The Evidence-Based Medicine Consultancy Ltd

Research for Impact

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From:

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To: Parliament

I am the Director of the Evidence-based Medicine Consultancy Ltd in Bath, United Kingdom. I have a medical degree (MBBCh) and a Doctorate in Philosophy (PhD) from the University of the Witwatersrand in Johannesburg, South Africa. Whilst I have practiced clinical Medicine in both the United Kingdom and South Africa, I now perform non-clinical research work only. My United Kingdom General Medical Council registration number is 3634680.

As the director of E-BMC Ltd, which I established in 2013, I am committed to improving the quality of healthcare globally through rigorous research. My research expertise is drawn from experience in both developing and developed countries, which uniquely positions me to evaluate and design research for a variety of healthcare settings. As a result, I am a frequent member of Technical Teams responsible for developing international clinical practice guidelines and am currently employed as the Guideline Methodologist on two World Health Organization (WHO) clinical practice guidelines due to be published in 2021. My peer-reviewed publications have received in excess of 3000 citations and my ResearchGate score is among the top 5% of ResearchGate members. Please note that E-BMC Ltd does not undertake pharmaceutical industry-sponsored work and I have no conflicts of interest to declare.

My involvement in the ivermectin story

On the 26th of December 2020, I watched Dr Pierre Kory's testimony on ivermectin before the United States Senate in which he asked that ivermectin be approved for the treatment of covid-19. Dr Pierre Kory is an intensive care specialist physician who is part of a group of called the Frontline Covid-19 Critical Care Alliance that has been monitoring potential treatments for covid-19. This group was the first to identify dexamethasone as a useful treatment for covid-19.

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I obtained a copy of the Kory/FLCCC review on ivermectin on the 26th December and was impressed with the number of studies included on ivermectin – I was surprised that I had not heard about ivermectin in the context of covid-19 before. I noted that a limitation of the FLCCC review was that the authors had not performed a meta-analysis of the included trials. Meta-analysis is a research method that involves pooling data from different studies to produce an overall estimate of the effect of a treatment for critical and important health outcomes. Evidence synthesis is one of my areas of expertise. Given the urgent need for therapeutics against covid-19, I undertook to do this evidence synthesis work for free during my Christmas holiday because I thought it might help to clarify whether ivermectin would be useful against covid-19 and in the context of the pandemic, speed was of the essence. I approached this work with professional equipoise.

Following my evaluation of the evidence, I concluded that ivermectin was an essential drug to reduce the morbidity and mortality from covid-19. Therefore, on Monday the 4th of January 2021, I emailed my report on ivermectin to Mr. Hancock, Mr. Ashworth, Mr. Rees Mogg (my MP based on my home address) and Mrs. Wera Hobhouse (my MP based on my business address). I titled the email 'URGENT - Ivermectin for COVID-19 will save lives and prevent COVID-19 infection'. I also emailed the report to one of my usual commissioning employers at the WHO, asking her to forward the report to the dedicated WHO Covid-19 Team. I enclose a summary excerpt from page 16 of the report:

This review and meta-analysis confirms that ivermectin substantially reduces the risk of a person dying from COVID-19 by probably somewhere in the region of 65% to 92% according to RCT data. The uncertainty in the evidence relates to the precise extent of the reduction, not in the effectiveness of ivermectin itself. Similarly, when ivermectin is used as prophylaxis among health care workers and contacts, it is clear that ivermectin substantially reduces COVID-19 infections, probably somewhere in the region of 88% (82% to 92%). Data from numerous currently active RCTs will help to determine the precise extent of its protective effect in these at-risk groups.

Despite the FLCCC's strong recommendation that ivermectin should be implemented globally to save lives from COVID-19, most governments and health professionals still appear to be unaware of this profoundly effective COVID-19 treatment. Not only is ivermectin a safe, effective and well-known medicine, at an estimated cost of less than 10 pence per person treated with a 12 mg tablet, it does indeed seem like a miracle drug in the context of the current global COVID-19 situation. Guidance and protocols on using ivermectin for COVID-19 can be found on the FLCCC website https://covid19criticalcare.com.

I received automated replies from the MPs but nothing more. As a medical doctor, I have a moral duty to help in times of health emergencies; I therefore recorded a brief appeal to the Prime Minister on the 6th of January 2021, in the hope of expediting communication about ivermectin with the Health Minister and authorities. The appeal can be found at this link:

https://www.youtube.com/channel/UCcCrBQZqQ1FTZ60WnC6JjDA

Whilst I again received no response from the Health Authorities, I was inundated with emails from health professionals and the public asking me how they can help and what further can be done to get ivermectin approved as soon as possible.

A limitation of my original report may have been perceived to be that I had done it rapidly in response to the FLCCC review and that data had not been double extracted (by me and one other). In addition, due to a lack of resources (everyone was on holiday, so I had struggled to find assistance with the work) and in the interests of haste, I had not conducted a literature search but, rather, had used the FLCCC review's list of identified studies in my analysis. Therefore, as I had not received a reply, I decided to gather a team of experienced systematic reviewers to conduct a review from scratch using Cochrane Systematic Review methods. The team included a statistician and health economist from Newcastle University, as well as clinicians and a consumer representative. I also invited Dr. Andrew Hill to be an author and he accepted the offer. We commenced work on the 14th of January, submitting a new rapid review protocol to the Cochrane Editor-in-Chief. A rapid review entitles review groups to use single data extraction methods, however, to ensure the highest methodological rigour, we double extracted the data. We also assessed the risk of bias of individual trials and graded the certainty of the evidence. The latter two procedures are not considered necessary under NICE's guidance on covid guidelines. See https://www.nice.org.uk/process/pmg35/chapter/finding-evidence

Dr. Andrew Hill and the World Health Organization/Unitaid's commissioned systematic review

I first 'met' Dr. Andrew Hill via email during the first week of 5th of January 2021, when I became aware that he was conducting a review on ivermectin for the WHO. I sent him my data extraction spreadsheet on the 4th January 2021 and offered him my assistance (gratis). On the 18th January his review, which found a reduction in deaths of 75%, was published on a preprint server called Research Square. I was surprised by the poor methodological quality of his review and the conclusions that stated that more trials were needed before the regulatory authorities could approve ivermectin for use in covid-19. To me he had admitted that there was evidence of a large effect on deaths. None of the existing drugs given emergency use authorization have half as much evidence of efficacy and safety as accumulated for ivermectin. I asked Dr. Hill how he came upon his conclusions which did not match the importance of the evidence (the large reduction in deaths, and significantly increased viral clearance). He told me that his sponsor (Unitaid) had influenced his conclusions and that, despite this, he would do everything he could to help get ivermectin approved. I informed him that, given his serious conflicts of interest, he could no longer continue as an author of our review. Dr. Kory and Dr. Marik from the FLCCC also wrote to Dr. Hill, challenging his conclusions and much of the content of the review, as there were many factual inaccuracies that they had previously discussed and clarified with him. The did not comprehend why he continued to present these in his paper. They also asked him to revise the manuscript. Unfortunately, despite the low quality of this unpublished review, it is currently used by the UK's Therapeutic Task Force to support the lack of use of ivermectin against covid-19.[i]

On the 18th January 2021, I informed the Cochrane Editors that Dr. Andrew Hill had serious conflicts of interest and, as such, could no longer be on the review author team. Thereafter, we worked night and day on the review, finding 21 randomised control trials of ivermectin for covid-19 – 18 were trials of treatment and 3 were trials of prevention. Meta-analysis of 13 trials found that ivermectin reduced deaths compared with no ivermectin by 68%; it also reduced covid-19 infection by 86% when used as prophylaxis. The evidence on clinical improvement and deterioration when used to treat covid patients with mild, moderate or severe disease also clearly favoured ivermectin. We concluded that the efficacy, safety and low cost of ivermectin for covid-19 suggested that ivermectin could have an important impact on the pandemic.

However, when we were ready to submit our work for peer review on the 8th February 2021, we were told by the Cochrane Editors that they were no longer interested in publishing our systematic review and meta-analysis. We prepared the review for the Lancet and submitted there instead. It was forwarded to Lancet Respiratory Medicine (LRM), underwent peer review by four peers and was found to be acceptable for publication. However, despite a positive peer review, the Editors declined to publish the paper. The LRM editors noted in their rejection email that "we have no doubt that this is an important paper that will be widely picked up". We have since submitted elsewhere and published the paper on the pre-print server in the meantime. (https://osf.io/k37ft/) It had been downloaded 1183 times by the 22nd January 2021.

Evidence used for NICE guidance

A systematic review and meta-analysis is considered to be the international standard for clinical practice guideline development. Most guideline developers, such as the WHO and NICE, recommend the use of these research syntheses to underpin guideline recommendations. Guideline development in response to a health and social care emergency requires an acceleration of the process while maintaining transparency of decision-making and reporting. This is one of the core principles underpinning the development of all NICE guidance and standards. NICE issued guidance on covid research in March 2020 stating that the hierarchy of evidence for evaluating interventions for covid would be systematic reviews, followed by randomized trials, observational studies and expert opinion. In the context of the pandemic, NICE states that they will not evaluate risk of study bias or grade (assess the quality or certainty of the evidence). Thus, the evidence provided by our systematic review and meta-analysis, with risk of bias assessment and grading of the certainty of the evidence represents the highest level of evidence that is used under normal circumstances and goes beyond the level of evidence required by NICE to make a recommendation on ivermectin during a pandemic.
https://www.nice.org.uk/process/pmg35/chapter/finding-evidence

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The British Ivermectin Recommendation Development (BIRD) Meeting

Aware that many people were (and are still) dying unnecessarily every day, I decided that a way to get through to the health authorities may be to prepare a DECIDE evidence to decision (EtD) framework. This is the gold standard of health care decision making for clinical practice guideline development. As health care recommendations are seldom made on the evidence on efficacy alone, these frameworks include evidence and considerations on stakeholder values and preferences, resource use, equity, acceptability and feasibility implications. On the 20th of February 2021, I presented this framework to a stakeholder panel from 16 countries. The meeting, which adhered to the process outlined in the WHO Handbook Guideline Development (2014), was convened at short notice (6 days) and was called the British Ivermectin Recommendation Development (BIRD) meeting. Invitees included relevant stakeholders in the UK; no representatives of UK authorities responded to the invitation. At the close of the BIRD meeting, at which stakeholders agreed that ivermectin should be recommended for both prevention and treatment of covid-19, the Steering Group undertook to communicate the evidence and the recommendation to the Health Authorities. We have yet to have a considered response from any UK Health Authorities, including the MHRA, Therapeutics Task Force, Public Health England, NICE, SAGE,etc.

I and many experts around the world would appreciate some assistance in conveying this important information to the relevant health authorities who seem to be creating barriers to the use of ivermectin, rather than facilitating its use. I reiterate that the evidence in support of using ivermectin for treatment of covid-19 is far stronger than the evidence on any other medicine given emergency use authorization to treat covid-19. In addition, ivermectin can be used in asymptomatic, mild, moderate and severe covid-19 infection – no other treatment has been shown to do this. In addition, ivermectin is very safe – it is currently being used by millions of people around the world for covid and other infections.

Data retrieved from WHO/Uppsala VigiAccess pharmacovigilance database (22.03.2021)				
Medicine	**Year reporting started**	**Deaths**	**Deaths per year**	**Adverse events**
Ivermectin	1992	16	< 1	4702
Aspirin	1968	1432	8	177606
Remdesivir	2020	467	467	5733
Tocilizumab	2005	769	48	47545
COVID-19 vaccines	2020	2402	9612	309403
Tetanus vaccine	1968	32	< 1	14725

A recent expert panel discussion on ivermectin for covid-19 in which I participated can be found here:

https://www.youtube.com/watch?v=ypxrJhSg5xU&t=19s

I trust that politicians will now respond to this information with the required urgency, so that further critical time in saving lives is not wasted.

Yours Sincerely,

Dr. Theresa Anne Lawrie

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[i] Email response from the Therapeutics Taskforce: "The Therapeutics Taskforce are monitoring the data from worldwide trials on ivermectin, including the WHO meta-analysis led by Dr Andrew Hill. We have monitored a collection of small studies which have now completed and provided some positive signals on the use of ivermectin as a treatment for COVID-19. This is a promising step; however, larger-scale studies are still needed to confirm the effectiveness and safety of this treatment. The Therapeutics Taskforce works with the independent RAPID-C19 group in assessing relevant trial evidence to provide advice on whether treatments are clinically effective." The RAPID-C19 group has already given NHS access to remdesivir, for which there is no evidence that it reduces deaths or improves outcomes for people with covid-19. The grounds for this emergency use authorisation of remdesivir are puzzling, especially when contrasted with ivermectin which has volumes of evidence not only from randomised trials, but also from large observational studies and country case studies. It is also much safer compared with all other medicines granted emergency use authorisation.