Editorial

Recommendations and regulations to decrease bias, increase access to clinical data and improve the quality of evidence-based medicine for all

In our endeavour to improve public health outcomes, we have to ensure that we are providing medicine and care which is evidence based. Therefore, we should strive to provide care for which there is unequivocal evidence that it improves the outcome of our patients. Unfortunately, in anaesthesia, there is surprisingly little good evidence of interventions that improve perioperative outcomes.[1]

Evidence-based medicine is built on two pillars; a hierarchy of evidence and a regard for values and preferences.[2] The principle of a hierarchy of evidence is to remove as much bias as possible from the data used in evidence-based medicine. The hierarchy of evidence should increase our confidence in evidence-based clinical management recommendations. The values and preferences pillar recognises that patient opinion is important as often a medical intervention trades risks and benefits. The most compelling example of this in perioperative medicine is the risk-benefit relationship associated with perioperative beta blockade, where acute administration is associated with a significant decrease in myocardial infarction, but at the cost of an increased risk of a stroke.[3] In this situation, patient values and preference are key factors in determining whether or not perioperative beta blockade is an acceptable intervention.

Despite the laudable objectives of evidence-based medicine, a number of clinicians continue to voice reservations about it. A large proportion of perceived failings of evidence-based medicine are not a function thereof, but rather a reflection of the limitations and failings of published research.[4] It is a sombre thought that as much as 80% of scientific publications are potentially false.[4] Access to all clinical data is required in order for credible evidence to be provided for evidence-based medicine. A lack of access to the totality of the clinical data undermines evidence-based medicine, as opposed to the concept or construct that evidence-based medicine is flawed.

For this reason, the new World Health Organization (WHO) statement on the public disclosure of clinical trials released in April 2015 is welcome.[5] This statement is a major step forward in ensuring that evidence-based medicine is not adversely affected by inaccessibility to clinical trial data, particularly secondary to selection bias (selective reporting) or attrition bias (the loss or inaccessibility of existing data).

The WHO statement demands that:

- Every clinical trial is publically registered before patient recruitment, so that all trials can be tracked, and so that it can be ensured that all outcome data are presented, as per protocol.
- All clinical trial registries are updated with trial-specific data, so that the number of participants is known.
- The trial results are reported within 12 months of trial completion, so that the data can be used to update the existing evidence base contemporaneously.

This statement attempts to ensure that even if the clinical trials results are perceived to be undesirable by the investigators, it will be known that the data exist, and there will be access to the data as it was originally intended to be presented, according to trial protocol. This will prevent investigators hiding undesirable data, or presenting only the most desirable outcomes, while ignoring the less desirable findings. Finally, the WHO has stated that past clinical trials should be registered retrospectively, and the results reported. This is important as missing data are associated with bias, and it is this bias which undermines evidence-based medicine.

The WHO statement is in line with campaigns such as AllTrials,[6] whose intention is to ensure that all the data from all clinical trials are publically available. Access to all clinical trial data is a just cause. Trial participants who have participated in a trial, and society organisations that have funded such trials, deserve to realise the benefits of the data derived from the clinical trial. It doesn't matter if the results of a trial are negative, as it is the summation of all the trial data which correctly informs clinical medicine and its practice. Data change practice. A study of publications in the *Archives of Internal Medicine* over a 10-year period showed that of the studies that evaluated current practice, 38% confirmed the current practice to be beneficial; 40% found it to be of no benefit, or worse, requiring a reversal of practice; and 22% were inconclusive.[7] Clearly, additional trial data have the power to change current clinical practice. Ensuring that all the data from clinical trials are freely accessible will contribute to decreasing existing bias in evidence-base medicine, and thereby increasing the robustness of evidence-based data.

This is important to anaesthesiologists as currently, only a small base of evidence-based practice is known that will improve perioperative outcomes.[1] By ascribing to the philosophy of the WHO statement,[5] and ensuring that we abide by it, we can improve upon this situation. Secondly, we need to participate in collaborative clinical trials which address perioperative outcomes. Every day, we practise with the best intentions of improving patient outcomes. In the absence of evidence, our clinical practice is often driven by our understanding of physiology, pathophysiology and medicine, and our interpretation of what

would therefore be reasonable clinical management. However, participation in clinical trials demonstrates that our interpretation of physiology, pathophysiology and clinical medicine, used to guide our practice, is often flawed. Unfortunately, clinical medicine is often more complex than our interpretation of physiology and pathophysiology. It could be believed, using sound first principles, that in the realm of perioperative cardiovascular medicine, preoperative beta blockade and aspirin would provide primary prevention for cardiovascular events. However, clinical trials have shown that preoperative beta blockers increase the incidence of a stroke,[8] and aspirin increases bleeding,[9] both of which compromise perioperative cardiovascular protection.

As anaesthesiologists, we need to positively contribute to building the evidence base for anaesthesia and surgery. We can start by supporting the WHO statement,[5] and having the courage to test our clinical practice by participation in clinical trials, when current practice is known to have a small or non-existent evidence base.

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