Finally, Javidroozi and colleagues[9] highlight statistical and clinical heterogeneity as limiting factors in our analyses. We performed multiple subgroup and sensitivity analyses to test the robustness of the primary analyses for the clinical setting, disease type, comorbidities, anaemia at baseline, the target of intervention, and trial quality. We showed that none of these factors contributed significantly to the analysis and heterogeneity of clinical outcomes. In fact, the most striking feature of the analysis was the consistent lack of any treatment effect for patient blood management on clinical outcomes.

The authors also identify the limitations of network meta-analyses to personalised medicine. We highlighted these points in the discussion. This does not, however, explain the observation that no single intervention had important clinical benefits.

In summary, the authors of these two letters do not, in our view, present evidence that undermines the validity of our findings. We, therefore, consider the title and manuscript to be an accurate representation of the available evidence.

Declarations of interest

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References

1. Trentino KM, Spahn DR, Mace H, Gombotz H, Hofmann A. Is patient blood management cost-effective? *Br J Anaesth* 2021; **126**: e7–9
2. Roman MA, Abbasciano RG, Pathak S, et al. Patient blood management interventions do not lead to important clinical benefits or cost-effectiveness for major surgery: a network meta-analysis. *Br J Anaesth* 2021; **126**: 149–56
3. National Institute for Care Excellence. *Costing statement: blood transfusion implementing the NICE guideline on blood transfusion (NG24)* 2015
4. Stokes EA, Wordsworth S, Bargo D, et al. Are lower levels of red blood cell transfusion more cost-effective than liberal levels after cardiac surgery? Findings from the TITRe2 randomised controlled trial. *BMJ Open* 2016; **6**, e011311
5. Reeves BC, Pike K, Rogers CA, et al. A multicentre randomised controlled trial of Transfusion Indication Threshold Reduction on transfusion rates, morbidity and health-care resource use following cardiac surgery (TITRe2). *Health Technol Assess* 2016; **20**: 1–260
6. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion* 2017; **57**: 1347–8
7. Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. *Transfusion* 2010; **50**: 753–65
8. Abraham I, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. *Transfusion* 2012; **52**: 1983–8
9. Javidroozi M, Hardy J, Ozawa S. Patient blood management interventions lead to important benefits for major surgery — a balanced view. *Br J Anaesth* 2021; **126**: e4–5
10. Kelley GA, Kelley KS. Statistical models for meta-analysis: a brief tutorial. *World J Methodol* 2012; **2**: 27–32

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Is patient blood management cost-effective? Comment on *Br J Anaesth* 2021; 126: 149–56

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Keywords: bleeding; cost-effectiveness analysis; economic evaluation; patient blood management; patient outcomes; transfusion

Editor—We read with interest the network meta-analysis by Roman and colleagues[1] describing the apparent lack of clinical benefit and cost-effectiveness of patient blood management (PBM) interventions. Whilst we have concerns with a number of items in their analysis, in this correspondence we would like to disagree with the authors' conclusions on the cost-effectiveness of PBM. The title implies that multiple cost-effectiveness analyses of PBM interventions were conducted, with none found to be cost-effective, and the abstract and the discussion sections reinforce this conclusion. This may lead readers to conclude that there are a number of cost-effectiveness analyses of trials investigating PBM as a standard of care when, in fact, a careful reading of the results section of this network analysis indicates that only 'one trial compared the cost-effectiveness of a PBM intervention to controls'.

Although incorrectly referenced in the article, the authors are referring to a cost-effectiveness analysis comparing a restrictive red blood cell transfusion strategy with a liberal transfusion strategy after cardiac surgery, based on the Transfusion Indication Threshold Reduction RCT.[2] This cost-effectiveness analysis compared costs and outcomes in a group of patients transfused a mean of two units of red cells per participant with a group receiving a mean of three units per participant. The costs collected included resource inputs from hospital admission to 3 months follow-up, with the difference in costs between groups mainly attributable to the difference in units of red cells transfused (mean difference: 1.00 unit). The clinical outcome measured was health-related quality of life. On reviewing this one cost-effectiveness analysis in detail, we found three reasons why we feel the conclusion PBM is not cost-effective is incorrect.

First, the authors mention in the results section of that cost-effectiveness analysis 'the point estimate for the base-case cost-effectiveness analysis suggested that the restrictive group was slightly more effective and slightly less costly than the liberal group and, therefore, cost-effective'.

Second, PBM is made up of 'care bundles of interventions'; therefore, a clinical trial investigating transfusion thresholds as a single therapy is not representative of PBM.[1,3] This is more properly seen as a study of transfusion management ('optimal blood use') rather than PBM.

Third, the cost-effectiveness analysis in question underestimates the cost of administering red blood cell transfusions. For example, the authors used a product acquisition cost of £123.31 for each unit of red blood cells and an administration cost of £22.00 for the first unit (49 min of nursing time and £6.00 of consumables) and £5.00 for subsequent units. This amount is substantially lower than published estimates and excludes many other cost inputs, such as laboratory costs. A systematic review on the cost of red blood cell transfusions in Western Europe highlighted that the cost of administering a transfusion is several times higher than the red blood cell product cost alone.[4] One study calculated the activity-based costs of administering a red blood cell transfusion were three to five times higher than the product acquisition costs.[5] Similar results have been found by others.[6] If these cost estimates were applied, the cost of administrating red blood cells (excluding the acquisition cost) would be approximately £270, not £22.00. Whilst the cost of transfusion can vary widely between institutions and countries, these data suggest the costs were greatly underestimated. This difference would likely significantly impact the results and conclusions of the cost-effectiveness analysis.

It is paradoxical that the results presented in this network meta-analysis may lead many clinicians and health economists to a very different conclusion than that made by the article title. In Figure 1 of the article, PBM interventions showed reductions in transfusions, reoperation for bleeding, and hospital and ICU length of stay, and 41 studies reporting the costs of PBM interventions 'all reported cost savings' (with the exception of cell salvage). Based on this, many would conclude that PBM interventions are likely to be cost-effective.

The article by Roman and colleagues[1] has drawn attention to the paucity of formal cost-effectiveness analyses in this field. Interestingly, one recent 5-yr study from Western Australia demonstrated a preoperative PBM clinic was cost-effective, potentially indicating that more cost-effectiveness analyses reporting the long-term results from comprehensive PBM programmes are on the horizon.[7] Such studies are needed, as the perception PBM is not cost-effective may represent a barrier to implementation, and therefore a barrier to improved patient care.

Declarations of interest

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References

1. Roman MA, Abbasciano RG, Pathak S, et al. Patient blood management interventions do not lead to important clinical benefits or cost-effectiveness for major surgery: a network meta-analysis. *Br J Anaesth* 2021; **126**: 149–56
2. Stokes EA, Wordsworth S, Bargo D, et al. Are lower levels of red blood cell transfusion more cost-effective than liberal levels after cardiac surgery? Findings from the TITRe2 randomised controlled trial. *BMJ Open* 2016; **6**, e011311
3. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion* 2017; **57**: 1347–58
4. Abraham I, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. *Transfusion* 2012; **52**: 1983–8
5. Shander A, Hofmann A, Ozawa S, et al. Activity-based costs of blood transfusions in surgical patients at four hospitals. *Transfusion* 2010; **50**: 753–65
6. Leahy MF, Mukhtar SA. From blood transfusion to patient blood management: a new paradigm for patient care and cost assessment of blood transfusion practice. *Intern Med J* 2012; **42**: 332–8
7. Trentino KM, Mace H, Symons K, et al. Screening and treating preoperative anaemia and suboptimal iron stores in elective colorectal surgery: a cost-effectiveness analysis. *Anaesthesia* August 2020. https://doi.org/10.1111/anae.15240

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Comparison between ultrasound-guided and digital palpation techniques for identification of the cricothyroid membrane: a meta-analysis

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Editor—Surgical cricothyrotomy is a potentially life-saving procedure in the 'cannot intubate/cannot oxygenate' scenario. As this procedure is not performed frequently, the conventional use of digital palpation to identify the cricothyroid membrane carries the risk of misidentification and failed cricothyrotomy.[1] The recent introduction of ultrasound-guided identification of the cricothyroid membrane could be a potential solution. A few published RCTs have shown the effectiveness of this ultrasound approach for improving the success rate of cricothyroid membrane identification compared with the conventional palpation technique.[2,3] However, most of these trials were small scale and conducted in different settings (e.g. emergency room or anaesthesia care unit),[4–8] and a number of studies failed to show significant differences in the accuracy of cricothyroid membrane identification between the two techniques.[1,3,4,8] Furthermore, there are concerns that the use of ultrasound technique may prolong the procedure time,[1,4,5,8] which can be life threatening in an emergency situation. We conducted this meta-analysis to analyse whether the ultrasound-guided approach is superior to the palpation technique in terms of procedural-related accuracy and procedure time.

Comparative trials that evaluated the accuracy of cricothyroid membrane identification by using ultrasound-guided or digital palpation techniques (i.e. ultrasound group *vs* palpation group) were identified from electronic databases, including Embase, MEDLINE, Cochrane Central Register of Controlled Trials, Google Scholar, and PubMed, from inception to June 2, 2020. No language restrictions were applied. A sensitive search strategy was conducted combining the following keywords with the