study by Koster and colleagues. This evidence comes from a very large number of RCTs and their meta-analysis and demonstrates that tranexamic acid safely reduces blood loss and transfusion associated with cardiac surgery.

Declaraton of interest
None declared.

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Safety of antifibrinolytic therapy during cardiac surgery and randomized controlled trials

Reply from the authors
Editor—We have read the thoughts of Drs Alston and McMullan regarding our article1 with great interest and agree with their reflections concerning the limitations of the results of observational studies. We have outlined this in a response2 to a previous letter and will avoid repetition in this regard.

However, the aprotinin tragedy, on which the final curtain has not fallen yet, demonstrates the limitations of the current concept of investigator-initiated or industry-sponsored randomized controlled trials (RCTs) to elucidate the safety profile of drugs in the multifaceted setting of complex cardiac surgery. The Blood Conservation Using Anti-fibrinolytics in a Randomized Controlled Trial (BART) was well published, but unfortunately not well performed. After review of all data and viewing imbalances in the grouping, Health Canada3 and the European Medicines Agency (EMA)4 lifted the suspension of aprotinin from the market, and have authorized the use of aprotinin only for basic coronary artery bypass grafting (CABG) surgery. Apparently, we all agree that effective blood conservation strategies are especially needed in the setting of complex cardiac surgery. Unfortunately, taking into account all available current data, both agencies expressed their concerns regarding aprotinin safety in complex cardiac surgery. Further studies into this matter are required. So, what does this mean in the end? The answer is evident: although aprotinin has been studied over decades in dozens of RCTs, and despite multiple sophisticated systematic reviews and meta-analyses, only drug effectiveness could be clearly demonstrated. These studies obviously failed to establish a clear safety profile, particularly in complex procedures. Complex cardiac surgery is performed using various different surgical and perfusion strategies. Additionally, patients most likely have numerous co-morbidities. Therefore, in this extremely heterogeneous setting, very high patient numbers are needed to clearly establish drug safety including effects on special organ systems.

A possible solution has been suggested by the EMA—the establishment of an international European register. Structured reporting of sophisticated sets of data from national key study centres may help to create such a large database. If these data produce suspicion of adverse drug effects, the pharmaceutical industry may be forced to initiate adequately powered RCTs to maintain authorization of the product in the special setting. Alternatively, industry and national insurance and health agencies may be asked to invest resources in a fund, which then is powered to perform adequate studies. The advantage of such a strategy would be that drug safety monitoring is more independent from the commercial interests of the pharmaceutical industry. This might guarantee that even older, well-established, and relatively inexpensive drugs such as tranexamic acid are continuously monitored.

The limitations of size and performance of the RCTs outlined for aprotinin also apply for tranexamic acid. Data, such as ours, show that, to date, the safety profile of tranexamic acid in the setting of complex surgery is inadequately studied. Therefore, we believe that an international register, not only for aprotinin, but also for the use of tranexamic acid in complex cardiac surgery, is badly needed. This seems to be all the more important as new alternative agents are not on the horizon. The development of possible successor drugs in cardiac surgery, such as the kallikrein inhibitor ecallantide and the antifibrinolytic agent MDCO-2010, has recently been stopped because of safety concerns.

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Colour-coded syringe labels: a modification to enhance patient safety

Editor—Medication errors during anaesthesia are being reported in the literature from time to time. Misidentification of a drug because of look alike/sound alike drugs, syringe swap, confusing, inaccurate, or incomplete drug labels have been found responsible for these errors on many occasions.\(^1\) Up to 86–94% anaesthesiologists have agreed for the need of standardized drug labels to decrease the incidence of medication errors.\(^2\)

Simple labels made from white adhesive tape or paper often fail to distinguish the different group of drugs, especially in critical situations. To prevent incidences of drug errors as a result of syringe and ampoule swap, Institute for Safe Medication Practices (ISMP) and American Society for Testing and Materials (ASTM) have recommended the standardized colour code for different anaesthetic drugs used in the operating theatre.\(^3\) Wassef and colleagues\(^4\) in a publication emphasized high-speed and accuracy of drug administration because of colour coding in simulated high-stress situations.

On the other hand, there have been problems with the colour-coding system. Colour differentiation has not been proved to prevent medication error completely.\(^5\) The colour label identifies a drug category, but it does not necessarily identify a specific drug in that group. Mix-ups occur because of selection errors among products within a class of drugs having different strength and action.\(^6\) Availability of the limited number of absolute identifiable colours and to remember these multiple or complex colour-coding systems is another limitation to colour-coding of drugs.\(^7\) Further, between 5% and 8% of the general male population is colour blind, although no authentic study has been done on colour blindness among the medical and paramedical personnel in anaesthesiology. To minimize the impact of colour blindness among anaesthesiologists, ASTM has proposed specific guidelines for the maximum contrast between text and background as specified in section 6.3.1 of ASTM International standards D6398.\(^8\)

In a letter published in the Anesthesia Patient Safety Foundation (APSF) newsletter, the author mentioned that anaesthesia providers may not read the label in critical situations because they only have time to recognize the colour and shape/size of the intended drug/syringe.\(^9\) Webster and Merry\(^10\) have recommended that colour coding should be used as a supplement to reading the label rather than substitute as the use of more than one cognitive cue (colour and text) always prevents the errors before they could occur.

Anaesthesiologists in many countries such as the UK, Australia, New Zealand, the USA, South Africa, Canada, and Denmark have been using standardized colour-coded syringe labels. Different forms of texts including drug name, concentration, date, and time of preparation have been printed on these colour labels for differentiation and identification of drugs. In India, no specific guidelines are available for the use of colour-coded syringe labels but we are using labels provided by a pharmaceutical company (Neon Labs, India). We often find difficulty in the identification of a particular drug within a group, for example, morphine, meperidine, and fentanyl, because of common colour and font size. We made a few modifications in the present colour-coded syringe labels to overcome these problems and to enhance the safety as follows (Fig. 1):

1. We divided the label into two sections in a ratio of 20% (white) and 80% (coloured).
2. In the coloured section, the generic drug name is printed in 12 font size, bold, Arial black letters all in upper case.
3. Below this, the concentration of the drug is printed in 12 font size, bold, Arial black letters all in lower case.
4. In the white section, either two or three letters from each drug name is printed in 24 font size, bold, Cooper standard black letters all in upper case.

Addition of these two/three big, bold, and capital letters of each drug against a white background as a second cue helped us to quickly identify a specific drug in a particular drug group by avoiding any element of colour blindness, thus further reducing the chances of drug error during anaesthesia because of syringe swap. We hope that anaesthesiologists will use these labels and share their experience with their fraternity.

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