Editorial

It is time for Africa to lead the way in pragmatic clinical trials

The African Surgical Outcomes Study (ASOS), which was published at the beginning of this year, showed that although African surgical patients are generally of a low surgical risk, one in five of these patients will develop complications, and the mortality following surgery is twice the global average.[1] In reality, mortality following surgery in Africa is probably more than twice the global average, as the data in ASOS is not risk adjusted for patient comorbidities. It is estimated that approximately five billion people globally are unable to access safe surgical treatment, and nearly 95% of these people live in low- and middle-income countries.[2] ASOS provides important data on how surgery may be made safer in Africa. In ASOS, nearly 95% of all deaths occurred after the day of the surgery, predominantly on the surgical ward.[1] ASOS also revealed that the number of specialists providing surgery and anaesthesia per 100 000 population were 20 to 50 fold less[3] than the recommended safe minimum as proposed by the Lancet Commission for Global Surgery.[2] It appears that the lack of human resources is a significant contributor to postoperative mortality in Africa.

For patients who are able to access surgery in Africa, the findings of ASOS leads to the hypothesis that a primary driver of mortality is 'failure to rescue' secondary to limited human resources. There are two potential solutions to this problem. First, we can increase the health personnel providing surgical care between 20 and 50 times the current number. Realistically this is neither practical nor possible. The alternative is to flag the patients at risk, and attempt to ensure that we do not miss postoperative complications or the progression of these complications. We have proposed the latter strategy for the African Surgical Outcomes Study (ASOS)-2 Trial.

Based on how dire the situation is in Africa, we need to conduct a pragmatic trial quickly. Traditional international collaborative clinical trials unfortunately move slowly. For example, the process from hypothesis to peer-reviewed publication often exceeds five years in mature collaborative clinical trial groups. The PeriOperativeISchemic Evaluation-2 (POISE-2) Trial took approximately six years, if one assumes that the conversion of the hypothesis to protocol took approximately a year (which would be unusually quick).[4] Furthermore, following peer-reviewed publication, one still needs to consider 'knowledge translation'. Knowledge translation relates to the length of time it takes for substantial uptake in clinical practice, once a therapy or intervention has sufficient evidence to be deemed clinically effective. This may be further prolonged in low- to middle-income countries.[5]

In a continent of 1.2 billion people, where approximately 95% of the population does not have access to safe and affordable surgery,[2] it could be considered ethically unacceptable to take as long as we have seen in previous large collaborative trials to address the simple signal of 'failure to rescue' which was seen in ASOS. We need a clinical trial that leads to a change in the culture of clinical trials research. In our context, we should focus on trials that rapidly establish robust clinical evidence and earlier uptake of effective interventions. It is time to break the mould. We must lead the change.

ASOS-2 is a trial powered for mortality, an outcome of social and clinical value. Powering the trial for mortality means that the required sample size is large (over 50 000 patients). In traditional perioperative randomized controlled trials this would be considered too big to conduct quickly, especially when one considers that the WOMAN (World Maternal Antifibrinolytic) Trial recruited 20 000 patients, and took six years to complete.[6] We, however, believe that we could conduct a 50 000 patient trial in Africa in two to three months, by ensuring absolute pragmatism. This requires a cluster randomized trial design. Providing standard of care in the control arm and a low risk intervention may mean that consent may be waived. We would require a large collaborative group of investigators who are not overly burdened by the number of patients needed for the success of the trial at each site. We propose 500 hospitals across Africa recruiting 100 patients each. Based on the ASOS data, it is expected that over 75% of the hospitals could complete trial patient recruitment within 10 weeks.[1] To ensure that it is not burdensome, the data collection needs to be lean; only capturing risk factors necessary for risk stratification, details of the intervention, and the simple outcome of mortality. The ASOS-2 Trial case record form will therefore be far leaner than ASOS. It is possible that this trial could be complete before the middle of 2019, if it ran in the first half of next year.

Finally, to ensure that knowledge translation is achieved, it is also time to embrace the power of mobile technologies. If mobile technologies could be used to establish the trial by providing trial site education and initiation, then these same mobile platforms could be used to communicate the outcomes to the entire African network following completion of the trial. It is possible then, that this platform could be used to educate the network to facilitate knowledge translation. We believe therefore, that we could move from a traditional 'six-year clinical trial model', to a pragmatic two-year model from hypothesis to knowledge translation by embracing pragmatism and employing mobile technologies. The ASOS-2 Trial could break the mould.

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