Fri 13 Jul 2018

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NIHR CLAHRC West Midlands News Blog

This work is funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) West Midlands. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health

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Welcome to the latest issue of your CLAHRC West Midlands News Blog where we look at the model used for health economics and access to care. We also look at recent research on the hygiene hypothesis and childbirth; observing mediating variables; reducing risk of postpartum haemorrhage; and using polio to treat cancer.

As usual, we also have details of the latest news and events; this issue's quiz question; replies to recent blogs; and highlight some of our latest publications.

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

Director's Blog

Health Economics and Access to Care: Are We Using the Wrong Model?

I woke one morning, many years ago, to the voice of a famous economist sounding off on my bedside radio. He spoiled the equanimity of my morning with his argument that the value of primary care should be evaluated by comparing the costs of the

service with the health gain achieved by the service (in terms of quality adjusted life years [QALYs]). That is cobblers! Quite apart from the facile idea that the health gain from primary care can be calibrated with any kind of accuracy, the economist's health economic model bypasses much of the purpose of healthcare. In this model, health care is simply as an instrument to improve health status. But a little thought will immediately show that health gain is a very incomplete understanding of the reason that people consult doctors. Health care serves a deep psychological need; human beings have turned to healers from the time that we became human beings. Health practitioners are not only valuable for the health gain they can now achieve, but also because they provide human warmth and support. The need for comfort, information, magic, and cure are all entangled. Not only do we need someone to turn out at times of mental or physical distress, but crucially, we also need to know that someone will be there for us when our time comes. And we need this assurance, even when we are perfectly healthy. We could perhaps wrap in the avoidance of catastrophic loss and call this the 'insurance value'. Nor should the value of information – news about your own body – be underestimated. Berwick & Weinstein found that half of the benefit of an antenatal scan was simply to get a picture of the baby and had nothing to do with its medical purpose.[1]

The classical health economic model of cost utility analysis is well adapted to rationing demand once the patient's condition has been defined. At that point calculating the relative value of different treatment options is a relatively straightforward issue (Figure 1). However, calculating the return-on-investment from simply providing access to healthcare is a different matter altogether. First, there is the extraordinarily difficult instrumental question of how to hypothecate the treatment effect over the full range of health conditions (Figure 2). Second, there is a need to factor in the value of:

1. Information.
2. Solace, comfort, support.
3. Knowing that access will be available when required – the insurance value.

At the very least, it should recognise that cost-utility analysis for a calculation of a QALY or a DALY is not up to the task. The topic of access is one area where health economics raises many unsolved problems. In a recent news blog we discussed another issue that exposes some of the deep philosophical conundrums at the heart of health economics – the thorny issue of infertility.[2]

Fig 1. Management of a Specific Condition: a task for standard health economics

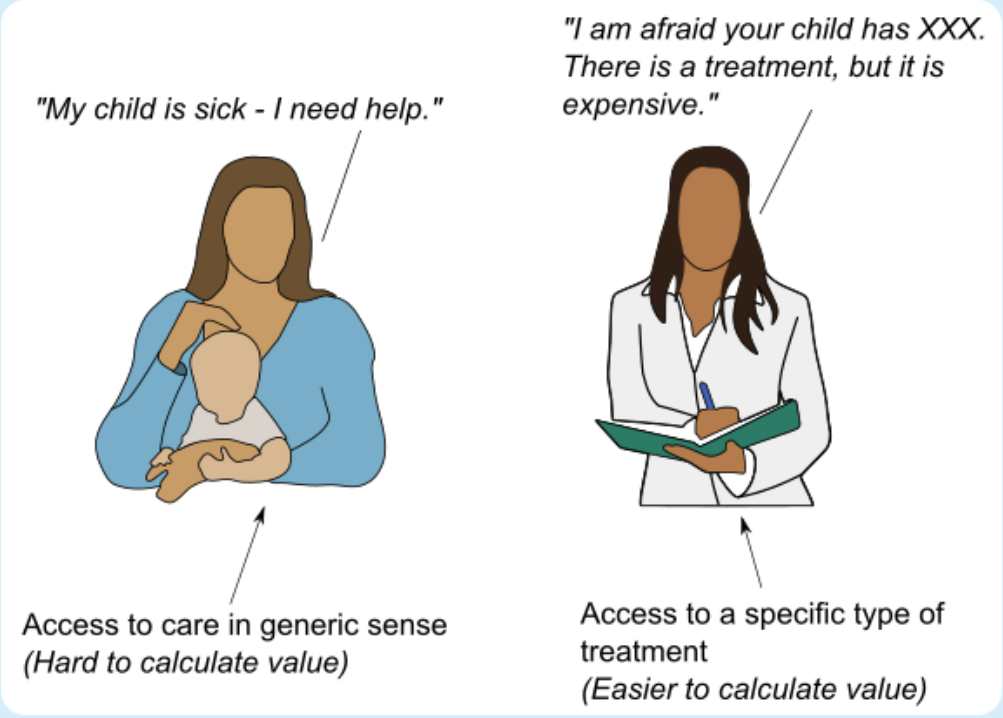
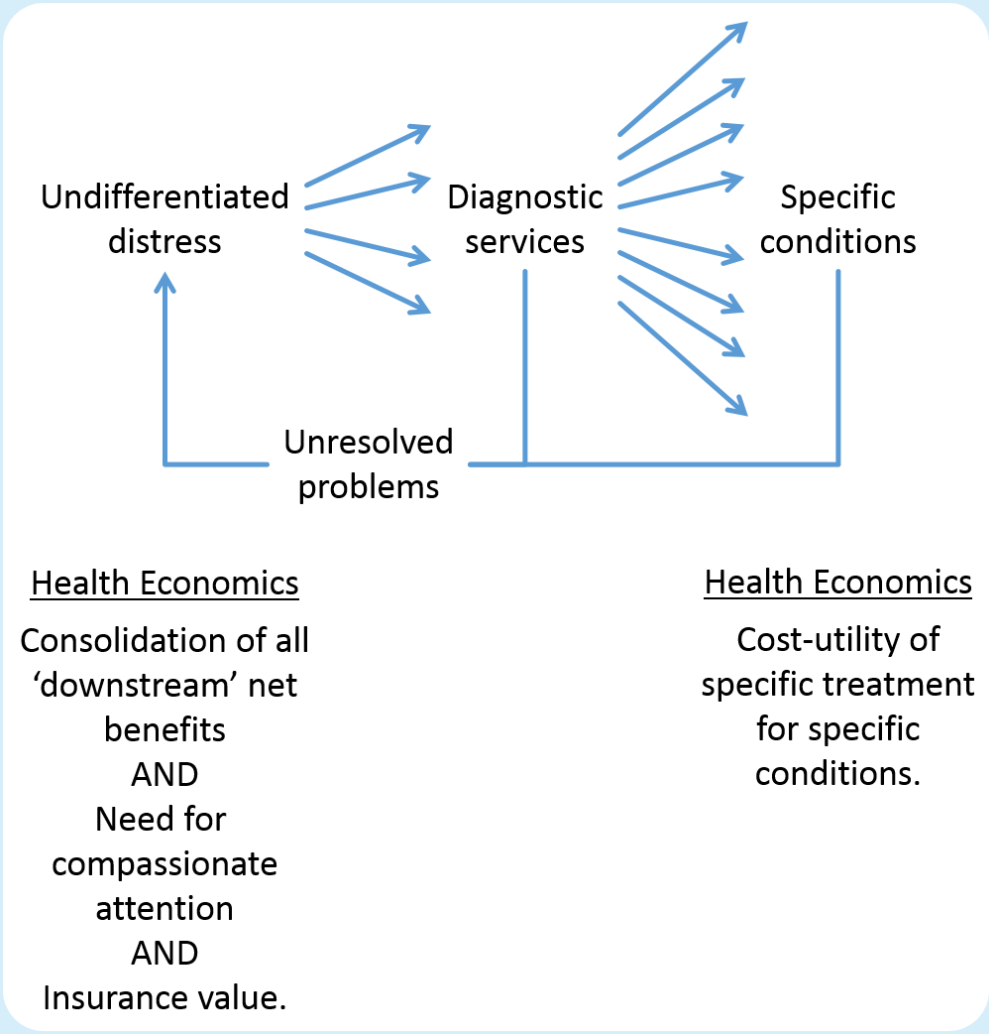


Fig 2. Providing Access to Healthcare: Health benefits are diffuse and hence hard to capture



-- Richard Lilford, CLAHRC WM Director

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CLAHRC WM Quiz

Which British physician provided the first clinical description of poliomyelitis in 1789?

Email CLAHRC WM your answer.

Answer to our previous quiz: While an estimated 74% of mothers in England start to breastfeed after birth, 36% continue to at least 6 months, but only 1% of children are exclusively breastfeed at 6 months. Congratulations to Nathalie Maillard whose answer was closest.

Director's Choice - From the Journals

More on the Hygiene Hypothesis and Exposure to Coliform Organisms from the Birth Canal

The putative advantages of a deep draught of coliform organisms during a baby's journey into the world has been discussed in a previous News Blog, with respect to prevention of allergy.[1] It now seems that it is not just allergy, but also cancer – more specifically the acute leukaemia of childhood – that is influenced by the process of birth.[2] And again, bypassing the birth canal by means of Caesarean section increases risk. The mechanism seems to conform with the three hits hypothesis, described in a past News Blog.[3] Here the hits might be:

1. Genetic predisposition.
2. Failure to 'benefit' from exposure to coliforms during birth.
3. Subsequent severe infection.

Regarding the third 'hit' above, it is known that acute lymphoblastic leukaemia of children occurs in semi-epidemic fashion, suggesting that an acute infection is the trigger.

Some decades ago I carried out a decision-analysis that argued that when the risk of intra-partum C-section exceeded a threshold of around 35%, then a planned C-section was the best option for mother and baby.[4] For the mother because intra-partum C-section is more risky than planned C-section; and for the baby because

situations where intra-partum C-section is common usually imply that the baby is also at increased risk – for example if the baby is coming by the breach. However, I can now see that my decision-analysis was incomplete – maybe I should have factored in the 'unknown unknowns'.

-- Richard Lilford, CLAHRC WM Director

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References

Mediating Variables

I have long argued that service delivery research, especially when generic interventions are evaluated, should examine the entire causal chain from intervention uptake to patient outcome.[1] Such an approach, of course, includes observation of mediating variables – variables (often residing in people's hearts and minds) that form part of the above causal chain. The advantages of such 'medication analysis' seems to be catching on – two papers in the journal 'Implementation Science' have covered this topic in the last year.[2][3] In one case the mediating variables explained most of the effect (Anselmi, et al.), while in the other (Lee, et al.) they explained none of it, suggesting that the intervention was working through a theoretical domain not previously considered. These papers used structural equations. However, I prefer Bayesian networks that our CLAHRC is pioneering.[4-6] This is for two reasons:

1. They can capture information from outside of the index study.
2. They can meld qualitative and quantitative information through elicitation of informative probability densities.

-- Richard Lilford, CLAHRC WM Director

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References

Reducing Risk of Postpartum Haemorrhage in LMICs

Worldwide around 127,000 women die each year due to postpartum haemorrhage (the loss of 500ml of blood within the first 24 hours after giving birth), making it the most common cause of maternal death.[1] It is especially prevalent in low- or middle-income countries (LMICs). The standard treatment is administration of oxytocin – however, the drug needs to be kept at 20-25°C, which can be difficult in some countries where refrigeration isn't reliable in either the hospital or whilst being transported. Thus, there is a need for an alternative option. Widmer and colleagues conducted a double-blind RCT of nearly 30,000 women across ten countries comparing postpartum administration of oxytocin with carbetocin, a heat-stable oxytocin analogue that can be stored at room temperature.[2] Both groups of women

showed similar frequencies of blood loss – 14.4% of those given oxytocin lost >500ml of blood, compared to 14.5% given carbetocin (relative risk 1.01, 95% CI 0.95-1.06); while, respectively, 1.45% and 1.51% lost >1000ml of blood (relative risk 1.04, 95% CI 0.87-1.25). There were also no significant differences in necessary interventions or adverse events.

Carbetocin could even perform better than oxytocin in LMICs as the oxytocin was stored in optimum conditions, which may not accurately reflect real-life settings. It will be interesting to track the implementation to uptake of this new finding – any takers?

-- Peter Chilton, Research Fellow

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Using Polio to Treat Cancer

Up until the mid-1950s polio was epidemic across many countries with an estimated 500,000 people paralysed or killed each year. Two vaccines were developed (one by Jonas Salk launched in 1957, the other by Albert Sabin in 1962), which lead to a dramatic decline in cases, and eventually eradication in many high-income countries. Following this the World Health Organization, UNICEF and the Rotary Foundation began an eradication campaign in 1988, and as a result there were only 22 reported polio cases worldwide in 2017. However, recent research has suggested that polio may be able to help patients with grade IV malignant gliomas.[1] Such patients have low survival rates – less than 20 months following diagnosis, and less than 12 months for recurrent gliomas. Current therapies are ineffective, inconsistent in improving survival and have many toxic effects. The trial was conducted using PVSRIPO, a modified live attenuated poliovirus type 1 vaccine. This is able to recognise CD155, a poliovirus receptor that is widely expressed in tumour cells. In total 61 patients were given a dose of PVSRIPO and followed up. Although 19% of patients had moderate-severe (grade 3 or higher) adverse events attributed to PVSRIPO, the overall survival of patients reached a plateau of 21% (95% CI 11-33) at 24 months, which was sustained at 36 months. This was higher than the rate among historical controls.

-- Peter Chilton, Research Fellow

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News & Events

Improving Quality and Safety of Care Workshop

A free workshop on 'The Positive Deviance Approach: Learning from Exceptional Performers to Improve the Quality and Safety of Care' is being held on **11 September 2018** in Leeds. This approach uses routinely collected data to identify and learn from those who demonstrate exceptional performance. Several teams from the Yorkshire Quality and Safety Research Group have been using pragmatic methods to apply this approach within various healthcare settings, and are looking to share and discuss their findings. For more information, and to register, please click here.

Learning Together for Quality Improvement

NIHR CLAHRC NWL are holding their Summer Collaborative Learning Event on 'Learning Together for Quality Improvement' on 18 July 2018 in London. For more information, and to register, please click here.

Improving Outcomes: the WM-AHSN Prevention and Self-Care Event

The West Midlands Academic Health Sciences Network are holding an event on 'putting prevention into practice- improving outcomes on Friday **14 September 2018** in Birmingham. This event will provide an opportunity to explore the impact and potential of prevention programmes and how they can changes the lives of everyone by improving their health, environments and/or services received. For more information, and to register, please click here.

Transforming Primary Care

Prof Paramjit Gill (Warwick Medical School) recently gave a talk at a King's Fund event on 'Transforming Primary Care with Population Health'. The event explored how patients at risk of certain conditions can be identified and supported to stay healthy, through the adoption of a population-level approach to health care. The event is still available to view online - to do so, please click here (note, registration is required).

Congratulations

Congratulations to Dr Rebecca Johnson (who works with CLAHRC WM Theme 3, Prevention and Detection of Diseases) who recently received a commendation from the Warwick Awards for Teaching Excellence.

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Selected Replies

Re: Interim Guidelines for Studies of the Uptake of New Knowledge Based on Routinely Collected Data

Very reasonable comment. Thank you.
It will be not full if you do not add the wordings like "real-world data", "big data". It is serious to filter out the buzz. I am afraid that some unexposed readers would not recognize that you are writing about the beloved "real-world data".

-- Vasily Vlassov

Re: Modern Chemotherapy for Severe Mental Disorders in a Prayer Camp

Dear Editor,
I wonder, can we consistently erase the naming of the medicine (today science based medicine) as allopathic medicine? The 'allopathic' was introduced by homeopaths for sake of propaganda. It was not and should not be used for the self-naming. I think.
When educated people from Russia-in-fear to England-in-Brexit try to limit the use of homeopathy, at least for public funded care, we need to have the homeopathy separated as much as possible, including in our language. I think.

-- Vasily Vlassov

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Recent Publications

Jolly K, Sidhu MS, Hewitt CA, Coventry PA, Daley A, Jordan R, Heneghan C, Singh S, Ives N, Adab P, Jowett S, Varghese J, Nunan D, Ahmed K, Dowson L, Fitzmaurice D. Self management of patients with mild COPD in primary care: randomised controlled trial. BMJ. 2018; **361**: k2241.

Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, Burroughs H, Jinks C. Saturation in qualitative research: exploring its conceptualization and operationalization. Quality & Quantity. 2018; **52**(4): 1893-1907.

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Available at: https://mailchi.mp/f477eef1e92e/clahrcwm-2018-07-13