Gmail **David Healy <david.healy54@googlemail.com>**

FW: Letter to M Hancock

David Healy (BCUHB - Mental Health & Learning Disabilities) <David.Healy@wales.nhs.uk>
To: David Healy <david.healy54@googlemail.com>

23 December 2019 at 14:29

From: David Healy (BCUHB - Mental Health & Learning Disabilities)
Sent: 23 December 2019 14:22
To: 'Andrew Dillon'; 'vaughan.gething@gov.wales'; 'richard.pengelly@health-ni.gov.uk'; 'june.raine@mhra.gsi.gov.uk'; Paul Chrisp; 'PSChiefMedicalOfficer@gov.wales'
Subject: RE: Letter to M Hancock

Dear Andrew

Many thanks for your response, which I read as an invitation to push at a partially open door. I might agree with your characterization of my concern as being with “bureaucratic medicine”, if you are willing to extend bureaucratic to include management. Health seems to me to have become a service industry and it’s the management (bureaucratic) processes common to such industries that are now putting us at risk.

In August 2018, I wrote to Vaughan Gething detailing similar concerns. I attach this letter – omitting the local service issues it also covered.

Dr Frank Atherton, the CMO in Wales, responded (letter attached) saying:

> I recognise some of the structural constraints you describe – these are not easily corrected, appearing as they do in all advanced healthcare systems. My suggestion would be for you to continue to engage with others who share similar views; collective analysis and advocacy are more likely to change systems than individual efforts.

With this advice in mind, and your response, this email seeks to engage a wider constituency.

We agree on what David Sackett said and I imagine you noted in my response to Leigh Smale that I referred to NICE Guidance rather than Guidelines. I am sure you are also aware that de facto NICE Guidelines have become something doctors either must, or feel they must, adhere to rigidly.

And even for doctors who view NICE as offering Guidance, the influence of the unpublished evidence can seriously skew that Guidance in a manner difficult to gainsay. By unpublished evidence I don’t mean trials that are never published, I am more concerned about trials published claiming efficacy and safety when the unpublished data suggests the opposite.

As regards unpublished evidence in general, I imagine the Dept of Health will be reassured by the points you make. I don’t wish to gainsay the impression that NICE are at least trying to do something, but I do need to spell out how from the point of view of someone concerned about safety, what has been done risks making the problems worse.

In the case of the articles on pharmaceuticals NICE works from, as you note Good Publication Practice boxes are more likely to be ticked than before – by the ghost writers. But the notional researchers (the apparent authors) are less likely to have seen or analysed the data from any of these trials than they were in 2004.

In agreeing with your suggestion that things have moved on since 2004, many readers of your email will likely forget that the pharmaceutical industry and health service companies have more incentive and resources to keep ahead of the game than anyone else – leading to "not easily corrected constraints that apply in most advanced healthcare systems" as Dr Atherton recognises.

In 2004, the BBC in particular were able to assist us all in tackling issues that appeared to be rotten apples in a barrel, but they seem unable now to get any purchase on what seem rotten barrel problems – tellingly illustrated for me in the failed efforts of two recent BBC programs to get answers from NICE on matters involving antidepressants and children.

Although NICE has access to regulatory material it didn't have in 2004, this is not the raw data. Having been involved in the consultation process regarding access to data that EMA began in 2012 and liaising regularly with colleagues who have availed of EMA's data offerings, I know that EMA now make available Company Study Reports (CSRs). They do not make available Clinical Record Forms (CRFs) which are closer to the data. CSRs written in the late 1990s were likely more innocent than CSRs written since companies became aware that their CSRs might later be scrutinized. But, even in 2004, the account CSRs offered were only slightly less rosy than published articles that led to indictments for fraud.

Your suggestion that regulators do not operate on the basis of the raw data accords with my understanding. Their use of any extra data to which they might have access is for audit purposes rather than analysis. In this respect nothing has changed since 2004.

For someone concerned about the safety of drugs, the AllTrials initiative you mention compounds the problems. RCTs and AllTrials focus on efficacy. This focus makes RCTs the gold standard way to hide adverse events – as outlined in a recent BMJ article I co-authored, (as part of a collective effort to analyse the problem). In adding to the premium put on RCTs, the impression generated by AllTrials, that we are now forcing companies to make key data available, as I see it adds to the inability of prescribers to see the harms they are causing – as demonstrated in the O'Neill Inquest.

From my point of view, if AllTrials hadn't existed the pharmaceutical industry might have had to invent it – and they were quick to sign up to it.

The post-marketing surveillance that might counter-balance the premium put on RCTs isn't working. My reason for initiating this correspondence was that the recent O'Neill inquest is a telling example of how things are getting worse rather than better.

The SSRIs give the lie to the standard response given to soothe policymakers and others that of course there are some events too rare to be picked up by RCTs, or that happen only after months or years of exposure, for which we need post-marketing surveillance. With SSRIs a genital numbness happens in close to 100% of people who take these drugs, within 30 minutes of the first pill, but it was close to completely missed by RCTs and is still, 30 years later, not included in the labels of these drugs.

This is not a matter of improving our post-marketing surveillance methods – it's a matter of re-empowering doctors and patients to notice problems happening commonly and in front of them – as Sackett would have wished – and developing methods to manage those problems as we did 50 years ago in the case of drugs like lithium but don't do now. In the absence of any Guidance on how to handle treatment induced suicidality, the doctors in the O'Neill case flailed around and it seems to me contributed to a death that should not have happened.

I don't hold industry or regulators to blame for this – I blame doctors and, in particular those who have held themselves out as experts on pharmacovigilance.

Most doctors now are too young to remember that 20 years ago we had a regular stream of publications like Drugs and Therapeutics Bulletins, reminding us that drugs are unavoidably unsafe. Very few of us read NICE Guidelines. Now every medical student learns NICE Guidelines and parrots them back in order to pass their exams. These essentially only outline the benefits of treatments – and few younger doctors have ever seen a DTB.

Most doctors work in Family Medicine and depend on specialists like me – who are either the very people whose names are on the ghostwritten articles or whom they will feel too uncomfortable to ask back to speak if my message is at odds with NICE Guidance. I'm reluctant to speak to doctors in training as they'd fail their exams if they listened to me.

When it comes to adverse effects, regulators, in practice, strip away the names of patients from reports of problems, transforming these into hearsay and making it impossible for the regulator ever to link an effect to treatment. MHRA have had reports of Post-SSRI Sexual Dysfunction (PSSD) on their books for 30 years, and may now have over 1000 such reports, but seem incapable of regarding these reports of a problem that is leading young people to seek assisted dying as anything other than a signal.

We would all be a lot safer if RCTs, increasingly conducted in developing world settings, with invented patients, and notional investigators unable to attest to the reality of anything that has happened in the trial, were regarded as hearsay.

It would also help if regulators made the kind of efforts that companies make to determine whether their drug causes a problem, which involves consulting with patients and doctors as to what has happened and often deciding their drug has in fact caused a problem.

I have not gone into the details above in order to castigate NICE. We agree this is not primarily a problem for NICE – other than perhaps being seen as a fall-guy for doctors who don't read or don't understand the small print in the Guidlines. It's rather difficult to pinpoint whose problem it is and I'd be grateful for any suggestions you might have in this respect.

As regards my efforts to engage a wider group of stakeholders, I will bundle up the recent correspondence about the O'Neill Inquest and ensure all Depts of Health in these islands get a copy. Unity on important issues seems lacking at the moment. Perhaps all 4 countries will be able to unite - in rejecting, or side-stepping, my concerns.

Other stakeholders that come to mind are some of the Royal Colleges, and the BMA.

Yours sincerely

David

From: Andrew Dillon [mailto:Andrew.Dillon@nice.org.uk]
Sent: 20 December 2019 12:22
To: David Healy (BCUHB - Mental Health & Learning Disabilities); 'vaughan.gething@gov.wales'; 'richard.pengelly@health-ni.gov.uk'; 'june.raine@mhra.gsi.gov.uk'; Paul Chrisp
Subject: RE: Letter to M Hancock

Dear Professor Healy

Thank you for this and your earlier emails. I am sorry that you didn't receive a response to your letter to David Haslam. He would have referred it to me for action and so the responsibility is mine.

The two main themes in your correspondence touch on the notion of 'bureaucratic medicine' and the provenance of the evidence that NICE takes into account when developing its guidance.

I know that you will be familiar with David Sackett's definition of evidence-based medicine (BMJ 1996; 312:71-72). His description of a "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" and his view that "the practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research" continue to be an important reference for NICE. Our guidelines are just one element of evidence-based care, alongside clinical judgement and the values and preferences of individual patients, a position we capture with these words, which appear in each guideline:

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

The issue of unpublished evidence is a challenge for anyone using evidence to inform treatment options. As you point out, the authors of our Depression in Children guideline drew attention to the problems caused by unpublished evidence some years ago. Since this guideline was published, there has been some progress in addressing the issue of unpublished evidence and positive bias in the published literature. Researchers are expected to follow the Good Publication Practice guidelines, which includes medical writers being named in the acknowledgements of papers. Since 2016, the EMA has made all clinical data submitted to them for the marketing authorisation applications of new medicines available through a dedicated website (https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication). This means that all clinical data that was used by regulators is accessible to everyone within 60 days of marketing authorisation (after registering for access to the database), whether or not is has been published.

Of course, these procedures were not in place when most SSRIs were approved, but post-marketing surveillance can trigger regulatory action and the EMA completed a referral procedure on SSRIs and suicide in 2005:

https://www.ema.europa.eu/en/medicines/human/referrals/serotonin-specific-reuptake-inhibitors-serotonin-noradrenaline-reuptake-inhibitors

We agree with you that it is not NICE's role to 'police' the academic literature, but we take the matter seriously and we are a AllTrials campaign which calls for all past and present clinical trials to be registered and their full methods and summary results reported.

Yours sincerely

Andrew Dillon

Chief Executive

National Institute for Health and Care Excellence

From: David Healy (BCUHB - Mental Health & Learning Disabilities) <David.Healy@wales.nhs.uk>
Sent: 17 December 2019 09:13
To: Andrew Dillon <Andrew.Dillon@nice.org.uk>; 'vaughan.gething@gov.wales' <vaughan.gething@gov.wales>; 'richard.pengelly@health-ni.gov.uk' <richard.pengelly@health-ni.gov.uk>; 'june.raine@mhra.gsi.gov.uk' <june.raine@mhra.gsi.gov.uk>
Cc: 'colleen.bell11@outlook.com' <colleen.bell11@outlook.com>
Subject: Letter to M Hancock

Attached a further piece of correspondence linked to recent correspondence sent to each of you

David Healy

David Healy MD FRCPsych

Professor of Psychiatry

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2 attachments

2018 Aug Healy to Gething edited.pdf
148K

2018 Atherton.pdf
42K