

## Reply from the authors

### A scientific journals' duty of neutrality

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Editor—In 2013 Wikkelsø and co-workers published a conclusive literature review about fibrinogen concentrate (FBC) therapy in

bleeding patients in the Cochrane database.<sup>1</sup> They unambiguously stated that up to now there is not one large, unbiased

study with adequate statistical power that justifies an indication for the use of FBC beyond the negligible group of patients with bleeding due to proven selective hypofibrinogenaemia. In conclusion they said, 'Included trials are of low quality with high risk of bias and are underpowered to detect mortality, benefit or harm. More research is urgently needed.' The entire group had no conflicts of interest. In response Kozek-Langenecker and colleagues<sup>2</sup> published an Editorial in the British Journal of Anaesthesia (BJA), expressing their unhappiness about the cautious conclusions of the authors. We learned that Wikkelso and co-workers were not notified by the editors of BJA let alone asked for a comment, though the title of the respective editorial, 'Fibrinogen concentrate: Clinical reality and cautious Cochrane recommendation' explicitly and critically address this group and this particular publication. This basically means that a highly prestigious anaesthetic journal gave a single group a forum for their personal opinion. In our mind BJA hereby left its duty of neutrality, probably unintended, by leaving the criticised group out.

The authors in question<sup>2</sup> – all – correctly disclosed their conflicts of interest. The liberal use of fibrinogen concentrate (FBC) in settings without proven benefit has been repeatedly promoted by them and affiliated groups,<sup>3,4</sup> and we are worried therapists may feel pressurised that way. We believe that the frequent and increasing application of FBC all over the world and its impressive sales figures are the consequence of 'scientific marketing' rather than scientific evidence. To shine a light on the financial dimensions of the issue, we considered one of the suggested indications, open heart surgery, and a single population. Administering 2 g FBC to each of 100 000 patients undergoing cardiac surgery per year in Germany would be equivalent to a sales volume of nearly 75 million Euros (75 000 000). Against this background therapists would be wise to contemplate alternative opinions.<sup>1,5–7</sup>

Attitude to benefits and indications of a drug can be characterised as either 'reluctant' or 'enthusiastic'. Regarding the generous use of FBC we are reluctant. To our liking enthusiasm for a drug so expensive, whose effects are only suggested but not yet proven<sup>1,8–11</sup> is not comprehensible.

It is explicitly not our intention to impute dubious motives to the 'enthusiastic' authors or to question their integrity. However, we have to face that candid critics judge medical literature to be undermined with flaws and bias,<sup>12</sup> saying that 'competition and conflicts of interest distort too many medical findings'.<sup>13</sup> The large amount of 'enthusiastic' FBC-literature, entirely sponsored by producers of the drug will further inspire this negative attitude.

We are convinced our system should be challenged. Is it really enough to simply declare conflicts of interest without consequences? Is the COPE statement still effective? Langer and colleagues reviewed 297 guidelines drawn up by German specialist societies in the years 2009–2011,<sup>14</sup> concluding, 'Standards to deal with conflicts of interest are lacking and should be urgently developed.' It is the duty of scientific bodies, universities, IRBs, journals/editors to make every effort to limit bias in scientific

literature. Disclosure of authors' research-related perks and publishing companies' economic ties to drug companies could be an additional instrument to adhere to the path of virtue.

## Declaration of interest

None declared.

## References

1. Wikkelso A, Lunde J, Johansen M, et al. Fibrinogen concentrate in bleeding patients. *Cochrane Database Syst Rev* 2013; **8**: CD008864
2. Kozek-Langenecker S, Fries D, Spahn DR, Zacharowski K III. Fibrinogen concentrate: clinical reality and cautious Cochrane recommendation. *Br J Anaesth* 2014; **112**: 784–7
3. Sadeghi M, Atefyekta R, Azimaraghi O, et al. A randomized, double blind trial of prophylactic fibrinogen to reduce bleeding in cardiac surgery. *Braz J Anesthesiol* 2014; **64**: 253–7
4. Spahn DR. Severe bleeding in surgical and trauma patients: the role of fibrinogen replacement therapy. *Thromb Res* 2012; **130**(Suppl 2): S15–9
5. Stanworth SJ, Hunt BJ. The desperate need for good-quality clinical trials to evaluate the optimal source and dose of fibrinogen in managing bleeding. *Crit Care* 2011; **15**: 1006
6. Ozier Y, Hunt BJ. Against: Fibrinogen concentrate for management of bleeding: against indiscriminate use. *J Thromb Haemost* 2011; **9**: 6–8
7. von Bormann B, Suksompong S, Zander R. Therapy with fibrinogen concentrate: clinical and ethical considerations. *Transfusion* 2013; **53**: 1137–8
8. Aubron C, Reade MC, Fraser JF, Cooper DJ. Efficacy and safety of fibrinogen concentrate in trauma patients—a systematic review. *J Crit Care* 2014; **29**: 471–7
9. Lunde J, Stensballe J, Wikkelso A, Johansen M, Afshari A. Fibrinogen concentrate for bleeding - a systematic review. *Acta Anaesthesiol Scand* 2014; **58**: 1061–74
10. Bilecen S, Peelen LM, Kalkman CJ, Spanjersberg AJ, Moons KG, Nierich AP. Fibrinogen concentrate therapy in complex cardiac surgery. *J Cardiothorac Vasc Anesth* 2013; **27**: 12–17
11. Wafaisade A, Lefering R, Maegele M, et al. Administration of fibrinogen concentrate in exsanguinating trauma patients is associated with improved survival at 6 hours but not at discharge. *J Trauma Acute Care Surg* 2013; **74**: 387–3
12. Kicinski M. How does under-reporting of negative and inconclusive results affect the false-positive rate in meta-analysis? A simulation study. *BMJ Open* 2014; **4**: e004831
13. Ioannidis JP. An epidemic of false claims. Competition and conflicts of interest distort too many medical findings. *Sci Am* 2011; **304**: 16
14. Langer T, Conrad S, Fishman L, et al. Conflicts of interest among authors of medical guidelines: an analysis of guidelines produced by German specialist societies. *Dtsch Arztebl Int* 2012; **109**: 836–42