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NIHR CLAHRC West Midlands News Blog

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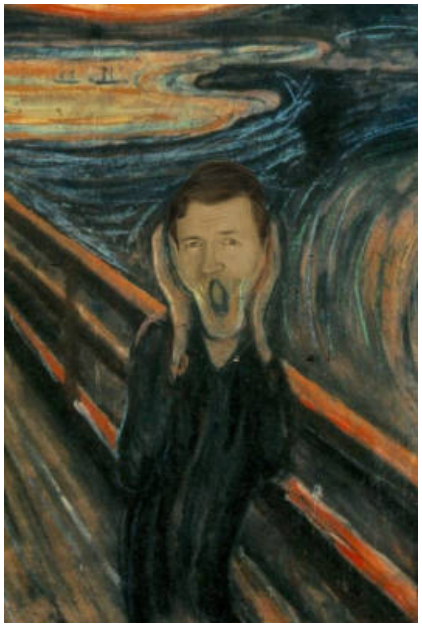
NHS National Institute for Health Research

Welcome to the latest issue of your NIHR CLAHRC West Midlands News Blog.



In this issue we look at how research in low- and middle-income countries can help high-income countries; and papers on the risk that effect sizes are exaggerated when small trials yield significant results; an RCT of providing immediate therapy for HIV-positive patients rather than waiting for CD4+ count to fall; a case-note review looking at preventable mortality; an update on sugar – this time a meta-analysis on the health risks of sugar-sweetened beverages; a summary of evidence concerning routine de-worming of children; and the use of check-lists.

We also bring you the latest news; profile Ula Othman; showcase upcoming events; and have our CLAHRC WM Quiz. Finally, we list some of our latest publications, and highlight some recent Tweets on Twitter.

We hope that you find these posts of interest, and we welcome any comments. You can find previous issues of our News Blog here.

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Director & Co-Directors' Blog

How Can Research in Low- and Middle-Income Countries (LMICs) Help People in High-Income Countries?

International research is undergoing a renaissance. Universities all over North America, Europe and Australia are establishing 'Centres for Global Research'. Such centres draw funds from local donors and it is reasonable to ask whether research conducted abroad is completely altruistic, or whether it might also benefit the high-income countries that sponsor the research. Knowledge exchange is a two-way street and we should expect increasing traffic on the North-bound carriageway. The CLAHRC WM Director proposes the following classification for the potential local benefits of overseas research:

1. The most obvious category relates to infectious disease. Research carried out abroad may provide early intelligence on impending risk so that countries may take steps to prevent spread, as in the recent Ebola epidemic (discussed in a previous post), or make preparations to contain the infection, as in the case of influenza, MARS and SARS.
2. Research carried out in countries where a disease is common may provide information on how to treat it in countries where the diseases is rare. This would obviously apply to all tropical diseases that may affect returning travellers, visitors or immigrants, such as malaria and schistosomiasis. It would also apply to infections, such as leishmaniasis or West Nile fever that can be contracted in Europe, but with less frequency than in tropical countries. This type of knowledge transfer would also benefit people at risk of non-infectious diseases arising from habits imported from abroad, such as use of the areca nut, as discussed in a previous post.
3. Providing larger populations to evaluate treatments where it would be very hard to accrue sufficient patients locally. Lelia Duley's trial of magnesium for

the treatment of eclampsia [1] and Ian Roberts' 'CRASH-2' trial of tranexamic acid for massive haemorrhage [2] were both carried out over three continents. Yet the results drive practice across the world, including the UK.

4. Providing a means to explore heterogeneity and thus glean deeper understanding of the role of context. For instance, the Cochrane review of trials of the effectiveness of providing additional support in labour through a layperson (so called doula) show that the service is effective in lowering the Caesarean rate where women are not accompanied by their partner, but not in countries like the UK where they usually are. The expeience of two people dying of terminal cancer, one in Kenya, the other in Scotland provides a further vivid example of the role of context.[3]
5. The success of an intervention in LMIC may encourage people to try it locally. For instance, the success of 'women's groups' in improving perinatal outcomes in India, Nepal and Bangladesh [4] have encouraged CLAHRC North Thames to replicate the method among Bangladeshi communities in East London, as mentioned in a previous post. But we should be alert to the danger of leaping too rapidly to the conclusion that what works in one place will necessarily work in another. Studies carried out in our CLAHRC shows that clinical research produces essentially the same results when carried out in North America or Europe,[5] but very different results across Europe and Asia.[6]
6. Research methodologies of generic utility may be developed to deal with issues in LMIC. The fabled stepped wedge design widely used in CLAHRC WM [7] was first used in West Africa.[8] The lesson that much more can be learned by juxtaposing quantitative and qualitative research in systematic reviews than by either method alone, was ably demonstrated by twin Cochrane reviews on the subject,[9] [10] (mentioned in a previous post).

More speculatively, the CLAHRC WM Director posits a category where there is no specific nugget of information that is returned, but rather tacit knowledge about universal features of the human condition. Certain general principles may be derived by examining health improvement projects across many countries, rich and poor, as recently pointed out by previous NHS Chief Executive, Lord Nigel Crisp. [11] More indirect still are the cultural and political benefits of human interaction, and putative benefits of seeing the world in less parochial ways.

I invite readers of this News Blog to share other types of benefits and help populate this framework with lots of examples where LMIC research has benefited UK patients.

-- Richard Lilford, CLAHRC WM Director

Leave a comment

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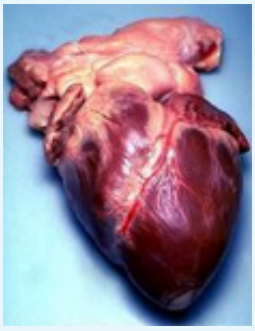

CLAHRC WM Quiz

Who was the first surgeon to carry out a human heart transplant?

Email CLAHRC WM your answer.

Answer to our previous quiz: The first successful kidney transplant in humans was carried out in 1954 by **Joseph Murray**, along with J. Hartwell Harrison, John Merrill and others. It succeeded because it was done between **identical twins**, Richard receiving a kidney from Ronald Herrick, which eliminated the problems of an immune reaction. Richard lived for a further eight years.
Congratulations to Melita Shirley who was first to answer correctly.

Director's Choice - From the Journals

A Fabulous Paper on P Values, Confidence Limits and, Yes, Bayes

I thank my friend and colleague Alan Girling for drawing my attention to a recent issue of the statistical journal '*Significance*'.

This issue of the journal followed close on the heels of the UK general election and so, not surprisingly, the failure of polls to predict the outcome provided the topic for the feature article. But it was another article on representing significance in the psychological and medical literature that Alan suggested I should read.[1] The author, Andrew Gelman, discusses small studies with statistically significant results.

Such studies tend to exaggerate effect sizes when the signal is associated with a lot of noise, and in the usual situation where true positive effects are of modest magnitude. Throw in a little publication bias and the literature becomes yet more severely distorted. I entirely agreed with the statement that use of confidence intervals “will not solve any problems: checking whether a 95% interval excludes zero is mathematically equivalent to checking whether p<0.05.” Gelman goes on to say that the problem of exaggerated claims is worse in psychology than medicine because there are fewer obstacles to carrying out small studies and, arguably, because the signals, relating as they do to latent mental constructs, tend to be more ‘noisy’ than those in medicine. Gelman comes down strongly in favour of the Bayesian approach, which brings sobriety to bear through the ‘prior’ probability density (see previous post).

-- Richard Lilford, CLAHRC WM Director

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Reference

Every Now and Then, an Earth-Shattering Trial with Immediate Implications for Policy

The CLAHRC WM Director has long thought that it made sense to treat **all** HIV patients with antiretrovirals and not wait until the CD4+ count had fallen to a specified threshold – a threshold that has been gradually increasing over the years. On this particular point, the Director was right. An RCT of 4,685 HIV-positive patients across 35 countries showed that immediate therapy, rather than therapy deferred until the CD4+ count had fallen below the current recommended threshold, reduced AIDS complications by over 50% within tight confidence intervals (P<0.001).[1] In addition, there is evidence that antiretroviral therapy can reduce the risk of HIV sexual transmission.[2]

-- Richard Lilford, CLAHRC WM Director

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References

Yet Again, Low Proportion of Hospital Deaths Judged Preventable

Hogan and colleagues have reported another study on preventable mortality based on case-note review among 34 hospitals.[1] Only 3.6% of deaths were thought to have been preventable on the balance of probability. Preventability rates did not vary widely between hospitals.

Of course, this might be something of an underestimate because deaths where

the probability of preventability was less than 50% are not included. The CLAHRC WM Director calculates preventability as the sum of all cases that may have been preventable, weighted by the probability that they were preventable. He also likes to adjust for the reviewer effect to minimise the influence of unusually 'hawkish' reviewers.

Despite these precautions, preventability is "in the eye of the reviewer,"[2] and may be over-estimated because of hindsight bias, or under-estimated because some practices that may increase the risk of death cannot be discerned from case-notes.

-- Richard Lilford, CLAHRC WM Director

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References

More, Yes More, on Pure, White and Deadly

Yes, the more you eat and the fatter you become, and the more likely you are to get diabetes. Subsidiary questions:

1. Are some diets more likely to make you fat than others? Yes, sugar is worse than other diets in making you fat (see previous posts). I think this is because they are less satiating, but they also have worse metabolic effects (again, see previous posts).
2. At a *given* level of weight gain, is a high intake of sugar more likely to cause diabetes?

A recent meta-analysis of prospective studies of sugar-sweetened beverages in seventeen cohorts including no less than 38,253 people were analysed. Each extra 'serving' of sugar-sweetened beverage was associated with an 18% increase in the risk of diabetes even after correcting for adiposity.[1]

The CLAHRC WM Director says "*think carefully before you correct for a variable on the causal chain between exposure and outcome because you will likely mask a true association*." These results are therefore impressive because they show an increased risk of diabetes with sugary drinks, net of the increased risk of obesity itself. Sugary drinks cause a very high spike of glucose, which may predispose to diabetes over a more gradual increase following, for example, a rice meal. Sugar is made up of a glucose and fructose molecule, and fructose increases insulin resistance. It is therefore likely to be more diabetogenic than the carbohydrate found in rice, wheat and potatoes, which is pure glucose. The astute reader will have noted that fruit juice will also cause a severe spike in glucose levels and also contains sugar, and hence fructose. Unlike whole fruit, which protects against diabetes, fruit juice also seems to be diabetogenic net of weight gain. Incidentally,

this is a beautifully conducted and analysed study from Japan, the USA and the UK, which is worth reading for this reason alone.

-- Richard Lilford, CLAHRC WM Director

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Reference

Nice Theory, but Ridding Children of Those Revolting Worms Does Not Seem to Affect Health

Wouldn't it be nice if we could find a simple physical cause for stunted-growth and impaired school performance? Worm infestations provide such a target; round worms (which may compete for the child's nutrition), and hook worms (which suck blood through the intestinal wall). Alas the attractive notion that we can do a great deal of good by the simple distribution of de-worming pills does not seem to be true. The recent meta-analysis from Paul Garner's group [1] provides little support for de-worming policies. Even among children known to be infected, de-worming does not do anything dramatic, and surprisingly (and disappointingly) the trials examining this issue are of poor quality.

It could be argued that de-worming does not do any harm, and that worms are revolting, and therefore that de-worming programmes should continue. But in a world of scarce resources, this argument might not hold. And then of course some people say that worms do some good by providing an inflammatory response that reduces atopic conditions, such as hay fever of asthma.[2]

Science cannot prove a negative, merely exclude effects of measurable size, and we may never have a conclusive answer to this question. Comments are invited on this controversial issue.

-- Richard Lilford, CLAHRC WM Director

Leave a comment

References

An Article on Check-lists in Nature (Yes Nature!)

Further to our recent post on check-lists, the topic has piqued the interest of the famous scientific journal Nature.[1] They discuss the variable success of check-lists and effectively conclude that "*it ain't what you do, it's the way that you do it*." This makes the CLAHRC WM Director consider what a check-list really is – is it an intervention or just one of many tools that can be used to change behaviour? When the CLAHRC WM Director was a pilot, check-lists were there to remind you of

things that might otherwise have been forgotten. However, it is possible to hypothesise that check-lists in most health contexts function more as a cultural tool. If so, they are but one of many routes to behaviour change. The CLAHRC WM Director posits that once the care has improved, check-lists can be removed with impunity – their effect is indelible. This is a testable hypothesis.

-- Richard Lilford, CLAHRC WM Director

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Patient and Public Involvement

Opportunity for Involvement in NIHR Advisory Committee/Panel

The NIHR are currently looking for members of the public to join the committees/panels for the following research programmes:

- Invention for Innovation (i4i): Product Development Awards Panel - two members.
- Research for Patient Benefit (RfPB): Regional Advisory Committees for West Midlands, East Midlands, London, East of England - two members for each committee.

Please click here for more information, including application forms and supporting documents.

PPI Advisor on Journal Review Panel

Congratulations to Imogen Chappelow, one of our CLAHRC WM PPI Advisors, who has recently joined the review panel for papers submitted to the new *Research Involvement and Engagement* journal.

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News

Medical and Ethical Decision-Making Summer School - Summary

During the second week of July, members of the Warwick Business School (WBS) Behavioural Science group hosted the third 'Summer School on Medical and

Ethical Decision-Making' for the University of Warwick in Venice (the programme is available online).

Professors Zvi Safra, Tigran Melkonyan and Ivo Vlaev were in charge of organising the Summer School. Financial and other support was provided by WBS, Institute of Advanced Study (University of Warwick), NIHR CLAHRC West Midlands, and Global Research Priorities (University of Warwick). In addition to presentations by WBS Behavioural Science faculty, the programme included presentations by a number of distinguished speakers, including Professors Gerd Gigerenzer from the Max Planck Institute for Human Development, John Fox from the University of Oxford, and Moshe Leshno from Tel Aviv University. Thirty six junior researchers, physicians, and health care professionals from the leading institutions in the United Kingdom and abroad participated in the School.

The event offered an exciting programme that covered a broad range of topics, including various theories of medical decision-making; understanding of health statistics; stochastic dominance and clinical guidelines; using behavioural change and decision theory to nudge doctors and patients; and over- and under-treatment of patients. Besides the lectures, the School included group projects that resulted in a number of practical suggestions and research projects of how to improve efficiency of NHS and medical decision-making. According to all parties involved in the programme, the Summer School was a huge success. In addition to acquiring practical knowledge and skills, the participants learned about a number of promising developments and directions at the forefront of medical decision-making. The School also provided a great opportunity to exchange ideas and to network face-to-face with young researchers and practitioners from around the world.

-- Ivo Vlaev, Professor of Behavioural Science, WBS

Health Policy and Potential Implications

Key actors attended a successful event on 30 July 2015 at University of Birmingham exploring the health policies of the new UK government and the potential implications for the CLAHRC WM initiative. The discussion was led by Prof Jon Glasby, Head of School of Social Policy at the University of Birmingham. Following a historical overview of health reforms since the start of New Labour in the 1990s, an exploratory discussion around the new government health policy agenda took place, including debate about 7 day services, capacity for innovation versus service delivery, and significance of the five year forward view. The implications of the Health and Social Care Act 2012 were also considered along with an energetic dialogue about the devolution agenda. Watch this space for further narrative.

Congratulations - Celia Taylor

Congratulations to Dr Celia Taylor who has been invited to join two committees: the *GMC Assessments Advisory Board*; and the *MSC Assessment / British Pharmacological Society Prescribing Safety Assessment Research Group*, of which she will also be chair.

Congratulations - Kaitesi Mukara

Congratulations to PhD student Kaitesi Mukara who was a member of the team who won best press release at the recent NIHR Doctoral Training Camp.

Kaitesi pictured second from right

Richard Lilford on Radio – Weekend hospital deaths

CLAHRC WM Director Richard Lilford recently spoke on BBC Radio Coventry & Warwickshire regarding weekend hospital deaths. If you are in the UK you can listen online until Saturday 15 August 2015. The interview starts at 02:05:27.

Summary – Patient Safety Seminar

Many thanks to Prof Charles Vincent for his recent seminar on patient safety, '*Safer Healthcare: Strategies for the Real World*', and thanks to all who attended. Prof Vincent is happy for people to contact him if there is anything they wish to discuss regarding safer healthcare at charles.vincent@psy.ox.ac.uk.

A (short) book is planned and will be made available under an Open Access Licence - we hope to share this with you when published.

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Selected Replies

Re: High Side-Effect Rates with Statins in Ordinary Practice but not in RCTs

Speaking as one who has taken the medication I experienced muscle pain as a consequence with no knowledge of the side effects. Hence do believe that it is a consequence of psychological expectations I believe is unfounded from my perspective. Having said that it makes an interesting study as I am sure psychological expectations are a certainty in many disciplines as a consequence of predicting an outcome in advance because it has already been stated as a likely outcome.

-- Neil Lilford

Re: Simulations May Not Predict Real Life...

Vis-à-vis mobile phone use, it isn't just the cognitive load imposed by parallel processing that matters, but the fact that not all are hands free, so the inattention whilst fiddling with the phone is alarming as I found out as a passenger in the back of a French taxi cab recently.

-- Lesley Fallowfield

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Personality of the Issue

Ola Uthman

Dr Olalekan (Ola) Uthman is an Assistant Professor in Research Synthesis at the Warwick (International) Centre for Applied Health Research and Delivery (W-CAHRD), University of Warwick.

As well as an interest in **Evidence synthesis** (in particular Bayesian network meta-analysis and generalised evidence synthesis), Ola's research interests include developing and applying **multi-level and natural experiments methods** for analysis of large and complex datasets; and non-communicable diseases

(especially cardiovascular epidemiology) and interaction with infectious diseases (especially HIV/AIDS).

Ola has worked across a wide range of health technology assessments with a focus on HIV/AIDS and other infectious diseases. He is the recipient of the FAS Marie Curie International Postdoc Fellowship to pursue research on the social and contextual determinants of HIV/AIDS, with a special emphasis on cardiovascular risk factors among HIV infected individuals in sub-Saharan Africa.

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Events

17 Aug 2015, 12:00-13:00
Maternal and Paternal Family Line Effects on Child Growth
A030, Warwick Medical School

Professor Barry Bogin (Professor of Biological Anthropology at Loughborough University) will be delivering a seminar on maternal and paternal family line effects on child growth at Warwick Medical School, hosted by W-CAHRD.

Please click here for more information. To book your place please email michelle.brown@warwick.ac.uk

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24-25 Feb 2016
2nd Behaviour Change Conference: Digital Health and Wellbeing
Senate House, London

The UCL Centre for Behaviour Change will be hosting its second behaviour change conference on 'digital health and wellbeing'. World-renowned academic experts will join key members of the public health and technology sectors in a wide variety of activities. Conference themes will include:

- using behaviour change theory to create high-quality interventions and products;
- multi-disciplinary approaches to digital health and wellbeing;
- developments in wearable and sensor technology;
- creating developer/industry partnerships.

Submissions for oral presentations, posters and satellite workshops open on Monday 3rd August 2015.

For more information, please click here.

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Publications

Halligan S, Dadswell E, Wooldrage K, et al. Computed tomographic colonography compared with colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients: two multicentre randomised trials with economic evaluation (the SIGGAR trials). *Health Technol Assess*. 2015; **19**(54): 1-134.

Morden A, Jinks C, Ong BN. 'Risk' and self-managing chronic joint pain: looking beyond individual lifestyles and 'behaviour'. *Sociol Health Illn*. 2015. [ePub].

Toulis KA, Nirantharakumar K, Ryan R, Marshall T, Hemming K. Bisphosphonates and Glucose Homeostasis: A Population-Based, Retrospective Cohort Study. *J Clin Endocrinol Metab*. 2015; **100**(5): 1933-40.

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Recent Tweets

HiSLAC study in the news again today: http://ow.ly/Q6VWf @MailOnline #7dayservices. For more info visit http://www.hislac.org
-- @HiSLACProject, 27 Jul 2015

Here @WarwickBSchool listening to Prof Charles Vincent on 'safer healthcare - strategies for the real world' ebook imminent @UniofOxford
-- @CLAHRC_WM, 20 Jul 2015

@rjlilford says we need to understand why patients admitted to hospital at the weekend more are likely to die http://ow.ly/PP0OE 2:05:27
-- @CLAHRC_WM, 20 Jul 2015

Major impact on youth mental health services in Bham @BSC_CCG @Bham_Childrens #0to25 - read our SUPER BITE now ow.ly/PFZXP
-- @CLAHRC_WM, 16 Jul 2015

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