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In Reply We thank Dr Andrea and colleagues for their comments on the postrandomization exclusions and withdrawals in our trial.[1] Figure 1 documented 40 of 837 (4.8%) patients included in our modified intention-to-treat analysis; of which, 28 (3.3%) were excluded postrandomization and 12 (1.4%) were withdrawn because we lacked permission to include their data.[1] The frequency of postrandomization exclusions and withdrawals was similar across treatment groups.

All 28 patients with postrandomization exclusions were ineligible. Three patients were mistakenly randomized twice and were excluded. Of the remaining 25 patients, 16 already underwent a spontaneous breathing trial (SBT) or were on SBT-equivalent settings, and 1 was extubated prerandomization. Of the 8 remaining patients, 5 received invasive mechanical ventilation for more than 2 weeks, 2 were already extubated, and 1 was receiving a level of positive end-expiratory pressure greater than 12 cm H_2O.

Of the 19 patients withdrawn from the trial, 7 consented to data retention and were included in the analyses. Three were enrolled under deferred consent, including 2 patients for whom consent was subsequently refused and 1 patient who died before written consent could be obtained. Of the remaining 9 patients, 4 were withdrawn because the consent form was improperly signed, 3 were withdrawn by family, and 2 were patient withdrawals.

The Cochrane risk-of-bias tool for randomized trials[2] states that analyses involving postrandomization exclusions of ineligible participants (when eligibility was not confirmed until after randomization and could not have been influenced by intervention group assignment) can be considered appropriate. Fergusson et al[3] highlight that patients who are randomized but did not receive a trial intervention can be excluded if the allocation cannot influence the likelihood that patients received the trial intervention. Furthermore, excluding ineligible patients from analyses who are mistakenly randomized does not introduce bias.[3]

We screened patients as soon as they could breathe spontaneously or trigger ventilators to minimize delays in the identification of patients who could undergo an SBT. We adopted strategies prerandomization (delayed randomization) and postrandomization (adjudication while blinded to assignment) to limit errors and minimize biased decision-making. Postrandomization, we excluded patients who already underwent an SBT or were on SBT-equivalent settings,[4] avoiding dilution of treatment effect induced by patients who already underwent an SBT. Also while blinded to patient assignment, we adjudicated ineligible patients at steering committee meetings and data and safety monitoring board meetings during the trial. Although it is not possible to specify a single threshold for exclusions and withdrawals below which the integrity of randomization is preserved, Schulz and Grimes[5] posit that losses of 5% or less, as occurred in our trial,[1] would not typically be concerning.

In a complex factorial trial of more than 800 participants, enrollment of some ineligible patients and patient withdrawals are inevitable and we appreciate the opportunity to provide details on how we handled such situations, addressing them as recruitment unfolded, and incorporating strategies to minimize them. We agree with Andrea and colleagues that investigators should adhere to the highest methodological standards of trial design and execution to minimize postrandomization exclusions and withdrawals.[3]

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Conflict of Interest Disclosures: None reported.

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Diagnosis and Treatment of Polycythemia Vera

To the Editor A recent Review of the diagnosis and treatment of polycythemia vera (PV)[1] focused on how to distinguish between primary and secondary erythrocytosis. However, there was no comment on the increasing incidence of erythrocytosis induced by use of sodium-glucose cotransporter 2 (SGLT2) inhibitors.

Based on the latest evidence, guidelines recommend use of SGLT2 inhibitors in most patients with diabetes, chronic kidney disease, and/or heart failure.[2] Post hoc analyses of clinical trials highlighted the increase of hemoglobin and hematocrit induced by these drugs. Gangat and Tefferi[3] first reported a large series of SGLT2 inhibitor–induced erythrocytosis as a differential diagnosis of PV. Indeed, these drugs can unmask hidden cases of PV. SGLT2 inhibitor–mediated erythrocytosis can be erythropoietin dependent or independent.[4]

In 2016, the World Health Organization lowered the threshold of hemoglobin for diagnosing erythrocytosis to 16.5 g/dL in men and 16 g/dL in women in an attempt to avoid overlooking the diagnosis of PV. However, some cases of PV may be missed in patients with diseases that reduce hemoglobin levels, such as chronic kidney disease. In these scenarios, starting SGLT2 inhibitors may cause an increase in hemoglobin to

levels characteristic of PV. With genetic testing, several patients have been diagnosed with PV after being treated with SGLT2 inhibitors.[3,4] Therefore, it is important to consider testing for the *JAK2* gene variant in patients with SGLT2 inhibitor-mediated erythrocytosis and symptoms suggestive of PV, such as pruritus, splenomegaly, leukocytosis, or thrombocytosis. Distinguishing primary from secondary erythrocytosis among patients treated with SGLT2 inhibitors is important to inform treatment of affected patients.

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To the Editor I appreciated the recent comprehensive Review of the diagnostic approach, risk stratification, and treatment options for PV.[1] The authors highlighted the use of exogenous androgens and erythropoietin as causes of secondary erythrocytosis. However, there was no mention of the use of SGLT2 inhibitors (canagliflozin, empagliflozin, dapagliflozin, ertugliflozin, and sotagliflozin) as a cause of drug-induced secondary polycythemia. Current guidelines strongly recommend an SGLT2 inhibitor in patients with type 2 diabetes and cardiovascular disease or for those at high risk of cardiovascular disease.[2] Due to their multiple health benefits, SGLT2 inhibitors are increasingly used not only for patients with diabetes but also for those with heart failure and chronic kidney disease. However, SGLT2 inhibitors are associated with erythrocytosis and increased hematocrit. The potential mechanisms behind erythrocytosis involve increased erythropoietin production through activation of hypoxia-inducible factor 2α and regulation of iron metabolism via hepcidin.[3] A 2021 meta-analysis of 40 randomized clinical trials with 21 050 participants demonstrated that SGLT2 inhibitors significantly increased hematocrit levels, especially at higher doses.[4] In a Mayo Clinic analysis of 100 consecutive patients without *JAK2* gene variants characteristic of PV who were treated with an SGLT2 inhibitor, the median increase of baseline hemoglobin and hematocrit was 2.5 g/dL (range, 0.4-7.3 g/dL) and 7.5% (range, 1.8%-21.1%), respectively.[5] Understanding that these increases are a known pharmacological response to SGLT2 inhibitors, rather than an indication of a pathological condition, is important to avoid unnecessary and expensive diagnostic tests. By informing clinicians and patients about this effect, we can prevent unnecessary stress for patients and their families and avoid unnecessary testing, allowing for more efficient use of health care resources and improving patient care and outcomes.

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In Reply The Letters in response to our recent Review on PV[1] from Dr Aoun and colleagues as well as Dr Ammatuna highlight emerging data on SGLT2 inhibitors as a cause of secondary erythrocytosis, which is particularly relevant given their increasing use for a variety of indications. Since first reported by Gupta et al[2] in 2020, many studies have reported *JAK2* variant-negative erythrocytosis after initiation of an SGLT2 inhibitor. In a single-center series of 100 patients, there was a median hemoglobin increase of 2.5 g/dL from baseline to a peak hemoglobin level of 18 g/dL that was recorded a median of 9 months after initiation of an SGLT2 inhibitor. Erythropoietin levels were inappropriately normal or elevated in all cases.[3]

Although SGLT2 inhibitors belong on the list of medications that can lead to erythrocytosis, along with exogenous androgens and erythropoietin-stimulating agents, it is important to note that this does not mean that an evaluation for PV should be deferred in patients taking these common medications. In fact, one of the earliest case reports of suspected

erythrocytosis secondary to an SGLT2 inhibitor was found to harbor the *JAK2* V617F variant.[4] Patients with concurrent leukocytosis, thrombocytosis, or symptoms concerning for PV, including aquagenic pruritus, splenomegaly, or thrombosis, should prompt evaluation for PV regardless of the use of an SGLT2 inhibitor.

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CORRECTION

Corrected Data Presentation: The Original Investigation titled "Nurse and Social Worker Palliative Telecare Team and Quality of Life in Patients With COPD, Heart Failure, or Interstitial Lung Disease: The ADAPT Randomized Clinical Trial,"[1] published January 16, 2024, has been updated to present the correct ethnicity data in Table 1 by study group and also to present the correct data for specialty care by group in the Results section of the text. This article was corrected online.

1. Bekelman DB, Feser W, Morgan B, et al. Nurse and social worker palliative telecare team and quality of life in patients with COPD, heart failure, or interstitial lung disease: the ADAPT randomized clinical trial. *JAMA*. 2024;331(3):212-223. doi:10.1001/jama.2023.24035

Incorrect Term: In the Patient Page titled "What Is Pericarditis?"[1] published in the March 4, 2025, issue of *JAMA*, an incorrect term was used. In the second paragraph of the section on diagnosis and treatment, both instances of "ECG" should have been "echocardiogram." This article has been corrected online.

1. Voelker R. What is pericarditis? *JAMA*. 2025;333(9):822. doi:10.1001/jama.2024.26822

Guidelines for Letters

Letters discussing a recent *JAMA* article should be submitted within 4 weeks of the article's publication. Letters received after 4 weeks will rarely be considered. Letters should not exceed 400 words of text and 5 references and may have no more than 3 authors. Letters reporting original research should not exceed 600 words of text and 6 references and may have no more than 7 authors. They may include up to 2 tables or figures but online supplementary material is not allowed. All letters should include a word count. Letters must not duplicate other material published or submitted for publication. Letters not meeting these specifications are generally not considered. Letters being considered for publication ordinarily will be sent to the authors of the *JAMA* article, who will be given the opportunity to reply. Letters will be published at the discretion of the editors and are subject to abridgement and editing. Further instructions can be found at http://jamanetwork.com/journals/jama/pages/instructions-for-authors. A signed statement for authorship criteria and responsibility, financial disclosure, copyright transfer, and acknowledgment is required before publication. Letters should be submitted via the *JAMA* online submission and review system at https://manuscripts.jama.com. For technical assistance, please contact jama-letters@jamanetwork.org.