Comparison of predicted and real propofol and remifentanil concentrations in plasma and brain tissue during target-controlled infusion: a reply

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We thank White et al. [1] for their interest in our study [2] and their thoughts on the implications it may have for the clinical use of total intravenous anaesthesia.

Online Supporting information Table S1 provides details of the exact type of surgery and medications of the patients in our study.

When discussing the development of pharmacokinetic models from data, it should be acknowledged that a balance must be sought between model complexity and parsimony. Some very simple models function very well clinically. An example is the Gepts model for sufentanil, which contains no covariates, meaning that for the same target concentration all patients receive the same dose. There is probably a very large number of factors that influence the pharmacokinetics of any one drug. The authors have suggested adding comorbidities and the effect of interacting drugs as covariates. While this may superficially seem simple, it is far from it, as the complexity can become almost infinite. If, for example, one considers adding interacting drugs as a covariate, there are several drugs that can cause PK and PD interactions, and for each there are additional variable factors (such as class of drug, exact drug used, dose of drug, duration of use, route of administration and duration since last dose). Similar complexity applies to comorbidities. Even when a drug has been used and studied in a very large population, and includes large numbers of patients in whom information about the covariables is available, there will always remain pitfalls associated with under-fitting (how would one then accurately model the influence of an interacting drug or comorbidity on PK parameters), but also with over-fitting (adding a covariate to a model structure, having wrongly attributed some of the residual variation to that covariate).

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. Type of surgery and medications of the patients.

Comparing the environmental impact of inhalational anaesthesia and propofol-based intravenous anaesthesia

We wish to comment on the recent editorial by White and Shelton [1] and the subsequent response by Tapley et al. [2] discussing the environmental effects of inhalational anaesthetic agents. We agree with the former that in order to accurately compare the various modalities of general anaesthesia in terms of their environmental impact, the universal comparator of carbon dioxide equivalent should be used. Data on the carbon footprint for various aspects of healthcare are increasingly available, allowing us to more accurately judge their effect on the environment.

The NHS has now accelerated its commitments to achieving net-zero carbon emissions, aiming for net-zero direct emissions by 2040. This includes anaesthetic gas emissions and, as such, we as anaesthetists need to urgently reduce these emissions by seeking lower-carbon alternatives.

We have taken the data used by Tapley et al. in their letter and applied the comparator of dioxide equivalents to their calculations for energy usage and waste disposal. We have used their own estimates of electrical consumption, and their estimates of what an anaesthetist might use during a 7-h-anaesthetic using total intravenous anaesthesia (TIVA) – ten 50-ml syringes, eight 50-ml vials of propofol, two 100-ml saline bags, one TIVA giving set and one set of processed electro-encephalography (pEEG) disposables. We acknowledge though that 'real-world' TIVA disposable usage may vary from these estimates, and we have not accounted for the small amount of non-plastic and non-glass components of the disposable equipment.

Taking emissions factors from the Department for Environment, Food and Rural Affairs (DEFRA) [3], we converted the mass of plastic and glass waste produced (as

Table 1 Carbon footprint calculations for components of a 7-h anaesthetic using propofol/remifentanil total intravenous anaesthesia (TIVA) or inhalational anaesthesia (desflurane or sevoflurane)

	Global warming potential	Weight per 7-h anaesthetic	kg CO_2e per 7-h anaesthetic
Propofol LCA	21	0.004 kg	0.084
Remifentanil LCA	103	0.000004 kg	0.000412
Plastic production	3.25	0.443 kg	1.44
Glass production	0.895	0.472 kg	0.42
Waste incineration	1.179	0.915 kg	1.079
		Energy per 7 h anaesthetic	
Electricity usage (UK grid)	0.4	0.45 kWh	0.18
TIVA total			3.2
Desflurane	2540		820.2
Sevoflurane	130		69.9

CO_2e, carbon dioxide equivalent; LCA, life cycle assessment.