target steatosis, inflammation, or fibrosis are in clinical development. In early clinical trials, glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP)–GLP-1 receptor agonists have shown efficacy in treating MASLD. Multiagonists that include glucagon receptor stimulation, such as retatrutide, may provide additional benefits.[2] We agree that combining such analogues of nutrient-stimulated hormones with agents that target potentially complementary mechanisms may provide even greater activity against MASLD. Multiple such combinations — including the GLP-1 receptor agonist semaglutide and cilofexor (a farnesoid X receptor agonist), firsocostat (an acetyl-coenzyme A carboxylase inhibitor), and a fibroblast growth factor 21 analogue — are currently in phase 2 trials (e.g., NCT05016882).[3] THR-β agonists, such as resmetirom, may also prove to be contributors to effective combination therapy for MASLD.

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Preoperative Treatment of Locally Advanced Rectal Cancer

TO THE EDITOR: I congratulate Schrag et al. (July 27 issue)[1] for successful completion of the PROSPECT trial (Chemotherapy Alone or Chemotherapy Plus Radiation Therapy in Treating Patients with Locally Advanced Rectal Cancer Undergoing Surgery). A major disappointment was the low percentage of Black participants — 4% of the total. Although a wide racial gap persists between Black patients and White patients in colorectal cancer (with Black patients having a 20% higher incidence and 40% higher mortality), Black participation in cancer trials remains low. A major reason is lack of trust. This mistrust isn't solely related to historical ethical maltreatment such as the U.S. Public Health Service Untreated Syphilis Study at Tuskegee. Currently, a higher percentage of Black patients than White patients receive their index colonoscopy from physicians in the lowest quartiles of polyp detection rate.[2] Furthermore, Black patients are less likely to undergo minimally invasive surgery and sphincter-preserving surgery than non-Black patients, even after adjustment for patient- and hospital-related factors.[3,4]

Solutions are not straightforward. A common proposal is increasing racial diversity among clinicians. Studies suggest that Black patients are more receptive to recommended treatments in racially concordant physician interactions.[5] On review, it appears that none of the 25 authors of the PROSPECT report are Black. Until substantial changes in the diversity of the oncology workforce occur, one hopes that current physicians are fully trained in cultural competency and that Black primary care practitioners and nurses can help with accrual rates.

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TO THE EDITOR: We wish to highlight that, on the basis of the European Society for Medical Oncology (ESMO) guidelines[1] that are widely applied internationally, neoadjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or chemoradiotherapy represents overtreatment of a substantial proportion of the PROSPECT trial population, including the 38% of patients with T3N0 rectal cancer, who would have a low incidence of local recurrence with initial total mesorectal excision. The use of neoadjuvant FOLFOX comes at the cost of a high incidence of adverse events of grade 3 or higher (41% with FOLFOX vs. 23% with chemoradiotherapy).

It is also confusing to describe the PROSPECT trial population as having "locally advanced" cancer because the most locally advanced rectal tumors (T4 and N2) were excluded and many patients had earlier stage disease (e.g., T2N1 and T3N0 without threatened resection margins).

Although we welcome the PROSPECT results, we strongly caution against applying these findings to the whole trial population. We believe that more information is needed to accurately define the patient subgroup that is most likely to benefit from a discussion about neodjuvant FOLFOX as a new option that includes balancing its increased duration and acute toxic effects as compared with the side-effect profile of chemoradiotherapy.

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THE AUTHOR REPLIES: Shah highlights the low accrual rates among Black patients in the PROSPECT trial. Three factors may play a role. First, persons from historically marginalized groups can have a high threshold to accept random assignment to selective omission of a treatment with established effectiveness.

Second, institutional support or per-case reimbursement for National Cancer Institute (NCI)–sponsored trials is almost always less than the costs required to execute protocols. Participation in trials such as PROSPECT that lack a commercial sponsor is challenging for minority-predominant institutions with constrained resources. Hospitals that treat larger proportions of Black patients are less able to maintain the staff necessary to conduct trials.[1] Until this structural barrier is overcome, it will be challenging to achieve equity in enrollment. The NCI might provide greater subsidies to hospitals that serve high proportions of Black patients and other marginalized populations.

Third, the dearth of Black physicians who specialize in cancer is an impediment to equity in accrual of trial participants, a major criterion for authorship. Of the 15,012 hematologists–oncologists in the United States in 2021, only 525 (3.5%) were Black. Of the 2057 physicians in a hematology–oncology graduate medical education program in December 2022, only 79 (3.8%) were Black, which suggests a persistent deficit in the training pipeline.[2] Intensified efforts to diversify trial participants as well as the clinician workforce are necessary to ensure the generalizability of trial findings.

Sebag-Montefiore et al. note that on the basis of the ESMO guidelines, some patients who were enrolled in the PROSPECT trial would have undergone up-front surgery. Neoadjuvant chemoradiation was deemed to be the standard-of-care option for all PROSPECT participants in the absence of trial enrollment. Management of rectal cancer requires navigating between the Scylla of undertreatment and the Charybdis of overtreatment. Even with high-quality magnetic resonance imaging, when patients have surgery first,

some cancers will be upstaged and require postoperative chemoradiation, which is associated with greater toxicity than preoperative administration.[3] The 43% incidence of neoadjuvant adverse events from FOLFOX reflects a 12-week administration period, and the 21% incidence of neoadjuvant adverse events from chemoradiation reflects a 6-week period. Moreover, these incidences reversed postoperatively and by 1 year had converged.[4] Notwithstanding the recent ESMO guidelines, ongoing European clinical trials recruit patients with T3N0 disease such as those included in the PROSPECT trial to receive neoadjuvant regimens. Finally, the results of the PROSPECT trial hold true for the subgroup of patients with both T3N0 and node-positive tumors.

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Community-Acquired Pneumonia

TO THE EDITOR: In the review of community-acquired pneumonia by File and Ramirez (Aug. 17 issue),[1] no reference was made to the role of "Hospital at Home" to treat the condition. This paradigm of care provides hospital-level care in a patient's home as a substitute for traditional inpatient care for selected patients by bringing all the elements of hospital care to the home.

Management of community-acquired pneumonia in Hospital at Home has been compared with traditional hospital care in multiple trials and has shown equivalent clinical outcomes, better patient and caregiver care experience, lower rates of complications, and lower costs; community-acquired pneumonia is one of the most common diagnoses among patients treated in Hospital at Home.[2,3] The Covid-19 pandemic saw dramatic growth in care of acute respiratory conditions in Hospital at Home settings.[4]

Hospital at Home is well established and scaled in countries such as Australia, Spain, and France. In the United States, Hospital at Home has expanded to nearly 300 hospitals under the Centers for Medicare and Medicaid Services Acute Hospital Care at Home waiver.[5] Physicians who care for patients presenting with community-acquired pneumonia should know that Hospital at Home units are well suited to manage the condition with the expectation of outcomes equivalent to those seen with traditional hospital-based care.

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Dr. Montalto reports being a consultant to the Kenes Group and the Singapore Ministry of Health. Dr. Leff reports being a consultant to the Kenes Group and the Chartis Group and serving on clinical advisory boards to the Medically Home Group and DispatchHealth. No other potential conflict of interest relevant to this letter was reported.

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