Introduction. Randomized controlled trials (RCTs) are usually considered the highest level of evidence for clinical practice. Patients assigned to control arm in RCTs should always receive the best available treatments to protect participants while also allowing for proper interpretation and applicability of study results. Here we analyzed RCTs published in oncology between 2017 and 2021, to describe the frequency of suboptimal control arms.

Methods. We identified phase III studies testing active treatments in patients with solid tumors among 11 major oncology journals. Each control arm was analyzed, and the standard of care was determined according to international guidelines and scientific evidences at accrual beginning and until accrual completion. We identified studies with suboptimal control arm from the beginning (type 1) and studies with an initially optimal control arm which became outdated during the accrual period (type 2).


Results. This analysis included 387 studies. 43 (11.1%) control arms were judged as suboptimal: 24 (6.2%) type 1 and 19 (4.9%) type 2. Suboptimality rates were higher in industry-sponsored compared to academic trials: 9.3% vs 1.9% for type 1 (p=0.003); 7.9% vs 0.6% for type 2 (p=0.001). Suboptimality rates were higher in studies with positive results: 8.1% vs 4.0% for type 1 (p=0.09); 7.6% vs 1.7% for type 2 (p=0.007).

Conclusion. A non-negligible percentage of control arms, even in journals with high impact factor, was suboptimal according to our criteria. Many patients were treated with suboptimal control treatments in those trials, and the interpretation and applicability of study results can be challenging.