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Title: Reply to Michael Poullis about lung metastasectomy

Tom Treasure[a*]

Fergus Macbeth[b]

Lesley Fallowfield[c]

[a] Clinical Operational Research Unit, Department of Mathematics, University College London, London WC1H 0BT, UK

[b] Centre for Trials Research, Cardiff University, Cardiff CF14 4YS, UK

[c] Sussex Health Outcomes Research and Education in Cancer, University of Sussex, Sussex BN1 9RX, UK

*Corresponding author. Tom Treasure.
Postal address: 111 Rue du Lieutenant Ménard, 62164 Audresselles, France
Telephone +33 6 08 94 13 11
e-mail: tom.treasure@gmail.com

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We appreciate the attention paid by Michael Poullis(1) to our Editorial(2) but we disagree with his comments about PulMiCC, made without references or reasoning. There were no flaws in the study's design or conduct. Despite randomising fewer patients than planned, PulMiCC provided good evidence that surgery was unlikely to increase overall survival by a clinically meaningful amount.(3) Cancer teams had difficulty in maintaining equipoise. Although initial recruitment was good—512 patients—clinicians overrode the protocol when it came to randomisation. If they are "no further ahead in managing pulmonary metastasectomy" it is because they are reluctant not to treat lung metastases surgically, and like Poullis appear to disregard the available controlled trial evidence.(4)

The question that interests Poullis is different: is there a subgroup of patients whose tumour doubling times suggest that they are more likely to benefit from metastasectomy? We recall his hypothesis and elegant theoretical model.(5) It is well known that sequential imaging to find tumours with a longer doubling time will identify patients whose tumours are slower growing.(6) But these patients are likely to have a better prognosis anyway.

Unfortunately, biology is "messy" with some knowns and many unidentified unknowns, throwing any idealised model off course. A randomised trial would still be the only certain way to determine whether lung metastasectomy would improve survival. In addition to the factors used in PulMiCC to minimise differences, you would have to *balance* the trial arms for doubling time *and* randomise to account for the unknown factors.

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