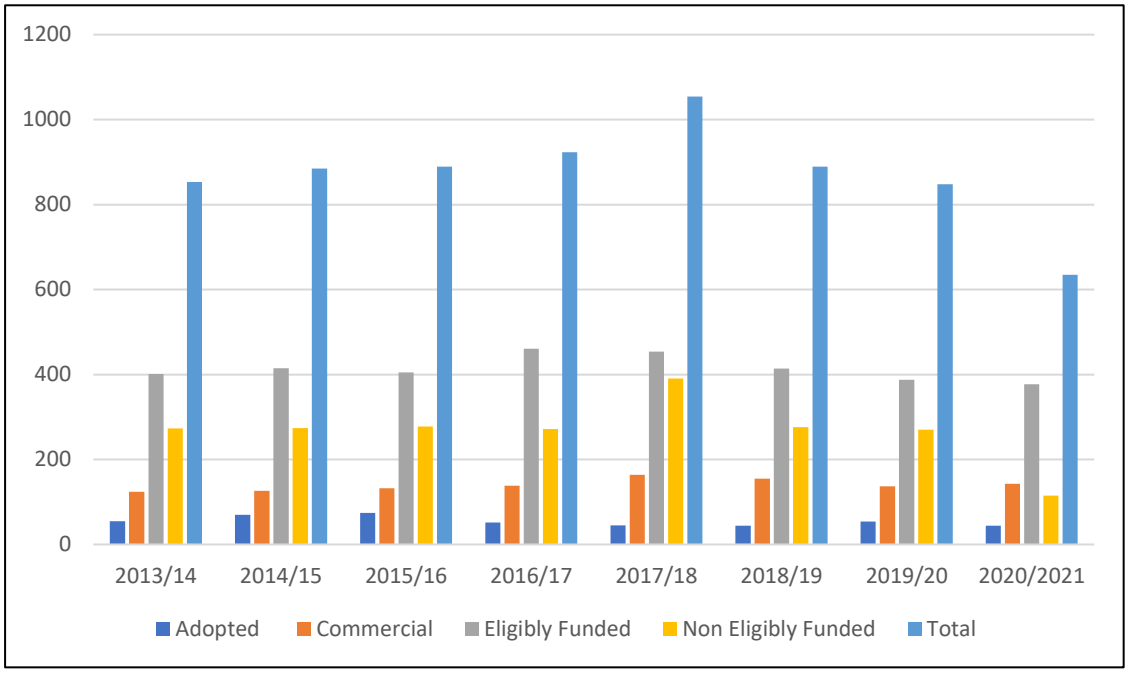


Figure 2: Study Recruitment by Year

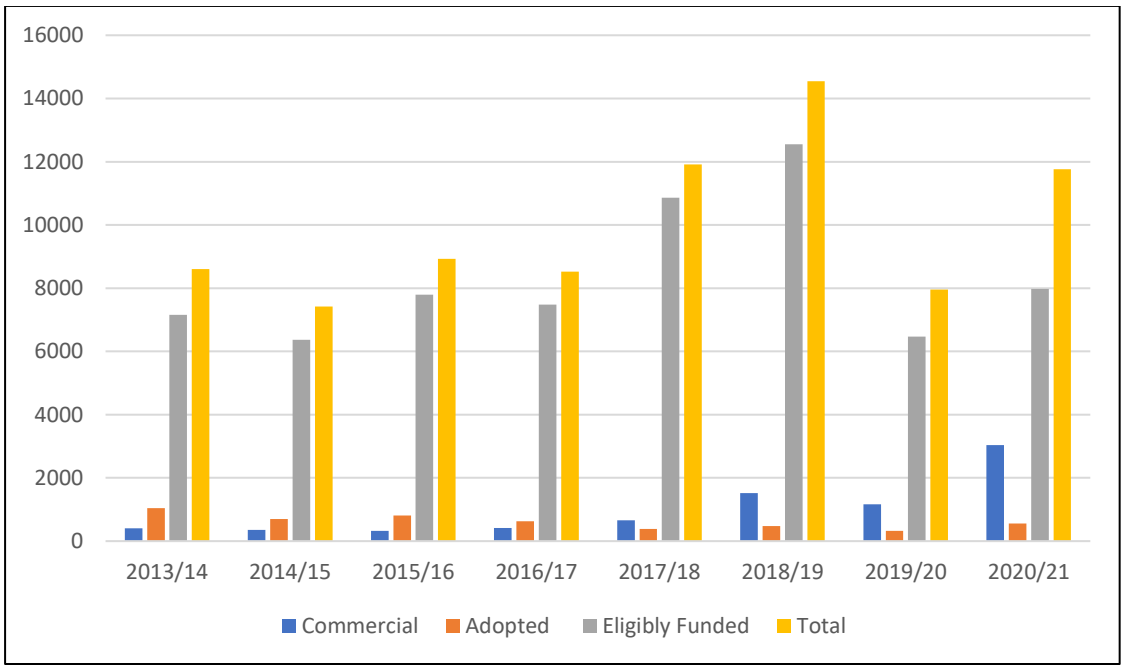


Figure 3: Annual NRS Allocation by Year

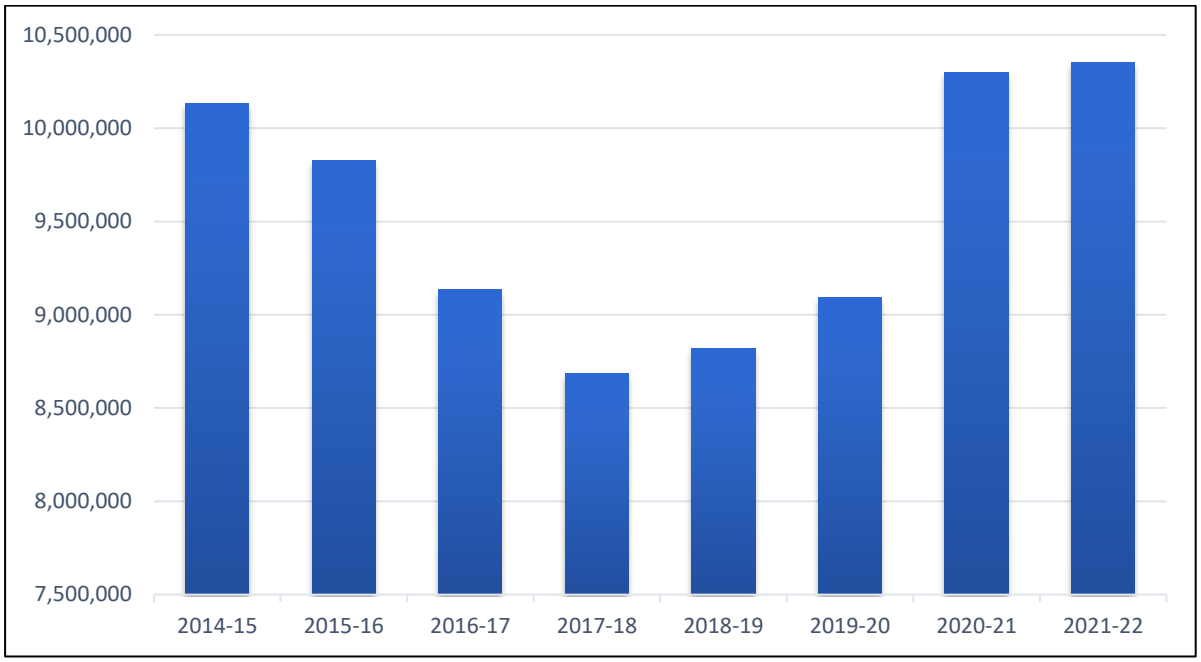
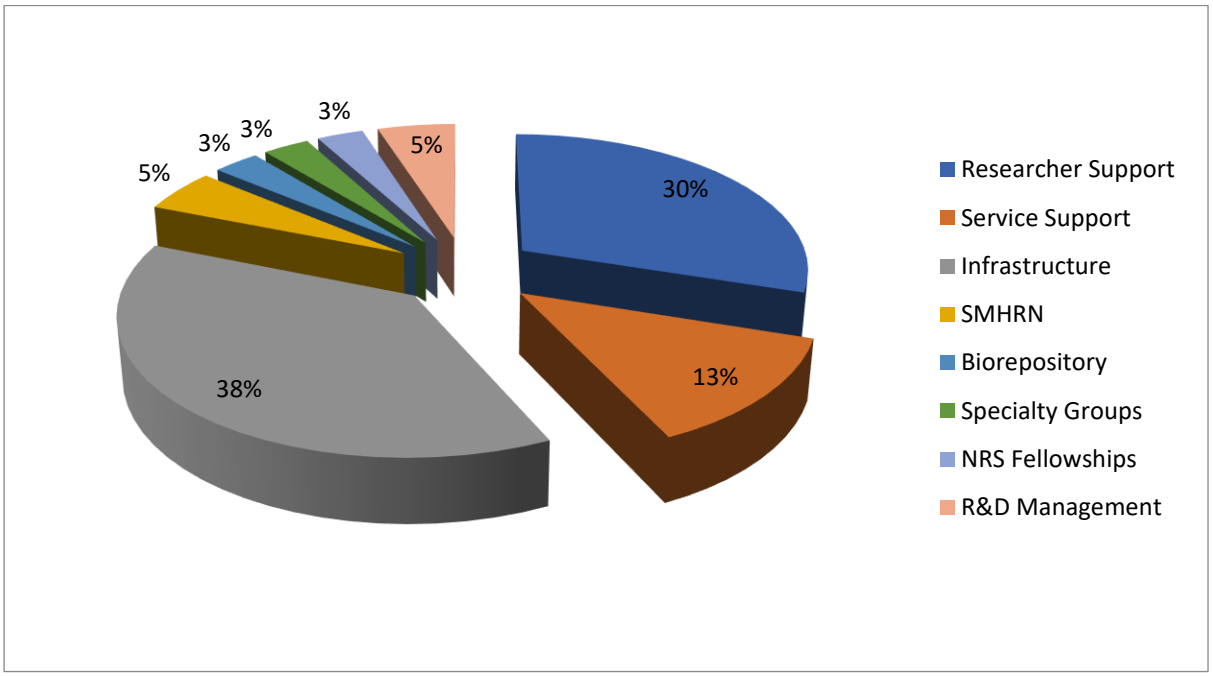


Figure 4: Distribution of NHS Lothian's NRS Funding Allocation 2021/ 22



Strategic plan priority areas

The work programmes below are aligned with the key areas detailed in 'Saving and Improving Lives: The Future of UK Clinical Research Delivery, 2021; the UK government's Life Science Vision, 2021. Locally, we will ensure synergies with the NHS Lothian's Our Health, Our Care, Our Future Our 10 year strategic plan and NHS Lothian Innovation plan (in development).

1. Research workforce

a. Review of current teams. We are currently reviewing all research posts who are supporting the delivery of clinical research within NHS Lothian to provide baseline information on service area, workload, training needs and contract types and their alignment with areas of NHS Lothian research priorities. We will work towards ensuring equality and diversity throughout our workforce. We will regularly monitor the composition of our research governance and delivery teams and our R&D supported clinicians. We will comply with our equality and diversity strategy currently in development.

b. Education and training. We will build on the highly successful WTCRF education programme to ensure ready access to research training and education materials to all staff. As part of this programme, we are currently undertaking a comprehensive scoping exercise that will inform an appropriate model of communication and delivery. An education and training strategic and implementation plan will be developed at the end of the scoping exercise.

c. Resilience in clinical research delivery teams. This will be delivered through several initiatives, including:
(1) Strategic R&D investment in emerging research groups, underpinned by clear business plans that are produced and updated by the investigators. Importantly these need to ensure collaboration and include sharing and pooling of resources between individual investigators (University and NHS);
(2) Ensuring succession planning of key posts through training and staff development; and
(3) Extending research team contract duration where possible.

d. Resilience in research oversight and governance teams. Work has already begun to restructure the research governance team. This will expand the team and improve skill mix alongside developing a progression and succession plan within the team. The overall aim is to have a more robust team with sustainable workloads and clear career progression pathways.

e. Develop career pathways. We will work towards providing sustainable research career pathways aligned with NHS Lothian research priorities. Where feasible we will look at developing rotational posts and entrance training posts that transition to promoted posts on completion of training. We will develop a research nurse career pathway model to ensure a clear pathway to progression.

We recognise the lack of opportunity for clinical research training for both doctors in training and non-medical health professionals. We therefore plan to fund a small number of research fellow, PhD fellowships and post-fellowship opportunities. We will seek matched funding for these posts.

Lastly, we plan to develop research assistant positions, embedded into research delivery teams. We will develop job specifications for these relatively new posts. Moreover, we will seek to develop novel entrance pathways into these roles such as a modern apprenticeship scheme.

f. Provision of suitable accommodation within NHS footprint to deliver research. There is a lack of support accommodation, especially on the RIE site to support research delivery teams. We will work with NHS Lothian and University of Edinburgh teams to attempt to address this issue.

NHS Lothian Research Exemplar – Information Summary 2.
Trials using routine data – HighSTEACS and HiSTORIC trials

- **Background:** Local researchers have pioneered data-enabled clinical trials. The term "data-enabled clinical trial" differentiates from standard randomised trial design by delivering results more efficiently, harnessing technology or routine data to increase scale or reduce the timeline for delivery. Enable evaluation of interventions in a broader group of patients than traditional trials.
- **Clinical context:** Chest pain is the most common presenting complaint to UK Emergency Departments (ED) (5% of all presentations). Most are evaluated for acute coronary syndrome.

High-STEACS

- This stepped-wedge, cluster randomised trial evaluated the introduction of high-sensitivity cardiac troponin into clinical practice in 10 Scottish hospitals.
- **Key findings:** Safely reduced length of stay by 33%
- Whilst in previous trials less than a third of patients recruited were women, enrolling consecutive patients minimised bias and identified a systematic under diagnosis of myocardial infarction in women.
- **Impact:** The Universal Definition of Myocardial Infarction, endorsed by the World Health Organisation, now recommends separate diagnosis criteria for myocardial infarction in men and women.

HiSTORIC

- This demonstrated the efficacy and safety of implementing the High-STEACS early-rule out pathway in 31,095 consecutive patients with suspected acute coronary syndrome across NHS Lothian and Greater Glasgow & Clyde.
- **Key findings:** Reduced ED length of stay by 3.1 hours and increased ED discharge from 50% to 71, as safely as previous clinical care.
- **Impact:** Recommended for use by the NICE DG40. Class IIa Level B recommendation by the European Society of Cardiology Guidelines.

See Appendix for more details

2. Patient and public involvement

NHS Lothian is committed to developing research in collaboration with patients and communities, to deliver research which meets their needs and improves the health and wellbeing of people across NHS Lothian.

a. Engagement with underserved populations to ensure equity of opportunity to research.

NHS Lothian wants to develop health research in collaboration with all our communities, but particularly those who are currently underserved by research, see "Improving inclusion of under-served groups in clinical research: Guidance from INCLUDE project". We want to create research-interested and engaged individuals and communities across Edinburgh and the Lothians, whether that interest is in being a participant, a Patient partner who works with researchers in developing and delivering their research or as someone interested in keeping up to date with developments in their health condition or areas of interest. This inclusion work will also support us to deliver on all our PPI in research deliverables. Research can often seem something others do; we want it to be something you feel part of and that serves you and your community. To do this we will:

1. Create a community of individuals, organisations, charities and third sector groups who are engaged and interested in research. We want to be co-producing studies with communities, to meet their needs, to do this we want to establish a network of communities, organisations and individuals we can work with on an ongoing basis to engage communities in participating in research and in PPI activities.

2. Create links with GP practices and healthcare providers in local communities – embedding research and understandings and contacts within the community. Working with NHS health providers in Deep-end GP practice areas and underserved communities, we will explore barriers to community engagement and to better understand how we can engage with communities in local healthcare settings to engage them in research.

3. Produce a Diversity and Inclusion strategy for clinical research which is produced by underserved communities and health and social care research communities.

b. Ensure robust and meaningful patient and public involvement in all research activity.

NHS Lothian has been supporting PPI in research for many years and over the last five years we have seen the increased demand for PPI support. We will continue to support and deliver PPI which meets the needs of patients and researchers in all research activity. Striving to support research which is meaningful for communities and patients means we must work in collaboration with local organisations and our strategic partners, including the University of Edinburgh. We will also strive to meet the best standards of PPI in research by following the UK Standards for Public Involvement. NHS Lothian has also signed the Shared Commitment to Public Involvement. (https://www.ukri.org/news/shared-commitment-to-improve-public-involvement-in-research/). We have committed to both delivering collaborative research and evaluating it and to continue to develop our PPI activities to meet future researcher and community needs.

c. Understanding and partnership around the use of patient data to enhance clinical outcomes through research.

Strategically supporting research teams across NHS Lothian working in data science, we will support the continued development of resources, tools and patient/community activities in data science research. This is to both enhance public understanding of the opportunities to use patient data to improve clinical outcomes but also to continue to collaborate with patients and

communities to ensure we are working in benefit of the public and striving to improve health outcomes via data science research.

d. Understanding and partnership around collaboration with industry and commercial partners to enhance clinical outcomes through research.
We will continue to encourage and support industry and commercial partners to work with patients and communities to harness research and innovation for improvements in health to benefit communities across NHS Lothian. We will encourage the co-creation, testing and implementation of innovative healthcare solutions to improve health across our community

e. Understanding and partnership around collaboration with university partners to enhance clinical outcomes through research.
Working strategically and collaboratively with university partners, we will continue to co-create PPI activities to enhance health outcomes for patients and communities. We will endeavour to develop new and efficient funding models which embed, support and deliver PPI activities which

- Support research interested communities across NHS Lothian
- Support patient and community involvement in clinical research and,
- Which build capacity to deliver PPI activities across clinical research

f. Investigator and research team training in patient and public engagement and involvement
NHS Lothian, through its collaborations with the University of Edinburgh and the Clinical Research Facility will continue to offer its extensive suite of training course for researchers:

- Self-directed - Bitesize Introduction to Patient Public Involvement in Research
- Patient Public Involvement in Clinical Trials
- Grant Applications and Patient Public involvement
- Creating and Running a Patient Public Involvement Group
- Doing Patient Public Involvement Virtually
- Patient Public Involvement in Research Summer School

In addition, we will develop education activities to meet future demands, on the topics of:

- Equality, Diversity and Inclusion of patients and participants across the research cycle
- Evaluating the impact and learning from our PPI in research and community engaged activities
- Chief Investigator Training - to develop Chief Investigators to lead the way in PPI in research

3. Communications

A new post, the ACCORD communication manager, is currently being recruited. This individual will be responsible, with the senior management team, for a communication strategy for ACCORD that will deliver in the following key areas:

a. Develop internal communication systems and processes between investigators and R&D oversight and governance teams. In conjunction with local investigator training, we plan to improve our communications around approvals, contracts and IT governance to make it easier for researchers to navigate and to access these systems and processes in NHS Lothian. We will ensure that local investigators can understand capabilities to develop and deliver their study at all stages and ensure they are connected with the right part of the system to help them at the right time. We will in conjunction with other key stakeholders e.g. Edinburgh Clinical Trials Unit ensure access to expertise to support the delivery of their study.

b. Develop communication to improve research access and opportunity for patients. This will support recruitment & retention of research participants across NHS Lothian. In particular, we require improvement in providing research opportunity to hard to reach groups (see section above).

c. Develop communication to improve feedback and dissemination of research findings to study participants. We will work with patients and public to develop processes to improve this and make it consistent and explicit for all research delivered in NHS Lothian.

d. Develop communication between research and clinical teams at specialty and service levels. Without an understanding of the benefits of research to patients, staff and services it is difficult to embed research into routine care. We plan a series of communications around these areas and to provide improved communication of local and national research findings to clinical teams. Evidence and disseminate the value of research to clinical services and management structures including drug budget savings, reductions in service utilisation e.g. bed days.

e. Develop communication to improve the understanding and enable the celebration of research delivered in NHS Lothian. Health Board wide dissemination of research findings and to NHS Research Scotland (NRS), specifically highlighting the following: the service cost reduction by being research active, patient access to new therapies and treatments, changes in practice to improve processes, and the overwhelming evidence that research active organisations have improved clinical outcomes.

f. Develop communication to enhance research collaboration between NHS Lothian, universities, third sector and industry. We will work with the NRS Communications Manager, UoE Communications and NHS Lothian Communications teams. See other sections of the strategic plan**.**

4. Efficient and safe research systems

NHS Lothian has an exemplar research governance system demonstrated by recent MHRA inspection and accreditation outcomes (see exemplars). We recognise the risk around prolonged governance approval, contract and IT security sign off times. We therefore plan to develop a system to achieve speed and predictability of research approvals and set-up, particularly commercial contract research, delivered in NHS Lothian.

a. Study approval and amendment review.

In order to create a clear pathway for research teams and sponsors seeking NHS Lothian R&D permission, our R&D governance team will be re-organised to function as two distinct teams; a commercial and a non-commercial team. In addition, to assist in timely review of research study amendments, we will develop existing systems to aid tracking and follow up of amendments as they are processed through the office. We plan to increase resource in the current team to fulfil this commitment by employing two new members of staff to new posts. By increasing capacity in the team, and reviewing and updating current processes, we aim to provide a robust and responsive system to process all R&D governance reviews within an acceptable timescale**.**

b. IT security and Caldicott review.

We are aware that more studies require access to data and will use a variety of digital technologies. In order to manage these appropriately and ensure that they comply with current data protection legislation and NHS Lothian policies we have recently appointed a full time R&D

Information Governance Lead who has delegated authority to issue Caldicott approval for research and we have also secured dedicated time from IT Security to help us to assess and approve the digital technologies that will be used in research projects. We will work with IT security and governance systems, alongside the Caldicott guardian to provide efficient and pragmatic review and approval.

NHS Lothian Research Exemplar – Information Summary 3.
Using routine clinical data - DATALOCH

The DataLoch puts routinely collected data at the heart of responses to health and social care challenges and improves decision-making, research, and support for colleagues providing care for patients. This is achieved by:

- Bringing together health and social care data for the South-East Scotland region,
- Working with experts in health and social care to understand and improve this data, and
- Providing safe and timely access to data for researchers.

Patient involvement

- Public Reference Group is now taking on an enhanced role, which will see members join the live application-review process and deliver an assessment of public value for all applications received.
- Further public engagement and involvement exercises will be delivered to better understand perspectives of the local population around potentially contentious concepts, such as commercial access to health and social care data.

Full launch – July 2022

- Then researchers (public-, industry-, and third-sectors) will be able to apply for secure access to DataLoch data.
- Data Controllers will include NHS Borders and NHS Fife, also the diversity of local authorities and private organisations that are involved in social care.
- Planned expansion of the data-access service beyond Lothian Research Safe Haven (now integrated within DataLoch). This expansion will allow customisation within a bespoke information governance framework, with improved opportunities for novel research designs such as, Natural Language Processing and other machine-learning techniques.
- Development of specialty-specific registries, such as for cancer and cardiology. These curated datasets will enable research activities, speeding up the impact on service delivery.
- Acceleration of Data-Driven Innovation programme – of which DataLoch is a part – through the building of new communities of interest that coalesce around specific themes, including frailty and mental health.

See Appendix for more details

NHS Lothian Research Exemplar – Information Summary 4.
The GenOMMIC study

Background:

- The Genetics Of Mortality In Critical Care (GenOMICC) study aims to find the human genetic determinants of susceptibility to, and outcome from, critical illness. The objective is to identify targets for drug therapy to improve outcomes in critical care.
- Study was designed to include Covid-19 – "critical illness caused by emerging infections such as SARS, MERS, or Ebola".
- Global collaborative study, led by Edinburgh researchers expanding during the COVID pandemic to 224 UK hospitals and multiple other countries.

Impact:

- 4 genes indicated that two molecular processes, antiviral immunity and lung inflammation, were key to critical illness development in COVID. This led to multiple potential targets for therapies including Baricitinib. Rapidly translated to clinical trials including RECOVERY and REMAP-CAP now proven to be effective at improving outcomes in sever COVID. The first example of a new treatment for an infectious disease being discovered using human genetics.
- A total of 41 genetic variants associated with critical illness have now been discovered for COVID (34 complete new) by GenOMMIC.

See Appendix for more details

5. Embedding research into clinical care

We aim wherever possible to normalise the facilitation and delivery of research within NHS Lothian, for patients, and workforce. Importantly, we aim to increase accountability for research across the health and care system and not just investigators, research teams and NHS Lothian R&D. The core aim is to embed research in the core conversation, culture and ethos of NHS Lothian.

a. Answer important questions for staff and patients – bottom up research. If staff and patient believe a research question is important to them, they are more likely to engage and be actively involved in research. Lothian.

b. Make it easier for patients to be involved. Increase awareness amongst patients that clinical research is something that the health and care system does as a normal part of delivering care and increase opportunities for patients to find out about and access studies of relevance to them. Develop novel pathways for recruitment, retention and follow up for patients to make research more accessible, patient friendly and convenient especially for underserved populations (see section 4).

c. Make it easier for clinical staff to be involved. We will consider a staff engagement process around how we can make research easier for them and how we can engage the broader system to see clinical research as part of routine care. Moreover, we need to improve understanding in clinical services regarding the importance of research to clinical care (See communication section).

d. Increase expectation, led via management structure that research is core NHS business. Our ambition is to normalise (make standard) the facilitation of research in all health and care roles, including direct care delivery, clinical support services (radiology, laboratory services), other support services (eHealth, Human Resources), and healthcare management and leadership.

Whenever possible, we plan to embed the delivery of research studies within routine care, where this is appropriate. This needs to be aligned with other parts of routine service activity such as quality and service improvement and innovation to improve clinical care and outcomes. Lastly, we aim to increase the accountability of clinical services, management structures and board, with research facilitation and delivery included in NHS Lothian oversight and reporting mechanisms.
At board level we need to ensure collaboration between research and strategic planning and service re-design and develop strong representation of research activity and value by NHS Lothian Board and senior executive team.

e. **Develop clinical research champions at ward and service level.** This will be across medical, nursing and AHP workforces. Without research champions and accountability across all levels of staff, truly making clinical research normal and "part of the day job" will be impossible. We plan to develop a programme for clinical research champions to support the communication and translation of the benefits of research for teams and their patients. We will also discuss with Lothian NHS board how we can recognise and value clinical research delivery as an integral part of professional development and revalidation.

NHS Lothian Research Exemplar – Information Summary 5.
Chief Scientist Office Precision Medicine Programme

- £6.9 million from the CSO Precision Medicine Alliance awards for three Lothian research programmes.
- Research to deliver a precision medicine approach for common Scottish diseases in underserved populations with clinical impact in five years.

Multiple Sclerosis

- Multiple sclerosis (MS) is the leading cause of acquired neurological disability in the young. Scotland has some of the highest rates of disease in the world.
- Novel radiology and blood biomarkers will support the targeted treatment to patients with the aim of achieving better control of patients' disease and reducing disability.

Liver disease

- Since 1970, deaths due to liver disease have increased by 400%. Liver disease kills 1 in 50 people in Scotland - where death rates are 70% higher than the UK average.
- Translate advanced precision therapies for treatment of liver disease across Scotland. By focusing on novel therapies targeting the liver that are at different stages of development, the team believe they have a real chance of facilitating new treatment options that will improve patient outcomes.

Critical Care

- 45,000 severely ill or injured patients will require specialist care and treatment in one of Scotland's critical care units of whom 40% will die before discharge and many more will have long term morbidity.
- This research programme will develop a platform investigate novel time-critical precision medicine treatments in patients in Scottish critical care units.

See Appendix for more details

6. Research collaborations

a. **Build seamless research delivery between NHS Lothian and the University of Edinburgh and other Universities in Edinburgh and Scotland.** We will continue to build on the learning from the recent clinical trials review and harness work with the joint oversight board between the University of Edinburgh and NHS Lothian to build seamless clinical trial capability. The organisations will work together to ensure joined up strategy to resource clinical trial capacity in terms of funding and shared responsibility. More broadly, we will ensure alignment of this strategic plan with the one currently in development in the University of Edinburgh**.** We will seek to update the Framework Agreement with QMU and develop framework agreements with Napier and Heriot Watt Universities'.

a. **Improve systems and opportunities to build cross-institution translational research to deliver clinical impact at speed**. We aim to further develop an efficient system to enable progression at speed from bench to bedside building on NHS Lothian exemplars in respiratory and critical care medicine and the recent CSO precision medicine alliance awards.

b. **Build collaboration and opportunity with third sector organisations and social care.** We will develop an engagement process for third sector organisations led by communications manager. We will ensure that any development in this area will be consistent with the NHS Research Scotland governance systems to support social care studies. We will support opportunities for people living in care homes to participate in research by connecting with the ENRICH Scotland. ENRICH (Enabling Research in Care Homes) was established with CSO support and it has recruited >100 care homes across Scotland as 'Research Ready'.
(https://www.nhsresearchscotland.org.uk/research-in-scotland/facilities/enrich).

c. **Develop relationship and opportunity with industry and commercial partners**
Participation in commercial research studies frequently offers patients access to novel diagnostics, devices, treatments and therapies that would not otherwise be available to them. In most of these studies the Board gains access to expensive trial medications free of charge. Our commercial partnerships provide opportunities to find solutions for service needs through the development of investigator led, commercially funded studies. We will continue to work closely with our industry and commercial colleagues to ensure that we undertake feasibilities for proposed studies in a timely and efficient manner. We will proactively match investigators to commercial opportunities.

We will work together with our NHS Research Scotland (NRS) colleagues to engage with key pharmaceutical and other commercial partners through the CSO Industry Partnership Forum. The Communications Manager and Portfolio Team will work with stakeholders to target their study pipelines and direct these to appropriate and interested investigators. The Communications Manager will develop marketing documentation detailing our research interests, capabilities and capacity so that we can target specific industry and commercial partners.

NHS Lothian will continue to represent NRS on the 4 Nations Contracting Leads Group which is responsible for developing and refining model research contracts which make the contracting process much quicker and efficient.

Risks to delivery

There are a number of risks that may reduce our ability to deliver this strategic plan that are outside the control of the NHS Lothian Research and Development team.

Descriptor	Moderate	Major
Workforce **(Very High Risk)**		Significant difficulty recruiting and retaining staff, continues staff workload mismatch
Finance **(High Risk)**		A relatively small research portfolio with varying commercial income stream, fluctuating annual CSO budget, set on a year to year basis
Clinical & Service Engagement **(Medium Risk)**		Clinical pressures with emphasis on other priorities
Clinical Research as Core NHS Business **(Medium Risk)**		If it is not this may cause significant difficulty in delivering the UK and local research plans
Ethical & Patient Data Policy **(High Risk)**		Public trust, reputational risk
COVID-19 **(Medium Risk)**	Continued constraints relating to the pandemic	
BREXIT **(High Risk)**	Increased costs & logistical challenges for delivering trials	

NHS Lothian Research Exemplar – Information Summary 6.
Phase 1 trials including

Phase I clinical trials are essential for the development of novel treatments for patients and to investigate novel pathophysiological pathways to improve understanding of health and disease. Requires the provision of a highly regulated environment - MHRA Phase I Accredited Edinburgh Clinical Research Facility - to ensure participant safety and data quality and integrity. Examples include:

Industry collaboration (Bristol-Myers Squibb)

- Longstanding collaboration around novel antiplatelet drug development to benefit cardiovascular disease
- Combining academic clinical model of thrombosis (an ex vivo model of deep arterial injury) together with a novel approach to platelet inhibition (protease activated receptor type 4 antagonism)
- Programme of research to understand the potential role of this novel pathway and the therapeutic potential of this new drug class for patients with cardiovascular disease.

MATCH

- Collaboration between the University of Edinburgh, NHS Lothian and Scottish National Blood Transfusion Service (SNBTS)
- Investigate the use autologous monocyte derived macrophages as a potential therapy for liver cirrhosis.
- Phase 1 dose-escalation trial of autologous macrophage therapy in 9 adults with cirrhosis. Safety and feasibility of peripheral infusion of ex vivo matured autologous monocyte-derived macrophages.
- Phase 2 multicentre, open-label, parallel-group trial investigating the efficacy of autologous macrophage therapy compared to standard medical care in adults almost complete.

DEFINE

- Phase 1 platform trial to define pharmacokinetics and pharmacodynamics and safety of repurposed medicines in small cohorts of patients with COVID-19 lung inflammation.
- Nafamostat and GB0139 were the first two re-purposed agents. Nafamostat is a potent serine protease enzyme (TMPRSS2) inhibitor that had the potential to inhibit viral entry and be anti-inflammatory and anticoagulant. GB0139 is an inhaled Galectin-3 inhibitor that had the potential to target inflammatory cell activation, viral entry and fibrotic pathways. 60 Edinburgh patients were recruited. There were promising results for further repurposing of GB0139 in viral lung injury.
- In collaboration with SNBTS, a viral specific T cell therapy arm has been added platform. Recruitment is due to start in May 2022 and will investigate safety and feasibility.
- Platform will act as a catalyst to accelerate experimental medicine in respiratory infection and inflammation in NHS Lothian

See Appendix for more details

Research Strategy delivery plan and success metrics

	2022	2023	2024
Research Workforce	A strategic implementation plan for education and training will be prepared by autumn 2022. We will appoint to critical R&D posts during 2022 including a Commercial Lead for the research governance team and a new Communications Manager.	We will work towards a comprehensive route map for clinical research training that aligns to profession, research role and career pathway. We will produce this by mid-2023. We will introduce an R&D Education Coordinator post in 2023 to support training & development within ACCORD, including progression of job descriptions and competencies for training posts.	Plans for the development of job descriptions for training posts and rotational posts are under discussion. We will work towards implementation of new entry-level posts by 2024.
Patient & Public Involvement	We will work towards a detailed plan for all elements of this work package by the end of 2022.	We will increase resource for the PPI work stream during 2023 to support the planned expansion of activity.	
Communications	We will work towards a detailed plan for all elements of this work package by the end of 2022. We will appoint a Communications Manager in 2022, with guidance & support from the NHS Lothian Communications Team.	We will produce a Communication Strategy for ACCORD in 2023.	
Efficient & Safe Research Systems	Capacity in our research governance team will remain under annual review and additional posts introduced as required, including Information Governance support roles. We will engage proactively with NRS and Research Data Scotland (RDS) to encourage standardisation of Information Governance and IT Security standards across Health Boards.		
	We are currently implementing an organisational change in our research governance team. We will expand capacity in this team during 2022 and work with NHS Research Scotland (NRS) colleagues throughout 2022/23 to prepare for forthcoming UK Wide study reviews.		

Embedding Research into Clinical Care	We will work towards a detailed plan for all elements of this work package by the end of 2022.	We will identify research champions at service level in 2023 and at ward level in 2023/24. We will explore the potential for joint appointments (50:50 research / clinical) in multidisciplinary roles during 2023. We will seek to increase the number of research sessions funded by clinical directorates each year. In 2022/23 will introduce an EDGE Project Manager to roll out use of this Clinical Research Management system across research groups in Lothian. Through EDGE we will demonstrate research related cost avoidance to Clinical Directors e.g. drug budget.	We will identify research champions at ward level in 2024.
Research Collaborations	We will work towards a detailed plan for all elements of this work package by the end of 2022.	We will produce a communication strategy in 2023 to support robust engagement with external parties, including industry organisations.	

Appendix
NHS Lothian research exemplars

1. Research Governance

Providing a single point of entry for researchers throughout the lifecycle of their studies, ACCORD acts to ensure that our investigators and institutions meet research governance and regulatory requirements, fulfilling legal, ethical and scientific obligations, whilst nurturing and attracting world class clinical research.

ACCORD operations are underpinned by the first joint Research Framework Agreement in Scotland with all clinical research activity co-sponsored by the UoE and NHSL. Benefits of this arrangement include the complementary indemnity provisions offered by the institutions: the UoE holds clinical trials insurance and NHSL is a member of the Clinical Negligence and Other Risks Indemnity Scheme (CNORIS). In combination, these provisions cover the breadth of clinical research activities led and undertaken by researchers in Edinburgh.

Co-sponsorship also lends itself to a single Quality Management System (QMS) and regulatory inspection model, bringing efficiencies in relation to time, resource management and shared inspection fees. Our most recent Medicines and Healthcare products Regulatory Agency (MHRA) inspection (October 2019) revealed no critical or major findings, an excellent achievement for a busy academic Sponsor.

Back in 2011, Edinburgh Clinical Research Facility (CRF) became the first non-commercial clinical research facility in the UK to be awarded Phase I Accreditation with the MHRA. Since then we have maintained this prestigious status, with extension of the scope of the accreditation to include our Children's Clinical Research Facility (CCRF). Phase I Accreditation is a recognised mark of quality that attracts commercial partners and strengthens our investigators' funding applications. We are delighted to provide gold standard CRFs for our academic researchers and industry colleagues. Edinburgh's CRF team is regularly invited to advise on the development of new facilities around the UK and many of their staff occupy key positions within the UKCRF Network.

Co-sponsorship Responsibilities

Under the Research Framework Agreement, Sponsorship obligations are assumed by the two institutions. The University of Edinburgh is charged with the authorisation for clinical trials, ethics committee opinion and pharmacovigilance whilst NHS Lothian Board leads on Good Clinical Practice (GCP) and clinical trials conduct.

2. Dataloch – Using routine data

The DataLoch puts routinely collected data at the heart of responses to health and social care challenges and improves decision-making, research, and support for colleagues providing care for patients. This is achieved by:

- Bringing together health and social care data for the South-East Scotland region,
- Working with experts in health and social care to understand and improve this data, and
- Providing safe and timely access to data for researchers.

Through bringing together key health and social care data, the DataLoch service allows a holistic data-driven approach to the prevention and treatment of different clinical conditions, as well as the broader provision of health and social care services.

During the beta phase of development, DataLoch has been open to applications from academics and clinicians in the South-East Scotland region, and has also:

- Further integrated primary and secondary care data within the main DataLoch-Core dataset.
- Improved the data structure and released a new Metadata Catalogue which includes TrakCare, SMR, and WardWatcher data, with more datasets regularly being added.
- Involved GPs within the Operational Delivery Board to embed primary care perspectives in DataLoch's foundations.
- Established a streamlined governance framework that includes NHS decision-making.
- Developed a new online application portal for applicants to submit proposals, communicate with the service team, and see the real-time progression of their proposal through the review process.
- Joined the UK Health Data Research Alliance to better develop the adoption of standards, tools, and technologies for trustworthy health data research.

The work started in the beta phase will continue beyond the full launch (in July 2022), which marks the point where approved researchers across the globe from public-, industry-, and third-sectors will be able to apply for secure access to the data that the DataLoch service hosts. Further datasets will be brought into DataLoch to enhance the capacity for research-ready and cradle-to-grave insights; these Data Controllers will include NHS Borders and NHS Fife, but also the diversity of local authorities and private organisations that are involved in social care. Work is also focused on the expansion of the data-access service beyond the parameters of the Lothian Research Safe Haven (now integrated within DataLoch). This expansion will permit greater levels of customisation within a bespoke information governance framework, which will offer improved opportunities for novel approaches, including Natural Language Processing and other machine-learning techniques.

Collaboration with expert partners will be focused on the development of specialty-specific registries, such as for cancer and cardiology. These curated datasets will enable research and development activities, speeding up the impact on service delivery. Further innovation will be advanced through the Data-Driven Innovation programme – of which DataLoch is a part – through the building of new communities of interest that coalesce around specific themes, including frailty and mental health. DataLoch's commitment to innovation is also reflected by ongoing collaboration with NHS partners through the supply of data to respond to NHS-defined priorities with a view to future deployment of solutions within frontline services.

From its early phases, DataLoch has involved public voices in the form of the Public Reference Group, which has provided important inputs around the team's public communications as well as offered retrospective assessments of the application-review decisions. The Public Reference Group is now taking on an enhanced role, which will see members join the live application-review process and deliver an assessment of public value for all applications received. Further public engagement and involvement exercises will be delivered (such as through surveys and deliberative workshops) to better understand perspectives of the local population around potentially contentious concepts, such as commercial access to health and social care data.

3. Trials using routine data – HighSTEACS and HiSTORIC trials

Randomised controlled trials are the cornerstone of evidence-based medicine and the most reliable method of evaluating the benefit or harm of new interventions. However, the cost of conducting a standard randomised controlled trial has escalated. Consequently these trials often have limited scope to address the questions that are most relevant to patient care, service delivery or healthcare policy. To address questions that will inform practice or policy decisions, we need to conduct pragmatic trials, which enrol everyone in whom the test or treatment is applied in clinical practice. In some trials, this is only possible through cluster randomisation where consent is at the site or institution level, and the effectiveness or safety of the intervention can only be evaluated through anonymised routinely collected healthcare data.

To address this, NHS Lothian have pioneered data-enabled clinical trials. The term "data-enabled clinical trial" differentiates from standard randomised controlled trial design by delivering results more efficiently, harnessing technology or routine data to increase scale or reduce the timeline for delivery. These trials evaluate the effectiveness of interventions in a broader group of patients than traditional trials. Clinical staff in NHS Lothian have led two major clinical trials that have changed practice using innovative approaches to trial design or the use of routinely collected healthcare data to evaluate interventions across multiple areas of healthcare.

Given that diagnostic tests can lead to under- or over-treatment with the potential for both benefit and harm, rigorous evaluation of their impact on patient management and outcomes in secondary care is needed. The High-STEACS stepped-wedge, cluster randomised trial evaluated the introduction of high-sensitivity cardiac troponin into clinical practice across ten hospitals in Scotland (Lancet. 2018;392:919-928). All consecutive patients were screened for suspected acute coronary syndrome using an electronic form integrated into the clinical care pathway and routine healthcare data was used to characterise the population and capture all outcomes. As the intervention was implemented at hospital level, consent was not sought from individual patients. This eliminated selection bias and ensured that the trial population was representative, comprising of both low- and high-risk individuals, and an equal proportion of men and women. Implementation of the high-sensitivity cardiac troponin assay reduced length of hospital stay by a third and was not associated with evidence of misdiagnosis or adverse outcomes (Lancet. 2018;392:919-928). Whilst in previous trials less than a third of patients recruited were women, enrolling consecutive patients minimised selection bias and identified a systematic under diagnosis of myocardial infarction in women (BMJ. 2015;350:g7873). Because of this data-enabled approach, the Universal Definition endorsed by the World Health Organisation, recommends separate diagnosis criteria for myocardial infarction in men and women.

Using the data-infrastructure created for this trial, the investigators have developed more efficient care pathways for patients with chest pain (JAMA. 2017;318(19):1913-1924). The HiSTORIC trial demonstrated the efficacy and safety of implementing this early-rule out pathway in 31,095 consecutive patients with suspected acute coronary syndrome across NHS Lothian and Greater Glasgow & Clyde (Circulation. 2021;143:2214-2224). Patient length of stay was reduced by 3.1 hours and the new pathway increased the proportion of patients discharged directly from the Emergency Department from 50% to 71% and through follow up at one year demonstrated this change in practice was not associated with any excess in hospital admission or death. Delivery of the HiSTORIC trial has impacted on our practice locally but has also been recommended for clinical use by the NICE DG40. It was given a Class IIa Level B recommendation by the European Society of Cardiology Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation.

4. Phase 1 trials

The conduct of early first-in-human and Phase I clinical trials is essential for the development and delivery of novel new treatments for the benefit of our patients as well as the investigation of novel pathophysiological pathways to understand health and disease better. This requires the provision of a highly regulated environment to ensure the safety of research participants and the quality-controlled integrity of the trial data. Successive first-in-human and Phase I clinical trials have been performed within the MHRA Phase I Accredited Edinburgh Clinical Research Facility to ensure the highest standards of trial delivery. This has included investigator-initiated and commercially sponsored clinical trials, often performed through scientific collaborations and under Clinical Trial Authorisations. As a case example, a series of Phase I clinical trials have been performed over the last 8 years in a collaboration with Bristol-Myers Squibb to understand the potential of novel anti-platelet therapies to improve outcomes in patients with coronary heart disease or stroke. Bringing together an academic clinical model of thrombosis (an ex vivo model of deep arterial injury) together with a novel approach to platelet inhibition (protease activated receptor type 4 antagonism), we have conducted a programme of studies to understand the potential role of this pathway and the therapeutic potential of this novel class of drug in patients with cardiovascular disease. This has been highly resource intensive, requiring numerous complex simultaneous measurements of pharmacokinetics, pharmacodynamics and multiple physiological endpoints. All studies have been delivered to time and target with excellent data completeness. The scientific insights have been impactful and led to two major publications (Arterioscler Thromb Vasc Biol. 2018;38:448-456; Arterioscler Thromb Vasc Biol. 2020;40:2678-2685.) which have established the important role of this pathway in platelet biology and thrombosis. These findings have also encouraged Bristol-Myers Squibb to expand their drug development pathway for this class of compound, resulting in a critical Phase I study being currently conducted within Edinburgh Clinical Research Facility and is due for completion later this year. If successful, this will lead to a large Phase II and Phase III programme of clinical trials to establish clinical efficacy in patients with atherosclerotic cardiovascular disease.

MATCH

Pre-clinical studies have suggested that macrophages can promote liver fibrosis regression. The MATCH study was designed to study the use of autologous monocyte derived macrophages as a potential therapy for liver cirrhosis. MATCH is a collaboration between investigators in the University of Edinburgh, SNBTS and the NHS Scotland. MATCH has completed a phase 1 dose-escalation trial of autologous macrophage therapy in nine adults with cirrhosis. The primary outcomes of safety and feasibility were met (Nat Med. 2019 Oct;25(10):1560-1565). The safety and feasibility of peripheral infusion of ex vivo matured autologous monocyte-derived macrophages in patients with compensated cirrhosis has been demonstrated. MATCH is just completing the phase 2 element of the study where the efficacy of autologous macrophage therapy is being compared to standard medical care in a cohort of adult patients with compensated cirrhosis in a multicentre, open-label, parallel-group, phase 2, randomised controlled trial. The primary outcome is the change in Model for End-Stage Liver Disease score at 90 days. Secondary endpoints studies include measurement over 12 months of liver function, non-invasive liver fibrosis markers and clinical outcomes (BMJ Open. 2021 Nov 8;11(11):e053190).

DEFINE

The Define COVID-19 platform started recruitment in September 2020 as a platform to define pharmacokinetics and pharmacodynamics and safety of repurposed medicines in small cohorts of patients with COVID-19 lung inflammation. DEFINE initially focused on evaluating two re-purposed therapies; Nafamostat and GB0139 compared to standard care. Nafamostat is a potent serine protease enzyme (TMPRSS2) inhibitor that had the potential to inhibit viral entry and be anti-inflammatory and anticoagulant. GB0139 is an inhaled Galectin-3 inhibitor that had the potential to target inflammatory cell activation, viral entry and fibrotic pathways. Sixty participants in medical wards at the Royal Infirmary Edinburgh and Western General Hospital, Edinburgh, were randomised

to either a treatment arm or standard care and recruitment was completed in February 2021. The Nafamostat group were significantly more likely to experience adverse events and developed significantly higher plasma creatinine levels. There were no other statistically significant differences in endpoints between Nafamostat and standard care. PK data demonstrated that intravenous Nafamostat was rapidly broken down to inactive metabolites and no significant anticoagulant effects were observed. The study provided clear and compelling evidence against the use of intravenous Nafamostat in COVID-19. For inhaled GB0139, plasma levels were measurable in all patients after inhaled exposure and demonstrated target engagement with decreased circulating galectin and a decrease in inflammatory mediators. The study showed promising PK/PD for further repurposing of GB0139 in viral lung injury. In collaboration with the Scottish National Blood Transfusion Service, a viral specific T cell therapy arm has been added to the Define platform and will begin recruitment in May 2022 to demonstrate safety and feasibility in patients with COVID-19. This platform has laid the foundations for experimental medicine in early phase evaluation of drugs in lung disease in Edinburgh. The teams' expertise will now focus on building on this capability to accelerate experimental medicine in respiratory infection and inflammation in NHS Lothian.

5. GENOMICS

GenOMICC

The Genetics Of Mortality In Critical Care (GenOMICC) study was initiated with support from ACCORD in 2014 to find the human genetic determinants of susceptibility to, and outcome from, critical illness. The ultimate objective is to transform critical care medicine by identifying targets for drug therapy to improve outcomes in critical care.

In order to recruit the large numbers of critically ill cases required to make robust genetic discoveries, GenOMICC was conceived as a global collaborative study with an open-source ethos (The Lancet Infectious Diseases. (2014);14:8–9). From the outset, GenOMICC was designed to include Covid-19: the first inclusion criterion was: "critical illness caused by emerging infections such as SARS, MERS, or Ebola". Hence, when the first cases of Covid-19 presented to intensive care units in the UK, they were recruited to GenOMICC. With support from ACCORD and NIHR, the study rapidly extended from covering half of the UK's intensive care capacity, to almost all of it. The study is now recruiting across 224 hospitals in the UK, and in Ireland, Canada, and Brazil. Setup in Pakistan, India and China is underway.

Within 5 months of the first critically ill cases in the UK, the GenOMICC study discovered 4 genes that make people susceptible to life-threatening COVID-19 (Nature. (2021);591:92–98). The first 2244 critically ill Covid cases in GenOMICC were compared with matched members of the population from three other studies (UK Biobank, Generation Scotland and 100,000 Genomes). The genes indicated that two molecular processes - antiviral immunity and lung inflammation - were important in determining the development of critical illness.

These genes led directly to multiple therapeutic targets, of which one stood out as being strongly supported by the genetic evidence and corroborated by preliminary clinical data: baricitinib (Nature. (2021);591:92–98). The GenOMICC team shared this result with the world as soon as it was available, specifically with the steering committee of the RECOVERY trial, the UK therapeutics prioritisation panel (UK-CTAP), SAGE, the REMAP-CAP trial, and the WHO committee on clinical management. Almost immediately, the decision was taken to include baricitinib in the RECOVERY trial (medrxiv.2022.03.02.22271623 (2022)), which has now demonstrated that baricitinib reduces mortality in patients hospitalised with severe Covid-19, in addition to existing therapies

(dexamethasone and anti-IL6 treatments). This is, to our knowledge, the first example of a new treatment for an infectious disease being discovered using human genetics.

In subsequent work, GenOMICC has discovered a total of 41 genetic variants associated with critical illness in Covid (COVID-19 Host Genetics Initiative. Nature (2021); Nature. (2022);1–10; medrxiv 2022.03.07.22271833 (2022)). 34 of these were discovered for the first time by GenOMICC, and the remaining discoveries depended on GenOMICC for verification. There are now more than 20,000 critically ill cases in GenOMICC, and many more discoveries are likely in 2022.

These additional discoveries identify a range of disease mechanisms and potential therapeutic targets, not only for Covid, but potentially for a broad range of critical illness problems. The GenOMICC study has led the world in host genetic discovery in Covid-19 and continues to lead the new field of critical care translational genomics.

The next phase of this work will extend GenOMICC recruitment worldwide, enabling discovery of underlying molecular mechanisms of a critical illness caused by sepsis, emerging infections, and sterile injury (such as pancreatitis and burns). Building on the UKRI-supported Outbreak Data Analysis Platform (ODAP) infrastructure at the Edinburgh Parallel Compute Centre, the GenOMICC team will work to rapidly translate new findings by identifying specific human proteins to target with therapy. Working with the translational healthcare technologies team in Edinburgh, they will work towards rapid translation into clinical practice by delivering microdoses of investigational drugs into the lungs of critically ill patients to determine efficacy. This “microtrials” experimental medicine concept has the potential to revolutionise drug discovery in critical illness, and to rapidly translate genetic discoveries into effective treatments.

6. Chief Scientist Office Precision Medicine Alliance programme

What can Scotland do about the fact that the incidence of multiple sclerosis in parts of the country are amongst the highest in the world? That liver disease is now the biggest killer of 35-49 year olds, with death rates in Scotland being 70% higher than the UK average? That survival rates for patients requiring ICU treatment are only 60%?

Three clinical research groups from Edinburgh, last year, were awarded a total of £6.9 million of funding from the CSO Precision Medicine Alliance research awards to support precision medicine research programmes. These programmes will run for the next five years with the potential to provide new treatment options for some of Scotland’s most common diseases with the poorest outcomes. Precision Medicine is an emerging approach for disease prevention and treatment that utilises individual variability in genes, patients’ phenotype, severity of illness and comorbidity. The approach allows clinicians and researchers to more accurately predict and therefore target which treatment and prevention strategies for a particular disease will work best in particular groups of patients.

Two of the research projects will focus on the use and impact of precision medicine on distinct medical conditions, with one concentrating on multiple sclerosis, and the other focusing on liver conditions including liver cirrhosis.

Multiple sclerosis (MS) is the leading cause of acquired neurological disability in young people and with rates in some of Scotland being amongst the highest in the world. More precise and accurate ways of measuring MS disease activity and determining if a particular treatment is suitable for an individual patient are urgently needed. This research project, led by David Hunt, will use radiology

and blood biomarkers to support decision making in relation to treatments with the aim of achieving better control of patients' disease and reducing disability.

Liver disease is a silent epidemic. Since 1970, deaths due to liver disease have increased by 400% and in people below the age of 65 they have risen five-fold. Liver disease kills 1 in 50 people in Scotland - where death rates are 70% higher than the UK average and 60% higher than 30 years ago. Liver transplant services cannot currently meet the numbers of Scottish patients with advanced liver disease, stressing the need for alternative treatment approaches. This research programme, led by Stuart Forbes, aims to translate advanced precision therapies for treatment of liver disease across Scotland. By focusing the research on therapies targeting the liver that are at different stages of development, the team believe they have a real chance of facilitating new treatment options that will improve patient outcomes within five years.

The third project, led by Manu Shankar-Hari, will focus on the impact of time-critical precision medical treatment for critically patients admitted to Intensive Care Units. Annually, around 45,000 severely ill or injured patients will require specialist care and treatment in one of Scotland's critical care units. These units provide a vital and highly specialised service both for emergencies and in support of planned elective procedures. However, survival rates for ICU patients are around 60%. For patients who do survive, they can experience substantial and long term physical and psychological morbidity after discharge from ICU. This research programme will begin by assessing two time-critical precision medicine treatments to understand their impact on survival rates, when administered alongside existing treatment and care. The hope is that through this research, new treatment options will emerge which will positively impact ICU survival rates.