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## COMMERCIAL INFLUENCE IN HEALTH: FROM TRANSPARENCY TO INDEPENDENCE

### Commercial influence and covid-19

Greater independence from commercial interests is more important than ever

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Although the covid-19 pandemic has provoked the best of human compassion, the hallmarks of unhealthy commercial influence have also emerged. This week, *The BMJ* published the initial list of signatories to our call for action to reduce commercial influence in how healthcare evidence is produced and used ([www.bmj.com/commercial-influence-call-to-action](http://www.bmj.com/commercial-influence-call-to-action)). Signatories include professors, patient advocates, clinicians, and researchers who want to see product evaluation, medical education, and clinical practice much freer from commercial interests.<sup>1</sup>

Previous *BMJ* investigations have highlighted systemic weaknesses in the regulation of drugs, devices, and tests,<sup>2</sup> and the experience with covid-19 may prove another powerful example of this problem. Statistician John Deeks, who is studying the evidence underpinning covid-19 tests, has expressed serious concerns that current regulatory mechanisms for tests are vulnerable to commercial influence.<sup>3,4</sup> For example, the UK government used “commercial confidentiality” to justify concealing the names of nine covid-19 antibody tests that had been found to be insufficiently accurate.<sup>3</sup> Manufacturers of antibody tests are not allowed to make false claims, but tests do not need to work well to be approved in Europe; nor is independent evaluation required.<sup>4</sup> Regulation in the US is usually more stringent but has been relaxed during the pandemic to facilitate approval of tests for covid-19.<sup>4</sup>

There are valid arguments for “regulatory agility” during emergencies such as covid-19,<sup>5</sup> but speed should not undermine basic standards for trustworthy evidence.<sup>6</sup> As a 2017 report on Ebola from the US National Academy of Sciences noted, “despite [the] sense of urgency, research during an epidemic is still subject to the same core scientific and ethical requirements that govern all research on human subjects.”<sup>7</sup> Clear evidence of the risk of bias in commercially funded research<sup>1</sup> should drive efforts to develop a new, but equally agile, system of independent evaluation of all tests and treatments.

#### Off balance

A serious imbalance in covid-19 research strongly favours the study of drug treatments over non-drug interventions, with many studies too small or too weak to produce reliable results.<sup>8</sup> Equally concerning is the release of partial or preliminary findings before peer review—often through commercial press releases—that is distorting public perceptions,

ongoing evaluations efforts, and political responses to the pandemic.

Remdesivir is a key example. The antiviral drug, made by US company Gilead, was unapproved at the start of the pandemic, but in early April the *New England Journal of Medicine* published a small descriptive study of a compassionate use scheme for patients with covid-19.<sup>9</sup> Gilead funded the study, a third of the authors were Gilead employees, and Gilead’s press release reported “clinical improvement in 68% of patients in this limited dataset.”<sup>10</sup> Despite being a non-randomised, uncontrolled, company funded study of just 53 patients, media headlines described “hopeful” signs and reported “two thirds” of patients showing improvement.<sup>11</sup>

Two weeks later, the *Lancet* published a randomised placebo controlled trial of remdesivir from China, finding no statistically significant clinical benefit in the primary outcome of time to clinical improvement.<sup>12</sup> Twelve per cent of participants taking remdesivir stopped treatment early because of adverse events, compared with 5% taking placebo. The trial was stopped before meeting recruitment targets, so results were inconclusive but did not rule out the possibility of benefit, according to an accompanying commentary.<sup>13</sup>

#### Spin

On the same day as the lacklustre *Lancet* findings were published, two other events helped sustain global hype about remdesivir. First, an upbeat media release by Gilead promoted preliminary results from another company funded study, still weeks away from submission for peer review.<sup>14</sup> Second, Anthony Fauci, a member of President Trump’s coronavirus task force, unexpectedly announced preliminary findings from a publicly funded trial being run in the US. Adding to Trump’s previous promotion of remdesivir as a potential “game-changer,” Fauci told the world the trial’s results suggested the drug could become the “standard of care” for covid-19, before any peer reviewed data were available for scrutiny.<sup>15</sup>

The publicly funded trial was published in *NEJM* almost a month later.<sup>16</sup> That report of preliminary results showed a difference of four fewer days in time to recovery among those taking remdesivir, compared with placebo, but no significant reduction in deaths. The paper revealed that the primary outcome had been changed during the trial, and, that following a data safety monitoring board recommendation and Fauci’s public announcement in April, treating physicians were allowed to switch trial participants

from placebo to remdesivir, bringing an early end to masking for some participants.

The published report also disclosed that Gilead supplied the drug for the trial, one of the trial investigators was a Gilead employee, and six other authors declared financial ties to Gilead. Finally, an additional note disclosed that employees of Gilead “participated in discussion about protocol development and in weekly protocol team calls,”<sup>16</sup> a level of engagement suggesting this drug trial could not be regarded as independent from the manufacturer.

## Call for independence

Whatever the evidence ultimately shows about remdesivir’s benefits and harms, commercial influence once again seems to be driving overly positive perceptions of a still unproved drug. Similar concerns over covid-19 tests and their reliability confirm the need for urgent reform of regulatory approval for diagnostic tests.<sup>4</sup> Both underscore the critical importance of rigorous and independent evaluation of tests and treatments.

*The BMJ* thanks all those who have signed the call for more independence from commercial interests in medical research, education, and practice, and encourages others to consider adding their signatures. (<https://www.bmj.com/commercial-influence>).<sup>1</sup> During this fast moving and lethal pandemic, independent and trustworthy evidence, interventions, and guidance are more important than ever.

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