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ARC West Midlands & Midlands PSRC News Blog

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A Union of Two Infrastructures

Richard Lilford, ARC WM Director, Midlands PSRC Co-Director
Alice Turner, Midlands PSRC Co-Director

As mentioned in the October 2022 issue of this Blog, the NIHR funded a new infrastructure grant - the Midlands Patient Safety Research Collaboration (PSRC), hosted at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The collaboration is co-directed by Professor Alice Turner and ARC WM Director Richard Lilford. The Midlands PSRC aims to bring together NHS trusts, universities, and private business to evaluate how digital tools can support clinical decision making and reduce risks for patients.

The NIHR infrastructure is designed to foster a thriving research environment, enabling scientists and clinicians to conduct high-quality research, improve patient care, and contribute to advancements in healthcare. By investing strategically in research infrastructure, the NIHR helps build the necessary platforms, facilities, and expertise required to advance scientific knowledge and improve healthcare outcomes. To help achieve the vision of the NIHR infrastructure, the term 'One NIHR' has come into existence. This refers to local NIHR funded infrastructure grants working together, enabling shared learning and sharing of best practice.

Locally, the University Hospitals Birmingham NHS Foundation Trust and University of Birmingham have been leading partners on a number of major infrastructure health research programmes enabled by external funding schemes. These include the Birmingham Biomedical Research Centre (BRC), the West Midlands ARC, the Midlands PSRC, the Birmingham Experimental Cancer Medicine Centre (ECMC), Trauma Management MedTech Co-operative (MIC), NIHR-MoD Surgical Reconstruction and Microbiology Research Centre (SRMRC) and Wellcome/NIHR Clinical Research Facility (CRF). These grants are building on the principle of a One NIHR approach and sharing resources and providing expertise to one another.

A key example of this is the established Birmingham NIHR Forum which acts as a coordinating body for all local NIHR infrastructure. It builds awareness of capability across the Forum, seeks opportunities for collaborative funding and novel partnerships including with industry, aligns strategies such as capacity building, equality diversity and inclusion and patient and public involvement and engagement. This maximises effectiveness and outputs from NIHR-funded assets for wider population benefit.

To continue the upward trend of the One NIHR approach, we propose making this Blog a joint venture between ARC WM and Midlands PSRC.

A Romp Through the BMJ

Richard Lilford, ARC WM Director

Regular ARC WM News Blog readers will know that I often quote from research in the BMJ. The issue from 23rd October has some fruit for thought.

The Cochrane logo is based on the forest plot for the meta-analysis of the antenatal steroid trials.[1] These trials showed, convincingly, that antenatal steroids protect against neonatal respiratory distress syndrome, and perhaps also provide some short-term brain protection by reducing hypoxia. But the short-term or initial studies do not always tell the whole story. For example, the endovascular aneurysm repair trial in the UK showed large gains for the intervention, which were not sustained over 15 years of follow up.[2] Likewise, the CRASH2 trial results showing that a clot stabilising medicine was effective in haemorrhage,[3] was not replicated in the United States,[4] perhaps because modern treatments with blood products make the medicine less useful. Now, we find that antenatal steroids might have harmful long-term effects on child development.[5, 6] It has always been known that giving steroids to pregnant mammals affects brain development in their offspring.[7] As the accompanying Editorial in the BMJ states, more studies are necessary,[8] but in the meantime, the medicine should be used selectively, and seldom repeatedly, in my opinion.

Also, in the BMJ, we find a very good article on long-term exposure to radiation in health workers.[9] There is a strong correlation between dose and the risk of subsequent solid organ cancer. This is unlikely to be an artefact of smoking, since lung cancer is not particularly affected, and there was no increase in chronic obstructive airways disease in relation to dose of radiation. I hypothesise that nearly all cancers are caused by radiation, such as that we get from space, and from the natural environment. If I am right, there is no place to hide, in heaven, or on earth!

Lastly, a further meta-analysis.[10] Therapeutic cannabis can prevent seizures and reduce pain in some conditions. However, it greatly increases psychiatric side effects, at least in the short-term. Driving after taking cannabis is associated with more road traffic accidents.[11] Cannabis contains carcinogens and is associated with the development of psychosis. Further, a recent study of its use in treating chronic pain suggested a link with higher risk of arrhythmia. [12] I have never thought that legalising this horrible weed was a good idea.

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ARC WM Quiz

Which medical term comes from the Greek word for "*without breathing*" and is included in the name of a condition where a person experiences brief pauses in breathing while they are asleep?

email your answer to: ARCWM@warwick.ac.uk

Answer to previous quiz: The most common zoonotic infection is thought to be *Leptospira*, which can cause leptospirosis (Weil's disease).

Congratulations to Alan Hargreaves who was first to answer correctly.

How Can Research Funders Do Important Evaluative Research in LMICs?

Richard Lilford, ARC WM Director

Whenever possible, we at ARC West Midlands try to apply lessons that we learn to our work in low- and middle-income countries (LMICs). We also apply lessons learnt abroad to our work here in the UK. In both contexts we like to evaluate interventions prospectively.[1,2]

This is because a prospective study enables data to be collected that cannot be harvested retrospectively (including qualitative data), and because it enables the evaluation to be built around a study design such as a cluster RCT. The problem lies in who might fund the intervention. In ARC West Midlands, the service funds the intervention in the form of co-funding. In global research, the NIHR allows a proportion of the research budget to be allocated to funding the intervention. There is a problem here, however. The intervention evaluated has to be inexpensive to fit within the constrained research budget. Therefore, either the intervention must be inexpensive (so that it can be funded from grant money) or the investigator must be lucky, such that the intervention is programmed to be rolled out at a time that coincides with the award of the grant. Therefore, as a general rule, the global programme does not evaluate big structural changes covering things like water and sewage, re-housing or cash transfers. These have to be left to funders like the Bill and Melinda Gates Foundation; their intervention WASH trials cost ~$100m.

So, my proposal is to establish a reactive fund, to enable researchers to evaluate interventions prospectively following rapid assessment applications. This would enable an evaluation to be put in place rapidly when an intervention is planned. In this way, research could accommodate the service imperative.

There will be a lot of opposition to this proposed rapid response policy from finance and possibly also from the Foreign Commonwealth Development Office because:

1. The funding would have to be released rapidly – the whole point is to get the evaluation in place before the intervention goes live, so it would be necessary to create a rapid, single stage, grant appraisal process. This in turn would require a more curtailed (and therefore risky) assessment process – akin to the Advanced Research and Invention Agency set up by the UK government in 2021.

2. It would be very hard to set a budget, since there would be no guarantee that any (or how many) fundable projects would be submitted over any one financial year.

However, bureaucracy should not trump expediency – the proposal should be tried. A mechanism to fund opportunistic reactive research would enable the global programme to evaluate really interesting things. No more community theatre or soup kitchens – they never endure beyond the funding envelope. Indeed, there are serious questions to be asked about the sustainability of any intervention that is a cost to a research grant. Yes, the application will bristle with letters from this and that policy maker. But such policy-makers are not psychologically invested to the degree of a policy maker who 'owns' the intervention and is using their department allocation to fund it.

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Using Trial Recruitment Thresholds for Performance Management

Richard Lilford, ARC WM Director
Paul Bird, Head of Programme Delivery

ARC funding, in common with many other types of NIHR infrastructure, is allocated to a lead NHS organisation. NHS organisations are subject to a performance target based on recruitment to the clinical trials that they host. The performance threshold requires that, across each organisation, 80% of trials will enter their first patient within three months of the trial opening. One of the sanctions connected to the target states that the quantum of money an ARC may apply for is limited by the extent to which the organisation is falling below the target at the time when the application is submitted.

Here in ARC WM we think this policy is not judicious because it violates good performance management principles as follows:

1. It places the penalty where it will be endured, rather than where it can be controlled. For example, a NHS host organisation could experience a reduction in funding of several hundred thousand pounds, but this might only represent a tiny component of the organisation's overall budget of over a billion pounds.

2. Targets are open to gaming as we have found in numerous ARC studies.[1,2] In the case of the above trial recruitment target, the obvious way to game the system would be to delay the starting date to accommodate the threshold.

We at ARC WM are not concerned about this target since our host organisation is already hovering at the target threshold and there is strong organisational focus on exceeding this.

Our point is more one of principle. In particular, that like most targets, it risks penalising honesty and rewards gaming.

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The WHO Is a Great Organisation, but It Needs to Stop Re-Writing the Dictionary

Richard Lilford, ARC WM Director

Unlike some people, I think the WHO is a force for good. It is not always right, and it has to bend to political imperatives originating with its funding organisations. But there is one thing I intensely dislike. The WHO has a bad habit of broadening the meaning of some common words.

My first example is health, defined as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". This is too broad. The reason it is too broad is first, that there are times when we simply want to talk about health abstracted from other things, and second, there is already a perfectly good language to describe the broader valued states that go beyond health; wellbeing for example.

Likewise, in the case of access, there are times we simply want to describe the ability to get to a health service, net of how good it is. Therefore, we dislike the new definition of access that includes service quality. We have perfectly good terms to describe the quality, safety, equitability, patient-centredness, and efficiency of care once accessed.

One may ask why WHO takes it on itself to re-write the dictionary. The reason is a type of self-righteousness. It is easy to generate a mental image of the committee in which these irenic decisions are made. Someone says: "health is not tantamount to absence of disease" or "how can you call it access if the care is poor quality – that is not access." It would take courage to push back and say "I share your aims, but we do not need to broaden existing terms in order to realise those aims." Better keep quiet and stay on the side of the angels.

Lastly, the term 'primary health care'. WHO has broadened the term to include public health measures, such as providing clean water and taxing unhealthy products such as those rich in sugar. And yet we had a perfectly good language to describe these non-rivalrous public goods aimed at improving health – namely public health or health policy. That means that primary health care can mean what it originally did – health care delivered by a health worker and hypothecated on individuals. It would encompass outreach to individuals to provide vaccination and screen for impending disease, as well as 'reactive' care when a person seeks healthcare from a healthcare provider like a doctor.

It's a pity that we cannot go back and clean up the language. In the meantime, it is best to define your terms every time you use them.

A Kind of Natural Experiment on Early Child (<5 years) 'Education'

Richard Lilford, ARC WM Director

Japan expanded access to government-funded nursery and schools/kindergartens in the era after World War Two. At the time, poorer areas were underserved and so the expansion was a partial corrective for this and was also designed to encourage girls' education. Assuming the roll-out was pretty much at random, the effect of when the intervention was rolled-out by area is a type of non-randomised step-wedge design.[1] Remarkably, researchers were able to link enrolment registers to a survey of the Japanese population about half a century later.[2]

The results support other literature, since it was found that attendance at a facility at an early age improved long-term earnings. A structural equation model showed that the effect was largely mediated by attendance at a further education college.

In a previous blog we reported that teaching maths to under-fives might actually be harmful long-term. So, maybe the theory goes that educational exposure is good so long as it is all fun! As often "*[it is not] what you do, it's the way that you do it*"!

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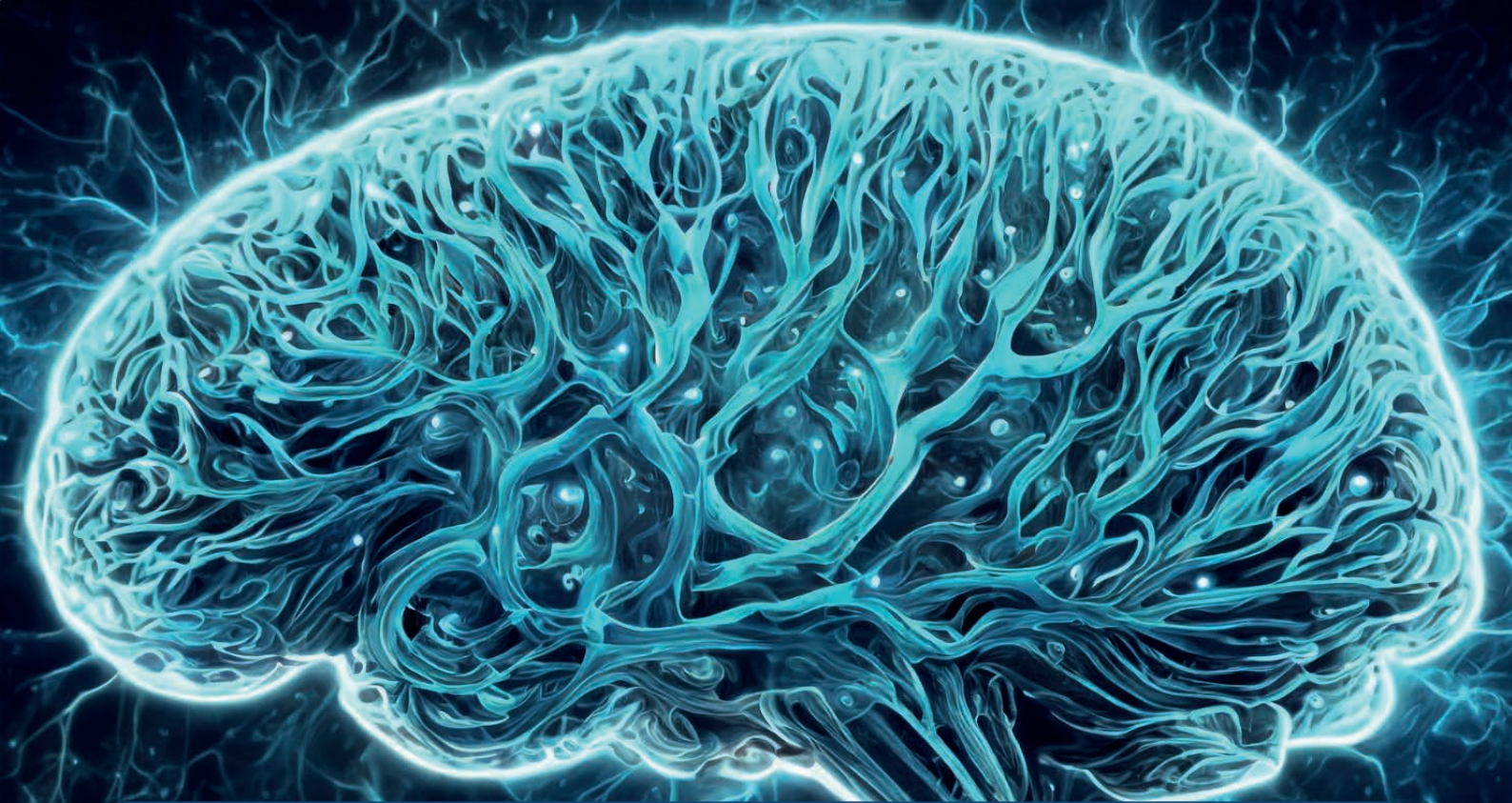
Using AI to Speak Again After Paralysis

Peter Chilton, Research Fellow

Much has been written about the different applications the new generation of artificial intelligence (AI) and machine learning may have in healthcare, and a recent case study published in Nature has revealed yet another.[1] Eighteen years ago, a 30-year-old woman suffered a stroke that left her with severe paralysis,[2] and even after years of therapy she was still unable to speak, communicating instead through head-tracking technology limiting her to a maximum of 14 words per minute. Researchers working in San Francisco and Berkeley (USA) developed a multimodal speech-decoding system, using an electrode array attached to part of the participant's cortex. Deep-learning models were trained on neural data from the participant attempting to silently speak specific sentences, and these were broken down into 39 phonemes (sub-units of sound) to improve accuracy and speed. The research team were also able to recreate a synthetic version of the participant's voice, using audio data from videos of her prior to her stroke, and combined this with AI-driven facial animation to create an avatar that could match movement of the jaw, lips, tongue, etc.

Results of the model showed a median rate of 78 words per minute, with a median error rate of 25%.

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Health Outcomes Worse in Bisexual Individuals

Peter Chilton, Research Fellow

According to a recent survey, around 10% of British adults aged 16-26 ('Gen Z') identify as bisexual, compared to ~5% of the adult population (aged 16-75) as a whole.[1] With this in mind, results from a recent cross-sectional study of the English General Practice Patient Survey (GPSS) dataset is of interest. [2] This dataset contains ~24,000 adults who identified as lesbian, gay, bisexual or "other" (LGB+), and researchers analysed their health outcomes as assessed through self-reported quality of life, physical and mental health, and their ability to manage their own health. After adjusting for age, ethnicity, working status and socioeconomic status, they found that people who identified as bisexual had worse physical and mental health outcomes compared to all other sexual orientations.

As a whole, people who did not identify as heterosexual were twice as likely to suffer long-term physical and mental health problems than people who identified as heterosexual, with bisexual women in particular being four-times more likely (OR=4.275, 95% CI 3.896-4.69, p<0.001). Further, bisexual women were half as likely to have no long-term health problem (OR=0.452, 95% CI 0.419-0.488, p<0.001). People who identified as LGB+ were also more likely to not feel confident in managing their own health, and had a significantly lower quality of life, compared to those who identified as heterosexual.

The authors suggest that the worse health outcomes for those who identified as bisexual may be due to additional marginalisation from biphobia experienced from both heterosexual and LGBTQ+ communities (i.e. in addition to that experienced by lesbian and gay individuals). Maybe, with more younger people identifying as bisexual, some of this stigma will be reduced and health outcomes may improve.

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Toolkit Helps Researchers Develop More Equitable and Representative Research

Researchers at the University of Birmingham have recently developed and released the **REP-EQUITY toolkit**, which aims to guide representative and equitable inclusion in clinical research. Clinical trials that proceed without representative participation do not truly reflect how medical interventions can affect patients, which can lead to biases and impact research quality. The REP-EQUITY toolkit consists of seven steps that researchers should consider to facilitate a representative and equitable sample selection.

The paper describing the toolkit is available in Nature Medicine: Retzer A, Ciytak B, Khatsuria F, et al. A toolkit for capturing a representative and equitable sample in health research. *Nat Med.* 2023; **29**: 3259-67; together with a corresponding Research Briefing.

A press release is also available from the University of Birmingham, with comments from the lead author, Dr Ameeta Retzer (ARC WM Equality, Diversity and Inclusion Lead).

Dr Ameeta Retzer has also filmed a short video on YouTube, together with Emily Lam, one of the Public Contributors, discussing the importance of this toolkit.

House of Lords Select Committee Report on Integrated Care

Prof Daniel Lasserson, ARC WM Acute Care Interfaces Theme Lead, recently provided evidence to the House of Lords Select Committee on integrated care regarding the Hospitals at Home study.

The report is now available at: https://publications.parliament.uk/pa/ld5804/ldselect/ldcareint/18/18.pdf

Latest National NIHR ARC Newsletter

The January issue of the national NIHR ARC newsletter is now available online at: http://eepurl.com/iD7IM-/. This special edition looks back at the 23 most popular (clicked-on) ARC newsletter stories from 2023, for your enjoyment

To subscribe to future issues, please visit: https://tinyurl.com/ARCsnewsletter.

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NIHR PSRC SafetyNet on Social Media

SafetyNet, a network of the six NIHR Patient Safety Research Collaborations, have launched a new X (*formerly Twitter*) account (https://twitter.com/nihrpsrcs) and YouTube account (https://www.youtube.com/@NIHRPSRCs). This aims to deliver research to improve patient safety across England.

Increasing Diversity in Community-Led Research

A number of NIHR centres at the University of Birmingham are aiming to help identify gaps in community-led research, in order to help engage groups that are under-represented. This project aims to find and bridge gaps in community engagement, create networks, and engage in communities.

For more information, please visit: www.birmingham.ac.uk/news/2023/birmingham-joins-partnership-to-increase-diversity-in-community-led-research

Funding Opportunities: NIHR i4i

The NIHR Invention for Innovation (i4i) programme have recently launched a funding opportunity for the Real World Evidence Programme, in collaboration with the Office for Life Sciences and NICE. This is aimed at generating evidence in real world settings for products recommended for early use in the NHS through the NICE Early Value Assessment (EVA) process.

For more information, please visit: www.nihr.ac.uk/funding/nihr-i4i-and-ols-real-world-evidence-programme/34713

Deadline for application is 1pm, **27 March 2024**.

Health Inequalities in Early Life Seminar

Booking for the latest series of national NIHR ARC webinars is now available. This is a set of three webinars, covering *health inequalities in early life* (8 May); *regional health inequalities* (5 June), and *health inequalities in later life* (10 July). ARC WM's Dr Abimbola Ayorinde will be speaking at the first seminar (8 May) on ethnic health inequalities in maternal and neonatal health in England.

For more information, and to book your place, please visit: https://www.eventbrite.com/cc/nihr-arcs-national-webinars-health-inequalities-2975089

Far Away From Home Webinar

ARC East Midlands are hosting a free webinar exploring the 'Far Away from Home' study, a collaboration between ARC East Midlands, East of England, Greater Manchester, Oxford & Thames Valley and West Midlands.

The study found a "stark shortage" of hospital beds on teenage mental health wards in the UK, which forces hundreds of teenagers to travel miles or wait weeks for admission.

The event takes place on **Thursday 21 March**, 12:30pm – 1:45pm.

For more information, and to book your place, please visit: https://arc-em.nihr.ac.uk/news-events/news/webinar-reveal-alarming-number-young-people-mental-health-wards-far-home

Digital Platform to Support Mental Health in Schools

ARC Kent, Surrey & Sussex have recently launched a free online tool, the **Whole School and College Approach (WSCA) Measurement** (https://wsca-measurement.co.uk), aiming to help schools and colleges measure and self-assess the impact of their approach to emotional wellbeing and mental health. Further information can be found at: https://arc-kss.nihr.ac.uk/news/digital-platform-launched-nationally-to-support-mental-health-in-schools-and-colleges

Keele Primary Care Research Fellowships

The NIHR School for Primary Care Research at Keele University are offering a number of fellowships:

- Post-doctoral 24 month fellowship

- Primary Care Clinicians Career Progression 12 month fellowship

The deadline for submissions is 1:00pm on **14 March 2024**.

For more information please see: https://spcr.nihr.ac.uk/career-development/funding

Integrated Care Conference 2024

Call for papers is now open for the 24th International Conference on Integrated Care (ICIC24), which will take place in Belfast on 22-24 April 2024. This year the overarching theme is '*Taking the leap: making integrated care a reality for people and communities*'.

For more information, including where to submit abstracts, please visit: https://integratedcarefoundation.org/events/icic24-24th-international-conference-on-integrated-care-belfast.

Recent Publications

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