Nottingham Biomedical Research Centre

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NHS National Institute for Health Research

VERSUS ARTHRITIS

Musculoskeletal Experimental Medicine Conference 2018

Jubilee Conference Centre, Triumph Road, The University of Nottingham, NG7 2TU
Friday 29th June 2018 - 10.00 am to 4.00 pm

CONFERENCE REPORT

Contents

Executive Summary

The UK biomedical research landscape is defined by significant infrastructural investment and valuable assets funded by the public sector, charitable bodies and commercial organisations. Collectively, these provide a broad opportunity for UK musculoskeletal experimental medicine to be recognised and sought as a global hub delivering at the forefront of musculoskeletal health and allowing an excellent environment for world-leading investigators to deliver powerful impact for patients, academics and commercial stakeholders.

Multiple structures and platforms exist, or are evolving, for local and collaborative design and delivery of new medicines. Nevertheless, overlaps and gaps do exist across the these NIHR and Arthritis Research UK translational research infrastructures and recognising these overlaps and exclusions, possible efficiencies and scope for improvements could be made to advance pace and productivity of MSK experimental medicine. To this end funders wished to explore "the alignment and opportunities to maximise, improve and add to the UK musculoskeletal experimental medicine investment in order to accelerate the translation of innovations for the benefit of patients, the public and the healthcare system." On the 29th June 2018, National Institute for Health Research (NIHR) and Versus Arthritis sponsored a meeting to explore needs and shape opportunities in musculoskeletal (MSK) experimental medicine, with over 50 experts and stakeholders across UK paediatric and adult academia, pharma and funders kindly hosted at the NIHR Biomedical Research Centre at Nottingham University. This report presents the background, aims, format and notes from the discussions of the day.

Discerning and constructive discussions were held in the domains of (i) models of delivery of collaborative experimental medicine research (ii) diverse research populations (iii) biobanking and biomolecular resources for experimental musculoskeletal medicine (iv) UK experimental musculoskeletal medicine infrastructure and technologies. Building on valuable insights, suggestions and proposals were offered into the very positive and progressive conversations.

The day highlighted, for funders, industry and academia, approaches to consider progressing. It also revealed remaining underlying areas of need (such as incorporation of a life course approach, capacity building), scope for system-wide adaption (to encompass a UK-wide approach, to connect with the clinical research facilities and networks, approaches to relationships and partnerships with industry) and some forward opportunities to act (for example in biobanking, patient involvement). There was consensus from stakeholders wishing to enhance the operational effectiveness in this area through collaboration and networking. There was collective recognition that there is opportunity to define and align activities against some common areas of need and derive benefit from a collaborative approach.

Summary Themes:
Themes of the day informing the next steps can be summarised as:

- *Adapt and Flex:* refrain from generating new initiatives and building afresh, learn from others whilst aligning, encompassing and testing changes to address the barriers and exploit the opportunities
- *Incorporate and Diversify:* there is distinct scope to develop a UK-wide and life course approach, encompassing a breadth of MSK specialities, new therapies and technologies with improved patient involvement
- *Clarify and Connect:* there is need to facilitate development of contacts between the infrastructures and provide clear sight of the points of engagement for stakeholders, such that relations develop in an efficient manner and speed translation

- *Invest and Enhance:* there is opportunity to prioritise development of and investment in beneficial underpinning activities and resources; as well as facilitating utilisation of existing investments there is a requirement for progressive investment to grow the UK capacity and advance different dedicated infrastructures

Next steps:

In the context of the evolving landscape there is a clear opportunity to align UK experimental medicine infrastructure and investments in MSK research at a national level with the goal of accelerating translation across the preclinical / clinical boundary for the benefit of patients.

NIHR and Versus Arthritis intend to form a small working group to consider approaches to take in developing and aligning UK MSK experimental medicine activities and opportunities, potentially defining and outlining a UK MSK TRC.

(* Versus Arthritis was launched on 19 September 2018, following the merger of two of the UK's largest arthritis charities, Arthritis Research UK and Arthritis Care - In relation to experimental medicine investment, established activity is presented with reference to Arthritis Research UK throughout, forward looking activity is presented with reference to Versus Arthritis)

Introduction

On June 29th 2018, the NIHR Biomedical Research Centre at Nottingham University kindly hosted the NIHR and Arthritis Research UK to bring together over 50 experts and stakeholders across UK paediatric and adult academia, pharma and funders to collectively explore and shape opportunities and activities in musculoskeletal (MSK) experimental medicine.

This report of the conference presents the background, aims and format for the day (with agenda, attendees and invitees) and captures notes of the plenary and breakout discussions.

The biomedical research landscape has many infrastructure investments and assets funded by the public sector and charitable bodies, working across different parts of the innovation pathway from discovery and invention to evaluation and adoption in the healthcare system. The MSK experimental medicine (definition in Appendix 1) field has been served relatively well, yet this presents some complexity, disjointedness and possibly inefficiency.

The landscape offers opportunities for the UK to be recognised globally as delivering at the forefront of MSK experimental medicine. There is however appreciation of the many overlaps, gaps and probable inefficiencies, that many investigators wear many 'hats' amongst the 'initiative soup', and there is opportunity to define activities against some common areas of need and derive benefit from a collaborative approach.

Background and Aims

Various models for collaborative design and delivery exist or are developing and evolving, with many infrastructure resources available to deliver across genomics, biomarker identification and development, imaging, informatics, well-phenotyped patients and access to industry assets. In musculoskeletal medicine, such resources are exemplified by the Arthritis Research UK Experimental Arthritis/Osteoarthritis Treatment Centres (EAOTCs), NIHR Biomedical Research Centres (BRCs) and Clinical Research Facilities (CRFs), NIHR Joint and Related Inflammatory Diseases Translational Research Collaboration (NIHR J-TRC), the newly formed Arthritis-Therapy Acceleration Programme (A-TAP). There is recognition of overlaps, repetition and crucial gaps and priority areas currently under-resourced, that investigators wear many 'hats' and the system can often be viewed as suffering from 'initiative soup'. This presents an opportunity to better define activities against some common areas of need and deliver with some collaborative approach.

In terms of funding support in England the NIHR has invested in BRCs (and Units), where the spend on MSK related themes has been approximately £7.5M per year and the forward investment over 2017-2022 is similar at approximately £40.5M, representing approximately 5% of the £816 million total BRC investment. For seven years the NIHR Office for Clinical Research Infrastructure (NOCRI) has supported the J-TRC (previously translational research collaboration (TRP)). An investment of £112.3 million by NIHR supports 23 NHS organisations to run CRFs, with 6 CRFs in Scotland, two in Wales and one in Northern Ireland, amongst these there are two dedicated paediatric CRFs.

Arthritis Research UK with Health and Care Research Wales and Chief Scientist Office Scotland has invested approximately £3M+ to establish nine EAOTCs (2012-2018) and a paediatric EATC (2013-2018). These centres have supported research fellows, physiotherapists, centre

and study managers, nurses, post-doctoral scientists, statisticians and technicians in activities such as management of patient cohorts, training in ultrasound, engagement of patients and public in experimental medicine and engagement with pharma in early phase studies.

The Kennedy Trust for Rheumatology Research provides £7m to support the A-TAP which provides a hub of expertise and infrastructure to support clinical inflammatory disease. Further initiatives and funding streams exist such as the MRC stratified medicine consortia across rheumatoid arthritis, juvenile idiopathic arthritis and its associated uveitis, psoriasis, systemic lupus erythematosus, Sjogren's syndrome and autoimmune hepatitis, the EMINENT programme accessing GSK's portfolio with the MRC to enable translational discovery, Innovate UK Catapults and syndicates (Medicine Discovery and Cell and Gene Therapy).

Multiple reports and meetings have presented reviews of the assets and issues:

Mapping of assets by the Precision Medicine Programme Coordination Group
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/483560/Precision_Medicines_Booklet_Final_Web__002_.pdf

http://pm.ktnlandscapes.com

November 2014 NIHR Stratified Medicine Capabilities Supporting innovation and expertise in stratified medicine
https://www.nihr.ac.uk/life-sciences-industry/documents/Brochures%20and%20flyers/NIHR_Stratified_Medicine_Capabilities_brochure.pdf

August 2015 ABPI report - Ensuring UK leadership in experimental medicine
https://www.bps.ac.uk/getmedia/39f8ae56-f93b-40e0-85ed-62bf26e07dde/Ensuring-UK-leadership-in-experimental-medicine-Aug-2015.pdf.aspx?ext=.pdf

November 2016 Developing a roadmap for delivery of stratified medicine studies within the NHS Workshop
http://www.uk-pgx-stratmed.co.uk/index.php/november-2016-workshop-videos

October 2017 UKRI report data - Mapping the Landscape of UK Health Data Research & Innovation A snapshot of activity in 2017
https://mrc.ukri.org/documents/pdf/mapping-the-landscape-of-uk-health-data-research-and-innovation-report/

NIHR Patient and Public Involvement and Engagement: NIHR Clinical Research Facilities for Experimental Medicine Annual Reports 2016/17
https://www.nihr.ac.uk/about-us/how-we-are-managed/managing-centres/nihr-central-commissioning-facility/PPIE-reports/CRFs_2016-17.pdf

ABPI report An experimental medicine model to support a stratified medicine approach
http://www.abpi.org.uk/media/1585/an-experimental-medicine-model-to-support-a-stratified-medicine-approach.pdf

AMS FORUM report with ABPI Bridging the preclinical/clinical boundary – workshop report
https://acmedsci.ac.uk/file-download/36971834

The purpose of the day was, as per the agenda, “to explore the alignment and opportunities to maximise, improve and add to the UK musculoskeletal experimental medicine investment in order to accelerate the translation of innovations for the benefit of patients, the public and the healthcare system.”

The day was not a showcase of what is in the system or how groups are working, a companion scoping document supported the day, presenting some of this broader context.

Conference Format

The conference was convened as a distinctive opportunity for participatory discussion, structured around four domains:

A - Models of delivery of collaborative experimental medicine research

B - Diverse research populations

C - Biobanking and biomolecular resources for experimental musculoskeletal medicine

D - UK experimental musculoskeletal medicine infrastructure and technologies

- There were no presentations during the day beyond the introductions.

- Reference was made, to the newly published AMS/ABPI workshop report from the AMS FORUM **"Bridging the preclinical-clinical boundary".**
  https://acmedsci.ac.uk/file-download/36971834

- The afternoon consisted of discussion in the four domains in plenary session, for each of which there was a panel representing activities /organisations active in that area who presented their thinking to facilitate discussions.
- In the morning there were breakout sessions in the four areas, to prepare and provide some groundwork for the afternoon collective discussion - attendees were free to join their preferred session of the four.
- Chairs of the afternoon panels also facilitated the breakout morning discussions, providing opening comments in the morning session and feeding in from the morning to the afternoon plenary session.
- Discussions sought to encompass capacity and skills within each area and the scope of the UK offer in these areas.

- Notes/key points were gathered in the breakouts and passed to chairs of panels to aid the introduction of the area and panel discussion in the afternoon.

- Agenda, Delegate list and Invitee list are as per Appendices 2-4.

Discussion notes: Models of delivery of collaborative experimental medicine research

This discussion sought to capture the skills and resources within current collaborations as well as explore the advantages of various collaborative models and identify opportunities to refine and align further the UK offer in MSK experimental medicine.

Facilitator: Professor Costantino Pitzalis

Note taker: Theo Bond

PANEL	***REPRESENTATION***
Professor Ian Bruce	*NIHR TRC Joint and Related Inflammatory Diseases, Manchester*
Professor John Isaacs	*Experimental Arthritis Treatment Centre Director, Newcastle*
Dr Alan McNair	*Senior Research Manager for the Chief Scientist Office*
Dr Claire Potter	*Arthritis Therapy Acceleration Programme, Birmingham*
Professor David Walsh	*Biomedical Research Centre, MSK Theme Lead, Nottingham*

Opening remarks:

- The UK MSK landscape for experimental medicine is complex, and people can find it difficult to access the right research team/researchers as there is no single point of entry to the covering the whole of the UK MSK. It was recognised that though this was the intention of the Translational Research Partnerships when they were set up. clusters of activity have developed, meaning the single point of contact has not been achieved.
- Considerations need to be made around regional vs national activity: there are localised models such as the Birmingham-Oxford A-TAP which support hospitals that aren't part of the EM infrastructure but add value/complement national initiatives.
- EATC funding has been key, enable bridging between all the centres, not just NIHR which is based in England.

Reflections on the nature of the models of delivery and collaboration:

NIHR BRC

- Funding to support experimental medicine based on scientific excellence.
- NIHR BRC contract with NHS organisation, the University is the partner.
- NIHR BRCs support a number of research areas beyond MSK.
- Encouraged to contribute to a national level and represent NIHR nationally.
- Local industry contacts get pulled into the national level.
- Local variability and some flexibility for how funding is spent.
- NIHR BRCs were required, as part of their funding bid, to outline the resources that they would provide to support the activity of the JI-TRC.

Arthritis Research UK EATC/EOTC

- Small level important enabling funding, but funding envelopes coming to an end / ended and continued uncertainty to date regarding renewal/extension.
- More flexibility for use of funding compared to NIHR.
- Includes new technology.

- Provides for Arthritis Research UK leadership role in experimental medicine.

NIHR TRC

- Single, central point of contact for industry.
- Allowing multi-centre studies through NIHR BRCs.
- NIHR TRC is England only.
- Funded through the NIHR BRCs funding stream.
- Specific to particular areas of MSK, although the strategy is being refreshed which could consider broadening the scope.
- Unclear to industry between the models and where the point of contact is.
- The current NIHR TRC structure does not act as a single point of contact, but there is an opportunity to consider how to build on this to act in this regard.
- To date, paediatric experimental medicine has not featured as part of the NIHR TRCs.
- Significant value-added opportunity recognised for UK to be internationally leading in this space by including paediatric experimental medicine.

A-TAP

- Allows more hospitals and more clinicians to get involved in research rather than just the recognised points in the infrastructure.

ECMC, cancer model

- Has become the face of cancer experimental medicine.
- Could be the same in MSK (an Arthritis Network).
- BRCs and CRFs deliver research within the ECMC network.

Scotland, Wales, Northern Ireland

- No competitive environment in this area, no real similarity to the NIHR BRC and CRFs, but have appropriate infrastructures for the size of the population.
- Join with / have similar funding programmes to NIHR.
- Work nationally via the Arthritis Research UK EATCs.

Needs:

- Experimental medicine academics don't know where to go to for help with the translational of their findings - need for a roadmap to help show the translation routes.
- SME and pharma ask where should they go for help - need for a clear roadmap for adult and paediatric experimental medicine, removal of confusion, showing a single point of contact for coordination of experimental medicine study design and delivery, provision of information to industry.
- NIHR TRC could benefit from more promotion so industry but would also benefit from broadening its scope beyond industry and beyond 'Joint and related inflammatory disease' – it was noted that the strategy is being refreshed at the moment so there is an opportunity to do this, including also paediatrics.
- UK approach needed which should build on the existing structures rather than trying to create something 'new' (which risks adding further complexity to the landscape).

Hurdles/barriers:

- Devolved nations have the issues that there is no competitive environment in this area, no real similarity to the BRC, CRFs. It was noted the level of investment in MSK research in England does significantly exceed the resources available in the devolved nations Enthusiasm for joining up expertise and facilities across the UK.
- Scotland, Wales, N.Ireland scope for involvement requires exploration.

- Governance of funding - hard to demonstrate impact of funding. Laborious reporting.
- Lack of sustainability.
- NHS vs University priorities - Division between experimental medicine and large-scale clinical trials in MSK - Academic vs NHS interest.
- CTU and NIHR CRN better delivery model for later stage studies. CTU very important in delivering later stage studies.
- Innovation isn't rewarded/encouraged at an academic level.

Opportunities:

- To review the strategy of the NIHR TRC to broaden scope (inclusion of children and young people was highlighted).
- To map all the resources, collaboration facilities so it is easy to understand.
- To maximise the 'life course' opportunities and approach across all centres to enhance the UK's USP in this area.
- Experimental medicine centres should reduce overlap of expertise in similar areas, 2-3 centres for each theme to reduce competition.
- NIHR CRN engagement with experimental medicine is an area for improvement.

Key points of feedback:

- It was noted that the NIHR TRC needs to evolve and could provide the basis for building a more national network rather than building something new/additional from scratch. It was highlighted this should cover the needs of industry, be UK wide, to include children and young people by ensuring life course approaches.
- Charity involvement would provide a mechanism to assist development of a single-point-of-contact that is well recognised in the community.
- Learning from cancer, MSK is more than just focus on clinical trials, oncology is in a different place to MSK.
- While the need for competition was recognised it was noted that this can be challenging to manage vs collaboration.
- There's a need to define experimental medicine better within the NIHR infrastructure.
- A roadmap for where academics can go to innovate is needed.
- A roadmap, or single point of access combing paediatric and adult expertise would be extremely beneficial to help show where people can go to with new innovations but also where there are to engage in the MSK experimental medicine landscape.

What should a collaboration look like?

How can the NIHR JI-TRC redevelop rather than building a network from scratch?

- No duplication, combine the charity and NIHR, specify what to achieve and how does it fit into the innovation pathway, utilising the delivery vehicles of BRCs, CRFs, and the expertise of the EATCs etc.
- TRC should define a set of recommendations to move forward, something that is sustainable and doesn't replicate the same issues of previous models. Sustainable and returnable.
- Include regulators and industry to influence the development.
- Identify where there can be alignment in research strategy nationally, while continuing to support local/regional clusters.

Discussion notes: Diverse research populations

This discussion sought to discuss requirements and innovative ways to integrate engagement across more diverse populations and include paediatric and adolescent research in the experimental musculoskeletal medicine arena to review the extent of activity across the life course. Outlining what is already taking place in the UK and discussing the work in paediatric and adolescent arthritis and related paediatric rheumatic disorders, the aim was to discuss how we can continue to make effective progression for research in diverse populations.

Facilitator: Professor Michael W Beresford

Note taker: Dr Bonnie Millar

PANEL	***REPRESENTATION***
Paula Wray	*Senior Public Involvement Manager*
Andy Wragg	*PPIE Manager Nottingham BRC*
Other members unable to attend	

Opening remarks:

The take home message is the requirement for “real world patients and real-world needs”.

Taking children and young people as a starting point: We need to step back from the phenomenal resources we have been reflecting on today and look at what is actually available and targeted at the needs of for children and young people across the UK. Children number some 20% of the population, and themselves have the whole array of complex rheumatology conditions with associated morbidity and mortality, that impact on their growth and development future employability, quality of life and life chances. In addition, they will grow into the very adults with all the complex MSK conditions we are considering, in which many precursors are already set in childhood and adolescence. The UK MSK community, in partnership with funders, industry and the public, needs to take a “life course approach” to consider both the young and the specific challenges of the very elderly. Both these groups have specific needs, specific challenges in participating in research, and both groups have tended to be marginalised or discriminated against in clinical research.

Needs:

There is a need to work collaboratively. If we don’t take a “life course approach” and incorporate children (and the very elderly) into MSK experimental medicine structures and specifically funding and resources, we will miss a key opportunity and necessity for addressing the needs of our population. Children are not currently included in the NIHR TRC strategy. Children’s specialities have their own challenges, but also can learn from and share their expertise with adult colleagues. It is always necessary to collaborate closely between paediatric and adult colleagues in addressing the challenges of transition for young people. In all of this there are both opportunities and challenges – why not integrate children and young people as much as possible into the infrastructure and UK-wide network of resources and expertise supporting MSK experimental research. Specific, enabling, even modest resources can also trigger important collaborations with existing (adult-predominant) experimental medicine infrastructure. For

example, with the MRC Stratified Medicine program for SLE (e.g. EATC for Children with Manchester BRC and the MasterPlans Consortium) and now for JIA and JIA-associated uveitis (e.g. EATC for Children and the BRCs of UCL, Manchester and Cambridge and the CLUSTER Consortium. Research involving children can produce models of working which are highly effective and exemplary.

Hurdles/barriers:

- We have highly established, internationally leading methodology for patient and public involvement and engagement in children and young people in the UK and within the paediatric MSK community, but with little or no specific funding and constant threat to its sustainability.
- Social diversity, ethnic diversity and inclusiveness are key factors. Exemplars are important. Going out into the community, taking information out to schools is fundamental. We need to have meaningfully diverse involvement. We need to get the right people involved to support research.
- We have the challenge of having to often having to adapt 'adult'-derived studies to the needs of children and/or an environment that tends not to address the specific needs of children and young people (and the very elderly).
- Buy in from NHS clinicians is required, but often difficult to protect, to cement relationships between clinicians and patients for taking part in clinical research.
- There are cross-cutting barriers relevant to all research i.e. age; medication formulation in children and elderly; access issues (isolated living alone).
- Real world people are often not connected to research.
- Other hurdles are multi-morbidities and ethnic diversity.
- Shortage of validated translations of outcome measures.

Opportunities:

The focus of tackling these challenges should be children, young people at the centre (and the very elderly for addressing their needs). Collaboration with INVOLVE and the extensive PPIE expertise nationally in Paediatrics, linking in already to MSK experimental medicine is fundamental.

Over the last 10 years has been significant progress in getting children and young people involved, but now we need to move forward to change attitudes to be as inclusive as possible and to get the right people, patients involved throughout life cycle of research.

Accessing studies to improve treatment options should be available for everyone. We need to give people the information they need to get involved. Clinical research in MSK experimental medicine is not just about medicines. There is a significant infrastructure out there so why not use it to help children and young people.

Key points of feedback:

- Need to take a true, integrated life course approach, considering the young and the very old.
- In this there is need to work collaboratively and inclusively of the paediatric experimental medicine expertise and community.
- The need to include children and young people's experimental medicine priorities and associated expertise across the UK within the next stage of development, and also specifically the NIHR TRC.

- There are intrinsic difficulties in linkage across the life course in the research landscape, which need specific attention and input from paediatric as well as adult colleagues.
- There is a problem with linkage between children and adult studies, important also for long term follow up but also comparative studies between paediatric and adult cohorts for experimental medicine, due to differences / changes in outcome measures across the ages.
- The cultural framework for research in children and young people is important. How do we truly empower the voice of young people? In the UK we have some excellent examples including “Generation R” and the “Invisible Illness” programme, linked in with the MSK experimental medicine community, which need to be supported and fostered.

Discussion notes: Biobanking and biomolecular resources for experimental musculoskeletal medicine

This discussion sought to outline and discuss the biomolecular resources within the UK infrastructure to deliver the deep phenotyping of patients and how we can further develop the utilisation of these resources. The conversation also aimed to focus on the various patient cohorts, samples and imaging resources amongst other across experimental musculoskeletal medicine and how these could be aligned to streamline access for research.

Facilitator: Professor Iain McInnes, Arthritis Research UK EATC Director

Note taker: Keith Pugh

PANEL	REPRESENTATION
Sancha Martin	*IMID-Bio-UK Project Manager*
Louise Knowles	*Head of Research Policy NIHR Infrastructure and Growth providing representation for NIHR BioResource*
Professor Maya Buch	*University of Leeds*
Dr Phil Quinlan	*UKCRC Tissue Directory*

Following discussions in the morning it became clear that there were needs, hurdles to overcome and also opportunities for greater coordination to create community resources. These were presented by the panel.

1) Cataloguing

The absence of a single catalogue of existing biobanks/cohorts and their available data and tissue has led to a fractured and confused landscape for researchers looking for access to specific bioresources. There is a clear need in which to catalogue the UK bioresources in a uniform and simple manner. It was recognised that this is the aim of the UKCRC Tissue Directory, but more is needed to be done to increase the adoption of collections into the UKCRC tissue directory.

2) Core phenotyping agreement

The heterogeneity of basic phenotype data across cohorts and the accuracy of this data within individual cohorts presents difficulty in working with the data. Clear discrepancies and absence of basic phenotype data such as sex, age and condition type make analysis difficult, have negative effects on the reliability of collections and make cataloguing an accurate stock of repositories difficult. Inconsistent datasets reinforce a fractured and confused landscape.

A national agreement for a minimal core set of phenotyping criteria for data is required.

3) Continuity

The lack of continuity in long terms funding across the biobanks, which makes it difficult to make these sustainable and to deliver long term milestones difficult. It was noted that this is a symptom of charity and government funding, as long-term commitment in the research charity sector is not feasible and government funding is often fixed at a specified fiscal cycle. However,

there are examples of continued funding after 5 years being awarded based on merit which provide opportunity for review.

4) Under use

The level at which the biobank resource (data and tissue) is being utilised within the UK is strikingly low, with only 20% of biobanks being reported at a 'good' rate of access across the existing biobanks within the UKCRC tissue directory. Furthermore, 75% of the biobank tissue and data granted to SMEs based in the UK was from outside of the UK. Reasons referenced for this are the lack of visibility of UK biobanks and an absence of a clear guidance on how to request access to the data and tissue. The under use of biobank resources could be having a direct effect on the sustainability and longevity of such collections because of a limited financial return from lower than anticipated access requests.

There is a clear need for increased visibility and publicity of collections and transparency of access processes.

5) Patient recall

The ability to recall individuals who have provided data and/or tissue to a biobank is an issue for many. Overcoming this issue will could aid recruitment of researcher participants from Phase I to Phase IV studies. The platform provided by the NIHR BioResource, which is still developing, was highlighted as an opportunity to create national cohorts who have consent to provide data and samples and to be recalled for research

Consenting practises are a clear hurdle in the ability to achieve sufficient and easy recall of research participants. A lack of clarity provided to consenting volunteers concerning the sharing and use of samples by external partners, particularly industry, has a negative effect on the access to collections and contributes to the under use of UK biobank repositories.

6) Academic reward

One clear barrier to harnessing the potential of UK biobanks and collections is the distinct lack of academic reward for the setting up and maintenance of a cohort of data and tissue. The limited reward and Research Excellence Framework (REF)-returnable impacts could lead to a number of detrimental effects on the power of individual cohorts and team science. The desire to initiate and maintain a cohort which is not recognisable on current impact scales will be affected, which could lead to a reduced number of cohorts and a greater number coming to an end prematurely.

Measuring impact through REF-returnable publications would overcoming this hurdle. The absence of clear authorship guidance for publications arising from biobanks/cohorts can be a deterrent to granting access to external researchers, thus reinforcing a cultural of ownership of cohorts and siloed research terms instead of a team science approach.

7) Independence of access

There is a need for a consistent approach to the membership of biobank access panels, specifically the need for independent membership on panels which are open to external applications for access. This relates to the need to dispel 'ownership' culture in which access being favoured to those within closed communities and limiting access to those external to it.

Discussion notes: UK experimental musculoskeletal medicine infrastructure and technologies

This discussion sought to review how to streamline access to infrastructure and novel technologies which are available within various research centres. What can be done to continue to support innovation and streamline access to various resources within the infrastructure and how can we stimulate or maximise further joint working within MSK experimental medicine research in the UK?

Facilitator: Professor Chris Buckley, Director of the Birmingham NIHR Wellcome Trust Clinical Research Facility

Note taker: Sarah Odoi

PANEL	REPRESENTATION
Mark Samuels	*Chief Business & Strategy Officer, Medicines Discovery Catapult*
Professor Dorothee Auer	*Director of Precision Imaging, Nottingham University Beacon of Excellence*
Professor Andrew McCaskie	*Director Arthritis Research UK Tissue Engineering Centre of Excellence*
Professor Medhi Tavakoli	*Knowledge Transfer Manager for Infrastructure, Med Tech & Therapies, Innovate UK, Knowledge Transfer Network*
Alan Reynolds	*Chief Scientific Officer and Director at AKL Research and Development Ltd and Illix Ltd*

Opening remarks:

How do you reward team behaviour? How best to utilise best practice for team science – infrastructure, and technologies can help address this. Non-contentious issues for investment e.g. how to recruit patients, how do we utilise technologies, imaging, pathology services. We should do more to recruit quickly and educate the next generation of experimental medicine researchers.

Needs:

- Need to encourage more team science, there is too much individualism in life science.
- Need a better overview of the structure.
- Need more money to invest in people.
- Need to understand how you transition clinical methods with new innovations?
- How do you work with people who deal with diagnostic imaging?

Hurdles/barriers:

- Infrastructure is not supportive of imaging and biomarker technologies.
- Some disconnection in the usage of physician reported and patient reported outcome measures.
- Much of the existing framework is focussed around the large BRCs (and related institutions), rather than looking across the who MSK experimental medicine expertise and landscape,

which would be better enhanced by a more integrated and inclusive approach, including those parts not associated with BRCs.
- Existing collaborations are often poorly supported and new collaborations can be hard to establish based on difficulties identifying shared interest outside the BRC landscape.

Opportunities:

- Reward successful collaborations, including especially those beyond just BRCs.
- Secondments for PhD students.
- Train rheumatologists in ultrasound and radiology.
- Use of the 'Manhattan project' approach – attract people with an aim and introduce them to compete in a friendly way.
- Collaboration with computer science and use of AI to generate disruptive technologies.
- Pilot a different approach where it is not PI-led, set a challenge and co-produce a solution.

Key points of feedback:

- Consideration to be made of what role the charity can play so that it is more aligned with NIHR.
- Experimental medicine is currently too broad.
- Pilot a few key clusters and then reward if successful e.g. bring a few of the ARUK centres of excellence and get them to collaborate.
- Ways in which team science can rewarded include
    - Use ARUK investment to fund PhDs in centres of excellence
    - Reward leadership that is comfortable with itself
    - Infrastructure is contingent on team science
    - Reward collaborative behaviour
    - Set younger people up for success, encourage leadership programmes as a mean to grow future leaders
- Better integration of cell and gene therapy, establish means to bring such technologies to patients.
- Better education for clinicians with new imaging technologies.
- Encourage accelerating clinical translation.
- Bring individuals such as health economists, biomarker specialists into experimental medicine.
- Work towards opportunities for collaboration beyond just BRCs, including expert centres that do not have a BRC (e.g. such as devolved nations; many paediatric centres).

Appendix 1 - What is Experimental Medicine?

Medical Research Council

https://mrc.ukri.org/research/initiatives/experimental-medicine/

Experimental medicine is a broad term and refers to:

Investigation undertaken in humans, relating where appropriate to model systems, to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments.

Advances in non-invasive techniques such as medical imaging, combined with powerful 'omics technologies, now allow us to approach the human as the ultimate experimental animal for improving human health. Doing so has the potential to dramatically increase the speed and efficiency by which medical discoveries are translated into healthcare.

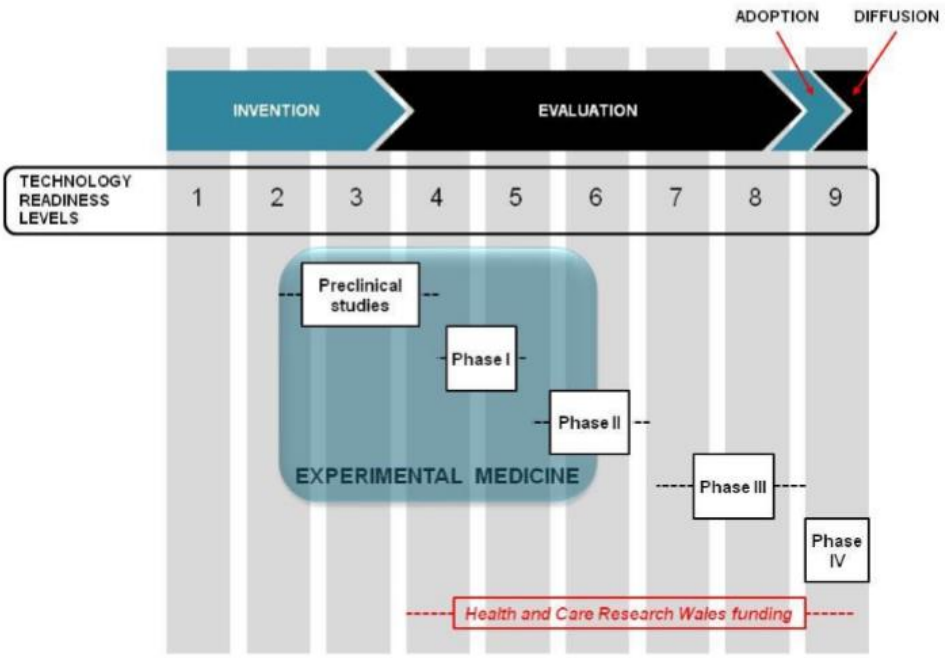
Health and Care Research Wales

https://www.healthandcareresearch.gov.wales/uploads/Policy%20%26%20Strategy/Precision%20Medicine/Precision_Medicine_strategic_direction_2015_09_16_Final.pdf

Position Paper - Future Initiatives in Experimental and Precision Medicine

Experimental medicine is a term used for studies which drive the translation of discoveries from basic science and clinical medicine into benefits for human health. This includes the study of mechanisms underlying disease in human tissue samples and/or patients and phase I/IIa trials to demonstrate proof-of-concept evidence for the validity and importance of new discoveries or treatments. Health and Care Research Wales also considers pre-clinical (animal) studies to investigate the mechanisms underlying disease and/or to demonstrate the effectiveness of new therapies to fall under the umbrella of experimental medicine, provided these studies are part of a larger body of work which includes the investigation of mechanisms underlying disease or novel treatments in humans.

Experimental medicine precedes and informs the development of late phase clinical trials. Effective translation of results from experimental medicine studies into later phase clinical research is an important outcome of experimental medicine, as is the generation of new ideas to be explored in the laboratory (otherwise known as reverse translation).


ADOPTION
DIFFUSION
INVENTION
EVALUATION
TECHNOLOGY READINESS LEVELS
1
2
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8
9
Preclinical studies
Phase I
Phase II
EXPERIMENTAL MEDICINE
Phase III
Phase IV
Health and Care Research Wales funding

Appendix 2 - Agenda and Invited Panel Members

Musculoskeletal Experimental Medicine Conference 2018	
Friday 29th June 2018 - 10.00 am to 4.00 pm Jubilee Conference Centre, Triumph Road, The University of Nottingham, NG7 2TU	
PURPOSE Explore the alignment and opportunities to maximise, improve and add to the UK musculoskeletal experimental medicine investment in order to accelerate the translation of innovations for the benefit of patients, the public and the healthcare system.	
9.30 am	Arrival and registration
	ITEM
10:00	**Welcome and Introductions - Bridging the preclinical-clinical boundary** Maintaining global recognition of the UK in delivering at the forefront of musculoskeletal experimental medicine. *Dr Stephen Simpson, Director of Research, Arthritis Research UK* *Louise Knowles, Head of Research Policy NIHR* *Mark Samuels, Chief Business and Strategy Officer, Medicines Discovery Catapult*
	2x Breakout Groups *To prime the afternoon discussion, exploring needs and scope for innovation, how to capitalise/change/deliver in the areas of opportunity, gathering strengths and weaknesses*
10.45	**BREAKOUT DISCUSSION 1** *(30 mins) (choice of four groups)* A - Models of delivery of collaborative experimental medicine research B - Research diverse populations C - Biobanking and biomolecular resources for experimental musculoskeletal medicine D - UK experimental musculoskeletal medicine infrastructure and technologies
11.20	**BREAKOUT DISCUSSION 2** *(30 mins) (choice of four groups)* A - Models of delivery of collaborative experimental medicine research B - Research diverse populations C - Biobanking and biomolecular resources for experimental musculoskeletal medicine D - UK experimental musculoskeletal medicine infrastructure and technologies
11:50	**Buffet Lunch**
	4x Panel discussions *Each panel discussion to provide some breakout group feedback and views from the panel to frame discussion to identify opportunities or solutions, how to create and exploit areas of opportunity*

12:50	**A - Models of delivery of collaborative experimental medicine research** *(40 mins)* In this discussion lead by Professor Costantino Pitzalis, we aim to explore the various model of collaboration which exist, discuss what we have learnt so far from these models, and explore how these existing models fit together to represent a UK offer. From this discussion we aim to capture the skills and resources within current collaborations as well as explore the advantages of various collaborative models and identify opportunities to refine and align further the UK offer in MSK experimental medicine.
1:30	**B - Research diverse populations** *(40 mins)* In this discussion lead by Professor Michael Beresford, we aim to discuss requirements and innovative ways to integrate engagement across more diverse populations and include paediatric and adolescent research in the experimental musculoskeletal medicine arena to review the extent of activity across the life course. Outlining what is already taking place in the UK and discussing the work in paediatric and adolescent arthritis we aim to discuss how we can continue to make effective progression for research in diverse populations.
2:10	**Tea and coffee**
2:30	**C - Biobanking and biomolecular resources for experimental musculoskeletal medicine** *(40 mins)* In this discussion lead by Professor Iain McInnes, we aim to outline and discuss the biomolecular resources within the UK infrastructure to deliver the deep phenotyping of patients and how we can further develop the utilisation of these resources. The conversation also aims to focus on the various patient cohorts, samples and imaging resources amongst other across experimental musculoskeletal medicine and how these could be aligned to streamline access for research.
3:10	**D - Panel discussion - UK experimental musculoskeletal medicine infrastructure and technologies** *(40 mins)* In this discussion lead by Professor Chris Buckley we aim to review how to streamline access to infrastructure and novel technologies which are available within various research centres. What can be done to continue to support innovation and streamline access to various resources within the infrastructure and how can we stimulate or maximise further joint working within MSK experimental medicine research in the UK?
3.50	**Closing remarks** *Dr Stephen Simpson, Director of Research, Arthritis Research UK* *Louise Knowles, Head of Research Policy NIHR*
4.00	Close

Invited Panel Members

NAME	REPRESENTATION
A - Models of delivery of collaborative experimental medicine research	
CHAIR	**Professor Costantino Pitzalis, incoming chair NIHR Translational Research Collaboration in Joint and Related Inflammatory Diseases**
Dr Alan McNair	*Senior Research Manager for the Chief Scientist Office*
Professor Ian Bruce	*NIHR TRC Joint and Related Inflammatory Diseases, Manchester*
Professor John Isaacs	*Experimental Arthritis Treatment Centre Director, Newcastle*
Professor David Walsh	*Biomedical Research Centre, MSK Theme Lead, Nottingham*
Dr Claire Potter	*Arthritis Therapy Acceleration Programme, Birmingham*
B - Diverse Research populations	
CHAIR	**Professor Michael Beresford, NIHR CRN Specialty Cluster Lead**
Paula Wray	*Senior Public Involvement Manager*
Andy Wragg	*PPIE Manager Nottingham BRC*
Professor Athimalaipet Ramanan	*Arthritis Research Clinical Study Group co-Lead, Associate Director of ARUK funded only Paediatric Experimental Arthritis Treatment Centre*
C - Biobanking and biomolecular resources for experimental musculoskeletal medicine	
CHAIR	**Professor Iain McInnes, Arthritis Research UK EATC Director**
Sancha Martin	*IMID-Bio-UK Project Manager*
Louise Knowles	*Head of Research Policy NIHR, oversight NIHR BioResource*
Professor Maya Buch	*University of Leeds*
Dr Phil Quinlan	*UKCRC Tissue Directory*
D - UK experimental musculoskeletal medicine infrastructure and technologies	
CHAIR	**Professor Chris Buckley, Director of the Birmingham NIHR Wellcome Trust Clinical Research Facility**
Mark Samuels	*Chief Business & Strategy Officer, Medicines Discovery Catapult*
Professor Dorothee Auer	*Director of Precision Imaging, Nottingham University Beacon of Excellence*
Professor Andrew McCaskie	*Director Arthritis Research UK Tissue Engineering Centre of Excellence*
Professor John Fisher	*Director Wellcome Trust/EPSRC Medical Engineering Centre*
Alan Reynolds	*Chief Scientific Officer and Director at AKL Research and Development Ltd and Illix Ltd*

Appendix 3 - Delegate List

Experimental Musculoskeletal Medicine Conference

The Jubilee Conference Centre - University of Nottingham

Friday, June 29, 2018

Title	First Name	Surname	Organisation
Dr	Lucy	Allen	Head of Collaborations, NIHR Office for Clinical Research Infrastructure (NOCRI)
Professor	Dorothee	Auer	University of Nottingham
Dr	Caroline	Aylott	Head of Research Awards, Arthritis Research UK
Professor	Michael	Beresford	University of Liverpool
Professor	Ian	Bruce	Manchester University
Professor	Maya	Buch	University of Leeds
Professor	Christopher	Buckley	University of Birmingham
Dr	Craig	Bullock	Research Programme Manager, Arthritis Research UK
Professor	Ernest	Choy	Cardiff University
Dr	Coziana	Ciurtin	UCL
Professor	Philip	Conaghan	University of Leeds
Dr	Francesco	Del Galdo	Leeds Institute of Rheumatic and Musculoskeletal Medicine
	Shanae	Dennis	NIHR Office for Clinical Research Infrastructure (NOCRI)
Dr	Sally-Anne	Dews	UK I&I Scientific Lead, Pfizer
Dr	Catherine	Emmerich	Medical Science Manager, Bristol-Myers Squibb
Professor	John	Fisher	University of Leeds
Dr	Rajinder	Flora	Programme Grants for Applied Research Assistant Director, NIHR
	Alessandra	Gaeta	Innovate UK, Medical Discovery Catapult
Professor	Christian	Hedrich	University of Liverpool
Dr	John	Ioannou	UCB
Professor	John	Isaacs	Newcastle University
Ms	Louise	Knowles	Head of Research Policy, NIHR
Dr	Rose	Maciewicz	VP Strategy Respiratory & Inflammation, AstraZeneca
Ms	Sancha	Martin	Project Manager, IMID Bio UK
Dr	Deborah	Mason	Cardiff University
Professor	Andrew	McCaskie	Cambridge University
Professor	Iain	McInnes	University of Glasgow

Dr	Alan	McNair	Senior Research Manager, Chief Scientist Office Scotland
Dr	Bonnie	Millar	Musculoskeletal Project Manager, NIHR Nottingham BRC
	Diar	Mohammed	Medical Advisor, AbbVie
Dr	Sarah	Odoi	IP Development Manager, Arthritis Research UK
Dr	Clare	Pain	Alder Hey Children's NHS Foundation Trust
Dr	Christopher	Penfold	University of Bristol
Professor	Costantino	Pitzalis	Queen Mary University of London
Dr	Claire	Potter	University of Birmingham
Dr	Keith	Pugh	Research Programme Manager, Arthritis Research UK
Dr	Philip	Quinlan	University of Nottingham, UKCRC Tissue Directory
Professor	Athimalaipet	Ramanan	University of Bristol, Arthritis Research UK Clinical Study Group Lead
Dr	Alan	Reynolds	AKL Research and Development Ltd, Illix Ltd
Dr	Sarah	Rudkin	Head of clinical studies and experimental medicine, Arthritis Research UK
Mr	Mark	Samuels	Chief Business and Strategy Officer, Medicines Discovery Catapult
Dr	Stephen	Simpson	Director of Research, Arthritis Research UK
Dr	James	Squires	Policy Officer, Academy Medical Science
Professor	Mehdi	Tavakoli	Knowledge Transfer Manager, Innovate Knowledge Transfer Network
Dr	Ed	Vital	University of Leeds
Professor	David	Walsh	University of Nottingham
Dr	Fiona	Watt	The Kennedy Institute of Rheumatology, Arthritis Research UK Research Advisory Group Lead
Mr	Andrew	Wragg	University of Nottingham
Dr	Paula	Wray	Senior Public Involvement Manager, INVOLVE, NIHR

Appendix 4 - Invitee List

Invitations were made to:

- Arthritis Research UK Experimental Arthritis Treatment Centres
- Arthritis Research UK Experimental Osteoarthritis Treatment Centres
- Arthritis Research UK Experimental Arthritis Treatment Centre - Paediatrics
- Arthritis Research UK Centres of Excellence
- Arthritis Research UK clinical study group / research advisory groups

- NIHR Biomedical Research Centre Directors/MSK theme leads
- NIHR translational research collaboration Members
- NIHR Medtech and In vitro diagnostics Co-operatives (MICs)
- Arthritis Therapy acceleration program
- Patient and Public Involvement
- Chief Scientist Office Scotland
- Health and Care Research Wales
- Health and Social Care, R and D, Northern Ireland
- Innovate UK (Medicines Discovery Catapult, Cell and Gene Therapy Catapult, Precision and Discovery Medicine, Knowledge Transfer Network)
- NIHR (EME, Programmes, NETSCC, TCC)
- MRC CRUK
- Pharma (UCB, BI, Roche, BMS, AZ, GSK, J&J, AbbVie, Sanofi, Pfizer, Novartis)
- Med Tech
- 100k genomes
- BioResource, UKCRC directory, UK Biobank, IMID Bio,
- LifeArc
- Academy of Medical Sciences
- Association of the British Pharmaceutical Industry

100,000 genomes project
AbbVie
Academy of Medical Sciences
Arthritis Research UK
Arthritis Research UK Adult Inflammatory Arthritis Research Advisory Group
Arthritis Research UK Autoimmune Research Advisory Group
Arthritis Research UK Centres of excellence
Arthritis Research UK Childrens Clinical Studies Group
Arthritis Research UK Experimental Arthritis Treatment Centre - Paediatrics
Arthritis Research UK Experimental Arthritis Treatment Centres
Arthritis Research UK Experimental Osteoarthritis Treatment Centres
Arthritis Research UK Musculoskeletal Research Advisory Group
AstraZeneca
Boehringer Ingelheim
Bristol-Myers Squibb

Cancer Research UK
Chief Scientist Office Scotland
Clinical Capital Projects - Imaging
Clinical Research Facilities
Department of Health and Social Care
GSK
Health and Care Research Wales
Immune-Mediated Inflammatory Disease Biobanks in the UK (IMIDBio-UK)
Innovate UK Cell Therapy catapult
Innovate UK Knowledge Transfer Network
Innovate UK Medicine Discovery Catapult
Innovate UK Precision Medicine
J&J Innovation
JRI Orthopaedic
LifeArc
Medical Research Council
NIHR Biomedical Research Centres - MSK (Director or Theme Lead)
NIHR Bioresource
NIHR Efficacy and mechanism evaluation programme
NIHR Evaluation, Trials and Studies Coordinating Centre
NIHR Health Informatics Collaborative
NIHR INVOLVE
NIHR Medtech and Invitro diagnostics Cooperatives
NIHR Office for Clinical Research Infrastructure
NIHR Programme grants for applied research scheme
NIHR Trainees coordinating centre
NIHR Translational Research Collaboration Academic Leads
Northern Ireland Health and Social Care R&D
Patient Insight Partners
Pfizer
Roche
Sanofi
Smith & Nephew
UCB Pharma
UK Biobank
UKCRC Tissue Directory