**Sampson and Cookson’s commentary: what is it good for?**

**Claxton K, Lomas J\*, Longo F, Salas Ortiz A**

\*Corresponding author

James Lomas, Department of Economics and Related Studies, Alcuin College, University of York, York, YO10 5DD, UK. +44 (0) 1904 321464 james.lomas@york.ac.uk

Sampson and Cookson [1] question the relevance of the estimates reported in Martin et al [2] to informing judgements about important policy questions. They suggest that the specification is too “weak” to inform policy choice, that the estimates are based on “imprecisely specified inputs and unobservable outputs” and point to unspecified structural uncertainties that are not reflected in the reported confidence intervals.

Our purpose in this and other related work, has been to identify the causal effect on mortality, by disease area, of an exogenous but marginal change in NHS expenditure, i.e., a change in expenditure when all other relevant factors are the same and the only difference is the level of expenditure. This can be estimated from variation in *observed* expenditure and *observed* mortality by disease area across local geographies. As with all empirical analysis, there are potential sources of structural uncertainty that are not reflected in the reported confidence intervals. This was fully acknowledged in Martin et al. Moreover, potential sources of structural uncertainty have been extensively examined. Our estimates are robust to alternative methods of model selection, heterogeneity of effects across different types of NHS expenditure and across the mortality distribution[2], [3]. As well as passing all relevant statistical tests, they have also been found to be robust to changes in geography [4] changes in the identification strategy [5] tests of over fitting using panel data [6] and sensitivity analysis of the validity of instruments used for identification [7], [8]. Estimates of effect by disease area are also found to be consistent with directly estimated effects on all-cause mortality [2], [3], [6].

To restrict attention to only the estimated mortality effects would be to make an implicit and implausible assumption that health care expenditure, which has a substantial causal effect on observed mortality, has no effect on other aspects of outcome (survival and quality of life) and that expenditure in disease areas without a mortality indicator have no effects at all. Instead, our body of work has made two explicitly stated assumptions: i) that the estimated effect on the mortality burden of disease is a good surrogate for the effects on the QALY burden of disease in those disease areas with a mortality indicator; and ii) that the estimated effect of expenditure on mortality burden of disease can be extrapolated to measures of QALY burden in disease areas without a mortality indicator. These assumptions have been subject to an extensive structured elicitation exercise with both clinical and policy experts and were found to be, if anything, conservative with respect to the likely health effects, i.e., the marginal cost per QALY (MCPQ) is, if anything, likely to be lower [9], [10].

Therefore, this and related work currently provides the best estimate of the expected health effects of exogenous changes in available health care expenditure. Nevertheless, Sampson and Cookson reject their relevance to informing judgements about a range of important policy questions.

They start by confusing marginal and average productivity and appear to misunderstand how measures of average productivity are constructed. Estimates of the (MCPQ) reflect the health effects of a marginal and exogenous change in expenditure. Other research [11], [12] estimates changes in the average productivity by constructing indices of the growth in outputs and inputs. These are not directly observed but require the aggregation of disparate activity data often based on valuations from costing data. These are related but very different measures of productivity, e.g., a lower estimate of the MCPQ does not necessarily mean that average productivity or technical efficiency has improved [13]. Consequently, we have made no claims about the overall productivity of the NHS and how it has changed over time. Nonetheless, the consistency of estimates of MCPQ over 14 years gives some confidence that they can help inform unavoidable judgements about the effects of changes in expenditure.

Sampson and Cookson question whether estimates of the marginal cost per QALY provide an indication of the likely health opportunity cost when the National Institute for Health and Care excellence (NICE) approves new drugs for widespread use and suggest that attention should, instead, be restricted to pharmaceutical expenditure. The funding requirement associated with NICE guidance means that the approval of a new drug, which has additional costs, is an exogenous reduction in the resources available *across the entire system* at a local level. Our estimates of the MCPQ indicate the expected impact on health outcomes of these additional costs as other care across the NHS is displaced. With the exception of the Cancer Drugs Fund [14], there is no ring-fenced budget for pharmaceutical expenditure. However, even if expenditure were increased or reallocated (as is the case for the Cancer Drugs Fund) to accommodate the costs of new drugs, the same question would arise; what health benefits could be achieved if the additional or reallocated expenditure was instead made available to the NHS [15]. This is what Martin et al and related work has estimated.

Sampson and Cookson imply that we, and others, claim that the approval norm or ‘threshold’ used to judge cost- effectiveness by NICE should only reflect the estimates of MCPQ reported in Martin et al. We do not. Indeed, in other work we, and others, demonstrate that different thresholds are required for different types of technology to achieve dynamic efficiency [16], [17]. We do, however, comment on the related but separate positive empirical question of what is the expected impact of NICE guidance on the public health objective of the NHS.

Sampson and Cookson are quite right to point out that cost effectiveness ‘thresholds’ do not necessarily reflect evidence of the likely health opportunity costs. This is certainly true in the UK where the NICE threshold range of £20,000 to £30,000 per QALY was originally based on implied values from early guidance [18] . Since then NICE has increased the threshold to £50,000 or even £300,000 in some circumstances. The weight of causal evidence of the expected scale of health opportunity costs from Martin et al and related work means we can say, with some confidence that NICE guidance does more harm than good with respect to the public health objective of the NHS. For example, an additional £1m spent on a new drug, which was approved with an estimated cost per QALY gained of £30,000, would offer just over 33 additional QALY. However, the £1m reduction in available resources across the entire system would be expected to reduce health outcomes by 125 QALYs (using an estimate of the marginal cost per QALYs of £8,000). The expected ratio of harm to benefit would remain whether the actual budget impact was smaller or larger. Although for larger non-marginal budget impacts, the health opportunity costs would be expected to be larger and the ratio of harm to benefit greater [19].

Sampson and Cookson are correct to point out that health benefits as measured by QALY are not the only consideration. Nonetheless, understanding health opportunity remains important in making these trade-offs, but it also extends the assessment of opportunity costs beyond QALYs. For example, previous work has shown that health opportunity costs also fall on areas of high disease severity, displace wider social benefits [20] and increase health inequality [3], [21]. Recent work examining the evidence of the effect of payment on incentives for innovation has found that the NHS is commonly paying too much for innovation, and that the net harms from premium prices during patent protection are not compensated for when cheaper generics enter the market [22]. In many cases the NHS is paying more than the total long term value of innovations, imposing harm in the short and long run, while incentivising innovation at prices which will increase this harm [16].

The £15,000 per QALY adopted by the UK Department of Health and Social Care is their estimate of the likely health effects of marginal changes in NHS expenditure and is used as a measure of health opportunity costs in their impact assessments [23], [24]. This estimate has been informed by our earlier work [4] and since this value is used for policy purposes we compare our more recent estimates to it. The £70,000 per QALY in the HM Treasury Green book is their preferred estimate of the consumption value of QALY based on revealed preferences in value of a statistical life studies [25]. These are indeed two very different quantities. The former reflects an estimate of how much it cost the NHS to generate one additional QALY, the latter reflects the UK Treasury view of how much an additional QALY is worth in terms of private consumption. Since the NHS can generate QALYs much more cheaply than they are valued by Treasury, it suggests that (from the perspective of the UK Treasury) there is a case for increasing public expenditure on health care. More formally we can say that the marginal value of public funds (MVPF) [26] devoted to health care is high (£70,000/£15,000 per QALY = 4.67) and appears to far exceed any estimate of the marginal cost of raising public finance (generally taken to be approximately 1.4) [27], [28].

There are other estimates of the consumption value of a QALY, which use different methods [29] but all suggest that the MVPF devoted to health care exceeds the marginal cost of raising them. There are also other objectives and benefits of health care expenditure such as equity [3], [21] marketed and non-marketed production [20] and reducing demand for social care [30] among many others. Accounting for these additional benefits would only increase any assessment of the MVPF [27] and strengthen the case for an increase in expenditure.

However, decisions about public expenditure and its allocation are ultimately political ones and there is no such thing as an “off-the-shelf policy” prescription from any piece of empirical work. Nonetheless, it seems important that they should be informed by evidence such as it is. We believe academics have a duty to address pressing policy questions with the data that is currently available, rigorously testing the robustness of their estimates and explicitly stating the assumption required – this we have done. Our findings in Martin et al and their relevance to policy questions are neither misplaced nor over stated and our discussion is appropriately nuanced to help policy makers come to more evidence based judgements when considering unavoidable policy choices.

However, for those primarily concerned with the fortunes of the pharmaceutical sector, and the prices and market access that can be obtained for new drugs in the NHS, evidence of the scale of health opportunity costs will, quite understandably, be a concern. The body of causal evidence of the health effects of changes in NHS expenditure combined with evidence of the effect of payment on incentives for future innovation suggests that the prices paid for new pharmaceuticals is not just too high but are doing long term net harms to population health and are undermining a key objective of the NHS [16], [22].

References

[1] C. Sampson and G. Cookson, “Marginal cost per QALY estimates: What are they good for?,” *Health Policy (New York)*, vol. 142, p. 105036, 2024, doi: https://doi.org/10.1016/j.healthpol.2024.105036.

[2] S. Martin, K. Claxton, J. Lomas, and F. Longo, “The impact of different types of NHS expenditure on health: Marginal cost per QALY estimates for England for 2016/17,” *Health Policy (New York)*, vol. 132, p. 104800, 2023, doi: https://doi.org/10.1016/j.healthpol.2023.104800.

[3] S. Martin, K. Claxton, J. Lomas, and F. Longo, “How Responsive is Mortality to Locally Administered Healthcare Expenditure? Estimates for England for 2014/15,” *Appl Health Econ Health Policy*, vol. 20, no. 4, pp. 557–572, 2022, doi: 10.1007/s40258-022-00723-2.

[4] J. Lomas, S. Martin, and K. Claxton, “Estimating the Marginal Productivity of the English National Health Service From 2003 to 2012,” *Value in Health*, vol. 22, no. 9, pp. 995–1002, Sep. 2019, doi: 10.1016/j.jval.2019.04.1926.

[5] K. Claxton, J. Lomas, and S. Martin, “The impact of NHS expenditure on health outcomes in England: Alternative approaches to identification in all-cause and disease specific models of mortality,” *Health Econ*, vol. 27, no. 6, pp. 1017–1023, Jun. 2018, doi: 10.1002/hec.3650.

[6] S. Martin, J. Lomas, K. Claxton, and F. Longo, “How Effective is Marginal Healthcare Expenditure? New Evidence from England for 2003/04 to 2012/13,” *Appl Health Econ Health Policy*, vol. 19, no. 6, pp. 885–903, Nov. 2021, doi: 10.1007/S40258-021-00663-3/FIGURES/2.

[7] K. Claxton *et al.*, “Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. Appendix 2.,” *Health Technol Assess*, vol. 19, no. 14, pp. 267–293, 2015, doi: 10.3310/hta19140.

[8] R. Rashimin, J. Lomas, M. Sculpher, and M. Soares, “Examining the methods to estimate the marginal productivity of NHS expenditure,” *Health Economists Study Group*, 2023.

[9] M. O. Soares, M. J. Sculpher, and K. Claxton, “Health Opportunity Costs: Assessing the Implications of Uncertainty Using Elicitation Methods with Experts,” *Medical Decision Making*, vol. 40, no. 4, pp. 448–459, May 2020, doi: 10.1177/0272989X20916450.

[10] M. O. Soares, M. J. Sculpher, and K. Claxton, “Authors’ Response to: ‘Health Opportunity Costs and Expert Elicitation: A Comment on Soares et al.’ by Sampson, Firth, and Towse,” *Medical Decision Making*, vol. 41, no. 3, pp. 258–260, Feb. 2021, doi: 10.1177/0272989X20987222.

[11] A. Castelli, M. Chalkley, J. Gaughan, and I. Rodriguez Santana, “Productivity of the English National Health Service: 2017/18 update.,” *CHE Research Paper*, vol. 171, 2020.

[12] A. Arabadzhyan, A. Castelli, J. Gaughan, M. Anaya Montes, and M. Chalkely, “Productivity of the English National Health Service: 2020/21 update.,” *CHE Research Paper*, vol. 190, 2023.

[13] M. Paulden, J. O’Mahony, and C. McCabe, “Determinants of Change in the Cost-effectiveness Threshold,” *Medical Decision Making*, vol. 37, no. 2, pp. 264–276, Feb. 2017, doi: 10.1177/0272989X16662242.

[14] R. Grieve *et al.*, “Cancer Drugs Fund requires further reform,” *BMJ*, vol. 354, p. i5090, Sep. 2016, doi: 10.1136/bmj.i5090.

[15] NAO, “Investigation into the Cancer Drugs Fund.”

[16] B. Woods, J. Lomas, M. Sculpher, H. Weatherly, and K. Claxton, “Achieving dynamic efficiency in pharmaceutical innovation: Identifying the optimal share of value and payments required,” *Health Econ*, vol. 33, no. 4, pp. 804–819, Apr. 2024, doi: https://doi.org/10.1002/hec.4795.

[17] M. Paulden, “A Framework for the Fair Pricing of Medicines,” *Pharmacoeconomics*, vol. 42, no. 2, pp. 145–164, 2024, doi: 10.1007/s40273-023-01325-z.

[18] M. D. Rawlins and A. J. Culyer, “National Institute for Clinical Excellence and its value judgments.,” *BMJ*, vol. 329, no. 7459, pp. 224–7, Jul. 2004, doi: 10.1136/bmj.329.7459.224.

[19] J. Lomas, K. Claxton, S. Martin, and M. Soares, “Resolving the ‘Cost-Effective but Unaffordable’ Paradox: Estimating the Health Opportunity Costs of Nonmarginal Budget Impacts,” *Value in Health*, vol. 21, no. 3, pp. 266–275, 2018, doi: https://doi.org/10.1016/j.jval.2017.10.006.

[20] K. Claxton, M. Sculpher, S. Palmer, and A. J. Culyer, “Causes for concern: is NICE failing to uphold its responsibilities to all NHS patients?,” *Health Econ*, vol. 24, no. 1, pp. 1–7, Jan. 2015, doi: 10.1002/hec.3130.

[21] J. Love-Koh, R. Cookson, K. Claxton, and S. Griffin, “Estimating Social Variation in the Health Effects of Changes in Health Care Expenditure,” *Medical Decision Making*, vol. 40, no. 2, pp. 170–182, Feb. 2020, doi: 10.1177/0272989X20904360.

[22] B. Woods, A. Fox, M. Sculpher, and K. Claxton, “Estimating the shares of the value of branded pharmaceuticals accruing to manufacturers and to patients served by health systems,” *Health Econ*, vol. 30, no. 11, pp. 2649–2666, Nov. 2021, doi: 10.1002/HEC.4393.

[23] DHSC, “Statutory scheme to control costs of branded health service medicines,” 2020. Accessed: May 05, 2022. [Online]. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachm

[24] DHSC, “Accelerated Access Collaborative for health technologies DH Impact Assessment,” 2017. Accessed: Jun. 22, 2021. [Online]. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\_data/file/663094/Accelerated\_Access\_Collaborative\_-\_impact\_asssessment.pdf

[25] H. Treasury, *The Green Book: appraisal and evaluation in central government*. 2022. [Online]. Available: https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-governent/the-green-book-2020

[26] A. Finkelstein and N. Hendren, “Welfare analysis meets causal inference,” *Journal of Economic Perspectives*, vol. 34, no. 4, pp. 146–167, Sep. 2020, doi: 10.1257/JEP.34.4.146.

[27] F. Longo, K. Claxton, S. Griffin, A. Mason, S. Walker, and H. Weatherly, “Social Decision-Making Analysis: A General Approach to Inform Decisions on Resources in the Public Sector,” *Value in Health*, 2024, doi: https://doi.org/10.1016/j.jval.2024.01.015.

[28] G. Ruggeri, “The Marginal Cost of Public Funds in Closed and Small Open Economies,” *Fisc Stud*, vol. 20, no. 1, pp. 41–60, Mar. 1999, doi: 10.1111/J.1475-5890.1999.TB00003.X.

[29] L. Ryen and M. Svensson, “The Willingness to Pay for a Quality Adjusted Life Year: A Review of the Empirical Literature,” *Health Econ*, vol. 24, no. 10, pp. 1289–1301, Oct. 2015, doi: 10.1002/hec.3085.

[30] F. Longo, K. Claxton, S. Martin, and J. Lomas, “More long-term care for better healthcare and vice versa: investigating the mortality effects of interactions between these public sectors,” *Fisc Stud*, vol. 44, no. 2, pp. 189–216, Jun. 2023, doi: https://doi.org/10.1111/1475-5890.12322.

**Acknowledgements**

We would like to thank Mark Sculpher, Dan Howdon, Tony Culyer, Mike Paulden, Simon Walker and Stephen Palmer for discussions that informed the writing of this manuscript.

Declarations of interest: none

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.