Homoeopathy and "the growth of truth"

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The comparison between homoeopathy and conventional medicine (allopathy) by Aijing Shang and colleagues[1] in today's *Lancet* goes to the root of the acquisition of knowledge in medicine. In 1846, John Forbes compared homoeopathy and allopathy, mostly informally, but also with a few shrewd experiments.[2] He found the results of homoeopathy for certain ailments as good as those of his own treatments. Because he considered the theory of increased potency by greater dilutions "an outrage to human reason", and therefore any effect of homoeopathy impossible, he proposed that his findings should lead to introspection about the effectiveness of the allopathic medicine of his time.[2] Now, 160 years later, Shang and colleagues compare homoeopathy and allopathy in a meta-analysis of two sets of 110 placebo-controlled trials.[1] At first sight, both homoeopathy and allopathy seem effective. However, a meta-regression and a subgroup of trials of higher quality showed higher sensitivity to potential bias for homoeopathic than for allopathic trials. This difference might be even larger than estimated because one cannot always reliably assess study quality from a publication. Thus Shang and colleagues arrive at a class judgment about homoeopathy that will be gladly accepted by many who always thought homoeopathic evidence was contaminated.[3] Others will claim that this analysis amounts to "data dredging".

Can a sophisticated application of statistics in meta-analysis in itself solve the problem that randomised trials might have provided a wrong answer? Evidence does not exist in isolation. The philosopher Susan Haack coined the crossword analogy wherein the clues are the analogue of experimental evidence, and the entries already completed are the analogue of background information (figure).[4] How reasonable an entry is depends on how well it is supported by the clue and by the background knowledge. We question the results of a randomised trial of homoeopathy because we know that pharmacological action of infinite dilutions is highly implausible.[5] This reasoning is also the explicit starting point of Shang and colleagues and their analyses only gain meaning because of that background. (Lest one concludes that basic science is always the ultimate arbiter: all work to identify carcinogens in tobacco smoke and specific mutations caused by smoking is only undertaken and can only be meaningfully interpreted because we know the epidemiology of smoking and lung cancer.[6])

Shang and colleagues present a subgroup of eight trials of homoeopathy in acute respiratory tract infections that withstands meta-analytical techniques for detecting bias. They are not prepared to accept these results either, because they declare the group of trials is too small, and they prefer to stick to their overall judgment about homoeopathy on the basis of all 110 trials. It seems unscientific to use the argument of "bias" against all investigations in a field. Nevertheless, the logician Douglas Walton proposed that a consistent track record of bias might lead to the conclusion that the bearer of the argument, and therefore the argument, has lesser credibility.[7] This comes close to Shang's proposal to apply judgment to a whole field.

Suppose that the respiratory trials were about a chemical investigated by an allopathic pharmaceutical company, with a meaningful mechanism and a record of effects in laboratory mice and early studies in volunteers. We might be equally mistaken in accepting the results: the trials will be sponsored by the industry, and industry trials have a strong record of coming out in favour of their product.[8] Various mechanisms account for this favouritism, and which might be responsible is usually impossible to judge from the publication.[9] But, should not we have been on safe ground already—the laboratory science is in complete concordance with the

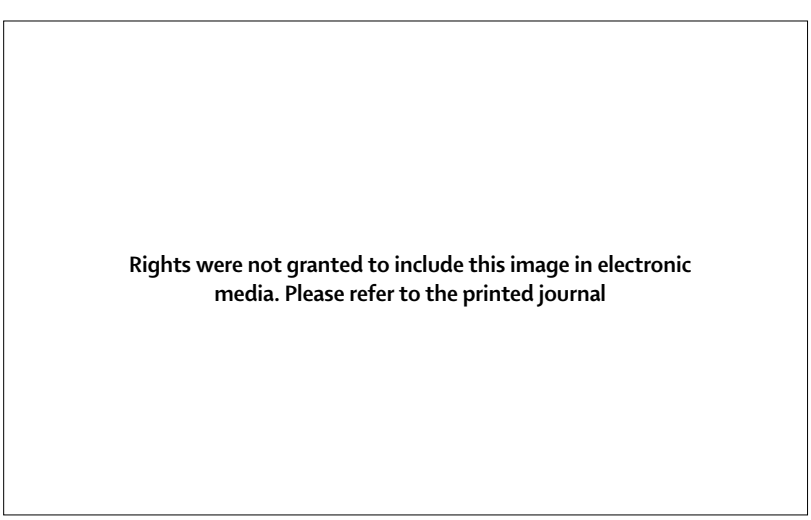

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Figure: Science progresses like solving a crossword puzzle

trial findings? Safer yes, but not infallibly so.[5,6] The construct might prove to be a "house of cards", as with cyclo-oxygenase 2 antagonists[10]—in which all evidence, from laboratory experiments to randomised trials, seems to have been selectively analysed and published.

Science is an intrinsically human affair. When new theories are created and new evidence sought, judgment will retain a subjective element. This does not mean that it is impossible to sift out which interpretation is more valuable: stimulated by debates and steered by opinions of protagonists, new insights and new data will emerge. These new insights and data will in turn be scrutinised and perhaps accused of bias. In 1906, William Osler delivered an oration on "The growth of truth" and stated: "Truth may suffer all the hazards incident to generation and gestation . . . [and] . . . all scientific truth is conditioned by the state of knowledge at the time of its announcement."[11] Stephen Gould echoed this sentiment at the brink of the 21st century: even if science progresses in a "fitful and meandering way", it achieves progressively more adequate understanding of an objective outside world.[12] The ultimate proof is that science makes progress in changing reality: in allopathic medicine by preventing, alleviating, and curing disease ever more effectively.

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T-cell depletion to prevent GVHD after unrelated-donor marrow transplantation

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Over the past three decades, allogeneic haemopoietic stem cell transplantation (allo-HSCT) has been increasingly used as the treatment of choice for patients affected by several haematological malignancies. With this procedure, the survival prospects of such patients have profoundly changed.[1]

Despite the successes achieved by allo-HSCT, the treatment is still associated with a remarkable incidence of failures, mainly attributable to the development of immune complications (ie, graft-versus-host disease [GVHD] and graft failure),[2] to relapse of malignancy,[3] or to the profound state of immune deficiency that characterises patients given an allograft and favours the occurrence of fatal infections.[4] GVHD is caused by donor-derived alloreactive T-cells contained in the graft attacking non-shared recipient antigens on target tissues. A two-step vicious circle generates the clinical syndrome: conditioning-induced tissue damage activates antigen-presenting cells (mainly of recipient origin) which present recipient alloantigens to donor T-cells transferred with the graft, and in response to recipient antigens, activated donor CD4+ cells expand and generate inflammatory cytokines that cause tissue damage and promote differentiation of cytotoxic CD8+ T-cells, which, in turn, kill recipient cells and further disrupt tissues.[5] In its most severe forms, GVHD may be largely refractory to immunosuppressive therapy, leading directly or indirectly, mainly because of infections, to the patient's death. On the other hand, GVHD has been reported to be associated with a graft-versus-leukaemia (GVL) effect, because of widely distributed histocompatibility antigens of the recipient