Observational studies usually involve some sort of multi-variable analysis. To make sense of the association between an explanatory variable (E) and an outcome (O), it is necessary to control for confounders – age for example in clinical studies. A confounder (C) is a variable that is associated with both E and O. Indeed it is causal of E and O as shown by the direction of arrows in Figure 1.

A common error is to mistake a confounder for a mediator. If the variable lies on the causal pathway between E and O, then it is a Mediator – M in Figure 2.

Failure to make this distinction, and to adjust for M, will reduce or remove the effect of E on the outcome. In a study of the effect of money spent on tobacco on lung cancer, it would be self-defeating to adjust for smoking! If we are interested in decomposing different causal pathways, then we should adapt the multi-variable analysis to examine how much of the effect of E or O is explained by the putative mediator (M in Figure 2) – a structural equation model or ‘mediator’ analysis.

There are some issues to consider:

1. It may not be possible to say for certain whether a variable is a mediator or confounder and some variables may be both. Then try the analysis three ways: omit it, treat it as a confounder, or treat it as a mediator.

2. It is hard to know which variables to include as confounders. A dataset was sent for analysis by 29 different teams of statisticians. They came up with different results that varied wildly. This was because they adjusted for different combinations of variables. The corollary is that choice of variables should not be left to statisticians – it turns on causal theory that distinguishes between variables that are likely to have arrows pointing from E and O via M, and those pointing from C to both E and O (Figure 2). Context matters!

3. There may be an interaction between variables, such that the causal effect of one variable on E or O is amplified or attenuated in the presence of another. Given four variables, each with four ‘levels’, yields 256 possible first order interactions. So, again, theory is needed to determine which variables to include in such interaction tests.
A variable may exist that is an independent cause of C or M (let’s call these C* and M*), as in Figure 3. There is no reason to adjust for these variables. Likewise, do not adjust for any variable that ‘precedes’ E, as also shown in Figure 3.

In this example, C* and M* are not causally linked to O, except through C and M respectively. But a situation may occur where such a link is possible. It is well known that maternal smoking is causally linked to both low birth-weight and to neonatal deaths, as per Figure 4. The theory is that smoking is toxic and leads to both a small baby and, via that pathway and other pathways, leads to neonatal death.

If this analysis is conducted controlling for ‘small baby’, then smoking is associated with lower mortality – it appears protective. The obvious fault was to control for a variable on the causal pathway, as per Figure 2. But this could explain why the association may be reduced, but not reversed.

The explanation for the reversal lies in a putative third variable (perhaps a ‘genetic’ defect, G), which predisposes to both a small baby and neonatal death (Figure 5). Note, that both E and G collide on M, and such a scenario leads to ‘collider bias’ – by controlling for one source of bias, the door is opened to another. It is well known that there may be unobserved (‘lurking’) confounders in any association. The same applies, of course, to a variable that might completely alter the meaning of an association once one has conditioned on another variable.

These analyses show that conducting a multi-variable analysis is not, or rather should never be, an entirely data-driven / empirical exercise. Choices have to be made, such that the statistical model informs on, but does not determine, the causal model. For a brilliant example of extensive causal chains involving confounders, colliders and mediators, see an example from Andrew Forbes and colleagues.[2]

Note, we are not arguing against adjustment per se. It is an essential part of the analysis. We argue against adjusting without reference to a causal model.

References:
High profile cultural programmes are said to ‘rejuvenate’ cities by bringing an influx of resources, attention and visitors. Early reports from the European Capitals of Culture and the nascent UK Cities of Culture show that there is some social and economic impact arising from these programmes. Yet their reach and legacy, that is, whether they make any lasting positive change, has also been questioned. One aspect that is largely missing from early analysis is whether and how such cultural programmes can impact the health and wellbeing of the local population in a sustained way. Our project aims to explore the legacy impact of the city of culture on the health and wellbeing of the local communities.

Early work has started to show positive links between health and well-being and cultural participation.[1,2] We know, for example, that cultural participation can reduce isolation, increase health literacy, create a sense of community and identity, and positively shape child development.[3] For example, there are studies that link higher socio-economic status and cultural participation.[4,5] Conversely, studies show a link between lower socio-economic status, reduced health and wellbeing, and reduced cultural participation.[6] Put simply, those who experience health inequalities are also less likely to engage in cultural activities that may benefit their health and well-being. From the perspective of high-profile cultural programmes, this is an important intersection to understand whether such programmes can reach those that may not usually have access to cultural activities.

The City of Culture Programme, because of its scope and duration, is a good empirical site to study the links between health inequalities and cultural participation. In December 2017 Coventry was awarded the title of City of Culture for 2021. The City of Culture Programme involves a year-long series of activities, as well as a build-up period and a legacy programme. The main goal of the Coventry City of Culture 2021 is to design and implement a programme of cultural activities that focus on the diversity and the youthfulness of Coventry, which are co-created with local communities. Additionally, one of the proposed impacts of the Coventry City of Culture 2021 is to reach the more deprived areas of the city and marginalised populations.
Using Coventry City of Culture 2021 as an empirical focus gives our research team a chance to focus on whether there is engagement with cultural activities in traditionally deprived areas in the city, and whether participation in the design and activities for the city of culture programme is perceived to have positive or negative change in health and well-being in the communities in these areas. The focus on communities means that we are interested in both individuals and local organisations. At the individual level, we are interested in if/how Coventry City of Culture 2021 changes the self-perceived health and well-being of local populations. In terms of organisations, we aim to understand how the city of culture utilises local community asset organisations (organisations that contribute to an improvement in the quality of community life) to deliver health and wellbeing outputs and importantly how local health and social care organisations leverage the year-long cultural intervention to address health inequalities within local communities.

We have designed the research project as a three phase, mixed-methods study (qualitative ethnography and quantitative household survey) to explore the type of impact and the reach Coventry City of Culture 2021. The organisations we have engaged with provide services to the populations most in need of local health and wellbeing services. Focusing on these organisations will allow us to examine the above impact and reach in relation to health inequalities and how inequality related issues are addressed by local organisations using high-profile cultural activities.

In the current phase we are interested in how local community asset organisations are engaging in design of the city of culture activities, to what extent health and wellbeing issues are being considered in the design of the activities, and how partnerships are being formed or not during this stage. Through early interviews, meetings and event observations we are starting to see emerging themes in the data, including how issues that create health inequalities, for example resources such as information, community amenities and transport, also play a role in whether or not people can access cultural activities. Another emerging theme is around community spaces. Perception of who the space belongs to plays a role in who accesses the space. Being part of the community, and feeling able to enter and access spaces (and the resources within them) are important for cultural participation and health and wellbeing of individuals. Finally, we note some interesting narratives around community development and local cultural participation emerging from the pandemic. From these initial findings we can already start to see the links between health inequalities, cultural participation, and areas of partnership tension and growth, as Coventry prepares for the City of Culture in Spring 2021.

References:


A recent paper in JAMA, concerning science denial, tackles a problem of immense importance.[1] For us scientists, science denial negates our reason for being. Far more important though, is the effect on society. We need to think only of the vaccination fiasco. The JAMA paper used the difficulties that people with certain neurological conditions have with processing information as an analogy for the challenges that people with low scientific literacy have with interpreting complex graphs. Such difficulties leave room for false beliefs, including beliefs in conspiracy theories. While this analogy might shed light on neural mechanisms, there are far more important determinants of science denial in the population at large. One issue is the effect of education. Lack of educational attainment is consistently associated with science denial and the propensity to believe in conspiracy theories. [2]

Of course, this does not prove that improving science education would solve the problem. It may simply be the case that the cause of low educational achievement is also the cause of a predisposition to believe conspiracy theories. For example, low self-esteem or cognitive ability may be determinants of both low educational attainment and science denial. More likely, education plays a part, and both nature and nurture are involved. In that case, educational achievement conditional on early-life cognitive ability should correlate with resistance to conspiracy theories. We do not know whether this possibility has been examined.

Debunking misinformation with evidence or education is not enough. In responding to COVID-19, behavioural scientists were quick to point out that debunking could even lead to a backlash and increase the belief in misinformation. While the evidence on backlash
is mixed, alternative approaches are still needed. One alternative is ‘pre-bunking’, which is analogous to medical inoculation: people are exposed to a little bit of misinformation that activates their ability to critique it, but not so much misinformation as to be overwhelming. Web-based games like ‘Get Bad News’ apply this approach and are used by governments and schools to reduce people’s susceptibility to fake news. Reminding people before they engage with information to assess the accuracy of sources may also help.

Yet, education, pre-bunking, and reminders are arguably ‘demand-side’ factors, which largely rely on the public selecting into engagement with science. These may be the very people least likely to denounce it. Given this, it is incumbent upon policymakers – and academics – to address the ‘supply-side’ factors, too. They must consider how to provide trustworthy, transparent, and accessible information, including to those with lower levels of education or cognitive ability. Sadly, this does not always happen; for example, little effort appears to have been directed towards testing some of the public health messaging about COVID-19 in the UK. Confusing messaging can breed uncertainty, which is easily filled with simple but false information – including scientific information. Critiquing conspiracy theorists for their ‘bad science’ is unlikely to be persuasive. Instead, we advocate building trust in rigorous science.

Engaging the public with science is critically important; we can hardly think of a more important issue. Here at ARC West Midlands we take public engagement very seriously. We continuously seek opportunities to engage on science. In previous news blogs, we tested some of the government’s COVID-19 messaging ourselves, and described our plans to use geospatially referenced maps to engage communities where COVID-19 infections are not under control. We are engaging the public in numerous implementation science projects, including one based on mathematical modelling and another on the role of chance in decision-making. In all of these, development of the service, engagement with decision-makers, and with the public, go hand in hand.

References:


The evidence-based movement has been spectacularly successful across many disciplines; medicine and education are arguably the prime exhibits. Randomised trials can produce nice clean outcomes regarding treatments and pedagogy. But randomised trials do not offer a one-stop shop for practising physicians in fields where the link between cause and effect is more complex. Improving health through behaviour change is one such field. Again, and again, high quality trials of specific interventions yield null results. This has led to a sense of impatience among scientists in the field. They know that behaviour change does is possible and can point to changes that have taken place with consequent health benefits. Consider smoking in high-income countries over the last 50 years. There has been a dramatic decline in smoking,[1] with an attendant drop in cancers [2] and cardiovascular disease.[3] So, what is going on here; individual trials show small or no effects while massive changes in behaviour have occurred over time?

The obvious answer relates to time and scale. The observed dramatic changes in behaviour are surely the combined effect of many individual human and institutional actions that, unfolding over time, have created a cultural change or social movement. There are long and interacting causal pathways linking interventions and outcomes, and information over time can flow from action to outcome and also from outcome to action. For example, a plethora of largely marketing/educational interventions led to greater use of seatbelts and an associated groundswell of opinion that fed back into legislation, which in turn resulted in still greater seat-belt use. It would have been difficult to get away with legislation until the necessary attitudes in society had been changed.

So where does this thinking leave individual trials of individual interventions carried out at a particular time and in a particular place? In this short article I acknowledge that it is hard for a single intervention in the single place to produce an effect sufficiently large enough to show up in a change in behaviour, let alone a change in health outcomes. Nevertheless, I still wish to encourage individual studies and oppose a sense of nihilism regarding trials.

In my opinion, a sense of inappropriate nihilism regarding trials of behavioural interventions results from a number of errors in scientific thinking.

**Error number one:** The results of a standard statistical hypothesis test are a prescription for action. The mistake here is to misinterpret a hypothesis test as a test of the probability that a treatment is effective. Many authors have drawn attention to this logical fallacy, which remains widely accepted.[4] An informative Bayesian approach does not dichotomise results into positive and negative and is a far better guide to the interpretation of scientific results, especially in a complex field such as public health. Many trials, each showing a tendency to improvement...
are valuable even if they underestimate what might eventually be achieved over time. Failure to find any signal at all may be a warning sign that the intervention is of little value.

**Error number two:** A study should nominate one primary outcome on which the interpretation of the findings should turn. This notion is completely inappropriate in a context where an intervention acts through a causal chain to produce both health and well-being outcomes. In order to produce an effect, an intervention needs to be adopted, impact on the hearts and minds of potential beneficiaries, and result in a change in behaviour and, finally, in outcome. There is information in all of these outcomes, and the data should be interpreted in light of the pattern of findings across a pre-specified causal chain. It is the causal chain, and not just the outcome, that should be pre-specified.

**Error number three:** A study is designed to answer a question. Even in clinical medicine there are a few examples where a single study has formed the basis for a change in practice. The notion that this is how the majority of decisions should be informed is even more inappropriate in public health. Given that the sum of interventions may be much more than the individual parts, and that intervention effects can become stronger over time, to regard a single study as the answer to the question, rather than a source of information to be synthesised with other findings, is clearly inappropriate.

So, the value of a public health trial lies not in the results of a hypothesis test on a primary outcome, but on how it may inform a broader causal pathway that will play out over a long period of time. For example, we have examined the effect of a financial incentive targeted on organisations to promote the health of their workforce.[5] We are writing the findings up for publication. But we will not concentrate solely on wellbeing and health or even on behaviour change. We will examine whether the intervention was delivered as intended and whether and to what extent employees noted a change in employer behaviour. Thus we will examine for the necessary as well as sufficient conditions for a change in health.

### References:


Medical errors can take many forms, including placing a medical order for the wrong patient (known as wrong-patient order entry). An estimate based on US data suggests that ~600,000 orders each year are placed for the wrong patient. [1] Various interventions have been shown to reduce the rate of these errors, but these often create interruptions (such as verification forms or alerts) that are time-consuming and can potentially result in alert fatigue.

A recent historical cohort study conducted in Boston, MA, evaluated the impact of displaying a photograph of a patient within their electronic health record.[2]

Over the two-year period more than 2.5 million orders were placed for ~70,000 patients, with 23.3% having a photograph displayed. Errors were determined using a validated measurement tool, which estimated the rate of near-miss, wrong-patient order events. Analysis of data found a significant decrease in errors due to wrong-patient order entry when a photograph of the patient was displayed in their electronic health record (odds ratio 0.72, 95% CI 0.57-0.89). This remained significant after adjusting for various confounders (race, ethnicity, sex, time, etc.) (OR 0.57, 95% CI 0.52-0.61). Patients who were acutely ill (scoring 1 or 2 on the emergency severity index) had lower odds of wrong-patient errors, as did patients who were documented as White.

This intervention seems to show the benefit of using patient photographs, placing no additional time burden on the practitioner, and not increasing the risk of alert fatigue.

**References:**


Air pollution is thought to be one of the major environmental causes of premature health, but its impact on mental health has not been as well researched. Researchers at King’s College London recently conducted a prospective, longitudinal survey of 1,698 adults living in South East London between 2008-2013 to look into this topic.[1]

Using a validated tool for assessing common mental disorders, researchers were able to score participants for overall severity of symptoms of common mental disorders, with a score higher than 12 being indicative of the presence of a common mental disorder. This data was then linked with levels of air pollution at the participants’ home address. Adjustments were made to take into account various confounders, including smoking status, socioeconomic status, frequency of drinking, previous mental illness, road traffic noise, and neighbourhood deprivation.

The study found that there was a significant increase in the likelihood of developing common mental disorders associated with an increase in air pollution, specifically very small particulate matter (odds ratio 1.18, 95% CI 1.02-1.37), and nitrogen dioxide (odds ratio 1.39, 95% CI 1.05-1.85). Researchers also estimated that there was a two-fold increase in common mental disorder cases that could be directly attributable to being exposed to very small particulate matter above 15.5μg/m³ annually (which was below the European target values of 25μg/m³).

Increases in very small particulate matter and nitrogen dioxide were also associated with a 19-30% increase in the likelihood of poor physical symptoms that can indicate mental distress (e.g. stomach pain, shortness of breath, sleep problems).

Although air pollution is only one of many factors that can have an impact on mental health, it is something that could be prevented or at least improved.

Reference:
HSJ Patient Safety Awards

Congratulations to the Birmingham Symptom Specific Obstetric Triage System (BSOTS) team who were recently awarded the Maternity and Midwifery Services Initiative of the Year at the Health Services Journal Patient Safety awards. This work is a collaboration between ARC WM, WM-AHSN, the University of Birmingham, the Birmingham Women’s and Children’s Foundation Trust, and the Royal Wolverhampton Trust.

The judges felt that “enthusiasm from the staff about this innovative project shone through. The initiative has reduced variation, improved safety, and generated a positive experience for women. It also shows a wide spread of use and positive affirmation from stakeholders across the UK.”

BALLETs Follow-up Study

The BALLETS (Birmingham And Lambeth Liver Evaluation Test Strategies) study was a five-year study that aimed to evaluate mildly abnormal liver function test results in general practice among patients who did not have known liver disease. Results were published in 2013.

We are now following up these patients to gain an improved understanding of longer-term health outcomes. In this study we will be electronically linking patients’ NHS numbers with two national databases to find out if they developed any liver-related health problems during the period 2007-2020.

More information on this follow-up study is available at: birmingham.ac.uk/research/applied-health/research/ballets.aspx

Although all people who took part in the original BALLETS study agreed to be followed up in the future, we did not make it explicit that we would be linking data in this way.

If you participated in the original project, you have the right to withdraw at any time, which you can do by contacting the BALLETS team: m.t.skrybant@bham.ac.uk or r.j.lilford@bham.ac.uk. When contacting the team, please provide your full name and preferred contact details.

This data will be used to ensure your previously obtained data is not used in this follow-up study. We will use the details provided to confirm this has taken place. We will store the fact that you have requested to opt out of the BALLETS study, but we will not send you any further information, nor will we use the data for any other purpose.
We have two full-time, three-year PhD studentships currently available:

1. One based in our Maternity theme at the University of Birmingham. This is focussed on the new universal 6-8 week check being introduced for new mothers in England. Closing date for applications is 30 November 2020. For more information, please visit this link.

2. One based at Warwick Medical School, with a focus on one of: supporting workplace health and wellbeing initiatives; knowledge required to evaluate health technologies; impact of HTA research from the NICE Technology Appraisal programme; implementation of co-production; or monitoring systems in ‘hospital at home’ care models. Closing date for applications is 27 November 2020. For more information, please visit this link.

The November issue of the national NIHR ARC newsletter is now available online.

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

The Margaret Peters Centre have recently released their first annual report, which is available at: arc-wm.nihr.ac.uk/news-events/latest-news/mpc_ar-1_-_nov_2020.pdf.

The Centre was launched in November 2019 as a collaborative centre for data analytics, and brings together the expertise of managers, clinicians and academics with questions that can be answered through the analysis of available data. It is needed to bridge the gap between the routine analysis and processing of data in hospitals, and the interesting questions that exist in clinical and academic teams. Its aim is to build on and enhance the existing capacity and expertise of informaticians and statisticians at University Hospitals Birmingham NHS Foundation Trust (UHBFT).

PhD Studentships

National NIHR ARC Newsletter

ARC WM Quiz

Where does the word ‘quarantine’ come from?

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

Answer to previous quiz: The first Chief Medical Officer in England was John Simon from 1855-1876. Congratulations to those who answered correctly.
Events & Funding Opportunities

Social Care Summit

ARC West Midlands are holding an online Social Care Summit on Thursday 25 February 2021. The event will focus on adult social care in the West Midlands and will provide an opportunity for practice and research to meet, discuss and create together. For further details, and to register, please visit: eventbrite.co.uk/e/adult-social-care-research-in-the-west-midlands-tickets-129275513541.

Fellowship opportunity – Care homes and primary care

The Healthcare Improvement Studies Institute (THIS Institute) have launched a new fellowship to co-produce a vision for high quality primary care for people who live in care homes, and to identify how it might be implemented and achieved within current resources and structures.

The fellowship is expected to begin during Spring 2021 and should be completed in 12-15 months. It can be undertaken full-time or part-time (minimum 0.6 FTE).

Applications close at 12pm on 10 January 2021.

For further details, and to apply, please visit: thisinstitute.cam.ac.uk/fellowships/covid-19-care-homes-and-primary-care/

NIHR/UKRI Research Call: Longer term effects of COVID-19 in non-hospitalised individuals

The NIHR and UK Research and Innovation (UKRI) have launched a joint research call to fund ambitious and comprehensive research into the longer term physical and mental effects of COVID-19. These ongoing problems, commonly termed ‘Long COVID’, may be experienced by patients regardless of how severe their COVID-19 infection was and irrespective of whether they were hospitalised. Projects are expected to start in early 2021, with funding for up to 3 years in the first instance.

Deadline for proposals is 9 December 2020.

For further details, and to apply, please visit: nihr.ac.uk/funding/research-into-the-longer-term-effects-of-covid-19-in-non-hospitalised-individuals/25904

PHR Programme Applications

The Public Health Research (PHR) Programme are accepting stage 1 applications for:

- **20/119** Public health interventions led by or involving the police.
- **20/120** Food taxes and subsidies.
- **20/121** Indoor air quality.
- **20/122** Multi-agency approaches to tackling illicit tobacco.

Deadline for proposals is 30 March 2021.


