

ria exist for evaluating the serotonin syndrome, these criteria may have varying usefulness when applied to different databases. The Hunter criteria were developed at a toxicology service using a data set of overdoses in which medical staff used a preformatted form that prompted staff to evaluate specific overdose symptoms.³ The criteria can be used for adverse drug reactions but have not been validated for that purpose.⁴ Because the serotonin syndrome reflects a clinical spectrum (mild, moderate, or severe), such strict criteria may lack appropriate sensitivity when applied to databases containing spontaneously reported adverse drug events from the public, such as the AERS.

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Clarifying Enrollment Procedures in the Trial of CT Screening for Lung Cancer

TO THE EDITOR: I would like to clarify the selection process leading to the inclusion of the patients in the previous report on survival in the trial of computed tomographic (CT) screening for lung cancer (Oct. 26, 2006, issue).¹ The process at 37 of the 38 participating sites was as follows. People interested in participating in the trial were first interviewed and were administered a precoded questionnaire by the study staff. The data from the questionnaires were entered, and data entry was checked, according to the standard protocol used at each center. The data were then transmitted electronically to the coordinating center. There, eligibility was assessed by means of a computer algorithm, and those who did not meet the eligibility criteria were excluded (Fig. 1). At the 38th site, the questionnaire was not administered, and therefore all the needed data were not recorded before enrollment.

For participants who received a diagnosis of lung cancer after baseline screening, study records were reviewed by the steering committee at one of its twice-yearly meetings. This review included confirmation of eligibility for the study — that is, asymptomatic status at the time of enrollment. If the symptoms resulting in exclusion had been present at enrollment but had not been recorded, the participant was excluded post hoc. This was the case for three patients among the 37 sites. Other features relevant to overall survival or survival itself were not used as a basis

for exclusion. At the 38th site, at which symptoms at enrollment had not been documented, eight participants were excluded on the basis of preexisting disqualifying symptoms, and one was excluded because pathological confirmation of lung cancer was not received by the coordinating center (Fig. 1). The symptomatic status of participants who did not receive a diagnosis of lung cancer was not reviewed, since this information had no bearing on the research question addressed by the study.

Except for the 12 patients excluded after enrollment (the 3 from the 37 sites at which the screening questionnaire had been administered and the 9 from the 38th site, at which the questionnaire was not administered), no patients were excluded from the study after they had been enrolled on the basis of the computer algorithm.

Inclusion of these 12 patients changes the 10-year survival rate for patients with lung cancer from the 80% (95% confidence interval [CI], 74 to 85) reported previously for 484 patients to 81% (95% CI, 75 to 86) for 496 patients. The other reported findings are not changed.

The article also reported that eight patients with clinical stage I lung cancer remained untreated and died within 5 years after diagnosis. However, only three had a pathological diagnosis of stage I lung cancer. Another four had stage I disease confirmed on CT, but further

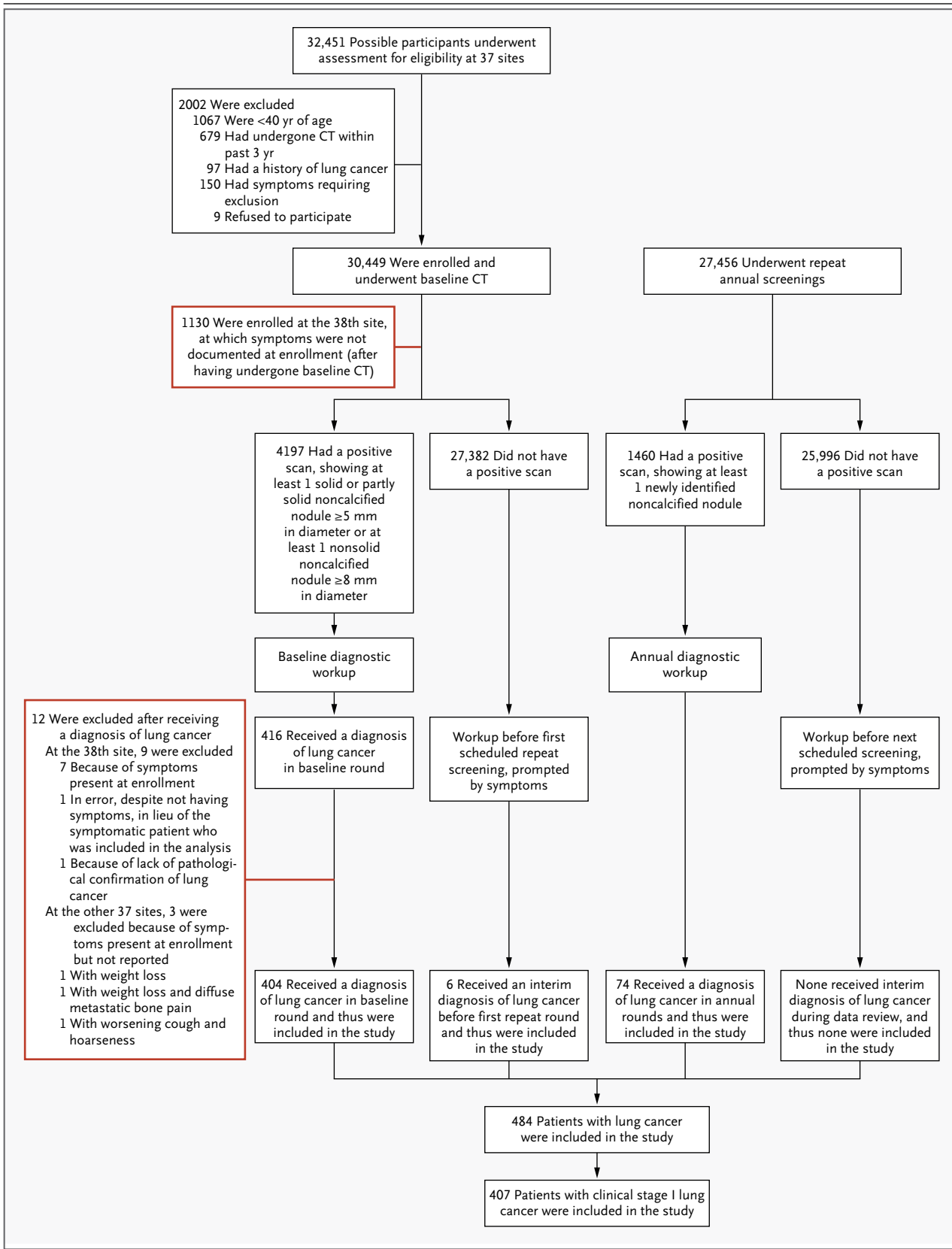


Figure 1 (facing page). Supplement to the Previously Published Figure 1, Showing the Numbers of Patients Enrolled and Evaluated at the 38th Site as Compared with the Numbers at the Other 37 Sites.

The "31,567 Asymptomatic participants [who] underwent baseline screening" in the previously published Figure 1 comprises the "30,449 [participants who] were enrolled and underwent baseline CT" at 37 sites plus the "1130 [participants who] were enrolled at the 38th site," minus the "12 [participants who] were excluded" (30,449 + 1130 - 12 = 31,567). CT denotes computed tomography.

workup was delayed despite repeated promptings, and pathological diagnosis was made only after the cancer had progressed to stage IV. The remaining patient had a solitary nodule on baseline CT that grew at a rate consistent with primary lung cancer, refused biopsy and treatment, and died of lung cancer 6 months after the last CT showing lung cancer. Thus, all eight patients died from lung cancer within 5 years after their actual or potential diagnosis during stage I.

Since, however, pathological diagnosis of lung cancer was required by the International Early Lung Cancer Action Project (I-ELCAP) investigators, I should have classified four of the

eight patients as having stage IV lung cancer and the remaining patient who had not received a pathological diagnosis during stage I as having an interim diagnosis. The remaining 483 patients received an antemortem pathological diagnosis of their lung cancer. Thus, the correct number of patients who were untreated and had a diagnosis of stage I lung cancer is 3, not 8, and the total number of patients who had clinical stage I lung cancer is 407, not 412 (Fig. 1).

These corrections increased the 10-year Kaplan–Meier survival rate for clinical stage I lung cancer from 88% to 90%. The overall Kaplan–Meier survival rate remained the same, since all patients with any stage of lung cancer were included in that analysis.

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