

# Standing physician orders did not improve guideline adherence in prescriptions to prevent febrile neutropenia

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Medical guidelines for the prophylactic use of colony-stimulating factors (CSFs) to prevent febrile neutropenia (FN) in patients starting chemotherapy are frequently not followed. Researchers from the SWOG Cancer Research Network, a clinical trials group funded by the National Cancer Institute (NCI), tested whether incorporating guideline recommendations as standing physician orders embedded in electronic medical records systems could improve prescribing practice for CSFs and thus lower the incidence of FN.

They found that the standing orders did not significantly change CSF prescribing patterns for patients on high FN risk chemotherapy, nor for patients on low FN risk therapy. For intermediate FN risk regimens, however, standing orders did significantly raise guideline adherence. Researchers also saw that standing orders did not significantly change the FN rate among patients on chemotherapy at any risk level.

The results will be presented in two poster sessions at the 2022 annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago on June 4 (abstracts 1525 and 1518).

The findings come from the SWOG S1415CD clinical trial, also known as the TrACER study, a multicenter, pragmatic (naturalistic) trial that involved 46 NCI Community Oncology Research Program (NCORP)

sites that were randomized to the intervention versus usual care, and an observational cohort group. The study was the first of this type of design—a highly novel design for cancer trials—to be performed by the NCORP.

The work was led by Scott D. Ramsey, MD, Ph.D., a SWOG investigator who is professor and director of the Hutchinson Institute for Cancer Outcomes Research at Fred Hutchinson Cancer Center, and by Dawn L. Hershman, MD, MS, a SWOG investigator who is deputy director for cancer care delivery and research, director of breast oncology, and co-leader of the Cancer Population Science Program at the Herbert Irving Comprehensive Cancer Center at Columbia University.

"There has been wide interest in the oncology community in the use of order entry systems to drive prescribing closer to practice guidelines," Ramsey said. "We found comparatively high rates of adherence for CSF prescribing and no significant impact for the entry system, suggesting that these systems should be used selectively if at all in oncology."

Febrile neutropenia—a fever coupled with a reduced neutrophil count—is a serious potential side effect of many types of chemotherapy. Colony-stimulating factors—special proteins that can signal the body to produce new white blood cells—can be used to treat or prevent it.

Standard-setting organizations such as the National Comprehensive Cancer Network (NCCN) have established clear practice guidelines, based on the FN risk level of the chemotherapy regimen, for when to prescribe CSFs prophylactically. Prior studies have found, however, that from 55 to 95 percent of prescriptions for CSFs are not in line with these guidelines.

The TrACER trial asked whether incorporating standing orders for when to use CSFs into computerized medical records systems could improve

prescribing practice and whether it could reduce the rate of FN in patients receiving chemotherapy.

For the study, SWOG researchers recruited 32 NCORP practices nationwide, cluster-randomizing them in a 3:1 ratio to an intervention arm that provided standing orders guiding CSF use versus a control arm that continued usual care. There were 14 additional clinics with pre-existing standing CSF order systems that served as an observational cohort comparison group. Together, these 46 NCORP centers enrolled almost 3,000 patients to the study over four years.

The study intervention changed each site's electronic medical record system to incorporate a standing order. Based on the NCCN guideline-indicated FN risk level (low, intermediate, or high) of the chemotherapy regimen that was to be started, the standing order explicitly stated that prophylactic CSF use was "recommended" or was "not recommend." Sites on the control arm made no change to their systems.

TrACER researchers found that in cases of patients on high FN risk regimens, the rate of prophylactic CSF use did not differ significantly between the intervention arm (89.2 percent) and the usual care arm (95.8 percent). The FN rates among patients on high-risk regimens were similar across the arms: 5.7 percent and 4.2 percent, respectively.

For patients on low FN risk regimens, the rates of prophylactic CSF use again did not differ significantly between arms: 6.3 percent on the intervention arm versus 5.5 percent on usual care. The FN rates for these patients were also similar across arms: 1.5 percent versus 0.8 percent. Notably, for both high-risk and low-risk regimens, rates of this side effect were substantially below rates reported in CSF use guidelines.

The trial included a sub-study to evaluate how effective prophylactic CSFs were for patients starting chemotherapy regimens that fell in the

intermediate FN risk category. The 24 NCORP sites on the trial's intervention arm were again randomized, with one-half using a standing order that recommended prophylactic CSFs for these patients and the other half a standing order that recommended they not be used for these patients.

Among these 24 sub-study sites, rates of prophylactic CSF use were significantly higher at sites where the standing order recommended their use with intermediate FN risk regimens (37.1 percent) compared to sites where the order recommended they not be used (9.9 percent). The FN rates among patients, however, were identical across these two sub-study arms: 3.7 percent on each arm.

Results from both the main TrACER study and the sub-study led researchers to conclude that standing orders related to primary prophylactic CSF use do not provide a benefit.

Additionally, lower-than-expected FN rates for patients on intermediate FN risk drug regimens led the team to conclude that prophylactic CSFs should not be used with these [patients](#).

The researchers noted that although the results provide important information about nonadherence to automated standing orders, they also provide data on FN rates that raise questions about current guidelines.

"We were surprised to see that the rates of febrile neutropenia were lower than expected in both arms," Dr. Hershman said, "and part of this may have been related to some selection factors or due to the fact that we only evaluated first-line therapy."

**More information:** [meetings.asco.org/abstracts-presentations/212455](https://meetings.asco.org/abstracts-presentations/212455)  
[meetings.asco.org/abstracts-presentations/209533](https://meetings.asco.org/abstracts-presentations/209533)

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