3. Prosser LA, Neumann PJ, Sanders GD, Siegel JE. Reporting cost-effectiveness analyses. In: Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats TG, eds. *Cost-Effectiveness in Health and Medicine*. 2d ed. Oxford University Press; 2016.

4. Vanness DJ, Lomas J, Ahn H. A health opportunity cost threshold for cost-effectiveness analysis in the United States. *Ann Intern Med*. 2021;174(1):25-32. doi:10.7326/M20-1392

THE AUTHORS RESPOND

We thank Kohli-Lynch et al for their letter (published in the *JMCP* August 2021 issue) and their interest in our study,¹ which estimated the incremental value of the novel oral semaglutide added to existing antihyperglycemic treatment for people with type 2 diabetes mellitus at increased risk for cardiovascular disease.

Our results demonstrated incremental benefits in major adverse cardiovascular events (MACE) avoided, along with greater quality-adjusted life-years (QALYs) compared with background antihyperglycemic treatment alone. Oral semaglutide use plus background treatment resulted in better outcomes than background treatment alone or sitagliptin plus background treatment, and similar outcomes to liraglutide plus background treatment or empagliflozin plus background treatment with overlapping 95% confidence ranges for QALYs. Oral semaglutide was estimated to be cost-effective compared with liraglutide plus background treatment and to have incremental cost-effectiveness ratios (ICERs) between \$100,000 and \$150,000 per QALY vs sitagliptin plus background treatment and background therapy alone, but was unlikely to meet these thresholds compared with empagliflozin plus background treatment.

We agree with Kohli-Lynch et al that extended dominance is an appropriate approach when evaluating the

full landscape of treatment options to identify the most cost-effective option within a class of drugs and/or for a particular indication. We also agree that empagliflozin would be the preferred add-on treatment in this analysis, since it gains comparable (though lower on average) QALYs with oral semaglutide at a lower (~\$35,500) lifetime cost.

However, this was not the aim of our analysis. We used pairwise comparisons of oral semaglutide vs each chosen comparator instead of calculating ICERs relative to the next least costly option because our overall goal was to separately evaluate the novel agent, oral semaglutide, compared with the 4 existing comparators. We did not perform an overall cross-class evaluation so as to determine the ordering of treatment value; rather, we sought to inform decision makers as they consider the place of oral semaglutide in the current treatment landscape.

Regarding the threshold cost, we thank Kohli-Lynch et al for bringing this to our attention. The calculated oral semaglutide price needed to reach a \$100,000 willingness-to-pay per QALY threshold was due to (a) the fact that empagliflozin had lower QALYs compared with oral semaglutide in 73% of simulations and (b) the micro-simulation modeling approach used to calculate each price threshold. Each threshold value was back-calculated from individual runs (15,000 total) of individual patient-level simulations per comparison. In the case of oral semaglutide vs empagliflozin, the 95% credible range for incremental QALYs spans zero, with 27% of the simulations having lower QALYs for oral semaglutide, whereas oral semaglutide had fully positive incremental QALY credible ranges vs the other comparators. Therefore, cost-effectiveness plane quadrant crossing unfortunately makes a threshold price

difficult to simply calculate from the overall costs and outcomes of the 2 treatments.

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REFERENCE

1. Guzauskas GF, Rind DM, Fazioli K, Chapman RH, Pearson SD, Hansen RN. Cost-effectiveness of oral semaglutide added to current antihyperglycemic treatment for type 2 diabetes. *J Manag Care Spec Pharm*. 2021;27(4):455-68.