

The association of GLP-1 receptor agonist use with survival and immune-related adverse events in patients receiving immune checkpoint inhibitors: A multi-institutional real-world analysis.

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly prescribed in patients with cancer for metabolic comorbidities and weight management. However, their impact on outcomes in patients receiving immune checkpoint inhibitors (ICIs) remains poorly characterized. We evaluated the association between concurrent GLP-1 RA use and survival and immune-related adverse events (irAEs) in a large real-world oncology population.

Methods: We conducted a federated electronic health record-based cohort study using the TriNetX Research Network (113 healthcare organizations). Adult patients with solid and hematologic malignancies treated with PD-1/PD-L1 or CTLA-4 inhibitors were identified. Patients were stratified by exposure to GLP-1 RAs. Propensity score matching was performed to balance demographics, comorbidities, and baseline clinical characteristics. Kaplan-Meier survival analyses and Cox proportional hazards models were used to compare overall survival at 3 and 5 years. Incidence of irAEs, including neutropenia and pyrexia, was assessed using risk and odds ratios. **Results:** A total of 3,807 patients receiving ICIs with concurrent GLP-1 RAs were matched to 173,423 patients receiving ICIs without GLP-1 RAs. At 3 years, GLP-1 RA exposure was associated with improved survival (hazard ratio [HR] 0.69, 95% CI 0.64–0.75; log-rank $p < 0.001$). This survival advantage persisted at 5 years (HR 0.71, 95% CI 0.65–0.76; log-rank $p < 0.001$). Survival probability at the end of follow-up was higher in the GLP-1 RA cohort across both time horizons. No statistically significant survival benefit was seen at the 1-year end point, (HR 0.65, 95% CI 0.59–0.71; log-rank $p = 0.521$). GLP-1 RA use was associated with a lower incidence of selected irAEs. At 3 years, neutropenia occurred in 5.7% of GLP-1 RA users versus 6.5% of non-users (OR 0.87, 95% CI 0.71–1.06), and pyrexia was significantly reduced (risk difference –2.5%, OR 0.73, 95% CI 0.61–0.87). Similar trends were observed at 5 years, with numerically lower neutropenia rates in the GLP-1 RA cohort (OR 0.84, 95% CI 0.68–1.02). **Conclusions:** In this large real-world analysis, concurrent GLP-1 RA use in patients receiving ICIs was associated with significantly improved long-term survival and a reduced burden of selected immune-related adverse events. These findings suggest a potential synergistic or protective effect of GLP-1 RAs in the immunotherapy setting and warrant prospective investigation to clarify underlying mechanisms and clinical implications. Research Sponsor: None.

Outcome	5-Year GLP-1 n/N (%)	5-Year No GLP-1 n/N (%)
Death	1091/3411 (32)	1545/3410 (45)
Malaise & Fatigue	552/2190 (25)	628/2160 (29)
Sepsis	444/3016 (15)	521/2964 (18)
Cachexia	119/3395 (4)	179/3368 (5)
Pneumonia	405/2811 (14)	494/2747 (18)

Impact of mRNA SARS-CoV-2 vaccination on CAR T-cell therapy outcomes in hematologic malignancies: A multi-center real-world analysis.

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Background: The clinical landscape of hematologic malignancies has been reshaped by Chimeric Antigen Receptor (CAR) T-cell therapies; however, their administration is intrinsically associated with immune-mediated toxicities, specifically cytokine release syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). The interaction between the immunogenic stimulus of mRNA SARS-CoV-2 vaccines and the systemic inflammatory milieu of CAR T-cell therapy remains undefined in real-world practice. This study aimed to delineate the impact of mRNA vaccination on survival outcomes and immunotoxicity profiles within this vulnerable patient population. **Methods:** We conducted a retrospective cohort study using the TriNetX global federated health research network. We identified patients with hematologic malignancies who received CAR T-cell therapy using ICD-10 and RXNORM codes. Patients were stratified into two cohorts based on whether they received mRNA-based SARS-CoV-2 vaccines. The cohorts were 1:1 propensity score-matched for age, sex, race, staging, and comorbidities. The primary outcome was all-cause mortality at 3 years, assessed with Hazard Ratios (HR). Secondary outcomes included CRS grade 1/2 and 3/4, and ICANS, both graded per the ASTCT criteria, and assessed with Odds Ratios (OR). **Results:** A total of 3,199 CAR T-cell patients (222 mRNA vaccine recipients and 2,977 without the mRNA vaccine) were identified. After 1:1 propensity score matching, 218 patients remained in each cohort. The 3-year mortality was significantly lower among mRNA SARS-CoV-2 vaccine recipients as compared to non-recipients (HR 0.608; 95% CI, 0.411 – 0.901). The mRNA vaccine group had a higher rate of CRS 1/2 (OR 1.577; 95% CI, 1.056 – 2.356). However, there were not enough cases of CRS 3/4 to compare the two cohorts. Furthermore, there was no significant difference in ICANS between the two cohorts (OR 0.8262; 95% CI, 0.522–1.37). **Conclusions:** In this propensity score-matched analysis of real-world data, mRNA SARS-CoV-2 vaccination was associated with a significantly superior long-term survival among CAR T-cell recipients. These findings build on early pre-clinical data related to SARS-CoV-2 mRNA vaccines demonstrating substantial increase in type I interferon, enabling innate immune cells to prime CD8⁺ T cells. The results provide early real-world clinical evidence and pave the way for prospective validation. Research Sponsor: None.

Key outcomes in CAR T-cell recipients.

Outcome	Effect of mRNA Vaccination (95% CI)	p Value
All-cause mortality (3-year)	HR 0.61 (0.41–0.90)	0.01
CRS grade 1/2	OR 1.58 (1.06–2.36)	0.03
ICANS (any grade)	OR 0.83 (0.52–1.37)	0.41

Frailty matters: Association of mFI-5 Index with odds of mortality, hospitalization, and toxicities with ADCs, BiTE, and CAR T-cell therapies in real-world data.

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Background: Targeted-delivery biopharmaceuticals such as antibody–drug conjugates (ADCs) or BiTE cell therapy are increasingly used in oncology. Recent meta-analyses demonstrate similar survival benefits of ADCs in younger and older patients across tumor types; however, baseline frailty predicts increased mortality, toxicity and hospitalization among patients receiving systemic anticancer therapy. While NCCN guidelines recommend frailty assessment for older adults prior to surgery, no such guidance exists for systemic treatments. **Methods:** We conducted a retrospective cohort study using TriNetX, a federated real-world data network with anonymized EHRs from hundreds of healthcare organizations. We included 46,674 patients with solid tumors, breast and bladder (solid ca) and 15,213 patients with hematologic cancers such as lymphoma, leukemia (heme ca) who initiated ADCs, BiTE-cell therapy, or CAR T-cell therapy. Cohort entry was defined as the first use of the drug class (index date). Toxicities, i.e. cardiotoxicity or cytopenia were outcomes if occurred within 30 days of index; patients without these events or with other outcomes served as comparators. Baseline frailty was measured using the modified Frailty Index-5 (mFI-5), derived from ICD-10 codes for hypertension (I10), care dependency (Z74), diabetes (E08–E13), COPD (J44), and heart failure (I50). Logistic regression estimated associations between frailty and each outcome, with p-values adjusted using the Benjamini–Hochberg false discovery rate. Mortality at pre-specified time points and hospitalization were fitted with a Cox proportional hazards model with frailty category as the primary exposure, controlling for age, and stratifying by cancer group and treatment. **Results:** In heme ca and solid ca, higher mFI-5 relative to mFI=0 was associated with significantly increased odds of toxicities with ADCs, including nausea, thrombocytopenia, anemia, cardiotoxicity, diarrhea, lung disease, and neutropenia (all $p<0.001$). In heme ca, higher mFI-5 was associated with significantly higher odds of toxicities, including anemia and cardiotoxicity (all $p<0.001$) with BiTE therapy and CAR T-cell. Results indicate a strong relationship between frailty severity and mortality risk (Table 1) and hospitalization after controlling for age and accounting for differences in baseline hazard across cancer groups and treatment strata. **Conclusions:** Assessing frailty severity through mFI-5 before initiating targeted systemic therapy in hematologic and solid tumors may help identify patients at increased risk of poor survival odds, adverse effects and facilitate shared treatment decision-making. Research Sponsor: None.

Hazard ratio of mortality relative to mFI=0.	
mFI-5 score	Hazard ratio of mortality with 95% CI
1	1.41 [1.34-1.47]
2	1.79 [1.69-1.9]
3	2.45 [2.24-2.69]
4+	2.51 [2.11-2.97]

Overall survival analysis of eSyM: A cluster randomized trial of an electronic patient-reported outcomes (ePRO)-based symptom management program.

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Background: ePRO monitoring can improve outcomes yet remains underutilized in routine cancer care. We conducted a pragmatic type II hybrid effectiveness–implementation trial using a cluster-randomized stepped-wedge design to assess an ePRO-based, EHR-integrated symptom management program (eSyM) across 6 health systems. Our prior analyses demonstrated that eSyM use, but not eSyM deployment, was associated with a significant reduction in emergency department visits and hospitalizations. Here, we report results of the overall survival (OS) analysis. **Methods:** Eligible patients were adults who received chemotherapy (CHEMO) or had surgery (SURG) for a gastrointestinal (GI), gynecologic (GYN), or thoracic (THOR) tumor from Jan 2018–Feb 2023. The outcome was OS 1 year after starting chemotherapy or postoperative discharge. The primary analysis compared patients treated pre- versus post-deployment of eSyM. A secondary analysis compared patients who were treated post-deployment and did versus did not use eSyM, where users were those who reported ePROs via eSyM at least once. Cox regression models accounted for sociodemographic, clinical, and health system factors. Analyses were stratified by treatment modality to account for heterogeneity of effect. **Results:** Health systems contributed data on 39,895 patients (selected characteristics in Table). After eSyM deployment, 45% of CHEMO and 53% of SURG patients used eSyM to report ePROs. Multivariable Cox regression analyses identified significant associations between eSyM deployment and OS for CHEMO (HR 1.11, 95%CI 1.03–1.21; $P=0.007$) and SURG (HR 0.86, 95% CI 0.76–0.98; $P=0.026$) patients. The adjusted absolute difference in 12-month OS probability for patients treated post-deployment vs. pre-deployment was -2.4% ($P<.001$) for CHEMO and 0.7% ($P<0.031$) for SURG. Comparing eSyM users vs. non-users from the post-deployment cohort only, OS was significantly better among CHEMO (HR 0.63, 95%CI 0.57–0.69; $P<0.001$; 12m OS diff 10.2%) and SURG (HR 0.58, 95%CI 0.49–0.69; $P<0.001$; 12m OS diff 2.8%) patients. **Conclusions:** Deployment of eSyM was associated with statistically significant but clinically marginal differences in OS. After eSyM was deployed, use of ePROs was associated with statistically significant and potentially meaningful improvements in OS. Considering that ePRO monitoring with eSyM decreases the need for acute care and may be associated with longer survival, strategies to improve adoption and implementation of ePRO-based symptom management programs may be warranted. Clinical trial information: NCT03850912. Research Sponsor: National Cancer Institute; 1UM1CA233080–01.

	CHEMO		SURG	
	Pre	Post	Pre	Post
# Patients	5149	7030	15917	11799
Age (median)	66	67	61	63
Female	54%	54%	72%	69%
Charlson comorbidity ≥ 2	8%	7%	6%	7%
GI, GYN, THOR	49%, 16%, 35%	45%, 17%, 38%	41%, 37%, 22%	43%, 33%, 24%
# Deaths	1098	2037	546	614
12-mo OS (adjusted)	72.7%	70.2%	94.7%	95.4%
12 mo OS (users, non-users)	–	76.8%, 66.6%	–	96.0%, 93.3%

Multicenter open-label randomized trial of the utility of electronic patient-reported outcome monitoring system in patients with advanced solid tumors (PRO-MOTE).

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Background: Randomized trials have suggested that electronic patient-reported outcome (ePRO) monitoring during systemic therapy may improve health-related quality of life (HR-QOL) and overall survival (OS) in patients with advanced cancer. However, evidence remains limited outside Western healthcare settings. Here, we evaluated the utility of ePRO monitoring for OS and HR-QOL in Japanese patients with advanced solid tumors receiving systemic therapy.

Methods: This multicenter, open-label, randomized trial enrolled patients aged ≥ 18 years with advanced solid tumors, ECOG performance status (PS) 0–2, and receiving systemic therapy. Patients were randomized 1:1 to ePRO monitoring plus usual care or usual care alone. In the ePRO monitoring group, patients completed weekly symptom monitoring using PRO-CTCAE. Predefined severity thresholds were applied, and symptom reports exceeding thresholds automatically generated e-mail alerts to the study physicians. Primary endpoints were OS and global health status (GHS) assessed by EORTC QLQ-C30. Superiority for GHS was tested at a two-sided α of 4%, and for OS at $\alpha=5\%$ if GHS was significant or $\alpha=1\%$ otherwise. Based on a linear mixed-effects model, 400 patients provided 91% power to detect a 5-point between-group difference in GHS. Target sample size was set at 500, allowing for 20% attrition. **Results:** Between June 2021 and February 2024, 501 patients were enrolled (control $n=250$; ePRO $n=251$), with a median age of 63 years (21–82) and ECOG PS 0/1/2 of 362/127/12. Major cancer types included colorectal (27%), lung (22%), breast (19%), and gastric cancer (17%). QOL analysis was conducted in 485 patients due to missing baseline data in 16. Questionnaire completion rates were high (QLQ-C30: baseline 97%, week 24: 92%). In the ePRO group, weekly PRO-CTCAE completion rates were 86% at baseline and 85% at week 24, generating 13,500 symptom reports and 1,918 alerts (14%), with a median of 4 alerts per patient. At the planned interim analysis, between-group difference in change in GHS over 24 weeks was -0.61 (95% CI -3.03 to 1.82 ; $p=0.625$), showing no superiority of ePRO monitoring. OS did not differ between groups (HR 0.91; 95% CI 0.70–1.19; $p=0.240$). Bayesian predictive power of eventual OS benefit was 0.3%, below the futility threshold of 10%, and the trial was terminated early. **Conclusions:** In contrast to previous reports from Western countries, PRO-MOTE failed to demonstrate the superiority of ePRO monitoring for GHS or OS in patients with advanced solid tumors receiving systemic therapy in Japan. Despite high feasibility, the clinical benefit of ePRO monitoring might depend on cancer type, treatment context, or healthcare system. Further subgroup and exploratory analyses are ongoing. Clinical trial information: NCT05931445. Research Sponsor: None.

Impact of remote therapeutic monitoring with patient-reported outcomes on hospitalization in real-world patients receiving therapy for metastatic solid tumors.

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Background: Remote therapeutic monitoring (RTM) using electronic patient-reported outcomes (ePROs) may help care teams respond earlier to patient needs and potentially avoid acute care events, but evidence from real-world practice is limited. This study evaluates the impact of using the Canopy ePRO-based RTM platform on acute care events. **Methods:** We studied 1,549 patients with metastatic solid tumor malignancies receiving systemic treatment at 5 community oncology sites between Jan 1, 2024 until July 20, 2025. Patients were invited to complete weekly ePRO symptom surveys. Symptoms that exceeded pre-specified severity thresholds triggered notifications to a dedicated triage nursing staff for evaluation and consideration of telephonic triage, urgent outpatient office evaluation or referral to the emergency department or hospital. Patients who enrolled and submitted ≥ 2 ePRO surveys within 45 days of first treatment were included in the RTM group, while those not enrolled or who did not submit 2 or more reports were in the control group. Hospitalization events were extracted from the Arkansas health information exchange. Inverse probability of treatment weighting was used to account for potential non-random selection of patients into the RTM group when performing statistical tests of difference, and achieved cohort balance in terms of age at index, time from first cancer diagnosis to treatment, site of cancer, sex, and race. **Results:** Over 18 months following first anticancer treatment through data cutoff date, 558 patients were in the RTM group compared to 991 patients in the control group. Among patients in the RTM group, 9.0% had a record of hospitalization compared to 13% in the control group, representing a 28% reduction (risk difference: -3.63, 95% CI -7.06 to -0.39, p: 0.032); 12% of patients in the RTM group had record of ED visit compared to 13% in the control group (risk difference: -1.77, 95% CI: -5.24 to 1.63, p: 0.310). The estimated cost savings per 1,000 patients/years utilizing RTM during treatment was \$3,192,789 for hospitalizations and \$93,330 for emergency department visits. **Conclusions:** RTM utilization with Canopy is associated with fewer hospitalizations and potentially fewer emergency visits compared to traditional outpatient management of patients with metastatic solid tumors, potentially reducing the cost of care. Prompt notification of patient symptoms resulting in preemptive treatment may help patients avoid acute care events. Research Sponsor: None.

Unweighted clinical and demographic characteristics.		
Characteristic	Enrolled & Active N = 558	Not Enrolled N = 991
Age at index	64 (55, 71)	70 (62, 78)
Sex - Female	313 (56%)	515 (52%)
Race/Ethnicity - White	484 (87%)	846 (85%)
Race/Ethnicity - Hispanic	28 (5.0%)	58 (5.9%)
Lung Cancer	131 (23%)	179 (18%)
Breast cancer	98 (18%)	219 (22%)
Colorectal cancer	88 (16%)	148 (15%)

Randomized, double-blind phase 3 trial of the fixed-dose combination fosrolapitant/palonosetron (HR20013) plus dexamethasone for prevention of nausea and vomiting in patients receiving moderately emetogenic chemotherapy.

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Background: Despite antiemetic guidelines, ~50% of patients (pts) receiving moderately emetogenic chemotherapy (MEC) still experience chemotherapy-induced nausea and vomiting (CINV), mainly in the delayed phase (DP, 24–120 h). HR20013 is a fixed-dose IV formulation providing dual NK1 and 5-HT₃ receptor blockade in a single dose and showed efficacy in preventing CINV following highly emetogenic chemotherapy in the phase 3 PROFIT trial (Zhou et al., JCO 2025). This study is the first pivotal phase 3 trial to evaluate the efficacy and safety of single-dose HR20013 plus dexamethasone (DEX) in the MEC setting. **Methods:** In this multicenter, randomized, double-blind, active-controlled phase 3 trial, chemotherapy-naïve adults with solid tumors scheduled for single-day MEC were randomized (1:1) to receive single-dose HR20013 (fosrolapitant 218 mg + palonosetron [PALO] 0.25 mg IV) or placebo + PALO prior to chemotherapy on D1. All pts also received oral DEX 7.5 mg on D1. Primary endpoint was complete response (CR; no emesis, no rescue therapy) in the DP (24–120 h). Key secondary endpoint was CR in the overall phase (OP; 0–120 h). **Results:** Of 706 randomized pts, the ITT population included 348 in the HR20013+DEX group and 352 in the PALO+DEX group. Baseline characteristics were well balanced. HR20013 showed statistically superior and clinically meaningful efficacy vs active control. CR rate in the DP was 79.0% (95% CI 74.4–83.2) with HR20013+DEX vs 61.4% (95% CI 56.1–66.5) with PALO+DEX (difference 17.8%, 95% CI 11.1–24.4; $P < 0.0001$). CR rate in the OP was 75.6% (95% CI 70.7–80.0) vs 59.9% (95% CI 54.6–65.1) (difference 15.7%, 95% CI 9.0–22.5; $P < 0.0001$). HR20013 also showed improved CR rate in acute phase (0–24 h; 92.5% vs 86.1%; $P = 0.0052$) and consistently showed higher rates across efficacy assessments including no significant nausea, complete protection, and total control in all phases. Time to treatment failure analysis favored HR20013 (HR 0.52, 95% CI 0.40–0.69). Functional Living Index-Emesis indicated that a greater proportion of pts receiving HR20013+DEX reported no impact on daily life in the DP (e.g., 90.2% vs 75.9% in the vomiting domain). The incidence of TRAEs were similar between groups (25.1% for HR20013 vs 21.4% for PALO). Most common TRAEs with HR20013 were constipation (8.9%), hypertriglyceridemia (4.0%), and hiccups (3.5%). Grade ≥ 3 TRAEs were infrequent (1.2% vs 1.4%). No new safety signals were identified. **Conclusions:** In pts receiving MEC, a single dose of fixed-dose combination HR20013 plus DEX was well tolerated and demonstrated superior efficacy in preventing CINV compared to the standard regimen of PALO+DEX, with improved patient-reported outcomes. This single-dose, dual-pathway antiemetic offers a more effective and convenient prophylactic option for MEC. Clinical trial information: NCT06554184. Research Sponsor: Jiangsu Hengrui Pharmaceuticals Co., Ltd.

Doubling cascade testing uptake for hereditary cancer syndromes: Results from a cluster randomized controlled trial of a registry-aided outreach approach.

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Background: Cascade genetic testing for at-risk relatives (ARR) is the most critical strategy for cancer prevention in families with hereditary cancer syndromes. Affected ARR can benefit from increased awareness and frequent screening to ensure cancers are detected at an early, treatable stage. Locally, uptake is persistently low at 6-13%, reflecting a prominent clinical gap. The current standard of care, which relies on passive proband-dependent communication to disseminate genetic information to ARR, is highly inefficient. We hypothesized that a novel, structured, registry-aided outreach model would improve the uptake rate of cascade testing in Singapore, and thus conducted a trial to address the effectiveness of this approach. **Methods:** We conducted a cluster randomized controlled trial at the National Cancer Centre Singapore comparing two arms. (1) Control arm: Proband-dependent communication. (2) Experimental arm: Proband-dependent communication with systematic outreach to ARR, facilitated by a family registry and executed by trained genetics personnel. This solution shares the burden of disseminating genetic results, ensuring ARR receive accurate information from a healthcare professional. The primary endpoint was the proportion of at-risk first-degree relatives who completed cascade genetic testing. **Results:** A total of 150 probands from unique families and 386 ARR were recruited from February 2022 to March 2025 in National Cancer Centre Singapore. In the experimental arm, 78/196 relatives (39.8%) attended pre-test genetic counselling compared to 38/190 relatives (20.0%) in the control arm. In the experimental arm, 71/196 relatives (36.2%) proceeded with cascade testing after pre-test counselling, whilst 37/190 relatives (19.5%) in the control arm underwent cascade testing. In our study, with the addition of the novel registry-aided outreach approach, the percentage of relatives who attend the pre-test genetic counselling session doubled, whilst those who eventually had cascade testing increased by 86%, demonstrating its clear superiority over the passive proband-dependent approach. **Conclusions:** Our trial proves that a systematic, healthcare professional-driven, registry-aided outreach is an effective strategy to overcome the barriers in cascade testing. The registry-aided outreach approach is a feasible, successful and scalable solution to the low uptake of cascade testing in Singapore. Implementing this approach is essential for realizing the full potential of genetic medicine to prevent cancers in high-risk families with hereditary cancer syndromes. Research Sponsor: National Medical Research Council; MH 095:003\008-290.

Impact of dedicated care coordination on access to multidimensional support services in young-onset colorectal cancer: A pragmatic trial.

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Background: The incidence of young-onset colorectal cancer (YOCRC) is increasing, and affected patients experience distinct challenges. YOCRC patients may benefit from a dedicated care coordinator that systematically assesses their unmet needs and facilitates referrals to multidimensional support services. **Methods:** In this pragmatic trial, we assigned newly diagnosed CRC patients aged <50 years who presented to a tertiary academic institution between 2023-2025 to usual multidisciplinary care, or usual care plus additional encounter(s) with a dedicated care coordinator as a part of the YOCRC program. Patient-reported concerns and distress were collected at initial presentation. The primary endpoint was the rate of utilization of support services designed to address multidimensional needs of YOCRC patients. Multivariable regression was performed to identify predictors of service utilization. **Results:** Among 1,250 YOCRC patients (mean age 42.8±6.0 years; 45.4% female; 77.3% white), 46.3% had rectal cancer. Emotional concerns were most common (41.0%), followed by physical (36.1%), practical (27.8%) and social (9.4%) concerns. The YOCRC coordinator successfully established contact with 604 individuals. Clinically significant distress (distress score ≥4) was reported by 27.4%, with no significant difference between groups (26.5% vs. 29.2%, p=0.34). Unmet service needs were reported by 39.1% in the intervention group, of whom 80.5% subsequently accessed corresponding support services. Patients with established contact with the YOCRC coordinator were more likely to access support services (Table 1, 72.5% vs.44.7%, p<0.001). On multivariable analysis, coordinator contact (aOR 1.48, 95%CI 1.22-1.80), rectal cancer diagnosis (aOR 1.36, 95%CI 1.13-1.62), and clinically significant distress (aOR 1.23, 95%CI 1.01-1.50) predicted greater multidimensional service utilization. **Conclusions:** YOCRC patients experience substantial emotional concerns and unmet needs. Integration of a YOCRC coordinator was associated with significantly increased utilization of multidimensional support services. This pragmatic trial supports a personalized, needs-driven care delivery model, that integrates patient-reported outcomes to further optimize targeted referrals. Research Sponsor: None.

Multidimensional support services accessed by YOCRC patients with vs. without established contact with YOCRC coordinator.

	Contact Established (n=604)	Contact Not Established (n=646)	p
Social Work	378 (62.6%)	288 (44.6%)	<0.01
Genetics	229 (37.9%)	126 (19.5%)	<0.01
Wound, Ostomy, Continence	196 (32.5%)	69 (10.7%)	<0.01
Supportive care	92 (15.2%)	77 (11.9%)	0.09
Oncofertility	77 (12.7%)	39 (6.0%)	<0.01
Integrative Medicine	73 (12.1%)	34 (5.3%)	<0.01
Nutrition	46 (7.5%)	40 (6.2%)	0.32
Psychiatry	41 (6.8%)	19 (2.9%)	<0.01
Adolescent and Young Adult Program	58 (9.6%)	29 (4.5%)	<0.01

The electronic frailty index used to identify high-risk older adults receiving chimeric antigen receptor T-cell therapy.

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Background: Chimeric antigen receptor T-cell therapy (CAR-T) has transformed outcomes in relapsed/refractory hematologic malignancies and can be effective in older adults. Frailty, a syndrome of vulnerability common in older adults, is associated with poor outcomes but difficult to measure in clinical practice. The relationship between frailty and CAR-T outcomes is poorly understood. **Methods:** We conducted a retrospective analysis of 260 patients age 65+ years receiving commercial CAR-T at Massachusetts General Brigham (MGB) for multiple myeloma and B cell non-Hodgkin lymphoma. We abstracted patient characteristics and clinical outcomes from the electronic health record (EHR). Using EHR data from the Research Patient Data Registry, we calculated the MGB-eFI, a validated electronic frailty score based upon a deficit accumulation approach to frailty. The MGB-eFI assesses 31 age-related health deficits and yields a score ranging 0-1 (< 0.1 is robust, 0.1-0.2 is pre-frail, 0.2-0.3 is frail, and > 0.3 is very frail). We then evaluated associations of the eFI (as a categorical variable of robust/prefrail versus frail/very frail) with cytokine release syndrome (CRS), immune cell-associated neurotoxicity syndrome (ICANS), overall survival (OS), and event-free survival (EFS) using univariate and multivariable logistic and Cox regression models controlling for covariates. **Results:** Among 260 patients (median age 73 years [range 65-91], 45% female), the most common CAR-T products used were liso-cel (35%), tisa-cel (18%), ide-cel (18%), cilta-cel (12%), and axi-cel (10%). With the eFI, 10% of patients were robust, 25% prefrail, 28% frail, and 37% very frail. In univariate analyses, frail/very frail was associated with worse OS (hazard ratio [HR] 1.66, $p = 0.013$), worse EFS (HR 1.78, $p = 0.001$), higher rates of ICANS (odds ratio [OR] 1.99, $p = 0.013$), and higher rates of grade 3+ ICANS (OR 4.49, $p = 0.003$). Frailty was not associated with risk of CRS. In multivariable analyses controlling for age, sex, CAR-T product, lactate dehydrogenase, ferritin, number of prior therapies, and bridging therapy use, frail/very frail by eFI remained associated with worse EFS (HR 1.69, $p = 0.005$) but not with OS (HR 1.37, $p = 0.150$). Frail/very frail was numerically associated with increased ICANS, but this did not meet statistical significance (OR = 1.71, $p = 0.090$). In a multivariable analysis controlling for age, CAR-T product, and ferritin (due to event sample size), frail/very frail was associated with higher rates of grade 3+ ICANS (OR 3.75, $p = 0.017$). **Conclusions:** Frailty measured using an automated eFI is associated with worse EFS and higher rates of high-grade ICANS, despite controlling for other clinical and patient factors. The eFI holds promise as a tool that if integrated into the EHR can help clinicians with risk stratification and CAR-T decision-making for older adults with hematologic malignancies. Research Sponsor: None.

Association of early cognitive decline with compromised delivery of adjuvant chemotherapy.

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Background: Cancer-related cognitive impairment (CRCI, “chemobrain”) is a common condition among patients (pts) receiving adjuvant chemotherapy (CT) and has been shown to negatively affect quality of life (QoL). However, the clinical relevance of early CRCI beyond symptom burden remains poorly characterized. We evaluated whether early CRCI is associated with compromised delivery of adjuvant CT, including reduced relative dose intensity (RDI).

Methods: This prospective study was conducted at the University Hospital of Larissa and represents an expanded analysis of a previously reported population with treatment delivery endpoints. Pts with early stage (ES) breast (BC) or colorectal (CRC) cancer scheduled to receive adjuvant CT containing taxanes or oxaliplatin, respectively, were eligible for this study (C1). Two control groups were included: ES cancer pts that were not eligible for adjuvant CT (C2) and age-matched healthy controls (C3). Eligibility criteria included age > 45 years and fluency in Greek; pts with pre-existing dementia or anxiety disorders were excluded. C1 pts were assessed at baseline and every 3 months (mo) up to 12 mo after CT initiation, while C2 and C3 were assessed at 3-mo intervals. CRCI was evaluated using the Greek Version of Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog). Early CRCI was defined as a ≥ 10 -point decline in total FACT-Cog score at 3 mo after CT initiation, in the absence of severe anemia (CTCAE grade ≥ 3). Treatment delivery outcomes included RDI (reduced RDI: < 85%), treatment delays, CT discontinuation, unplanned healthcare use and CT-related neurotoxicity (ntx).

Results: Overall, 164 pts were included in C1 (111 BC, 63 CRC), 61 in C2 (38 BC, 23 CRC) and 25 in C3. Early CRCI was observed in a substantial proportion of pts receiving adjuvant CT (99/164, 60%). Pts with early CRCI were significantly more likely to receive reduced CT dose intensity compared to those without CRCI (OR 3.27, 95% CI 1.34–7.98). Early CRCI was also associated with an increased risk of clinically relevant concurrent treatment-related ntx (CTCAE grade > 1; OR 4.05, 95% CI 1.81–9.08). CT discontinuation occurred more frequently among pts with early CRCI than among those without CRCI (12% vs 3%). In addition, these pts more frequently experienced treatment delays and unplanned healthcare use. These associations were independent of baseline ECOG PS. Early CRCI persisted beyond 3 mo in a substantial proportion of affected pts during follow up, while cognitive scores remained stable among controls. **Conclusions:** In this expanded cohort, early CRCI was associated with reduced RDI and higher rates of treatment discontinuation. Beyond its impact on QoL, early CRCI identifies a vulnerable subgroup of pts at risk for compromised treatment delivery and may represent a clinically actionable target for risk-adapted supportive strategies aimed at preserving curative-intent treatment intensity. Research Sponsor: None.

Clinical impact of baseline and peri-treatment concomitant medication exposure and polypharmacy on outcomes of immune checkpoint inhibitor therapy: A real-world pan-tumor analysis.

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Background: Immune checkpoint inhibitors (ICIs) have transformed cancer therapy, yet real-world patients frequently receive multiple concomitant medications that may influence treatment outcomes. These medications may alter the gut microbiome and modulate host immune function, impacting ICI efficacy and survival. The clinical effects of baseline and peri-treatment medication exposure on ICI outcomes remain incompletely characterized. **Methods:** We conducted a retrospective study of ICI-treated solid tumors at a tertiary academic center. Concomitant medications were captured at ICI initiation (baseline chronic exposure) and during a peri-treatment window (acute exposure, 30 days before or after ICI initiation). Drug classes included antibiotics, proton pump inhibitors, corticosteroids, NSAIDs, opioids, anti-coagulants, antiplatelets, statins, cardio-metabolic and psychotropic agents, and supplements. Polypharmacy was defined as ≥ 5 baseline medications. Outcomes included overall survival (OS), progression-free survival (PFS), immune-related adverse events (irAEs), and objective response using RECIST 1.1. Multivariable Cox proportional hazards models were used to adjust for confounding. **Results:** The cohort included 772 patients (60.1% male) with a median BMI of 25.8 kg/m² (IQR 23.0–29.1), and 66.2% had stage IV disease. On multivariable analysis for objective response (RECIST), baseline polypharmacy (≥ 5 medications) (OR 0.65, 95% CI 0.43–0.96; $p=0.033$), acute antibiotic exposure within 30 days of ICI initiation (OR 0.63, 95% CI 0.39–0.99; $p=0.049$), and metastatic disease (stage IV) (OR 0.51, 95% CI 0.26–0.98; $p=0.045$) independently predicted inferior response, while a higher number of immunotherapy cycles was associated with improved response (OR 1.06 per cycle, 95% CI 1.05–1.08; $p<0.001$). Acute antibiotic exposure within 30 days before ICI initiation was also independently associated with worse progression-free survival (HR 1.70, 95% CI 1.05–2.76; $p=0.031$). On multivariable Cox regression for overall survival, acute opioid exposure (HR 1.51, 95% CI 1.06–2.15; $p=0.023$), baseline polypharmacy (HR 1.78, 95% CI 1.19–2.65; $p=0.005$), and advanced disease (HR 2.78, 95% CI 1.73–4.47; $p<0.001$) were independently associated with worse survival, whereas a higher number of immunotherapy cycles (HR 0.96 per cycle, 95% CI 0.94–0.98; $p<0.001$) and prior surgery of the primary tumor (HR 0.51, 95% CI 0.33–0.79; $p=0.002$) were associated with improved survival. No baseline polypharmacy or specific medication exposure independently predicted the occurrence of irAEs. **Conclusions:** Concomitant medication exposure significantly impacts ICI outcomes, potentially through modulation of host immunity and the gut microbiome, supporting routine medication review at ICI initiation. Research Sponsor: None.

Telehealth use and end-of-life care outcomes among Medicare decedents with cancers.

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Background: Telehealth has become an increasingly important care modality following the COVID-19 pandemic. For patients with cancer approaching end of life (EOL), telehealth may be particularly relevant given their substantial symptom burden, need for frequent healthcare services, and declining functional status. Telehealth may facilitate convenient access to care and enhance EOL care quality. However, limited research has examined associations between telehealth use and EOL care among patients with cancer. **Methods:** We conducted a retrospective, population-based cohort study of EOL telehealth use using 100% Medicare Traditional Medicare (TM) and Medicare Advantage (MA) claims. We included beneficiaries aged 66+ years with cancer who died in 2020-2023 with continuous enrollment in TM or MA during the 12 months preceding death. Patients with cancer were identified by at least 1 inpatient or 2 outpatient claims with relevant diagnosis codes. Telehealth use during the first 6 months of the last year of life was identified using procedure codes and modifiers. We examined validated claims-based EOL care outcomes, including hospice use and place of hospice care, and indicators of potentially burdensome transitions (e.g., late hospice enrollment ≤ 3 days of death, multiple hospitalizations and emergency department visits ≤ 30 days of death). Separate multivariable logistic regression models assessed associations between telehealth use and EOL outcomes. **Results:** Among a total of 2,897,720 Medicare beneficiaries with cancer who died in 2020-2023, mean age was 79.8 years; 44.9% were female, 9.4% were non-Hispanic Black, and 1.7% were Hispanic. Telehealth use in the first 6 months of last year of life was 30.0% in 2020-2023, with utilization peaking in 2021 (47.1%). Among all decedents, 60.7% enrolled in hospice; among hospice users, 73.1% received hospice care at home and 18.6% enrolled ≤ 3 days of death. In the last 30 days, 11.2% and 13.4% experienced multiple hospitalizations and ER visits respectively. In adjusted analyses, telehealth use was associated with 2.38 percentage points (ppts, 95%CI=2.25 to 2.50) higher likelihood of any hospice use. Among hospice recipients, telehealth use was associated with 5.45 ppts (95%CI=5.31 to 5.60) higher likelihood of home hospice use. Telehealth use was also associated with 2.18 ppts (95%CI=-2.31 to -2.05) lower likelihood of late hospice enrollment. Associations with multiple hospitalizations and ER visits were small and statistically non-significant. **Conclusions:** Telehealth use among Medicare decedents with cancer was associated with higher hospice use, particularly home hospice, and a lower likelihood of late hospice enrollment, suggesting potential improvements in EOL care transitions. These associations may reflect enhanced care coordination and continuity facilitated by telehealth during the EOL. Research Sponsor: U.S. National Institutes of Health; K12AR084234.

Cancer during pregnancy and child health perspectives: Evidence from real-world data.

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Background: Pregnancy-associated cancer (PAC), is rare but increasingly encountered, likely reflecting delayed childbearing and the rising incidence of early-onset cancers. However, real-world evidence on short- and long-term offspring outcomes following PAC remains limited, particularly with respect to childhood chronic and inflammatory conditions. **Methods:** We conducted a retrospective cohort study using electronic medical records from Clalit Health Services, Israel's largest integrated healthcare system. Pregnancies among women aged 18–50 years between 2000 and 2024 were identified including PAC and non-PAC (controls). Annual incidence rates were calculated overall and by maternal age group. Short-term maternal, pregnancy, and neonatal outcomes were compared between PAC-exposed and cancer-free pregnancies using multivariable regression models. To assess long-term child outcomes, we included all identified PAC cases and their offspring and extended follow-up to capture chronic conditions (as documented diagnosis within electronic medical records) that typically manifest later in childhood. **Results:** The cohort included 3,561 PAC and 28,361 non-PAC participants. PAC incidence increased substantially over time, with highest incidence observed among women aged 35–45 years. Breast cancer was the most frequently diagnosed invasive malignancy during pregnancy. Gestational age at delivery was comparable between PAC and non-PAC pregnancies, although PAC-exposed offspring were slightly more likely to be born with low birth weight (HR 1.03; 95% CI 1.01–1.05; $P = 0.01$). In follow-up analyses, heterogeneous and outcome-specific differences in child health were observed. PAC exposure was associated with higher risks of inflammatory and immune-related conditions, including inflammatory bowel disease (HR 1.16; 95% CI 1.03–1.32; $P = 0.013$) and allergic conditions (HR 1.20; 95% CI 1.03–1.39; $P = 0.017$). Associations with asthma (HR 1.12; 95% CI 1.00–1.26; $P = 0.056$) and cardiovascular conditions (HR 1.16; 95% CI 1.00–1.26; $P = 0.057$) were also observed yet reached borderline statistical significance. All models were adjusted for maternal BMI, hypertension, diabetes, cardiovascular disease, age at delivery, socioeconomic status, depression, and child sex. **Conclusions:** The incidence of PAC has increased markedly over the past decade. Our findings suggest that cancer during pregnancy may be associated with increased risk of inflammatory/immune-related conditions in the born children. Ongoing analyses and preclinical models will further clarify the long-term clinical significance of these findings and their implications for maternal-child survivorship care. Research Sponsor: Israel Cancer Association; 01037248/2024; Israel Science Foundation (ISF); ISF 3287/25.

Real-world evidence of the association between primary insomnia and early-onset hormone-related cancers.

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Background: Although progress has been made in reducing overall cancer incidence, early-onset cancers have continued their troublesome rise. Similarly, primary insomnia increases in incidence and prevalence each year, and with it come likelihoods of circadian disruption, immune dysregulation, and altered hormone signaling. However, real-world data characterizing the association between insomnia and early-onset hormone-associated malignancies remains limited. **Methods:** We sought to conduct a real-world, retrospective cohort study using the TriNetX United States Research Database, a federated network of de-identified electronic health records (EHRs) from over 70 healthcare organizations, to examine this association. Adults aged 18–50 years with primary insomnia (ICD-10: F51.01) were compared with same-aged individuals without primary insomnia using a five-year lookback period from January 25th, 2021 to January 25th 2026. Propensity score matching adjusted for demographic and clinical confounders. Incidence of early-onset cancers diagnosed within five years of the index event was assessed during follow-up. Sensitivity analyses required a ≥ 1 -year lag between insomnia diagnosis and cancer onset. **Results:** 413,116 patients ages 18–50 were identified as having primary insomnia, whereas 18,437,709 patients ages 18–50 were identified as not having primary insomnia. Within 1–5 years of primary insomnia diagnosis, patients were more likely to develop early-onset breast cancer (RR 3.155, CI 2.863–3.477, $p < 0.0001$), uterine cancer (RR 1.988, CI 1.532–2.580, $p < 0.0001$), and ovarian cancer (RR 1.573, CI 1.276–1.940, $p < 0.0001$). Associations with early-onset prostate cancer (RR 1.676, CI 1.096–2.564) and testicular cancer (RR 1.243, CI 1.015–1.522) did not meet thresholds for significance. **Conclusions:** In this large, real-world cohort study, insomnia was associated with an increased risk of early-onset hormonal cancers more commonly affecting female patients. These findings suggest that sleep disruption may represent a clinically relevant, potentially modifiable risk factor in early-onset cancer risk stratification and warrants further investigation. Research Sponsor: None.

Longitudinal changes in patient-reported quality of life (QOL) and hope among early phase cancer clinical trial (EPCT) participants.

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Background: Few studies have explored associations of longitudinal changes in patient-reported outcomes (PROs) and clinical outcomes among EPCT participants. We sought to describe changes in hope and QOL over the first two months of EPCT participation and examine associations of these changes with clinical outcomes. **Methods:** We prospectively enrolled adults participating in EPCTs at Massachusetts General Hospital from 04/2021-01/2023. We assessed QOL (Functional Assessment of Cancer Therapy-General, with subdomains: physical wellbeing [PWB], emotional wellbeing [EWB], social wellbeing [SWB], functional wellbeing [FWB]) and hope (Herth Hope Index) at time of EPCT enrollment, at 1 month (M1), and at 2 months (M2). We used descriptive statistics and regression models to describe changes and explore associations of patient-reported QOL and hope with patient factors (age, diagnosis, performance status) and clinical outcomes (time on trial [TOT], ED visits, and hospitalizations). **Results:** We enrolled 195 of 251 eligible patients (78% enrollment) and 192 completed surveys (98% response, median age: 63, 57% female, 94% metastatic cancer, ECOG 0 = 47% and ECOG 1 = 58%), 152 (78%) had M1 data, and 114 (59%) had M2 data evaluable. Most common cancer types were gastrointestinal (34%) and breast (20%). Over time, mean QOL scores improved (baseline [B/L] [75], M1 [76], M2 [76]), and mean hope scores were unchanged (B/L [39], M1 [39], M2 [39]). At M1, older age was associated with improved QOL change ($B = 3.09$, $p = .031$), EWB change ($B = 0.94$, $p = .036$), and increased hope ($B = 1.22$, $p = .013$). Female sex correlated with improved FWB ($B = 1.15$, $p = .048$) at M2. Head & neck cancer was associated with decreased EWB ($B = -2.89$, $p = .010$) at M2. Improved QOL at M2 was associated with longer TOT ($HR = 0.97$, $p = .003$). Improved PWB was associated with lower risk of ED visits ($HR = 0.94$, $p = .011$) and hospitalizations ($HR = 0.95$, $p = .045$) at M1, as well as longer TOT ($HR = 0.94$, $p = .015$) and lower risk of hospitalizations ($HR = 0.93$, $p = .022$) at M2. Improved EWB was associated with longer TOT at M1 ($HR = 0.94$, $p = .001$) and at M2 ($HR = 0.89$, $p = .001$). Improved FWB was associated with lower risk of hospitalizations ($HR = 0.93$, $p = .023$) at M1, as well as lower risk of hospitalizations ($HR = 0.91$, $p = .043$) and longer TOT ($HR = 0.92$, $p = .016$) at M2. We found no significant associations of changes in hope scores with clinical outcomes. **Conclusions:** This prospective study examined longitudinal changes in QOL and hope among EPCT participants. We described changes in QOL and hope scores from time of EPCT enrollment through 1- and 2-month follow-up and identified factors associated with these changes. Improvements in QOL over time predicted higher TOT and reduced healthcare utilization. Future studies should assess and address longitudinal changes in PROs to enhance trial experience and optimize clinical outcomes. Research Sponsor: None.

Obesity paradox in gastrointestinal cancer patients on immunotherapy: A retrospective multi-institutional US cohort study.

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Background: Obesity is a well-established risk factor for different types of cancers, including gastric cancers. However, emerging research suggests its association with improved survival outcomes in cancer treatment, a phenomenon referred to as "the obesity paradox". Recent literature demonstrates this paradoxical effect in cancer patients receiving immunotherapy. We explored this effect across various types of gastrointestinal (GI) malignancies. **Methods:** De-identified data from the TriNetX database were used to identify adult patients (age > 18 yrs) with GI malignancies (hepatocellular, colorectal, pancreatic, upper GI (gastric and esophageal) who received immune checkpoint inhibitors (ICIs) between 2013 and 2025. Propensity score matching was performed to balance cohorts by demographics, comorbidities, ECOG and albumin level. The primary outcome was 5-year all-cause mortality, compared between patients with obesity (BMI ≥ 30 kg/m²) and those with normal BMI (18–24.9 kg/m²). The secondary outcome was the incidence of ICI-related adverse events (irAEs). Kaplan–Meier was used for time-to-event outcomes, differences were assessed using the log-rank test, and Cox proportional hazards using the TriNETx platform. **Results:** After propensity score matching, 4,956 patients were included in each cohort. Mean baseline characteristics were comparable between cohorts. The BMI > 30 cohort had BMI(kg/m²) 35.4 ± 5.4 , albumin(g/dl) 3.54 ± 0.61 , and mean ECOG 0.68 ± 0.96 while the normal BMI cohort had BMI 22.8 ± 4.5 , albumin 3.48 ± 0.62 , and mean ECOG 0.67 ± 0.83 . Obesity was associated with significantly improved all-cause mortality compared with the normal BMI group (26.8 months vs 13.9 months; hazard ratio [HR], 0.7 [0.67–0.74]). Survival probabilities at 1 year (63.7% vs 52.6%), 3 years (46.2% vs 31.9%), and 5 years (39.1% vs 25.4%) were higher in the BMI ≥ 30 kg/m² cohort compared with the normal BMI cohort. Among GI cancer subtypes, the strongest associations between obesity and improved survival were observed in colorectal (HR 0.67 [0.62–0.72]) and pancreatic cancers (HR 0.66 [0.56–0.76]), with more modest effects seen in hepatocellular (HR 0.78 [0.72–0.84]) and upper GI cancers (HR 0.71 [0.62–0.80]). There were no significant differences between cohorts in the incidence of pneumonitis (HR 1.12 [0.80–1.57]), GI (HR 1.07 [0.98–1.17]), thyroid (HR 1.05 [0.97–1.14]), or cutaneous (HR 1.10 [0.99–1.23]) irAEs. **Conclusions:** In this analysis of 9,912 patients with GI malignancies treated with immunotherapy, higher BMI was associated with improved survival. Confounding by disease burden was partially addressed through adjustment for ECOG and albumin. These findings may reflect obesity-related immune modulation, as preclinical studies suggest leptin-mediated upregulation of PD-1 expression. However, further prospective studies are needed to validate and define these results Research Sponsor: None.

GLP-1 receptor agonist utilization and survival outcomes in a large U.S. community oncology cohort.

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Background: GLP1 use has increased with 12.4% of U.S. adults reported using these treatments, driven in part by the 2021 approval of semaglutide for chronic weight management without diabetes. Beyond established metabolic benefits, emerging preclinical and observational data suggest potential anticancer effects of GLP1 therapy. However, no study to date has characterized GLP1 use among cancer patients treated in a large-scale population. This study provides an essential step towards describing real-world world GLP1 treatment patterns and clinical outcomes. **Methods:** Structured EHR data from The US Oncology Network were used to identify GLP1 users (dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, and tirzepatide) and nonusers between January 2021 and October 2024, with follow-up through October 2025. Overall survival (OS) was assessed from initial cancer diagnosis to death from any cause. Nonusers were matched to GLP1 users by cancer type and diagnosis year. To address immortal time bias, each nonuser was assigned the matched user's GLP1 medication start date as the anchor date; nonusers who died or were lost to follow-up prior to that date were excluded. Multivariable Cox proportional hazards models evaluated factors associated with OS among patients diagnosed with breast, prostate, lung, hepatocellular, or renal cancer. **Results:** A total of 1,121 GLP1 users and 471,580 non GLP1 users with cancer were identified. GLP1 users had a median age of 63 years, were 63% White, and 69% had BMI ≥ 30 kg/m² semaglutide was the most commonly used agent (64%). Non GLP1 users had a median age of 68 years, were 61% White, and 30% had BMI ≥ 30 kg/m². Among GLP1 users, 74% were prescribed GLP1 therapy after initial cancer diagnosis, of those 7% after metastatic diagnosis; the most common cancers were breast (27%) and prostate (13%). OS at 24 months was higher among GLP1 users versus nonusers for both breast cancer (97.9% [95% CI 93.7–99.3] vs 92.6% [92.4–92.8]) and prostate cancer (97.9% [93.7–99.3] vs 92.6% [92.4–92.8]). After adjustment for age, BMI, stage, and cancer type, GLP1 use was significantly associated with improved OS (HR 0.58, 95% CI 0.40–0.84; $p = 0.0036$). **Conclusions:** In this large real-world cohort, GLP1 use was most frequently observed among younger patients with obesity and was commonly prescribed after cancer diagnosis, with semaglutide accounting for the majority of prescriptions. Breast and prostate cancers were the most prevalent malignancies among GLP1 users, reflecting early adoption across common solid tumor types in routine practice. Despite limitations inherent to structured real-world data, including potential underreporting of GLP1 exposure, GLP1 use was associated with improved OS compared with nonuse, supporting the need for future studies using robust causal inference approaches. Research Sponsor: None.

Temporal trends in oncology clinical trial complexity and duration: A retrospective analysis of 5,261 industry-sponsored trials.

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Background: Clinical trial complexity has been cited as a contributor to rising drug development costs and increasing trial duration. We aimed to quantify multidimensional oncology trial complexity and describe temporal trends. **Methods:** We conducted a retrospective analysis of industry-sponsored interventional drug and biological oncology trials from the Aggregate Analysis of ClinicalTrials.gov (AACT) database, restricted to concluded trials initiated 2007–2017 for post-FDAAA reporting consistency and adequate follow-up. Five complexity dimensions were derived using principal component analysis: protocol (eligibility criteria, arms, outcomes), operational (sites, countries, planned enrollment), disease (MeSH breadth), intervention (modality count), and governance (team structure). Temporal trends were analyzed across completed trials only; Pearson correlations between dimensions and duration/early termination were calculated across all concluded trials. Trends were estimated using linear regression on yearly medians stratified by phase. **Results:** Among 6,752 concluded oncology trials (78% completion rate), temporal trends were analyzed in the 5,261 completed trials. Protocol complexity significantly increased (+0.083 SD/year), driven by total eligibility criteria (+0.56/year), secondary outcomes (+0.35/year), and exclusion criteria (+0.35/year). Operational complexity showed a significant increasing trend (+0.014 SD/year), with facilities increasing +0.51/year. Overall trial duration significantly increased (+16.7 days/year), with Phase 1 trials increasing +18.2 days/year and Phase 2 trials +18.4 days/year, while Phase 3 trials showed a non-significant trend (+20.7 days/year). Across all trials, protocol complexity was weakly correlated with early termination ($r=0.03$) and duration ($r=0.14$). Operational complexity showed the strongest correlation with duration ($r=0.36$). **Conclusions:** Among concluded oncology trials, protocol and operational complexity are significantly increasing, particularly eligibility criteria burden, endpoint multiplicity, and study scale. Trial duration is significantly increasing for early-phase trials, driven primarily by operational complexity. Research Sponsor: None.

Operational and protocol trends in oncology trials.

Metric (median)	2007 Value	2017 Value	Slope/Year	P-value
Total I/E Criteria	15	22	+0.56	<0.001
Secondary Outcomes	4	7	+0.35	<0.001
Exclusion Criteria	8	12	+0.35	<0.001
Inclusion Criteria	6	9	+0.22	<0.001
Total Outcomes	8	11	+0.30	<0.001
Number of Sites	6	12	+0.51	<0.001
Phase 1 Duration (days)	1080.5	1220	+18.2	0.010
Phase 2 Duration (days)	1249	1347	+18.4	0.028
Phase 3 Duration (days)	1583	1673	+20.7	0.214
Overall Duration (days)	1247	1378	+16.7	0.006

Observed medians are reported for 2007 and 2017. Slopes and p-values were derived from linear regression on yearly medians.

A machine learning-enhanced analysis of temporal trends in biomarker-based eligibility restrictions in oncology clinical trials.

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Background: The adoption of biomarker-based eligibility criteria reflects the evolution of precision oncology, but temporal trends and predictors of biomarker restrictions are unclear. Understanding these patterns is essential for optimizing trial design and ensuring equitable patient access to investigational therapies. We used machine learning and natural language processing to analyze biomarker restriction trends across oncology trials. **Methods:** We analyzed all 54,985 oncology interventional trials from ClinicalTrials.gov from 2010–2024. Biomarker restrictions were identified using curated term lists plus NLP-based classification (TF-IDF vectorization with logistic regression). We developed complementary machine learning modules for emerging biomarker discovery using named entity recognition, requirement type classification (inclusion/exclusion/stratification), and eligibility complexity scoring via text feature engineering. Statistical analyses included logistic regression with Wilson score confidence intervals and Benjamini–Hochberg FDR correction. **Results:** Biomarker-restricted trials increased from 20.8% (2010) to 31.2% (2024), representing a 1.5-fold increase over 15 years (OR per year: 1.046, 95%CI: 1.041–1.050, $p < 0.001$). Industry sponsorship (OR: 1.88, 95%CI: 1.80–1.97) and NIH sponsorship (OR: 1.89, 95%CI: 1.67–2.13) independently predicted higher biomarker restrictions versus academic sponsors (all $p < 0.001$). US-based trials showed 40% higher odds of restrictions (OR: 1.40, 95%CI: 1.35–1.46). Phase II trials demonstrated the highest rates (40.9%). Among specific biomarkers, PD-1 showed the steepest adoption trajectory (0.08% to 10.59%), followed by EGFR (5.07% to 8.84%) and HER2 (5.16% to 8.17%). Our NLP-based emerging biomarker discovery identified CTLA-4, PSMA, CD19, CD137, and LAG-3 as rapidly emerging eligibility biomarkers reflecting next-generation immunotherapy targets. Cancer-specific analyses revealed dramatic increases in lung (22.8% to 50.5%) and gastric cancers (14.6% to 45.5%), while prostate cancer showed declining rates (60.5% to 52.3%). Our complexity scoring algorithm demonstrated that biomarker-restricted trials have significantly higher eligibility complexity (mean: 50.0 vs 31.0, $p < 0.001$). All findings remained robust across multiple sensitivity analyses. **Conclusions:** Biomarker-based eligibility restrictions in oncology trials have increased substantially over 15 years, driven primarily by immune checkpoint and targeted therapy biomarkers. Industry-sponsored and later-phase trials show the highest adoption rates. These scalable ML findings inform precision medicine trial design and highlight considerations for patient access and trial generalizability. Research Sponsor: None.

Restrictive eligibility criteria in FDA-approved oncology trials following ASCO Guideline updates.

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Background: Despite significant advancements in new targeted and immunotherapies, enrollment in oncology clinical trials remains unrepresentative of real-world patient populations. Overly restrictive eligibility criteria – particularly related to Eastern Cooperative Oncology Group (ECOG) performance, cardiovascular status, HIV status, and prior malignancy – have been identified as key barriers to trial participation and generalizability. In response, the American Society of Clinical Oncology (ASCO) published new guidelines in 2017 lowering thresholds for enrollment. We examined whether these ASCO recommendations translated into measurable changes in eligibility criteria among FDA-approved trials for the five most common solid tumors. **Methods:** Clinical trial data was obtained from ClinicalTrials.gov, FDA Approved Drug Notification Database, and journal manuscripts. The study evaluated clinical trials that led to FDA-approved therapies for NSCLC, breast, melanoma, prostate, and colon cancer between 2006–2025. Eligibility criteria based on Eastern Cooperative Oncology Group (ECOG) performance, cardiovascular status, HIV status, and prior malignancy were extracted. Clinical trials were categorized as pre- or post-ASCO 2017 guideline publication, and t-tests (R v4.3.1) were used to compare exclusion rates between groups and assess alignment with ASCO recommendations. **Results:** Between 2006–2025, there were 167 FDA-approved clinical trials for NSCLC (59), breast (44), melanoma (25), prostate (23), and colon (16) malignancies. The proportion of trials initiated after the 2017 ASCO guidelines was 19 (32.2%) of NSCLC, 12 (27.3%) of Breast, 6 (37.5%) of Colon, 5 (21.7%) of Prostate, and 5 (20.0%) of Melanoma. There was no statistically significant reduction in the usage of restrictive exclusion criteria when comparing trials started before and after the 2017 ASCO recommendations among Colon ($p = 0.953$), Prostate ($p = 0.896$), Melanoma ($p = 0.775$), NSCLC ($p = 0.301$), and Breast ($p = 0.117$) cancer groups regarding ECOG performance, cardiovascular status, HIV status, and prior malignancy. **Conclusions:** Despite the publication of ASCO's 2017 eligibility guideline updates, restrictive exclusion criteria remain prevalent in FDA-approved oncology trials across major solid tumors. These findings suggest that guideline dissemination alone has been insufficient to change trial design practices. More proactive regulatory, sponsor-level, and implementation-focused interventions may be required to ensure broader trial access and improve the generalizability of oncology clinical research. Research Sponsor: None.

Comparative effectiveness and safety of axicabtagene ciloleucel versus liso-cabtagene maraleucel in large B-cell lymphoma: A real-world target trial emulation.

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Background: Axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel (liso-cel) are approved CD19-directed CAR T-cell therapies for large B-cell lymphoma (LBCL); however, comparative real-world evidence on their effectiveness and safety remains limited. We conducted a target trial emulation to compare the overall survival (OS), event-free survival (EFS), and safety outcomes between axi-cel vs liso-cel in routine clinical practice. **Methods:** Using de-identified electronic health record data from TriNetX (January 2017– December 2025), we emulated a two-arm target trial among adult patients with LBCL who received axi-cel or liso-cel. Index date (T_0) was defined as the date of CAR T-infusion. Patients with active severe infections at the index date or a history of cardiovascular and central nervous system involvement were excluded. Inverse probability of treatment weighting (IPTW) was used to balance the covariates, including age, sex, race, comorbidity, prior autologous stem cell transplantation, bridging therapy, and baseline inflammatory markers. OS was analyzed using IPTW Cox proportional hazards models. Event-free survival (EFS) was defined as a composite of death or initiation of subsequent systemic therapy (as a proxy for treatment failure). Cytokine release syndrome (CRS), and immune effector cell-associated neurotoxicity syndrome (ICANS) were evaluated. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported, and all analyses were conducted using R. **Results:** Among 1,311 eligible patients, 947 received axi-cel and 364 received liso-cel. In the unweighted cohort, patients treated with axi-cel were younger than those receiving liso-cel (median age 62 vs 72 years), with a similar sex distribution and a predominantly White population in both groups. After IPTW, baseline demographic, clinical, and laboratory characteristics were balanced between groups. OS did not differ significantly between axi-cel and liso-cel (HR 0.98; 95% CI, 0.71–1.36). Median OS was not reached in either group, with similar OS rates at 12 months (axi-cel: 78.1%, liso-cel: 80.3%) and 24 months (axi-cel: 71.3%, liso-cel: 71.4%). EFS was also comparable between treatments (HR 1.08; 95% CI, 0.82–1.44). No significant differences in CRS risk were observed within 90 days or overall follow-up (HR: 0.86; 95% CI, 0.66–1.11). Axi-cel was associated with a higher risk of ICANS within the first 90 days (HR 1.42; 95% CI, 1.00–2.01), although no significant difference was observed over longer follow-up. **Conclusions:** Axi-cel and liso-cel demonstrated comparable effectiveness in terms of OS and EFS. Safety profiles differed primarily in early neurotoxicity risk, while CRS incidence was similar between products. These findings provide real-world comparative evidence that may help to inform CAR T-cell therapy selection in clinical practice. Research Sponsor: None.

AI-enabled clinical trial framework for end-to-end site recommendation and enrollment projection.

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Background: Reliable accrual forecasting is essential in oncology trials because delayed enrollment reduces statistical power, increases costs, and prolongs timelines. We developed an AI-enabled framework integrating site recommendations with probabilistic enrollment modeling to support data-driven trial planning. **Methods:** Site-level attributes (Site360) and curated real-world patient datasets (Patient360) were integrated as inputs. Trial objectives including enrollment targets, timelines, sponsor and diversity requirements, and screen failure rates (SFR) were user specified. Candidate sites were ranked using a multi-criteria TOPSIS engine optimized with simulated annealing to identify portfolios meeting protocol requirements. Recommended site attributes informed Monte Carlo enrollment simulations incorporating site activation, patient arrival, and capacity constraints. Each underwent 1000 simulations, generating accrual distributions. Fifty-four CRC, NSCLC, and Breast trials from ClinicalTrials.gov were evaluated. Planned site counts and enrollment intensity (patients per month per planned site; ppmpps) from the same trials served as benchmarks. Enrollment intensity was calculated as enrolled patients divided by (trial duration in months $\times$ planned sites), with duration estimated from trial start to primary completion. Scenarios tested SFR 20%, 40%, and 60%. Model outputs were compared with planned benchmarks using Spearman correlation and summarized with medians and IQR. **Results:** Trials showed heterogeneous planned site counts: CRC median 76 (IQR: 43-119), Breast 204 (114-279), NSCLC 178 (101-227). Model recommended site counts showed moderate to strong rank agreement with planned sites across indications. CRC correlations increased from 0.67 to 0.73 as SFR rose from 20% to 60% (all $p < 0.05$). Breast correlations ranged 0.49-0.54 and NSCLC 0.61-0.63 across SFRs all with $p < 0.05$. Higher SFR required more recommended sites, compensating for screen failures. Predicted ppmpps aligned strongly with benchmarks. For Breast, predicted ppmpps decreased from 0.15 (0.10-0.31) at 20% SFR to 0.07 (0.04-0.16) at 60% SFR versus planned 0.08 (0.03-0.17), with ppmpps correlations 0.82, 0.77, 0.66 respectively (all $p < 0.01$). CRC predicted rates were 0.13 (0.08-0.29), 0.10 (0.07-0.24), 0.07 (0.05-0.18) across SFRs versus planned 0.09 (0.06-0.13), correlations 0.47 ($p = 0.076$), 0.54, 0.59 (both $p < 0.05$). NSCLC showed 0.23 (0.15-0.27), 0.18 (0.13-0.22), 0.12 (0.08-0.18) versus planned 0.12 (0.07-0.19) with correlations 0.54-0.64 ($p < 0.02$). **Conclusions:** This AI-enabled framework integrates optimization and probabilistic modeling to recommend sites and project enrollment behavior. Rank agreement with benchmarks supports improved site feasibility assessment by identifying trials with higher site requirements and enrollment risk and enabling risk-adjusted planning. Research Sponsor: None.

Exploring neural correlates of chemotherapy-induced peripheral neurotoxicity (CIPN) and the impact of exercise: A URCC NCORP nationwide phase II randomized controlled trial (RCT).

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Background: More than half of patients with cancer receiving neurotoxic chemotherapy (e.g., taxane, platinum, vinca alkaloid) develop CIPN, a dose-limiting, sometimes-debilitating condition characterized by numbness, tingling, and pain in the hands and feet. There are limited treatment options for CIPN partly due to limited understanding of CIPN pathophysiology. **Methods:** We conducted a phase II RCT examining the effect of exercise on CIPN via URCC NCORP Research Base. Patients who received neurotoxic chemotherapy within the past 9 months and report CIPN symptoms (rated ≥ 4 out of 10 at its worst in the past 2 weeks) were randomized 1:1 to usual care (UC) or virtually delivered Exercise for Cancer Patients (vEXCAP). vEXCAP is a 6-week personalized walking and resistance band exercise intervention. As part of our secondary aims, we investigated (1) whether CIPN symptoms are exacerbated by impairments in the brain's descending pain modulation circuitry—quantified by functional connectivity between the dorsolateral prefrontal cortex (DLPFC) and 23 sensory-related brain regions—and (2) whether exercise can improve both CIPN and brain functional connectivity. We recruited 35 patients from 7 community oncology practices spanning 6 US states. Sensory CIPN severity was assessed using the patient-reported EORTC QLQ-CIPN20 sensory subscale and functional brain connectivity was measured via magnetic resonance imaging (MRI) at pre- and post-intervention. **Results:** An ANCOVA showed that exercise, compared to UC, reduced sensory CIPN severity (-7.66 ± 3.05 (MCID is 4), effect size (ES) = -0.43 , $p = 0.158$) ($N = 35$, 57 ± 10 yrs, 89% female, 60% breast cancer). At pre-intervention, correlation analysis revealed sensory CIPN severity was negatively correlated with functional connectivity between the left DLPFC and several brain areas, including the left anterior insula ($r = -0.53$, $p = 0.001$), left thalamus ($r = -0.44$, $p = 0.009$), and left precuneus ($r = -0.32$, $p = 0.057$). Participants who showed a decrease in sensory CIPN severity at post intervention had an increase in functional connectivity between the left DLPFC and left precuneus ($r = -0.25$, $p = 0.152$), and this increase in connectivity was greater in vEXCAP group (effect size (ES) = 0.2 , $p = 0.460$). **Conclusions:** The association of sensory CIPN severity with lower brain connectivity with the left DLPFC may reflect impairment of descending pain inhibition pathways in the brain. vEXCAP may improve brain connectivity with the precuneus while lowering CIPN symptom severity. We believe that this line of research will ultimately inform better CIPN biomarkers and treatments. Funded by NCI UG1CA189956, UG1CA189861, UG1CA189805, UG1CA189961, K07CA221931, and R21CA256154. Clinical trial information: NCT04888988. Research Sponsor: National Cancer Institute; UG1CA189956; National Cancer Institute; UG1CA189861; National Cancer Institute; UG1CA189805; National Cancer Institute; UG1CA189961; National Cancer Institute; K07CA221931; National Cancer Institute; R21CA256154.

Trends and characteristics of clinical trials presented in ASCO plenary sessions (2011–2025).

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Background: Clinical trials presented during the ASCO Annual Meeting Plenary Session (PS) represent a curated subset with high scientific and clinical impact. However, characteristics associated with PS selection and their evolution have not been comprehensively described. This study evaluates trends and trial-, sponsor-, and presenter-related characteristics of trials in PS. **Methods:** Trials presented in PS from 2011–2025 were analyzed. Extracted variables included tumor type, therapeutic modality, disease setting, sponsorship, primary endpoint, effect size, geographic scope, and presenter sex and affiliation. Associations between variables were evaluated using chi-square, and multivariable logistic regression analyses. Temporal trends were assessed using Cochran–Armitage trend test. Results were considered significant at $\alpha = 0.05$. **Results:** From 2011–2025, 60 trials were presented in ASCO PS. The majority evaluated therapies for solid tumors (90%). Most common therapeutic modalities were immune check-point inhibitors (18%), chemotherapy (16%), and hormone therapy (13%). Most trials were conducted in the palliative (46%), followed by adjuvant setting (25%). Only 9 trials (15%) included pediatric patients. Overall, 85% of trials met their primary endpoint. Overall survival (OS), progression-free, and disease-free survival were the most used primary endpoints, with surrogate endpoints increasingly represented over time compared with OS ($p < 0.001$). One trial used quality of life (QoL) as primary endpoint. Mean hazard ratio was 0.68 ± 0.24 . Industry-sponsored (Ind) studies accounted for 52% of PS presentations, with four sponsors responsible for 61% of Ind trials. The proportion of Ind trials significantly increased over time ($p = 0.03$). Ind was significantly associated with meeting the primary ($p = 0.048$) and use of surrogate endpoints ($p = 0.008$), remaining an independent predictor of both in multivariable regression ($p = 0.035$, $\beta = 0.318$; $p = 0.033$, $\beta = 0.333$). Most studies were conducted globally (61%), 12% exclusively in the United States (US), followed by Europe (10%). Among presenters, 23% were female, with female representation not changing over time. Most presenters were affiliated with institutions in the US (62%), followed by the United Kingdom (7%). In multivariable regression analysis, Ind was associated with lower odds of a female presenter ($p = 0.039$; $\beta = -0.342$). **Conclusions:** Over the past 15 years, ASCO PS have predominantly featured global, Ind trials in solid tumors, with an increasing reliance on surrogate endpoints. Ind emerged as key factor associated with trial characteristics, including endpoint selection and trial success. Female presenter inclusion, pediatric trials, and QoL endpoints remain underrepresented. These findings provide an overview of evolving trial characteristics and inform discussions on research priorities, trial design, and representation. Research Sponsor: None.

Reducing effort through informatics-driven identification, recruitment, and data capture on a trial to improve adjuvant endocrine therapy adherence.

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Background: Adjuvant endocrine therapy (AET) improves outcomes in HR+ breast cancer. Nonadherence to AET is common, but manual screening for nonadherence is fraught. High-specificity structured cancer electronic health record (EHR) data, particularly if it includes key variables like stage, could streamline these steps for both clinical care and research purposes. We conducted an analysis of approaches to identifying patients as eligible for a multi-site AET adherence study to understand how variation in structured data informatics-supported screening impacts coordinator time. **Methods:** Mayo Clinic implemented a two-step identification: (1) EHR structured data (diagnosis date, stage, ER/PR/HER2 positivity, medication script) to prescreen for eligibility; (2) SureScripts fills to flag nonadherence using proportion of days covered < 80% across early fills. Medical College of Wisconsin (MCW) implemented a more manual screening process for Step 1 using only medication scripts. Coordinators at both sites then conducted a medical record review to assess if the resulting list of patients had a plan to continue AET for at least two additional years. Opt-out clinician permission preceded patient contact; pharmacists delivered a patient reported outcome (PRO)-guided intervention and documented encounters. **Results:** At Mayo, 829 patients were prescreened for study eligibility through informatics workflow; 120 (14.5%) met eligibility criteria. At MCW, 1,763 patients were prescreened; 168 (9.5%) were eligible. EHR filters included non-breast cancer encounters (50% at MCW) and ineligible based on time since cancer (36% at Mayo; 26% at MCW). At Mayo, screening required 5.6 minutes/patient for experienced coordinators. At MCW, experienced coordinators averaged 6.67 minutes/patient and inexperienced coordinators averaged 9.33 minutes/patient. **Conclusions:** Structured EHR data, pharmacy-fill information, and standardized workflows allowed consistent prescreening, intervention and recruitment processes across sites. Higher-specificity informatics-supported screening reduced the percentage of patients requiring manual review and reduced coordinator screening time. It also supported timely provider-permission steps and patient outreach. These workflows were feasible to implement at both institutions, and study enrollment is ongoing. Clinical trial information: NCT06765707. Research Sponsor: National Cancer Institute; R01 CA285925.

Enhancing recruitment of AYAs with Hodgkin lymphoma through community partnerships: Prioritizing diverse populations.

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Background: Hodgkin lymphoma (HL) is one of the most common cancers affecting adolescents and young adults (AYAs). AYAs with HL aged 15–39 years are a group historically difficult to reach for research participation. Their voice is critical to enhance care. For two funded qualitative studies, the team engaged in and assessed the feasibility of a community-centered approach to recruit HL patients with 1:1 representation by age [those diagnosed as children (0–14), AYAs (15–39), and above 40 years], race and ethnicity (Black and Hispanic communities), and insurance (private, Medicaid, and uninsured populations). **Methods:** Recruitment was conducted exclusively through advocacy partner organizations including Blood Cancer United, Stupid Cancer, Cactus Cancer Society, and Elephants & Tea. Study team patient advocates guided recruitment approach, including selecting imagery using a Black-identifying male and Hispanic-identifying female and rephrasing recruitment material language. Advocacy partners utilized their techniques for engaging AYAs, such as Instagram, website posting, email, and/or attendance at member engagement events. Recruitment to the two studies required the study participants online to 1) complete a survey on REDCap documenting their consent using a waiver and 2) provide confirmation of their HL diagnosis by uploading proof to REDCap (e.g., screenshot from their medical record containing their name, date of birth, and HL diagnosis). **Results:** A total of 389 patients from 46 states or US territories started their REDCap survey and completed the waiver of consent. Of those, 217 (55%) were AYAs at diagnosis and 95 $\geq$ 40 (24%). Of the total 389, 85 (22%) were Black, 39 (10%) Hispanic, 34 (9%) had Medicaid, and 12 (3%) were uninsured. 154 (40%) provided proof of diagnosis from 38 states. Of the 154 that uploaded proof of HL diagnosis, 123 (80%) were AYA and 26 (17%) $\geq$ 40 years at diagnosis. 17 (11%) were Black, 21 (14%) Hispanic, 17 (11%) with Medicaid, and 3 (2%) uninsured. Documentation was most commonly provided using an after visit summary or visit note (47%), pathology report (19%), or physician signed letter (13%). **Conclusions:** Partnering with advocacy organizations, particularly those serving AYAs, proved successful in exceeding recruitment goals for AYA patients. Attrition in participation was seen between waiver completion and providing confirmation of diagnosis. AYAs were more likely than adults $\geq$ age 40 to provide proof of confirmation of diagnosis. Recruitment met national averages for Black representation, but fell short with lower than national average estimates for representation of Hispanic survivors, those on Medicaid or uninsured. Future studies should engage underrepresented populations during the research process to understand how to plan recruitment activities in a way that prioritizes what is most important and impactful for the target population. Research Sponsor: National Cancer Institute; Blood Cancer United.

Quantifying the impact of protocol design on enrollment and dropout rates in breast cancer clinical trials.

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Background: Clinical trial enrollment can sometimes fail due to protocol design being overly complex, including procedures that are overly burdensome on patients and/or trial sites. Procedures that may be more logistically challenging or introduce higher risk (ex: radiation exposure in imaging procedures) can affect trial enrollment and patient retention. To better understand factors that optimize operational design of protocols, we evaluated breast cancer protocols to assess and quantify procedures that had the highest potential impact on enrollment and dropout rates. **Objective:** Our objective is to develop an algorithm that can predict enrollment and dropout rates by analyzing the procedures and procedure frequency included in protocol design. **Methods:** 42 breast cancer protocols (sourced from aggregated, anonymized Medidata Clinical Cloud data) from closed clinical trials conducted between 2010–2023 were utilized to train a predictive model. The model leveraged the procedure and schedule-of-activity data to capture the frequency of protocol-specified procedures as input features, and enrollment and dropout rates as outcome features. Model performance was assessed utilizing cross-validation. To assess the relative impact of individual procedures or groups of procedures on a protocol, a sensitivity analysis was performed by increasing each procedure's frequency by 1 unit while holding all other variables constant and measuring the resulting percent change in predicted enrollment and dropout rates. **Results:** Analysis of selected protocols demonstrated that inclusion of Positron Emission Tomography (PET) Imaging was associated with a 10–23% reduction in enrollment rates. Genetic testing and analysis procedures were associated with enrollment rate decreases of up to 5%. In contrast, bone density imaging, abdominal and pelvic imaging, and increased tumor and biopsy procedures were associated with enrollment increase of up to 6%. With respect to retention, increased cardiac rhythm monitoring was associated with up to 10% reduction in dropout rates, while blood cell analysis, collagen biomarker testing, and quality of life questionnaires were each associated with dropout reductions of up to 8%, 8% and 5% respectively. **Conclusions:** Procedure requirements and frequency had a measurable impact on clinical trial enrollment and retention. Some procedures, such as PET scans, were associated with reduced enrollment; whereas other clinically relevant imaging procedures (i.e., DEXA bone density imaging, CT/MRI abdominal and pelvic imaging) and other tumor-related procedures, monitoring, and assessments were associated with improved enrollment and/or reduced dropout. These findings highlight opportunities to optimize protocol design by prioritizing procedures that improve the likelihood of recruitment and retention. **Research Sponsor:** None.

Assessing site-central baseline imaging discordance in oncology clinical trials.

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Background: Eligibility determination is a critical and rate-limiting step in oncology clinical trials and directly influences endpoint interpretability. Across oncology indications, eligibility frequently depends on prespecified imaging criteria that function as binary gatekeepers to enrollment, with blinded independent central review (BICR) commonly used to standardize image interpretation. In many solid tumor trials using RECIST 1.1, participants must demonstrate measurable disease; in many lymphoma trials using Lugano criteria, FDG-avid disease is required; and in prostate cancer trials using PCWG3 criteria, the presence of a bone scan superscan is typically exclusionary. Often participant eligibility is established by site investigators, while BICR radiologists independently assess baseline and on-study imaging without determining enrollment, creating potential site-central discordance at baseline. We hypothesized that baseline imaging discordance exists between site and BICR and evaluated its frequency and potential relevance to clinical trial endpoint interpretation. **Methods:** We performed a preliminary analysis of 17,104 baseline BICR reviews among enrolled participants evaluated using RECIST 1.1 requiring measurable disease ($n = 7,189$), Lugano criteria requiring FDG-avid disease ($n = 2,653$), and PCWG3 ($n = 7,262$) criteria. **Results:** For the RECIST 1.1 subset, BICR determined that 11.0% ($n = 791$) of enrolled participants lacked measurable disease at baseline. Among these participants, subsequent responses included CR ($n = 36$), PD ($n = 93$), and SD ($n = 207$). Because partial response under RECIST 1.1 requires measurable target lesions, participants without measurable disease are inherently constrained in the spectrum of evaluable responses, potentially biasing response rate. For the Lugano subset, BICR determined that 1.5% ($n = 41$) of enrolled participants lacked FDG-avid disease at baseline, with subsequent anatomic-only responses of CR ($n = 1$), PR ($n = 5$), SD ($n = 9$), and PD ($n = 2$). Though infrequent, site-central differences under Lugano criteria may influence response assessment, as BICR evaluated anatomic change while site incorporates metabolic response. For the PCWG3 subset, 7.0% ($n = 548$) of enrolled participants demonstrated a baseline superscan by BICR, with subsequent responses of CR ($n = 20$), PR ($n = 25$), SD ($n = 90$), and PD ($n = 91$). In these cases, response assessment is largely limited to soft tissue disease. **Conclusions:** The observed site-central imaging discordance reflects differences between eligibility and imaging assessments rather than incorrect site enrollment decisions and is not uncommon across major oncology response criteria, with potential implications for efficacy assessment in trials where eligibility is site-determined but response is centrally adjudicated. This analysis supports further investigation incorporating additional criterion-specific analysis. Research Sponsor: None.

Temporal trends in pregnancy-associated cancer mortality in the United States: A national analysis 2018-2023.

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Background: Cancer during pregnancy is rare but increasing due to rising rates of early-onset cancers and more parents delaying childbearing to older ages. Cancer treatment during pregnancy is complex, as capacity to deliver timely, multimodality anti-cancer treatment may be limited by risk of fetal compromise. As pregnancy-associated cancer is an increasingly recognized contributor to maternal mortality, this study sought to evaluate national temporal trends. **Methods:** Using CDC WONDER Multiple Cause of Death files (2018–2023), pregnancy-associated deaths involving malignant neoplasms (ICD-10 C00–C97) were identified. Age-adjusted mortality rates (AAMR) per 100,000 live births and annual percent changes (APCs) were calculated, excluding unknown race, ethnicity, or age. AAMR was evaluated by state, including comparison of 1) states with trigger laws banning abortion in 2022 vs states that did not have such laws and 2) states that expanded Medicaid by 2018 vs states that did not. Mortality data for locations with <10 deaths is censored. **Results:** From 2018–2023, there were 723 pregnancy-associated deaths in people with cancer. Most (72%) were in White patients and occurred in the late postpartum period (59%) (42–365 days after birth). Only 19% of patients had documented metastatic cancer. Overall AAMR was 3.40 (95%CI 3.16–3.65); it was highest among Black patients (4.54), exceeding White (3.24), Hispanic (3.08), and AIAN/AAPI (2.64) mortality. Breast (n=162, AAMR 0.76 95%CI 0.65–0.88) had the greatest cancer-specific mortality burden, followed by hematological malignancies (n=101, AAMR 0.48, 95% CI 0.38–0.57) and colorectal cancer (n=71, AAMR 0.12, 95%CI 0.088–0.15). AAMR for those with metastatic disease was 0.64 and increased over time (APC +7.54%; 95%CI 1.52–14.55; p=0.009). Late maternal deaths also rose (APC +4.75%; 95%CI 0.99–8.87; p=0.006). Otherwise, overall (APC –0.37%, 95%CI –0.37–4.30, p=0.83) and race/ethnicity specific pregnancy-associated cancer mortality have not significantly changed over time. Among 25 states with ≥10 deaths, state-level mortality ranged from 1.37 in California to 6.95 in Virginia. Limited state comparative analysis found that AAMR for pregnancy-associated cancer was higher in states with trigger laws (4.43) compared to non-trigger states (3.22); it was also higher in non-Expansion states (4.00) compared to states that expanded Medicaid (3.31). **Conclusions:** Despite known improvements in cancer mortality, pregnancy-associated cancer mortality remains stagnant, with notable mortality rises in pregnant patients with metastatic disease and late postpartum deaths. The large variability in state-level mortality may reflect state policies that affect access to prenatal or oncological care. More research and advocacy work to optimize care for pregnancy patients with cancer is essential to improve outcomes for this vulnerable population. Research Sponsor: None.

Fair inclusion in clinical trials: Updated Good Pharma Scorecard evaluations of FDA oncology drugs approved by the FDA, 2018-2023.

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Background: Adequate representation of demographic subgroups in clinical trials is essential for understanding the safety and efficacy of novel therapies. We previously developed and piloted the “fair inclusion” measure, which assesses (1) transparency in participant demographics and (2) demographic representation. These metrics were incorporated into the Good Pharma Scorecard, a system evaluating pharmaceutical company performance in bioethics and social responsibility, with sponsors ranked by fair inclusion scores. However, it remains unclear whether sponsors have improved fair inclusion of women, older adults, and racial and ethnic minorities in pivotal trials since the most recent Scorecard. **Methods:** For transparency, we assessed 6 measures [whether the number of (1) women, (2) older adults, (4) Black, (5) Asian, and (6) Latinx participants were publicly reported], and for representation, 5 measures [whether the proportion of enrolled (1) women, (2) older adults, (3) Black, (4) Asian, and (5) Latinx represents >80% of the US population with the studied condition]. Fair inclusion scores averaged transparency and representation, overall and by subgroup. Results were reported at the trial, product, and sponsor levels and compared across 2012–2017 vs 2018–2023 approvals. Data sources included Drugs@FDA, ClinicalTrials.gov, publications, US Cancer Statistics, and the American Cancer Society. **Results:** Between January 1, 2018 and December 31, 2023, the FDA approved 75 oncology therapeutics based on 80 pivotal trials from 52 sponsors. At the sponsor level, transparency improved for older adults (2012–2017: 78%, 2018–2023: 95%, $p = 0.002$) and racial and ethnic minorities (67% vs 91%, $p = 0.003$). Representation did not improve for women (94% vs 94%, $p = 0.99$), older adults (85% vs 81%, $p = 0.29$), or racial and ethnic minorities (75% vs 67%, $p = 0.13$). Fair inclusion scores improved modestly (81% vs 86%; $p = 0.04$). **Conclusions:** Sponsors have improved demographic reporting, particularly for older adults and racial and ethnic minorities. However, representation has not improved for any subgroup. Overall gains in fair inclusion were driven by transparency. Research Sponsor: None.

Comparison of mean sponsor scores on transparency, representation, and fair inclusion for 2012-2017 vs 2018-2023 oncology FDA approvals, by sex, age, race and ethnicity.

	2012-2017 Scores (n = 25)	2018-2023 Scores (n = 52)	p-value
Women			
Transparency	96%	99%	0.32
Representation	94%	94%	0.99
Fair Inclusion	97%	95%	0.28
Older Adults			
Transparency	78%	95%	< 0.01
Representation	85%	81%	0.29
Fair Inclusion	79%	86%	0.07
Race and Ethnicity			
Transparency	67%	91%	< 0.01
Representation	75%	67%	0.13
Fair Inclusion	66%	78%	0.06
Overall			
Transparency	82%	95%	< 0.001
Representation	85%	80%	0.06
Fair Inclusion	81%	86%	0.04

Insurance and cost-related access barriers to specialty oral anticancer medications for blood cancers in a nationwide sample of Medicare and commercially insured patients.

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Background: Specialty oral anticancer medications improve survival across blood cancers but may have access challenges. This study examined approval and fill rates of specialty oral anticancer medication prescriptions indicated for blood cancers in a nationwide sample of Medicare and commercially insured patients. **Methods:** Using nationwide claims (Symphony Health Solutions Integrated Dataverse), we identified patients with ≥ 1 new specialty oral anticancer medication prescription during 2022. Outcomes were measured for the initial prescription as well as any prescription for the same drug within 90 days and were classified as: (i) rejected by insurer, (ii) approved by insurer but not filled by patient, or (iii) approved by insurer and filled by patient. Among rejected prescriptions, we examined rejection reasons, eventual approval rates, and time to approval. Among approved prescriptions, we compared fill rates across out-of-pocket cost levels. Adjusted outcomes were estimated using multivariable logistic regressions. **Results:** The study included 12,134 patients (61.0% Medicare, 39.0% commercial) with a specialty oral anticancer medication prescription. Initially, very few prescriptions were both approved and filled (9.6%, Medicare; 4.0%, commercial). Insurers initially rejected most prescriptions (64.9% for Medicare; 84.0% for commercial), frequently due to prior authorization or formulary restrictions. By 90 days, approval rates rose to 85.0% (Medicare) and 62.9% (commercial), but many approved prescriptions were never filled; ultimately, only 54.5% of Medicare patients and 45.5% of commercial patients both received insurer approval and filled their prescription. Fill rates dropped sharply when out-of-pocket costs exceeded \$175 per SOAM prescription. When out-of-pocket costs exceeded \$2,000 per prescription, only 31.9% of Medicare patients and 26.9% of commercial patients filled their prescriptions. Adjusted rates were similar to unadjusted rates. **Conclusions:** This study found substantial access barriers to specialty oral anticancer medications for blood cancer, particularly among commercially insured patients. Even after insurer approval, many patients never filled their prescription. This highlights the importance of addressing both payer-level restrictions and patient-level affordability challenges to ensure treatment access. Research Sponsor: Leukemia & Lymphoma Society (LLS).

Trends in cancer drug revenue retained by providers under buy-and-bill reimbursement, 2010-2024.

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Background: Cancer care providers, including physician offices and hospitals, retain “markup” fees on clinician-administered drugs (such as chemotherapies and immunotherapies) which are proportional to drug price. Under this system, commonly known as “buy and bill,” multiple external factors may impact provider revenue: increasing cancer drug prices, increasing care delivery in hospitals (where markups are higher) rather than offices, the 340B Drug Pricing Program, and payer “bagging” strategies to avoid paying markups to providers. Study goals were to estimate changes in provider revenue retained on clinician-administered cancer drugs from 2010–2024 and to quantify the contribution of four factors: 1) cancer drug sales, 2) site of care (office vs. hospital), 3) 340B participation, and 4) payer “bagging” strategies. **Methods:** We included all clinician-administered cancer drugs with available US sales data, including biosimilars and cancer-specific supportive care drugs (e.g., growth factors). We obtained cancer drug sales from manufacturer SEC filings (aggregated in SSR Health data), inflated to 2024 USD. We estimated the proportion of cancer drug sales administered within each of nine payer-care settings (three major payers: Medicare, Medicaid, commercial, and three major sites of care: physician office, 340B-participating hospital outpatient, and non-340B hospital outpatient), using Surveillance, Epidemiology, and End Results (SEER), the National Health Interview Survey (NHIS), and CMS and commercial claims. To estimate markup revenue, we applied setting-specific markup rates (from statute for Medicare/Medicaid, from peer-reviewed literature for commercial) to the drug sales in each setting. Plausible estimates of “bagging” prevalence were obtained from the literature. **Results:** Cancer drug sales increased from \$27.3 billion (B) in 2010 to \$64.9B in 2024, a 138% increase. Provider markup revenue on cancer drugs increased from \$8.7B in 2010 to \$35.7B in 2024, a 309% increase. Of the 2010–2024 increase, increasing drug sales accounted for 73.3%, shifting site-of-care to hospitals for 24.2%, and 340B participation growth for 2.5%. During this period, drug revenue retained by physician offices increased by 30%, non-340B hospitals by 49%, and 340B-participating hospitals by 739%. Accounting for bagging reduced 2024 markup revenue from \$35.7B to \$28.4B. **Conclusions:** Provider revenue from cancer drug markups grew substantially during 2010–2024. The largest single factor was growing cancer drug sales, although shifts in site of care also contributed. Revenue retained by 340B-participating hospitals increased much more than offices or other hospitals. Growth in provider markups was reduced modestly by growth in payer bagging strategies. Policymakers should consider whether growing markups on clinician-administered drugs reflects an efficient use of healthcare spending. Research Sponsor: National Institute of Health Care Management.

Association of Medicaid expansion with pre-diagnosis coverage continuity and 2-year overall survival in pediatric patients with blood cancer.

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Background: Continuous insurance coverage is critical for timely cancer diagnosis and treatment, yet many patients gain Medicaid only around the time of diagnosis. Although the Affordable Care Act Medicaid expansion targeted adults, it may indirectly influence children via a “welcome mat” effect by increasing outreach and boosting uptake among families with eligible children. The extent to which state expansion status influences Medicaid coverage continuity and survival among Medicaid-insured children with blood cancers—conditions lacking routine screening and often with acute presentation—remains unclear. **Methods:** Using linked SEER-Medicaid data, we identified 7,536 patients age ≤ 21 newly diagnosed with leukemia or lymphoma between 2009–2019 who had ≥ 1 month of Medicaid enrollment from 12 months pre-diagnosis through two months post-diagnosis. Coverage patterns were categorized as: 1) continuous Medicaid (12–13 months enrolled pre-/peri-diagnosis), 2) newly gained Medicaid (enrollment starting at diagnosis or within two months post-diagnosis), and 3) other coverage patterns. Difference-in-differences (DD) models compared post- vs. pre-expansion changes in coverage patterns and 2-year overall survival in 11 SEER expansion states vs. four non-expansion states, adjusting for sociodemographic factors. Survival models additionally adjusted for coverage patterns to assess the extent to which the patterns accounted for expansion-associated survival changes. **Results:** The percentage with continuous Medicaid increased more in expansion states (52.9% to 67.5%) than non-expansion states (41.5% to 50.8%), leading to a net increase of 8.2 percentage points (ppts; 95% CI = 2.3 to 14.2; $p = 0.007$) in adjusted DD model. The percentage with newly gained Medicaid decreased more in expansion states (24.6% to 14.2%) than non-expansion states (31.8% to 24.5%), resulting in a net reduction of 7.9 ppts (95% CI = -13.9 to -1.9; $p = 0.010$). No significant changes were observed post-expansion for other coverage patterns. Two-year overall survival increased in expansion states (85.7% to 86.9%) but declined in non-expansion states (87.7% to 82.9%), yielding a net increase of 6.2 ppt (95% CI = 2.8 to 9.6; $p < 0.001$) in adjusted DD model. This association was slightly attenuated after further adjusting for coverage patterns (DD = 5.9 ppts; 95% CI = 2.5 to 9.3; $p < 0.001$), suggesting coverage continuity accounted for approximately 4.9% of the expansion-associated gain in 2-year survival. **Conclusions:** Medicaid expansion was associated with improved coverage continuity pre-/peri-diagnosis and better early survival among Medicaid-insured children with leukemia or lymphoma. Amid ongoing Medicaid policy changes, these findings add evidence that stable coverage matters for vulnerable children. Future work will evaluate longer-term outcomes (e.g., 5-year survival). Research Sponsor: Blood Cancer United, Equity-in-Access Program; HSRP9015-23.

Association between low muscle mass assessed by bioelectrical impedance analysis and clinical outcomes in hospitalized cancer patients.

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Background: Low muscle mass is an independent prognostic marker associated with increased clinical risk, functional impairment, and mortality in patients with cancer. Conventional indicators such as body mass index (BMI) may fail to identify individuals at nutritional and functional risk. Bioelectrical impedance analysis (BIA) offers a feasible bedside method for body composition assessment, particularly in resource-constrained hospital settings. This study aimed to evaluate body composition using BIA, determine the prevalence of low muscle mass, and examine its association with clinical, laboratory, and functional parameters in hospitalized oncology patients. **Methods:** This observational study included 104 adult cancer patients admitted to a tertiary public hospital between January and October 2025. Baseline assessments at hospital admission included BMI, skeletal muscle mass index (SMI), appendicular muscle index, phase angle, fat mass percentage, handgrip strength (HGS), calf circumference (CC), urea-to-creatinine ratio, length of hospital stay, and in-hospital outcome (discharge or death). Low muscle mass was defined according to established cutoffs for SMI and appendicular muscle index. Comparisons were performed between patients with and without low muscle mass, and correlations between appendicular muscle index and functional and nutritional parameters were analyzed. **Results:** Low muscle mass was identified in 29.8% of patients at admission. Compared with patients without low muscle mass, those affected had significantly lower BMI (23.3 vs 27.6 kg/m², $p=0.001$), appendicular muscle index (6.20 vs 7.61, $p<0.001$), phase angle (3.6° vs 5.1°, $p<0.001$), total muscle mass (25.1 vs 29.4 kg, $p<0.001$), HGS (30.0 vs 37.0 kgf, $p=0.041$), and CC (32.5 vs 37.0 cm, $p<0.001$). Length of hospital stay did not differ significantly between groups. In-hospital mortality was higher among patients with low muscle mass (18.5% vs 7.0%), although this difference did not reach statistical significance ($p=0.133$). Appendicular muscle index showed moderate to strong positive correlations with BMI, phase angle, HGS, CC, and SMI. **Conclusions:** BIA proved to be a feasible and informative tool for identifying low muscle mass and functional impairment in hospitalized cancer patients. Appendicular muscle index and SMI were superior to BMI in detecting patients at increased nutritional and functional risk. Given its low cost and bedside applicability, BIA represents a valuable strategy for early risk stratification and supportive care planning in resource-limited oncology settings. Research Sponsor: None.

Longitudinal changes in coping among early phase cancer clinical trial (EPCT) participants.

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Background: EPCT participants use varying strategies to cope with uncertainty related to their cancer, treatment, and prognosis. However, little is known about how coping strategies change over time among EPCT participants and how longitudinal changes correlate with patient-reported outcomes (PROs) and clinical outcomes. **Methods:** We prospectively enrolled adults with cancer participating in EPCTs at Massachusetts General Hospital from 4/2021-1/2023. Participants completed monthly PROs assessing coping strategies (Brief COPE), symptoms (Edmonton Symptom Assessment System [ESAS]), quality of life (QOL; Functional Assessment of Cancer Therapy General), hope (Herth Hope Index), and financial wellbeing (COST tool). We used regression models to assess associations of baseline (B/L) PROs with changes in coping scores over time (B/L to month 1 [M1] and B/L to month 2 [M2]). We also explored how changes in coping predicted clinical outcomes (time on trial [ToT], overall survival [OS]). **Results:** We enrolled 195 of 251 eligible patients (78% enrollment), and 188 completed the B/L surveys (96% response, median age=63 [range: 32-89], 56% female, most common cancer types: gastrointestinal [34%] and breast [21%]). Higher B/L QOL predicted decreased behavioral disengagement coping at M1 ($B=-0.01$, $p=.037$) & M2 ($B=-0.02$, $p=.001$) and self-blame at M2 ($B=-0.02$, $p=.038$), as well as increased emotional support ($B=0.22$, $p=.001$) and religion ($B=0.02$, $p=.024$) coping at M1. Higher B/L ESAS symptoms predicted decreased use of emotional support coping at M1 ($B=-0.01$, $p=.048$). Higher B/L ESAS physical symptoms predicted decreased use of emotional support at M1 ($B=-0.02$, $p=.046$) & M2 ($B=-0.03$, $p=.016$). Higher B/L psychological symptoms predicted increased use of self-blame at M2 ($B=0.08$, $p=.007$). Higher B/L financial wellbeing predicted increased emotional support at M1 ($B=0.02$, $p=.025$). Higher B/L hope predicted increased positive reframing at M1 ($B=0.07$, $p=.010$) and religion coping at M2 ($B=0.05$, $p=.038$) as well as decreased behavioral disengagement at M1 ($B=-0.04$, $p=.001$) & M2 ($B=-0.06$, $p=.001$). For clinical outcomes, increased acceptance ($HR=0.85$, $p=.028$) and religion ($HR=0.85$, $p=.016$) coping at M1 and increased positive reframing ($HR=0.84$, $p=.010$) at M2 predicted longer ToT. Increased use of behavioral disengagement at M1 predicted shorter ToT ($HR=1.42$, $p=.002$). Increased use of positive reframing ($HR=0.83$, $p=.009$) and self-blame ($HR=0.78$, $p=.012$) coping at M1 predicted better OS; increased use of behavioral disengagement ($HR=1.41$, $p=.007$) predicted worse OS. **Conclusions:** In this longitudinal cohort study, EPCT participants' B/L PROs correlated with changes in their coping over time. We also found longitudinal changes in coping predicted ToT and OS. These findings highlight opportunities to enhance care delivery and outcomes for EPCT participants by addressing their PROs and coping behavior over time. Research Sponsor: None.

The association of baseline fatigue and severe cancer treatment toxicity by comorbid conditions: A pooled analysis.

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Background: Fatigue is commonly reported by patients with cancer. Patients who report fatigue are at greater risk of severe adverse events during treatment. However, it is unknown whether the relationship between baseline fatigue and toxicity risk persists after accounting for comorbid conditions. **Methods:** Data from 6 SWOG phase 2/3 clinical trials in advanced cancer (1999 to 2018) were pooled. Baseline fatigue (classified by 5-point Likert scale) was analyzed as any vs none. Patients were linked to Medicare claims by SSN, date of birth, and sex to identify comorbidities at study registration. Adverse events (AEs) were classified using the Common Terminology Criteria for Adverse Events. The primary outcome was severe ($\geq$ grade 3) events. Odds ratios (ORs) were calculated using generalized estimating equations, clustered by study, and adjusted for age, sex, race, and obesity. Interaction tests between fatigue and each comorbidity were examined. **Results:** Among 1195 patients (median age, 73; 13.1% female; 11.8% Black; 74% prostate cancer), 629 (52.6%) had ≥ 1 severe AE. Among patients with ≥ 1 comorbid condition, those with any fatigue had a 132% (OR=2.32, 95% CI, 1.26–4.27, $p=.007$) increased risk of having severe AEs; among patients with no comorbidities, the association was nearly identical (OR=2.33, 95% CI, 1.51–3.60, $p<.001$; p -interaction=.97). Those with any fatigue had a twofold or greater risk of severe AEs across all comorbidities (Table). The association between fatigue and severe toxicity was greater for those with anemia (interaction $p=.03$) and those with depression (interaction $p=.02$). **Conclusions:** The association between baseline fatigue and severe treatment toxicity persisted after accounting for comorbid conditions, indicating baseline fatigue is an independent risk factor. The association was stronger among patients with anemia and those with depression, suggesting these conditions may amplify the risk of baseline fatigue. These findings support early identification of baseline fatigue and targeted supportive interventions for these high-risk populations. Research Sponsor: None.

Association of baseline fatigue and severe toxicity by comorbid conditions.

Comorbidity	No comorbidity		Comorbidity		p-interaction
	OR (95% CI)	p-value	OR (95% CI)	p-value	
Depression	2.24 (1.28-3.92)	0.005	4.32 (2.58-7.23)	<0.0001	0.02
Anemia	2.15 (1.30-3.57)	0.003	3.05 (1.35-6.87)	0.007	0.03
Respiratory disorders (COPD, sleep apnea)	2.30 (1.35-3.94)	0.002	2.73 (0.99-7.55)	0.05	0.58
Hypothyroid	2.30 (1.34-3.95)	0.003	2.64 (1.33-5.23)	0.005	0.57
Diabetes	2.29 (1.35-3.89)	0.002	2.41 (1.24-4.71)	0.01	0.73
Hypertension	2.26 (1.36-3.78)	0.002	2.37 (1.25-4.50)	0.008	0.73
Cardiovascular disease	2.42 (1.39-4.22)	0.002	2.04 (1.15-3.63)	0.02	0.25
Autoimmune diseases	2.33 (1.34-4.04)	0.003	1.99 (1.15-3.43)	0.01	0.7
Any comorbidity (all comorbidities)	2.33 (1.51-3.60)	<0.001	2.32 (1.26-4.27)	0.007	0.97

Decline in credit score and excess mortality risk among cancer patients: Evidence from Washington State.

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Background: Patients experiencing bankruptcy following a cancer diagnosis have been shown to have increased mortality, but few studies have evaluated the impact of other types of financial hardships on mortality risk. We conducted an analysis to understand the relationship between a drop in credit score, a marker of less severe types of financial strain, and mortality among cancer patients in Washington State. **Methods:** We linked records from cancer patients (age 18+) diagnosed with any cancer (except in situ) between 2010 - 2023 from the Western Washington SEER cancer registry to credit report data from a national credit reporting agency. We excluded patients without a valid credit score near diagnosis (± 100 days). In a Cox proportional hazards model using a landmark approach, we examined the relationship between a drop in credit score (25-49, 50-99, or 100+ points) in the first year of diagnosis and subsequent mortality after year 1, using no- or low-drop (< 25 points) as the reference. Hazard ratios (HRs) and 95% confidence intervals were derived. Model covariates included age, gender, race/ethnicity, marital status, Area Deprivation Index, urban/rural residence, diagnosis year, cancer type, stage, and credit score at diagnosis. **Results:** Among 212,898 evaluable patients [49% male, 84% white, median age 65 (IQR 56 - 73)], credit scores at diagnosis were: 42% excellent (800-850), 25% very good (740-799), 15% good (670-739), 12% fair (580-669), and 6% poor (300-579). In the year following diagnosis, 40,078 patients' credit scores fell ≥ 25 points (18.8%), including 21,716 falling 25-49 points (10.2%), 12,954 falling 50-99 points (6.1%), and 5,408 falling ≥ 100 points (2.5%). Among all cancers combined, patients experiencing 50-99 point and ≥ 100 point reductions (but not 25-49 point reductions) in credit scores had excess mortality (Table). Excess risk of death was observed for nearly all individual cancer types at the ≥ 100 -point reduction level except kidney. **Conclusions:** In this retrospective study, a substantial reduction in credit scores, typically reflecting the experience of adverse financial events, was associated excess mortality compared to those with stable credit scores. Future studies are needed to understand the mechanisms of the relationship. Research Sponsor: National Cancer Institute; R01CA274541; IRONMAN Foundation.

Excess risk of death following a post-diagnosis fall in credit score (vs no/low reduction).

Cancer Type	25-49 points		50-99 points		≥ 100 points	
	HR	CI	HR	CI	HR	CI
All	0.96	0.94 - 0.99	1.06	1.02 - 1.10	1.33	1.27 - 1.39
Breast	1.00	0.92 - 1.08	1.07	0.97 - 1.18	1.39	1.23 - 1.59
Colorectal	1.02	0.93 - 1.11	1.11	0.99 - 1.23	1.31	1.14 - 1.51
Kidney	0.85	0.73 - 1.00	0.86	0.70 - 1.05	1.23	0.95 - 1.59
Leukemia/lymphoma	0.87	0.79 - 0.96	0.94	0.82 - 1.07	1.29	1.09 - 1.54
Lung	1.00	0.93 - 1.08	1.13	1.04 - 1.24	1.15	1.02 - 1.30
Melanoma	0.90	0.78 - 1.04	1.01	0.85 - 1.20	1.60	1.23 - 2.09
Prostate	0.95	0.87 - 1.03	1.06	0.96 - 1.17	1.39	1.20 - 1.61
Other	0.97	0.92 - 1.01	1.05	1.00 - 1.11	1.31	1.22 - 1.42

Cost-effectiveness analysis of teclistamab plus daratumumab in relapsed or refractory multiple myeloma.

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Background: Relapsed or refractory multiple myeloma (RRMM) remains a significant therapeutic and economic challenge as patients progress through successive lines of therapy. Teclistamab, a CD3×B-cell maturation antigen (BCMA) bispecific antibody, has demonstrated deep and durable responses in heavily pretreated patients in the phase 1–2 MajesTEC-1 trial. Daratumumab, an anti-CD38 monoclonal antibody, is a cornerstone of modern myeloma treatment. The phase 3 MajesTEC-3 trial evaluated teclistamab plus daratumumab versus daratumumab-based regimens, including daratumumab with pomalidomide and dexamethasone (DPd) or with bortezomib and dexamethasone (Dvd) in patients with RRMM. While teclistamab-based combinations have demonstrated strong clinical efficacy, their economic value relative to standard daratumumab-based regimens remains uncertain. **Methods:** We extracted event-free survival (EFS) and overall survival (OS) data from published Kaplan–Meier curves and reconstructed individual patient data using a validated algorithm (IPD-fromKM). A Markov model was developed to compare lifetime costs and health outcomes between treatment strategies. Model inputs were obtained from the Centers for Medicare & Medicaid Services, the Medicare Physician Fee Schedule, and published literature. Health state utilities, adverse event rates, treatment discontinuation probabilities, and toxicity costs were derived from the MajesTEC-3 trial and peer-reviewed sources. Analyses were conducted from a U.S. third-party payer perspective, with costs reported in 2025 U.S. dollars. Cost-effectiveness was assessed using incremental cost-effectiveness ratios (ICERs) with a \$150,000/QALY willingness-to-pay (WTP) threshold, and robustness was examined through one-way and probabilistic sensitivity analyses. **Results:** Gompertz and lognormal distributions were selected based on Akaike Information Criterion to extrapolate EFS and OS for the teclistamab–daratumumab and DPd/DVd arms, respectively. Using a Markov model, teclistamab plus daratumumab yielded an incremental gain of 1.16 QALYs compared with DPd/DVd, at an additional cost of \$95,376, resulting in an ICER of \$82,074 per QALY, well below the WTP threshold. Probabilistic sensitivity analysis showed that 88.9% of simulations favored teclistamab plus daratumumab at the \$150,000/QALY threshold. Treatment discontinuation rates and the cost of daratumumab in the DVd regimen were the primary drivers of ICER estimates. **Conclusions:** From a U.S. payer perspective, teclistamab plus daratumumab is cost-effective compared with DPd or DVd in patients with RRMM, supporting its broader adoption in clinical settings. Research Sponsor: None.

Base-case model.					
Strategy	Cost, USD	Incremental cost, USD	Effectiveness, QALY	Incremental effectiveness, QALY	ICER, USD/QALY
Teclistamab-Daratumumab	445,405	95,376	16.72	1.16	82,074
DPd or DVd	350,029		15.55		

Association of baseline clinical factors and treatment-related variables with survival in phase I solid tumor trials.

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Background: Phase I trials in solid oncology increasingly use biomarker-based enrollment and evaluate diverse therapeutic mechanisms. However, outcomes among patients with advanced solid tumors remain heterogeneous, and the relative contribution of baseline patient factors versus treatment-related variables to survival is incompletely defined. **Methods:** We conducted a retrospective analysis of patients with advanced solid tumors treated on Phase I clinical trials in UCLA's Drug Development Program between Jan 2013 and Sept 2025. Outcomes included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS). Survival was estimated using the Kaplan-Meier method. Multivariable Cox proportional hazards models identified factors independently associated with OS, adjusting for clinical variables, treatment characteristics (including combination vs monotherapy, mechanism of action [MOA] of study therapy, and participation in biomarker-selected trials vs unselected patients), and baseline laboratory values. **Results:** 726 patients were included across 106 trials. ORR was 13.3%, and DCR was 61.7%. Median PFS was 2.9 months (95% CI 2.66–3.39), and median OS was 10.4 months (95% CI 9.15–12.34). In univariable analysis, treatment-related characteristics, including combination therapy, were associated with OS, whereas participation in biomarker-selected trials and specific MOA was not consistently associated with survival. In multivariable analysis, OS was independently associated with baseline performance status (ECOG 1 vs 0: HR 1.35, 95% CI 1.12–1.63, $p = 0.0015$), combination therapy (HR 0.81, 95% CI 0.68–0.98, $p = 0.0283$) and female sex (HR 0.79, 95% CI 0.65–0.96, $p = 0.0164$). Baseline physiological parameters were strong predictors of OS, including higher hemoglobin (HR 0.90 per 1g/dL increase, 95% CI 0.85–0.96, $p = 0.0018$), higher albumin (HR 0.48 per 1g/dL increase, 95% CI 0.38–0.61, $p < 0.0001$), and higher lymphocyte count (HR 0.75 per 1.0K/ μ L increase, $p = 0.0005$). **Conclusions:** In this large retrospective cohort of patients treated on Phase I solid oncology trials, survival outcomes were primarily dictated by baseline physiological reserve and functional status rather than trial design features. While combination-based regimens were independently associated with OS, participation in biomarker-selected trials and MOA of study therapy did not retain prognostic significance after adjustment for clinical and laboratory factors. These findings suggest that baseline function and nutritional status remain the primary determinants of survival in early phase trials, highlighting the importance of rigorous clinical selection even in the era of increasingly diverse and novel therapeutic mechanisms. Ongoing analyses will further delineate prognostic factors associated with survival in this cohort. Research Sponsor: None.

Reduced treatment adherence and cancer mortality in patients with depression.

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Background: Depression affects up to 20% of cancer patients and is associated with poorer cancer outcomes. The lack of mechanistic explanations for this interaction greatly limits clinical interventions. We hypothesize that patients with late-stage malignancies have lower treatment adherence that may increase risk of cancer-specific mortality (CSM). **Methods:** We selected patients age 66+ years diagnosed with breast, colon, rectal, prostate, or non-small cell lung cancer (NSCLC) from 2010–2017 using Surveillance, Epidemiology, and End Results (SEER)–Medicare. International Classification of Diseases (ICD)–9 or ICD–10 codes identified depression. Late-stage included locally advanced (Stage III+ or high-risk prostate) or metastatic. Locally advanced treatment adherence was defined as receiving curative therapy <1 year from diagnosis. In metastatic patients, this was defined as receiving systemic therapy along with number of cycles/months, <6 months from diagnosis. Multivariate Fine Gray regression with non-cancer death as a competing event evaluated CSM. Multivariate logistic regressions modeled the impact of depression on receiving therapy, and multivariate linear regression modeled its role on cycles/months of systemics received. **Results:** The cohort included 93,384 patients, with median age of 74 years and follow-up of 4.2 years. In total, 21,690 patients (23.2%) had depression, highest in NSCLC (27.1%) and lowest in prostate (13.4%). Depression was associated with 6–36% increased risk ($p < 0.01$) of CSM (Table 1). Locally advanced patients with depression had 15–32% lower odds ($p < 0.01$) of receiving curative treatment. Patients with metastatic disease and depression had significantly lower odds of receiving systemic therapy, reduced cycles/months of systemics, or both (Table 1). **Conclusions:** Depression was associated with increased risk of CSM across five tumor histologies. Patients with depression exhibited decreased treatment adherence for all subtypes, underscoring a possible mechanistic explanation for increased CSM in this population. Research Sponsor: None.

Multivariate regressions for depression effect.

Endpoint	CSM: SHR 95% CI, p	Received treatment: Locally advanced OR 95% CI, p	Received treatment: Metastatic OR 95% CI, p	Therapy cycles/months: Metastatic, B Coefficient, p
Histology				
Breast	1.11 [1.02-1.24], <0.01	0.78 [0.65-0.92], <0.01	0.85 [0.71-1.03], 0.10	-0.52, <0.01
Colon	1.15 [1.10-1.20], <0.01	0.71 [0.63-0.79], <0.01	0.67 [0.59-0.75], <0.01	-0.63, <0.01
Rectal	1.13 [1.02-1.25], <0.01	0.68 [0.53-0.87], <0.01	0.67 [0.52-0.88], <0.01	-0.24, 0.33
Prostate	1.36 [1.25-1.48], <0.01	0.85 [0.78-0.93], <0.01	0.94 [0.69-1.31], 0.71	-0.22, 0.02
NSCLC	1.06 [1.04-1.09], <0.01	0.75 [0.67-0.84], <0.01	0.94 [0.88-0.999], 0.045	-0.21, <0.01

SHR: Subdistribution hazard ratio; OR: odds ratio; CI: confidence interval.

APS-TMA phenotypes as a failure-to-rescue signal during U.S. cancer hospitalizations: National Inpatient Sample, 2018–2022.

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Background: Failure-to-rescue (FTR), defined as mortality following major inpatient complications, reflects both patient disease pathology and hospital rescue capacity. Antiphospholipid syndrome (APS) and thrombotic microangiopathy (TMA) phenotypes are rare, high-acuity thrombotic syndromes observed during cancer hospitalizations, but whether excess mortality reflects independent risk factor versus complication-mediated risk is unclear.

Methods: A serial cross-sectional, hospitalization-level analysis was performed using the 2018–2022 Healthcare Cost and Utilization Project National Inpatient Sample (NIS). Adult hospitalizations with a principal diagnosis of malignancy were identified using ICD-10-CM codes (C00–C97; D45–D47). APS and TMA phenotypes were defined using any-diagnosis ICD-10-CM proxies for APS and TMA, including TTP/HUS, and combined as an APS/TMA phenotype. Because laboratory and medication data are unavailable in the NIS, exposures were analyzed as inpatient phenotypes rather than presumed diagnoses. Major complications included mechanical ventilation and acute kidney injury requiring dialysis. Failure-to-rescue was defined as in-hospital mortality among admissions with ≥ 1 major complication. National estimates incorporated discharge weights, hospital clustering, and stratification; multivariable models adjusted for All Patient Refined Diagnosis Related Group (APR-DRG) severity. **Results:** Among an estimated 4.81 million principal malignancy hospitalizations nationally, APS/TMA phenotypes occurred in 0.48% of admissions. Compared with non-phenotype admissions, APS/TMA phenotype hospitalizations had higher mortality (9.43% vs 4.35%) and higher rates of major complications, including mechanical ventilation (5.85% vs 2.57%) and dialysis-requiring acute kidney injury (2.11% vs 0.61%). In severity-adjusted modeling incorporating APR-DRG severity, APS/TMA phenotype was not independently associated with mortality (adjusted OR 0.99, 95% CI 0.70–1.40), indicating that excess mortality was largely mediated by complications and underlying illness severity. **Conclusions:** APS/TMA phenotypes identify a rare but high-acuity subgroup of cancer hospitalizations characterized by disproportionate ICU-level support and dialysis utilization, functioning as a national failure-to-rescue signal rather than an independent driver of mortality after severity adjustment. These findings highlight the importance of early recognition and severity-directed rescue strategies for high-risk thrombotic phenotypes during cancer admissions. Research Sponsor: None.

Premature cancer mortality in the United States, 1999–2023: Analysis of CDC WONDER data.

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Background: Premature cancer deaths (defined as mortality in adults aged 20–69 years) represent significant years of potential life lost (YPLL) and substantial disease burden, yet comprehensive national trends remain insufficiently characterized. **Methods:** CDC WONDER cancer mortality database (1999–2023) was queried for cancer-related deaths among individuals aged 20–69 years across USA. Age-standardized mortality rates (ASMR) per 100,000 person-years were calculated using 2000 U.S. Census standard population. Join point regression analysis identified temporal trend inflection points with annual percentage change (APC) and 95% confidence intervals (CI). Stratification included sex, race/ethnicity, geographic region, and 15 major cancer types. **Results:** From 1999–2023, 3,847,200 premature cancer deaths occurred in the U.S. (mean 153,888/year). Annual deaths increased 12.4% (152,100 in 1999 to 171,000 in 2023), while age-standardized mortality declined 18.6% (ASMR 87.3 to 71.1 per 100,000). Joinpoint analysis identified three phases: stability in 1999–2005 (APC –0.42%), accelerated decline in 2005–2015 (APC –2.18%), and slower improvement in 2015–2023 (APC –0.73%). Males had higher mortality than females in 1999 (ASMR 105.4 vs 69.2), with declines in both sexes (APC –1.89% males; –2.34% females), narrowing the male–female gap from 52.2% to 37.8% by 2023. Racial/ethnic disparities persisted: Black Americans had the highest ASMR in 2023 (84.3), 18.6% higher than Whites (71.1), with slower declines (APC –1.23% vs –2.07%); Hispanics/Latinos had the lowest ASMR (52.8) and fastest declines (APC –3.12%); American Indian/Alaska Native populations showed persistently high rates (89.2) with minimal change (APC –0.18%). In 2023, leading contributors were lung (38,200 deaths; ASMR 17.5; APC –3.78%), breast (23,100; 10.5; –2.45%), colorectal (11,800; 5.3; –3.12%), pancreatic (8,400; 3.8; –0.28%), and ovarian cancer (6,200; 2.8; –1.86%), together accounting for 58.2% of premature deaths. Cervical cancer declined sharply (APC –4.23%), while melanoma increased (APC +2.15%). **Conclusions:** Premature cancer mortality in the United States declined 18.6% from 1999–2023, yet significant and widening disparities persist by race/ethnicity, geography, and socioeconomic status. Alarming stagnation in declining rates post-2015, coupled with increasing absolute deaths among aging cohorts, signals necessity for intensified prevention efforts targeting modifiable risk factors. Research Sponsor: None.

Dose-response relationship of serum iron, ferritin, and transferrin saturation with cancer-related mortality: An analysis of population-based data.

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Background: Altered iron homeostasis has been linked to cancer outcomes, with epidemiologic evidence suggesting that both reduced iron availability (low transferrin saturation or anemia) and elevated iron markers, particularly ferritin, may correspond to higher cancer mortality. However, population-level data quantifying dose-response relationships between continuous iron indices and cancer-related mortality remain limited. This study evaluates the dose-response association of serum iron, transferrin saturation (TSAT), and ferritin with cancer mortality using nationally representative NHANES data. **Methods:** NHANES laboratory data were linked to National Death Index mortality files (1999–2019). Survey-weighted Cox proportional hazards models and Fine-Gray competing-risk models were used to assess linear, quintile-based, and restricted cubic spline-modeled non-linear relationships between iron biomarkers and cancer mortality. Models were further adjusted to evaluate independent effects of each biomarker. **Results:** A total of 52,593 participants were included, with 6,875 recorded deaths. In survey-weighted log₂ Cox models, serum iron (HR 1.41; 95% CI 0.17–11.68) and ferritin (HR 1.14; 95% CI 0.84–1.55) showed no significant linear association with cancer mortality, while TSAT suggested a nonsignificant inverse trend (HR 0.30; 95% CI 0.02–5.43). Quintile analyses revealed no consistent dose-response pattern for serum iron or TSAT; ferritin showed lower mortality in the second quintile (HR 0.33; 95% CI 0.12–0.92) without a graded pattern across higher quintiles. In mutually adjusted models including all three biomarkers, none demonstrated independent linear associations. Fine-Gray analyses identified a statistically significant but clinically small association for ferritin, whereas serum iron and TSAT remained nonsignificant. Restricted cubic spline models showed no clear non-linear dose-response for any biomarker. **Conclusions:** Among the iron indices evaluated, ferritin demonstrated the strongest and most consistent association with cancer-related mortality, although no clear linear or non-linear dose-response pattern emerged. Ferritin may serve as a more informative marker for risk stratification, but further mechanistic and longitudinal studies are warranted. Research Sponsor: None.

Predictors of mechanical ventilation in metastatic cancer hospitalizations: A National Inpatient Sample study.

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Background: Invasive mechanical ventilation (MV) represents a major escalation of supportive care in metastatic cancer and is consistently associated with high short-term mortality in prior observational cohorts. We sought to identify patient and hospital factors associated with MV utilization in metastatic cancer hospitalizations using national inpatient data. **Methods:** We analyzed the National Inpatient Sample (2016–2020), including adult hospitalizations with metastatic cancer (ICD-10-CM C77–C79). MV was identified using ICD procedure codes. Survey-weighted multivariable logistic regression estimated adjusted odds ratios (aOR) for MV utilization, adjusting for age group, sex, race/ethnicity, payer, hospital bed size, hospital region, and comorbidity burden using vwcheck (van Walraven score derived from Elixhauser comorbidities). **Results:** In the complete-case regression cohort (weighted N=6,859,238), MV utilization varied across demographic and health-system factors. MV was less likely with older age (≥ 65 vs 18–44: aOR 0.80, 95% CI 0.75–0.87) and in females (aOR 0.96, 95% CI 0.93–0.99). Black race was associated with higher MV odds compared with White race (aOR 1.18, 95% CI 1.13–1.23). Compared with Medicare, Medicaid (aOR 1.08, 95% CI 1.01–1.14) and self-pay (aOR 1.17, 95% CI 1.05–1.30) had higher MV odds. MV was more likely in medium vs small hospitals (aOR 1.08, 95% CI 1.03–1.14) and large vs small hospitals (aOR 1.08, 95% CI 1.03–1.13). Regional variation persisted (South vs Northeast: aOR 1.11, 95% CI 1.06–1.17; West vs Northeast: aOR 1.07, 95% CI 1.01–1.13). Higher vwcheck was strongly associated with MV (aOR 1.07 per unit). **Conclusions:** Among hospitalized patients with metastatic cancer, the use of mechanical ventilation varied by patient demographics, payer status, hospital size, and region, even after adjustment for comorbidity burden. These differences suggest heterogeneity in illness severity and/or thresholds for escalation of care across health systems. Mechanical ventilation remains a marker of high-risk hospitalization in advanced cancer, and understanding the factors associated with its use may help inform inpatient supportive-care planning and quality improvement efforts. Research Sponsor: None.

Predictors of mechanical ventilation in metastatic cancer hospitalizations (NIS 2016–2020).

Predictor	Adjusted OR (95% CI)	p-value
Age ≥ 65 vs 18–44	0.80 (0.75–0.87)	<0.001
Female vs male	0.96 (0.93–0.99)	0.01
Black vs White	1.18 (1.13–1.23)	<0.001
Medicaid vs Medicare	1.08 (1.01–1.14)	0.02
Self-pay vs Medicare	1.17 (1.05–1.30)	0.004
Medium vs small hospital	1.08 (1.03–1.14)	0.002
Large vs small hospital	1.08 (1.03–1.13)	0.001
South vs Northeast	1.11 (1.06–1.17)	<0.001
West vs Northeast	1.07 (1.01–1.13)	0.01
van Walraven score (per unit)	1.07 (1.06–1.08)	<0.001

Addressing housing instability as a quality-of-care determinant in cancer: A meta-analysis across national and Veterans Affairs cohorts.

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Background: Housing instability is an under-recognized determinant of cancer outcomes that directly affects screening adherence, treatment delivery, and survival. Over 650,000 Americans experience homelessness nightly, yet its impact on oncologic quality-of-care metrics remains poorly quantified. We conducted a meta-analysis to evaluate disparities in cancer screening, treatment, and survival among persons experiencing homelessness (PEH) versus housed individuals, and to assess whether housing status functions as a system-level quality indicator. **Methods:** Real-world evidence from the Veterans Health Administration (VHA), National Inpatient Sample (NIS), and community cohorts (2011–2024) was pooled using random-effects DerSimonian–Laird models. Eligible studies reported odds ratios (ORs) or hazard ratios (HRs) comparing PEH with housed counterparts. Heterogeneity was summarized using I^2 statistics, and all analyses were performed in Stata. **Results:** Six cohorts contributed sixteen effect estimates encompassing >200,000 cancer cases. PEH were less likely to be up to date for colorectal cancer screening (pooled OR 0.56, 95% CI 0.23–1.31; $I^2 = 93.9\%$). Homelessness was associated with markedly lower odds of surgery or other invasive procedures (pooled OR 0.42, 95% CI 0.26–0.66; $I^2 = 98.4\%$) and substantially higher odds of discharge against medical advice (pooled OR 5.37, 95% CI 3.39–8.50; $I^2 = 92.9\%$). In gastrointestinal cancer admissions, PEH also had longer hospital stays and higher costs. Within VHA datasets, homelessness independently predicted higher all-cause mortality after lung (HR 1.09–1.29) and colorectal cancer (HR 1.18–1.22). Veterans who gained housing after diagnosis achieved survival comparable to continuously housed peers (HR ≈ 1.0). **Conclusions:** Across diverse U.S. datasets, homelessness is consistently associated with lower screening uptake, reduced treatment receipt, and higher mortality—outcomes that represent measurable quality-of-care failures. Stable housing acts as a protective, modifiable factor influencing survival independent of access or insurance. Incorporating housing status screening into oncology intake workflows can close equity gaps, improve safety, and advance value-based cancer care. Housing stability should be recognized as a core quality metric in oncology. Research Sponsor: None.

Cohorts included in the meta-analysis of homelessness and cancer outcomes.			
Study	Cancer Type(s)	Main Outcomes	Effect (95% CI)
Asgary 2014 VA Cohort 2011–21	Colorectal CRC, Breast	Screening Screening / Colonoscopy	OR 0.35 (0.23–0.53) aIRR 0.84 (0.83–0.84); 0.88 (0.84–0.92)
Shah 2024	All cancers	Procedure / Therapy / AMA	AOR 0.53; 0.73; 4.29
Mevawalla 2019 VA Mortality 2011–20	GI Lung	Surgery / AMA Mortality	OR 0.33; AOR 6.86 HR 1.21 (0.93–1.57)
Health Affairs 2024	Lung, CRC, Breast	Mortality by housing	HR 1.09–1.29 (lung); 1.22 (CRC)

Impact of symptom burden, psychological distress, and treatment accessibility on quality of life in people with cancer in Syria.

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Background: In low-resource and conflict-affected settings, barriers to cancer care may amplify symptom burden and psychological distress, leading to poor quality of life (QoL). This study aimed to evaluate the impact of symptom burden (fatigue), psychological distress (depression), sources of psychological support, and treatment accessibility on the quality of life (QoL) of people with cancer in Syria. **Methods:** A cross-sectional study was conducted between April and May 2025 at Albairwni Hospital, Syria's national cancer center. Adult outpatient oncology patients completed validated Arabic versions of the Patient Health Questionnaire-9 (PHQ-9), Brief Fatigue Inventory (BFI), and Functional Assessment of Cancer Therapy-General 7 (FACT-G7). Socio-demographic and clinical data included cancer type, stage, metastasis, relapse, complications, treatment accessibility, and sources of psychological support. Statistical analyses included group comparisons and Spearman correlation. **Results:** Among 225 participants (median age 53; 71.6% female; 65.8% rural). 41.8% reported difficult access to treatment, while only 18.7% reported easy access. Psychosocial support was primarily provided by family (87.1%), followed by religious sources (37.3%) and healthcare providers (18.2%). Breast cancer comprised 49.3% of cases. By PHQ-9, 77.3% had depressive symptoms (mild 26.7%, moderate 25.8%, moderately severe 17.8%, severe 7.1%). Mean BFI total score was 32.5 ± 23.6 . Worse depression, greater fatigue and poorer QoL were associated with difficult treatment access (PHQ-9 $P = 0.01$; BFI $P = 0.01$; FACT-G7 $P = 0.005$), advanced stage (PHQ-9 & FACT-G7 $P < 0.001$; BFI $P = 0.001$), presence of metastases (PHQ-9 $P = 0.001$; BFI $P = 0.01$; FACT-G7 $P < 0.001$). Relapse was associated with higher depression and greater fatigue (PHQ-9 $P = 0.04$; BFI $P = 0.03$), while cancer-related complications were associated with worse scores across all scales (PHQ-9 $P < 0.001$; BFI $P = 0.001$; FACT-G7 $P < 0.001$). Health-provider support was associated with lower symptom severity and better QoL (BFI $P = 0.01$; FACT-G7 $P = 0.003$). Spearman correlations showed strong inverse relationships between fatigue measures and QoL (BFI total vs. FACT-G7 $\rho = -0.71$, $P < 0.001$), while QoL scores showed a graded decline as depression severity increased ($P < 0.001$). **Conclusions:** Depressive symptoms and fatigue are strongly associated with poorer QoL in cancer patients. Modifiable factors-notably treatment accessibility and health provider support- correlate with better outcomes and may be targets for interventions to improve patient wellbeing in low-resource oncology settings. Research Sponsor: None.

The AI paradox in precision oncology: Prospective blinded validation of large language models against molecular tumor board.

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Background: Molecular tumor boards (MTBs) are central to precision oncology but remain limited in accessibility. Large language models (LLMs) are increasingly proposed as scalable clinical decision-support tools, yet prospective validation is sparse. We evaluated multiple LLMs against MTB consensus, focusing on molecular pathway interpretation, actionability, and evidence strength. **Methods:** This prospective, blinded, cross-sectional validation study included consecutive cases discussed at a Tamil Nadu Medical and Pediatric Oncologist Society-initiated national MTB (July 2025–January 2026). Anonymized clinical and genomic data were analyzed using a standardized prompt across 4 latest LLM versions [ChatGPT (5, 5.1, 5.2), Perplexity, Gemini (2.5 Flash, 3 Pro), and DeepSeek], each queried in 2 independent runs to assess reproducibility; AI systems were blinded to MTB decisions, and reviewers to AI identity. Concordance was classified as concordant, discordant, AI non-evaluable (extraction failure or non-reproducible), or MTB non-evaluable (no predominant molecular pathway). The primary endpoint was end-to-end concordance; conditional concordance excluding non-evaluable outputs was secondary. Predictors of concordance were evaluated using univariate and multivariate logistic regression. **Results:** Of 108 cases, 80 were evaluable for AI comparison. Mean age was 56 years; 65% were male; 90% had ECOG 0–2; 73% had metastatic disease; and 82% were treated with palliative intent. The cohort was heavily pretreated, with 48% receiving ≥ 3 prior lines. Common pathways included EGFR/RAS/RAF/MAPK (34%), PI3K/AKT/mTOR (23%), and HRD/DDR (18%). End-to-end concordance was 88%, 74%, 83%, and 55% across the four LLMs. AI non-evaluable outputs due to extraction failure or non-reproducibility across two independent runs occurred in 3.8% to 21.3% of cases across platforms, highlighting important limitations in reliability. Citation-level hallucination rates were high (41%, 36%, 49%, and 48%). On univariate analysis, higher evidence level predicted concordance across all models (all $P \leq 0.03$). ESCAT tier was also significantly associated with concordance for LLM-2, LLM-3, and LLM-4. On multivariate analysis, evidence level remained the only consistent independent predictor for three LLMs, while ESCAT tier retained significance for one model. Inter-rater reliability was excellent (96.3%; $\kappa = 0.93$). **Conclusions:** LLM concordance is highest in guideline-supported, high-actionability settings but declines in low-evidence, poor-targetability scenarios—precisely where clinical support is most needed. This “AI paradox,” combined with substantial hallucination risk, indicates that while LLMs may assist first-pass molecular interpretation, expert multidisciplinary MTBs remain essential for safe and reliable precision oncology. Research Sponsor: None.

Evolution of immune checkpoint inhibitor trials in oncology from 2011 to 2025: A cross-sectional study.

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Background: Immune checkpoint inhibitors (ICIs) have transformed the oncology therapeutic landscape since the first FDA approval in 2011. Over the past decade, ICIs have expanded rapidly across tumor types, disease settings, and therapeutic strategies. However, a comprehensive evaluation of the long-term evolution and key characteristics of global ICI clinical trials remains limited. We conducted a cross-sectional analysis to characterize temporal trends and fundamental features of ICI oncology trials registered on ClinicalTrials.gov from 2011 to 2025. **Methods:** All interventional oncology trials with a primary treatment purpose registered on ClinicalTrials.gov between January 1, 2011, and December 31, 2025, were included. ICI trials were defined as studies investigating agents targeting CTLA-4, PD-1, PD-L1, or next-generation immune checkpoints (e.g., LAG-3, TIGIT, TIM-3). Trials were categorized by phase, randomization, enrollment, funding source, geography, tumor type, treatment setting, and primary endpoints. Descriptive statistics summarized trial characteristics and temporal trends. **Results:** A total of 8,756 interventional treatment-purpose ICI trials were identified. Annual trial starts increased from 32 in 2011 to a peak of 955 in 2021, remaining consistently high thereafter (858 in 2022, 848 in 2023, and 817 in 2024), and reaching 940 in 2025. Most trials were Phase 2 (4,174/8,756; 47.7%), Phase 1 (1,756; 20.1%), or Phase 1/2 (1,374; 15.7%), while Phase 3 trials only accounted for 870 (9.9%) overall. The number of Phase 3 trials increased from 4 in 2011 to 100 in 2019, declined during 2020–2022, and subsequently rebounded to 101 in 2023, 110 in 2024, and a peak of 137 in 2025, reflecting ongoing maturation toward late-stage development. Funding was most frequently categorized as other (5,291; 60.4%), followed by industry (3,065; 35.0%) and US federal sources (400; 4.6%). The most common tumor groups were non–small cell lung cancer (NSCLC) (1,014; 11.6%), melanoma (579; 6.6%), breast cancer (498; 5.7%), and colorectal cancer (431; 4.9%). Among trials with available location data (n=8,152), the United States (4,173; 51.2%) and China (2,647; 32.5%) were the most frequent trial locations. **Conclusions:** Over the past 15 years, ICI clinical trials have expanded markedly in number and across tumor types; however, the majority remain early-phase, open-label, and small in scale, with Phase 3 studies comprising less than 10% of all trials. Encouragingly, the recent increase in late-phase trials suggests continued maturation of the immuno-oncology field and sustained progress toward regulatory approval. Persistent geographic concentration highlights the need to broaden global participation and strengthen the generation of confirmatory evidence to maximize the clinical impact of ICIs in cancer care. Research Sponsor: National Natural Science Foundation of China; 82202827.

Baseline financial and credit status of participants enrolled in SWOG S1912CD.

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Background: Financial hardship is associated with adverse outcomes in cancer patients. While there is a critical need for interventions to prevent financial hardship, their scale and impact depend on the baseline financial status of patients. CREDIT (SWOG S1912CD) is a national prospective, randomized pragmatic trial evaluating the impact of a financial navigation intervention versus usual care on financial, clinical, and psychosocial outcomes. We report baseline demographic and financial characteristics of trial enrollees, using a combination of self-reported and credit data. **Methods:** Enrollees were within 6 months of diagnosis of a metastatic/stage IV solid tumor or hematologic malignancy. A total of 329 patients were randomized between July 2021 and December 2024 (165 control, 164 intervention). We assessed baseline income, employment, debt, homeowner status, financial fragility (ability to come up with \$2,000 in 30 days), mean Comprehensive Score for Financial Toxicity (COST), and financial coping strategies (e.g. loans, cost-related nonadherence). We also examined the proportion of patients with adverse credit indicators (bankruptcies, third-party collections, repossessions, tax liens, delinquent mortgage payments) in their baseline credit reports. We compared mean COST score for patients with versus without adverse credit indicators. **Results:** Most patients (median age 61.5) were White (78%), 51% had commercial insurance while 33% had Medicare. The most common cancer types were gastrointestinal (23%), lung (12%), and breast (11%). Median household income was \$50,001–\$75,000, 70% were homeowners, and 32% reported a change in employment following cancer diagnosis and prior to enrollment. 39% reported financial fragility, 71% reported debt (32% with debt greater than \$25K), and 20% reported taking loans from friends or family in the prior 3 months. Mean COST score was 19.6, with 45% of patients reporting scores ≤ 17.5 , consistent with significant financial toxicity. 18.5% of patients had utilized $\geq 75\%$ of credit limit on credit cards. The proportion of patients with prior bankruptcy, third-party collection, repossession, or delinquent mortgage payment were 3.3%, 16%, 2.7%, and 2.5% respectively. Mean COST score was significantly lower in patients with an adverse credit indicator compared to those without (21.4 vs. 13.0, $p < 0.0001$) suggesting good correlation between credit data and patient-reported outcome measure. **Conclusions:** A significant proportion of patients newly diagnosed with cancer reported debt, financial fragility, and significant financial toxicity. A smaller proportion had more severe financial challenges identifiable in their baseline credit reports. There is clearly a need for interventions to address and mitigate financial hardship in this population. Final primary analysis of the impact of CREDIT in this financially challenged population is forthcoming. Clinical trial information: NCT04960787. Research Sponsor: National Cancer Institute.

Palliative care for advanced cancer: Medicare Advantage and provider networks.

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Background: Palliative care is a specialized medical approach to improve symptoms and quality of life for patients with serious illnesses, including cancer, yet its utilization remains low. While enrollment in Medicare Advantage (MA) has grown and surpassed Traditional Medicare (TM), less is known about differences in palliative care between MA and TM and the extent to which MA plan design, particularly provider networks, contributes to these differences. **Methods:** Using the 2025 SEER–Medicare linkage, we identified Medicare beneficiaries aged ≥ 66 years diagnosed with distant-stage breast, colorectal, lung, pancreatic, or prostate cancer between 2016 and 2021. We included patients who survived at least 2 months after diagnosis and had continuous enrollment in TM or MA from 1 year before diagnosis to death/end of follow-up. The primary outcome was the cumulative incidence of palliative care billing within 6 months of diagnosis. To assess the role of provider networks, we first assigned each patient a treating oncologist based on the plurality of visits with cancer diagnosis codes; we then conducted 1:1 matching of patients enrolled in a given MA plan to patients in TM treated by the same oncologists within the same county. Multivariable Cox proportional hazards models estimated differences in palliative care billing between TM and MA overall and by MA plan type, before and after matching, adjusting for sociodemographic and clinical characteristics. **Results:** Among 135,402 beneficiaries with advanced cancer, 67.7% were enrolled in TM and 32.3% in MA; over half were female, 7.3% Hispanic, and 9.5% non-Hispanic Black. The 6-month cumulative incidence of palliative care billing was 13.3% among MA beneficiaries and 9.3% among TM beneficiaries. In adjusted analyses, MA enrollment was associated with higher palliative care billing (hazard ratio [HR], 1.39; 95% CI, 1.34–1.44). When stratified by plan types, palliative care was particularly higher among patients in health maintenance organization (HMO) plans (HR=1.66, 95%CI=1.60–1.72) but not other plan types. After matching on treating oncologists, 23,033 TM and 23,033 MA patients were included. Matched MA beneficiaries were less likely to have HMO plans than those not matched (49.1% vs. 76.7%). Differences in palliative care were attenuated and statistically non-significant, with cumulative incidence of 11.0% and 10.4% among MA and TM, and an adjusted hazard ratio of 1.05 (95%CI=0.99, 1.11). Similar attenuation was observed in HMO plans (1.16, 95%CI=1.08, 1.24). **Conclusions:** Palliative care billing was significantly higher among MA than TM beneficiaries, but these differences were substantially reduced after accounting for provider networks. These findings suggest that between-provider variation accounts for the majority of the difference in palliative care receipt between TM and MA beneficiaries. Research Sponsor: U.S. National Institutes of Health; K12AR084234.

Household costs of breast cancer and coping mechanisms in Kenya: A case of Kenyatta National Hospital.

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Background: In 2020, cancer was the third leading cause of mortality in Kenya, with breast cancer the most prevalent cancer and the second leading cause of cancer-related deaths. Patients and the health system faced a substantial economic burden due to breast cancer, which requires long-term medical attention as a chronic condition. Research has identified cost as a primary obstacle to accessing breast cancer healthcare services, particularly in low- and middle-income countries (LMICs). **Objectives:** The objective of this study was to examine the household costs of breast cancer among patients receiving treatment at Kenyatta National Hospital, Kenya's national referral hospital. Specifically focusing on cost incurred, drivers of cost and cost coping mechanisms. **Methods:** Cross-sectional descriptive research design was utilized to quantify the cost of breast cancer among 103 breast cancer patients at the Kenyatta National Hospital in 2024. Data were collected via a semi-structured questionnaire on the direct medical costs, direct non-medical costs, and indirect costs incurred, as well as cost coping mechanisms. To assess the drivers of cost, multivariable linear regression model was used to determine associations between the independent variables and cost outcomes. **Results:** The mean total costs of breast cancer were estimated to be USD 14,255 (KES 2,138,330). Direct medical costs (USD 8,916/KES 1,337,475) were the largest component, followed by direct non-medical costs (USD 1,917/KES 287,625) and indirect costs (USD 3,421/KES 513,229). Targeted therapy was the largest cost component within direct medical costs, representing 45.37% of direct medical costs. Luminal B and Stage IV breast cancer incurred the highest total costs. Patients primarily relied on public health insurance and personal income and savings to cater for the costs. Despite all participants using the National Health Insurance Fund (NHIF), now Social Health Authority (SHA), it only covered 25-50% of the direct medical costs. Out-of-pocket expenditures were significant, with 97% of respondents using personal income and savings, 29% liquidating assets, and 22% taking loans. **Conclusions:** Breast cancer patients and their households incur significant costs in Kenya. This underscores the need for urgent health financing reforms that ensure broadened insurance coverage, and social protection systems that ensure Kenyans have access to comprehensive cancer care and prevent cancer-related financial toxicity and impoverishment. Research Sponsor: Kenyatta National Hospital; KNH/R&P/23/24-25/10/5.

Disparities in race and insurance status among hospitalized patients with pancreatic cancer and protein–energy malnutrition: A nationwide analysis, 2016–2022.

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Background: Protein–energy malnutrition (PEM) is frequently encountered in patients with pancreatic cancer and is associated with worse clinical outcomes. Although sociodemographic differences in malnutrition risk have been described, it is unclear whether racial and insurance-based disparities persist after accounting for clinical complexity, socioeconomic factors, and hospital characteristics. We sought to identify independent predictors of PEM among hospitalized patients with pancreatic cancer using a nationally representative inpatient cohort with multivariable adjustment for relevant covariates. **Methods:** We conducted a retrospective cohort study using the National Inpatient Sample (NIS) from 2016 to 2022. Adult hospitalizations with pancreatic cancer were identified using ICD-10-CM code C25, and PEM was defined using ICD-10-CM codes E40–E46. Multivariable regression models evaluated independent predictors of PEM and its associations with in-hospital mortality, length of stay, discharge disposition, and hospital charges. Models adjusted for demographic factors, comorbidities, and hospital characteristics, with survey weights applied to generate national estimates. **Results:** Among an estimated 263,890 hospitalizations for pancreatic cancer, 37% were associated with PEM. After adjustment, Black patients (adjusted odds ratio [aOR] 1.39, 95% CI 1.31–1.48) and Asian/Pacific Islander patients (aOR 1.41, 95% CI 1.27–1.56) had higher odds of PEM compared with White patients. Medicaid insurance was associated with increased odds of PEM (aOR 1.12, 95% CI 1.03–1.22), whereas private insurance was associated with lower odds (aOR 0.85, 95% CI 0.80–0.91) relative to Medicare. Higher comorbidity burden (Charlson Comorbidity Index ≥ 3) was the strongest predictor of PEM (aOR 1.54, 95% CI 1.45–1.64). Median household income was not independently associated with PEM. PEM was more common in urban hospitals and those with larger bed size. **Conclusions:** In this national inpatient cohort, PEM was common among patients hospitalized with pancreatic cancer and demonstrated racial and insurance-based disparities that persisted after adjustment for income, comorbidities, and hospital characteristics. These findings highlight potential gaps in nutritional risk recognition and underscore the importance of standardized inpatient nutritional screening and targeted interventions for high-risk populations. Research Sponsor: None.

Variable	aOR	95% CI	P value
Age 50–64	1.20	1.03–1.38	0.016
Age ≥ 65	1.25	1.08–1.46	0.004
Female sex	0.94	0.91–0.98	0.006
Black race	1.39	1.31–1.48	<0.001
Asian/Pacific Islander	1.41	1.27–1.56	<0.001
Other race	1.23	1.10–1.38	<0.001
Medicaid insurance	1.12	1.03–1.22	0.010
Private insurance	0.85	0.80–0.91	<0.001
Charlson Index ≥ 3	1.54	1.45–1.64	<0.001

Malnutrition and cachexia as drivers of failure-to-rescue in gynecologic cancer hospitalizations, 2016–2023.

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Background: Malnutrition and cancer cachexia are underrecognized in administrative data yet may identify hospitalized oncology patients with limited physiologic reserve. Rather than acting solely as baseline comorbidities, these conditions may amplify the lethality of inpatient complications. The prevalence, temporal trends, and outcome-modifying role of malnutrition were evaluated among U.S. gynecologic oncology hospitalizations using a failure-to-rescue framework. **Methods:** A retrospective, survey-weighted analysis of the National Inpatient Sample (NIS), 2016–2023, was conducted. Adult hospitalizations with gynecologic malignancies (ICD-10-CM C51–C58) were included; palliative encounters (Z51.5) were excluded. Malnutrition was defined using a narrow phenotype (E43, E44.*, E46) and a broader definition including cachexia (R64). Outcomes included in-hospital mortality, ICU escalation (mechanical ventilation and/or shock), major complications (sepsis, bleeding/transfusion, venous thromboembolism, acute kidney injury, bowel injury/peritonitis, respiratory failure), length of stay (LOS), hospitalization cost, and failure-to-rescue (death following ≥ 1 complication among surgical admissions). Survey-weighted estimates with 95% confidence intervals (CI) were reported. **Results:** The cohort included 1,019,030 weighted hospitalizations. Malnutrition prevalence was 12.75% (95% CI, 12.53–12.98) using the narrow definition and increased from 9.61% in 2016 to 15.32% in 2023. In-hospital mortality was higher among malnourished admissions (4.36% [95% CI, 4.11–4.63] vs 1.55% [95% CI, 1.48–1.61]). Malnutrition was associated with greater ICU escalation (5.63% [95% CI, 5.35–5.92] vs 2.48% [95% CI, 2.41–2.56]), AKI (31.53% [95% CI, 30.93–32.13] vs 17.54% [95% CI, 17.33–17.76]), and any major complication (64.97% [95% CI, 64.35–65.60] vs 44.07% [95% CI, 43.74–44.40]). Resource utilization was higher with malnutrition (LOS 8.98 vs 4.71 days; cost \$28,155 vs \$18,740). Among admissions with complications, mortality was higher with malnutrition (6.27% [95% CI, 5.90–6.65] vs 3.16% [95% CI, 3.03–3.29]). In the surgical subcohort, failure-to-rescue mortality was 2.55% (95% CI, 1.98–3.28) with malnutrition versus 0.82% (95% CI, 0.70–0.95). **Conclusions:** In U.S. gynecologic oncology hospitalizations, malnutrition and cachexia identify a high-risk inpatient phenotype with disproportionate complication burden and post-complication mortality. These findings support malnutrition as a modifier of failure-to-rescue rather than an isolated baseline risk factor and highlight inpatient nutritional vulnerability as a target for early risk stratification and supportive intervention. Research Sponsor: None.

Comprehensive molecular profiling in advanced non-small cell lung cancer (NSCLC): Measurable survival and value impacts of implementation.

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Background: Comprehensive molecular profiling (CMP) is key to precision oncology in advanced non-small cell lung cancer (NSCLC), enabling identification of actionable driver alterations and delivery of matched targeted therapies that improve survival. CMP has been universally recommended by international guidelines for over a decade. Despite mature evidence and widespread availability, real-world adoption remains strikingly low. We evaluated the real-world impact of molecular profiling on survival, healthcare utilization, and cost in NSCLC, and quantified the magnitude of its ongoing underuse. **Methods:** We analyzed NSCLC patients aged ≥ 18 years treated between January 2019 and December 2025 using two independent real-world datasets: TriNetX and Highmark Health. Patients were categorized based on receipt of broad-panel molecular profiling consistent with guideline-directed indications. Outcomes included overall survival (OS), emergency department (ED) visits, inpatient admissions, and healthcare costs. Survival was assessed using Kaplan-Meier methods, with multivariable regression to adjust for clinical factors. **Results:** Among 33,977 NSCLC patients in TriNetX, only 2,354 (6.9%) underwent molecular profiling, despite the majority of NSCLC patients presenting with advanced disease. Molecularly profiled patients experienced a substantial survival advantage, with median OS of 1,784 days versus 1,074 days in untested patients (adjusted hazard ratio 0.61; $p < 0.001$). Molecular profiling was also associated with significantly fewer inpatient admissions (0.651 vs 0.875; $p < 0.001$) and ED visits (0.437 vs 0.583; $p = 0.047$). Highmark Health data independently validated these findings, demonstrating significantly improved 4-year OS in molecularly tested patients (55% vs 43%; $p < 0.001$). Importantly, these survival gains were achieved without a statistically significant increase in total cost per patient per month at follow-up ($p = 0.083$). **Conclusions:** Across two large, independent real-world datasets, comprehensive molecular profiling in NSCLC was associated with meaningful improvements in survival and reductions in healthcare utilization, even when applied primarily in advanced disease. These benefits were achieved without a significant increase in overall costs, supporting the value-based impact of precision oncology. Yet fewer than 1 in 15 eligible NSCLC patients underwent molecular profiling between 2019 and 2025, revealing a profound and persistent failure to implement guideline-concordant care. This underuse directly translates into avoidable mortality and unnecessary healthcare utilization. System-level solutions, including standardized and reflexive molecular testing at diagnosis, are urgently needed to ensure precision medicine is delivered as standard care in advanced NSCLC patients. Research Sponsor: None.

Overall survival of Black patients with newly diagnosed multiple myeloma in the era of triplet and quadruplet therapies.

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Background: Black individuals have been shown to have a higher incidence of multiple myeloma, as well as worse survival, compared with White patients. A single VA-based study demonstrated that with equal access to myeloma therapy, Black patients have superior survival compared to White individuals. Nevertheless, it is unknown whether this finding holds in other settings. **Methods:** This retrospective cohort study included adult patients newly diagnosed with multiple myeloma between January 1, 2017, and December 31st, 2023, in one health system in Ohio and Florida. We captured receipt of triplet or quadruplet therapy within one year of diagnosis, as well as patients' overall survival (OS) through September 30, 2025, using the Cleveland Clinic electronic health record, including linked state and federal death records. A multivariable logistic regression model examined the association of race with the receipt of either triplet or quadruplet therapy within one year of diagnosis, and a multivariable Cox regression model examined the association of race with 5-year all-cause mortality. The Cox model was adjusted for receipt of either a triplet or quadruplet regimen within 1 year, age at diagnosis, sex, Charlson comorbidity index (CCI), ECOG performance status, baseline eGFR, urbanicity of patient's residence, area deprivation index based on Census Block Group, insurance type, and year of diagnosis. **Results:** We identified 1230 patients, 54.1% male, 74.1% White, 22.8% Black, 3.1% other races. Mean (SD) age at diagnosis of 67.2 (11.1); it was 67.7 (10.8) for White and 65.9 (11.7) for Black patients. Overall, 66.3% of the cohort had an ECOG performance score of 0-1, 59.9% had baseline eGFR ≥ 60 , and 51.1% had a CCI of ≤ 2 . Within one year of diagnosis, 707 patients (57.5% of the cohort) received either triplet or quadruplet therapy, including 56.6% (n=516) of White and 58.9% (n=165) of Black individuals. Both univariable and multivariable analyses did not indicate a significant association between race and receipt of either a triplet or quadruplet therapy (aOR for Black race vs. White, 0.91, 95% CI, 0.64-1.28). According to Kaplan-Meier estimate, the probability of 5-year OS in the overall cohort was 62.1% (95% CI, 59.0%-65.4%). In the multivariable Cox regression model for all-cause mortality at 5 years, aHR for death for Black patients vs. White was 0.76 (95% CI, 0.58-1.00). **Conclusions:** In this large and diverse cohort of patients who had equal access to triplet or quadruplet therapies for newly diagnosed multiple myeloma, Black patients did not have a higher risk of all-cause mortality at 5 years compared to White individuals. Our findings indicate that health equity initiatives aimed at improving access to multiple myeloma care among minority patients have the promise of addressing race-based disparities in survival. Research Sponsor: National Cancer Institute.

Impact of U.S. most-favored-nation (MFN) drug pricing on global oncology access.

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Background: U.S. cancer drug prices substantially exceed those in other OECD countries. In May 2025, a U.S. Presidential Executive Order mandated adoption of a Most-Favored-Nation (MFN) pricing policy, linking U.S. drug prices to those of economically comparable countries. In December 2025, the Centers for Medicare & Medicaid Services (CMS) proposed two MFN-based frameworks: the Global Benchmark for Efficient Drug Pricing (GLOBE) for Medicare Part B drugs and Guarding U.S. Medicare Against Rising Drug Costs (GUARD) for Part D drugs. Both require manufacturer rebates when U.S. prices exceed GDP-adjusted international benchmarks, creating potential incentives for manufacturers to alter global oncology pricing and launch strategies. This study assesses which international markets may face pricing pressure or delayed access to new oncology therapies following MFN implementation. **Methods:** The top 50 best-selling U.S. drugs in 2024 were reviewed, and 12 oncology drugs without generic or biosimilar competition were selected. List prices were collected from the 19 OECD reference countries included in GLOBE and GUARD. Prices were adjusted for GDP per capita using purchasing power parity (PPP). For each drug, the two lowest GDP-adjusted international prices were identified and compared with U.S. prices, using January 2026 Medicare Average Sales Price (ASP) data for Part B drugs and December 2025 Federal Supply Schedule (FSS) prices for Part D drugs. **Results:** Across all 12 drugs, GDP-adjusted benchmark prices were 48% to 90% lower than U.S. prices. Pembrolizumab, the top-selling oncology drug in 2024, had a U.S. Medicare price of \$5,972 per 100 mg; the lowest adjusted prices were observed in South Korea (\$2,116) and Japan (\$2,271), representing reductions of 65% and 62%, respectively. Daratumumab, the second top-selling oncology drug, was priced at \$2,831 per 400 mg in the U.S., compared with \$1,467 in South Korea and \$1,603 in the Netherlands (48% and 43% lower). The lowest benchmark prices most frequently originated from South Korea (n=5) and the Netherlands (n=4). Norway, Germany, and Japan each provided the lowest benchmark for one drug. Second-lowest benchmark prices were observed in Japan (n=4), South Korea (n=3), the Netherlands (n=2), Germany (n=2), and Norway (n=1). **Conclusions:** Countries serving as the lowest-price benchmarks— particularly South Korea, Japan, the Netherlands, Norway, and Germany— may face increased risk of upward pricing pressure or delayed access to innovative oncology therapies as manufacturers seek to limit U.S. MFN rebate exposure. Expanded use of confidential discounts, confidential rebates and other managed-entry agreements may help preserve access while reducing MFN benchmark risk. Research Sponsor: None.

When does time become a burden? Evaluating the association between time spent on cancer care and patient distress.

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Background: While cancer care is time-intensive, the specific impact of various tasks on patient well-being is poorly understood. We evaluated how time spent on specific cancer-care tasks contributes to patient distress and identified patient populations most vulnerable to these time burdens. **Methods:** We enrolled individuals receiving treatment for advanced-stage ovarian or metastatic breast cancer at the University of Minnesota and the University of Alabama-Birmingham. Participants used a mobile app for 28 days to log time spent on out-of-home and at-home cancer-care related tasks. Daily distress was measured via the National Comprehensive Cancer Network (NCCN) Distress Thermometer (0-10; 0=no distress, 10=extreme distress). The primary outcome was clinically significant distress (NCCN distress score <4 vs. ≥ 4). Predictors included any time spent on each task type on a given day for both out-of-home healthcare tasks (lab, clinic, treatment, research, imaging, other) and at-home tasks (taking medications, scheduling appointments, managing medical bills/insurance claims, symptom management, monitoring health status, seeking information, and arranging help/transportation). A multi-level model with a random intercept for participants was used, adjusting for age, employment, education, dependent and partner status. Odds ratios and 95% confidence intervals are reported. **Results:** Analysis included 1,869 days from 60 participants (median age 59; 42% employed; 35% with dependents). Experience of significant distress was more likely on days including out-of-home treatment compared to days without treatment (OR: 2.54 [1.47, 4.39]). Participants were also more likely to experience significant distress on days including time spent on symptom management (OR: 2.59 [1.85, 3.64]), health monitoring (OR: 2.50 [1.56, 3.98]), and managing bills/claims (OR: 2.24 [1.22, 4.12]) compared to days without those tasks. Vulnerability varied: employed patients were more distressed by managing bills/claims and information seeking, while non-working patients experienced more distress on treatment days. Among those with dependents, scheduling was a unique stressor. **Conclusions:** Out-of-home treatment and at-home cancer-care tasks are significantly associated with patient distress. Findings suggest that interventions reducing at-home administrative and symptom burdens would reduce patient distress, and resources may need to be tailored based on employment and caregiving status. Clinical trial information: NCT05708703. Research Sponsor: U.S. National Institutes of Health; 1R01CA277714, P30 CA77598, P30 CA013148, UM1TR004405.

An AI-powered, human-in-the-loop, real-time registry platform to enable clinical trials, pragmatic studies, and prospective external control arms (ProECA) at scale in US community practices.

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Background: Drug development is requiring novel approaches such as prospective external controls to reduce development timelines and de-risk phase transitions. The majority of oncology patients in the US are seen at community oncology centers, many of which have limited clinical research infrastructure. The Kaleido registry was initiated to address these challenges through a hybrid operational technology model combining on-site staff, clinical note preparation, pre-visit abstraction, and automated workflows to facilitate pre-screening, data capture and research operations. **Methods:** The Kaleido registry enrolls patients at US community oncology practices with variable research infrastructure and is actively enabling seven studies. Real-time abstraction is performed prior to each patient visit across an expanding set of indications, including non-small cell lung cancer (NSCLC), colorectal cancer (CRC), prostate cancer, and myeloproliferative neoplasms, enabling standardized data collection and systematic/unbiased trial prescreening. An automated prescreening tool was developed and validated against manual chart review. Standardized draft notes are generated to reduce clinical documentation burden. A patient questionnaire captures social determinants of health (SDOH) and self-reported performance status. **Results:** As of 1/1 2026 more than 16,000 patients (60% female, median age 70 years, range 19-105) from 28 sites have been consented. Most common diagnoses are breast (29%), colorectal (9%), prostate (6%) and lung cancer (6%). 99% of approached patients filled out the patient questionnaire and missingness of race/ethnicity/education/marital status was <4%. Comprehensive biomarker testing exceeded 85% for patients with metastatic NSCLC. Time from specimen collection to NGS results (median 18 days, range 5-45) or PD-L1 (median 21 days, range 4-45) was a key driver of delays in evaluating trial-eligibility. Patients were consistently identified prior to starting next line of therapy. The model identified additional trial-eligible patients beyond standard workflows even at high-performing sites. In 2025, more than 500 patients were included in trials, ProECAs and pragmatic studies with enhanced data depth within the registry. **Conclusions:** The Kaleido registry demonstrates a scalable, integrated infrastructure for real time patient identification and comprehensive prospective data collection in the community setting. By facilitating community trial enrollment, pragmatic studies and prospective external controls while reducing operational burden of clinical teams, Kaleido has the potential to significantly accelerate drug development. Research Sponsor: None.

Association of drug industry payments to oncologists and use of guideline-preferred cancer treatments.

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Background: Payments from the drug industry to oncologists are common and influence physicians' prescribing decisions. However, whether payments affect the likelihood that patients receive optimal cancer treatment has not been assessed. **Methods:** This was a population-based cohort study. We used fee-for-service Medicare claims to identify patients with incident cancer diagnosis (new cancer diagnosis code after ≥ 1 year with no cancer diagnosis codes) from 2014–2020. We used National Comprehensive Cancer Network (NCCN) Guidelines to identify treatment scenarios (e.g., metastatic melanoma, stage III colon adjuvant therapy) with variation in the clinical benefit among recommended treatment options. The patient cohort corresponding to each scenario was identified using claims. We used NCCN Guidelines to identify the “optimal” treatment for each scenario (defined as the designated “preferred” treatment, with NCCN Evidence Blocks scores used for tiebreaks) at each time point across the study period. The primary outcome was whether a patient received the treatment that was, as of their diagnosis date, the optimal treatment for their cancer (vs. any non-optimal treatment). The primary exposure[s] were whether a patient's medical oncologist received personal (“general”) payments (source: linked Open Payments data) related to 1) optimal treatment or 2) any non-optimal treatment, during the year prior to the patient's cancer diagnosis. We fit Poisson-family generalized estimating equations, with physician-level clustering and adjustment for scenario, year, and patient characteristics, to estimate the relative risk (RR) of optimal treatment. **Results:** There were 14 clinical scenarios comprising 15,835 patients. There were 3,429 (21.7%) patients whose oncologist received payment for the optimal treatment, 4,891 (30.9%) for non-optimal payments, and 1,993 (12.6%) to both payment types. Oncologist receipt of payment for optimal treatment was associated with a greater likelihood (RR=1.07, 95%CI:1.01–1.13), and payment for non-optimal treatment was associated with lower likelihood (RR= 0.94, 95%CI:0.89–0.98) of patients receiving optimal treatment. Associations became stronger as payment dollar value increased; for optimal payments $\geq \$10,000$, RR=1.26 (95%CI:1.02–1.57), and for non-optimal payments $\geq \$10,000$, RR=0.70 (95%CI: 0.49–1.00). An estimated 41.6% of unexposed patients received optimal treatment; versus 52.6%, 29.3%, and 33.8% among patients exposed to $\geq \$10,000$ of payments for optimal treatment only, $\geq \$10,000$ non-optimal payments only, and $\geq \$10,000$ of both payment types, respectively. **Conclusions:** Industry payments related to the optimal cancer treatment were associated with increased use of the optimal treatment. However, payments related to non-optimal treatments were more common and were associated with decreased use of optimal treatment. Research Sponsor: NIH – National Cancer Institute; R37CA264563; National Institute of Health Care Management; GC260700; NIH – National Cancer Institute; P30CA008748.

Format matters: Digital vs print delivery of a job retention intervention during breast cancer therapy.

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Background: Talking to Employers and Medical Staff about Work (TEAMWork) is an English/Spanish intervention, delivered as a booklet or mobile app, which was developed to improve work outcomes among women undergoing (neo)adjuvant breast cancer therapy. TEAMWork provides education on work accommodations based on vocational rehabilitation principles, employer negotiation strategies, symptom self-management tools, and guidance on communicating with clinicians to enhance support (e.g., obtain work documentation). Here we present data on predictors of intervention use during systemic therapy from an ongoing randomized controlled trial comparing the TEAMWork app to the booklet. **Methods:** Eligible participants were women aged 18–65 years with stage I–III breast cancer who spoke English and/or Spanish, were employed pre-diagnosis, and undergoing or planning to undergo systemic (neo)adjuvant chemotherapy. Patients were recruited between October 2021 – March 2025 from multiple New York City sites. Data on socio-demographics, work characteristics, and intervention use were collected through patient surveys at baseline and after completion of chemotherapy. Multivariable logistic regression was used to assess predictors of intervention use during systemic therapy. **Results:** Of 372 participants (89% English; 11% Spanish), 54% identified as White, 17% Black, and 20% Hispanic/Latina. The mean age was 48 years. 70% were college-educated. All were employed at diagnosis, but only 77% were actively working (e.g., not on leave) at baseline. Participants worked in various occupations: managerial/professional (50%), sales/technical/administrative support (24%), service providers (21%), arts/media/athletics (5%), and operators/fabricators/laborers (1%). All participants received chemotherapy, with 53% starting therapy before the baseline survey. Slightly over half of participants (53%) reported using TEAMWork during systemic therapy; 120/187 (64%) in the mobile app arm and 76/185 (41%) in the booklet arm. In multivariable analysis, assignment to the mobile app arm was positively associated with intervention use during treatment (OR 2.54, 95% CI 1.61–4.05, $p < .001$). However, age, race, ethnicity, language, US-born (yes/no), educational attainment, occupational category, and chemotherapy initiation prior to randomization were not independently associated with intervention use. **Conclusions:** After adjusting for sociodemographic, occupational, and treatment-related characteristics, participants randomized to the mobile app arm had more than double the odds of using TEAMWork compared to those in the booklet arm. These findings underscore the importance of delivery format in the design of supportive interventions. Although mobile app development can be time- and resource-intensive, this approach may offer meaningful advantages in promoting patient engagement during therapy. Research Sponsor: National Cancer Institute; R01 CA214785; National Cancer Institute; R37 CA214785; National Cancer Institute; P30 CA008748; National Cancer Institute; T32CA275764.

Co-creating patient partnership within a national cancer trials network: Experience from Cancer Trials Ireland in partnership with the Irish Cancer Society.

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Background: Structured patient partnership is increasingly recognised in oncology research, yet less is known about how cancer trials groups and cancer charities can collaborate to sustain partnership system-wide. Cancer Trials Ireland (CTI) has established a patient partnership model through its Patient Consultants Committee, supported by the Irish Cancer Society (ICS), enabling integration of research infrastructure, charity support, and advocacy. **Methods:** The development and implementation of patient partnership at CTI from inception in 2016 was reviewed. The role of the ICS in enabling this model through funding, strategic alignment and public engagement was considered. Organisational learnings, barriers and facilitators to integration, research and strategic outputs, public outreach, clinical trial impacts, national and international collaborations, and engagement with early career investigators were synthesised from descriptive programme data and documented outputs. **Results:** By 2026, 33 patient partners were embedded across all adult Disease-Specific Subgroups, with patient and ICS representation in CTI governance. Key facilitators included a funded coordination role, enhanced partner recruitment, aligned public messaging, shared advocacy for clinical trial access and funding, and international research network engagement. Barriers to integration included challenges in patient diversity, competing commitments, and sustainable funding. Several were mitigated through partnership resourcing, advocacy and alignment of strategic priorities. Since 2023, patient partners have contributed to four investigator-initiated trial concepts and participated in Trial Management Groups. They contributed to grant applications, trainee research projects, and the development of a CTI climate change charter. Five patient-led, trainee-integrated research projects were delivered, resulting in international conference presentations and peer-reviewed publications. The CTI-ICS partnership supported sustainability and visibility through public engagement and policy activity, including contributions to the National Clinical Trials Oversight Group, engagement on GDPR barriers, election manifesto advocacy, and the *Value of Cancer Trials* campaign (co-launched with ICS and a patient partner). These findings demonstrate feasible integration of patient partners into a national cancer trials network at scale. **Conclusions:** A structured partnership between a national cancer trials organisation and a cancer charity can accelerate and sustain patient partnership beyond individual studies, embedding patient perspectives across trial selection, development, and dissemination. This experience complements cooperative group frameworks and offers a replicable approach for oncology research systems. Research Sponsor: Irish Cancer Society; Health Research Board (HRB).

Commercial price variation in precision oncology testing across US hospitals.

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Background: Precision oncology testing using clinically validated biomarker tests is standard of care for solid tumors and is endorsed by clinical guidelines and professional societies. However, these tests represent a substantial and growing component of cancer care costs. Commercial payer-negotiated prices for these tests and their variation across hospitals and payers have not been examined. **Methods:** We conducted a cross-sectional analysis of hospital-reported commercial payer-negotiated prices, aggregated by Turquoise Health as of January 2026, for biomarker tests commonly used in breast, colon, and non-small cell lung cancer and identified using the National Comprehensive Cancer Network Biomarkers Compendium and Centers for Medicare and Medicaid Services Clinical Laboratory Fee Schedule. We included tests with unique Current Procedural Terminology codes and extracted prices negotiated between short-term acute care hospitals and the four largest US payers (Aetna, Blue Cross Blue Shield, Cigna, UnitedHealthcare). Prices were adjusted using ZIP code-level Geographic Adjustment Factors. We assessed within- and between-hospital variation in prices for each test using the median 90th-to-10th percentile price ratio and compared prices across payers using Kruskal-Wallis tests. **Results:** We identified 422,515 payer-negotiated prices for 28 biomarker tests from 2,142 US hospitals. Oncotype DX Breast Recurrence Score and CEA expression testing were the most frequently reported panel- and non-panel-based tests, with median (interquartile range [IQR]) prices of \$4,129 (\$3,869–\$10,680) and \$28 (\$20–\$59), respectively, across hospitals. The percentage of hospitals reporting negotiated prices, price amounts, and price variation are summarized in the Table. Cigna had the highest prices for 20 (71.4%) tests, whereas UnitedHealthcare had the lowest price for all tests. **Conclusions:** Commercial payer-negotiated prices for precision oncology testing varied substantially across payers and hospitals, with greater variation between than within hospitals for the same tests. Given the central role of these biomarker tests in guideline-recommended cancer care, price variation has important implications for payer spending, clinical decision-making, patient out-of-pocket costs, and equitable care access. Research Sponsor: None.

Price variation for precision oncology testing.				
Biomarker Tests	Percentage of hospitals in Turquoise Health database reporting negotiated price, Median (IQR)	Negotiated price, USD, Median (IQR)	Within-hospital ratios, Median (IQR) ¹	Between-hospital ratios, Median (IQR) ¹
Panel-based (N=13)	18.3% (17.2%-18.8%)	\$3,704 (\$3,096-\$4,129)	1.5 (1.4-1.5)	5.5 (5.5-5.6)
Non-panel-based (N=15)	30.3% (22.2%-37.8%)	\$301 (\$157-\$485)	1.6 (1.5-1.7)	5.2 (5.1-5.4)

¹Median (IQR) of ratios of the 90th:10th percentile payer-negotiated prices within each hospital and across all hospitals for the same test.

Economic evaluation of a designated oncology pharmacist in hemato-oncology outpatient care: A randomized clinical trial.

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Background: Adverse drug reactions (ADRs) and medication errors are major contributors to morbidity and healthcare utilization in hemato-oncology. In a randomized clinical trial, we previously demonstrated that integrating a designated oncology pharmacist significantly reduced ADRs and intercepted potentially serious medication errors. The economic value of this intervention has not yet been established. **Methods:** We conducted a trial-based cost-effectiveness analysis alongside a single-center randomized clinical trial (n=182), in which adult patients with hematologic malignancies were randomized 1:1 to comprehensive pharmaceutical care delivered by a designated oncology pharmacist versus standard care. Patients were followed for 5 months (4-month intervention plus 1-month follow-up). The primary economic outcome was incremental cost per ADR avoided; secondary outcomes included cost per emergency department visit and hospitalization avoided. The analysis was conducted from the public healthcare system perspective and included only the pharmacist program cost, estimated at \$105 per patient over the 5-month study period. Incremental cost-effectiveness ratios (ICERs) were calculated using absolute risk reduction, with uncertainty assessed by nonparametric bootstrap resampling (5,000 replications). Costs are reported in 2022 USD. **Results:** ADRs occurred in 47.3% of control patients compared with 23.1% of intervention patients, corresponding to an absolute risk reduction of 24.2% and a number needed to treat of 4.1. The ICER was \$434 per ADR avoided (bootstrap 95% CI: \$281–\$956), with a >99.9% probability that the intervention reduced ADRs. Secondary outcomes also favored the intervention: emergency department visits (37.4% vs 28.6%; ICER \$1,194 per visit avoided) and hospitalizations (28.6% vs 23.1%; ICER \$1,911 per hospitalization avoided). In addition, the pharmacist intercepted 287 medication errors in real time, including 13 potentially severe errors, with a physician acceptance rate of 94.8%. **Conclusions:** This economic evaluation demonstrates that integrating a designated oncology pharmacist in hemato-oncology outpatient care is a cost-effective strategy for preventing ADRs and reducing acute healthcare utilization. These findings support broader implementation of oncology pharmacists as a high-value patient safety intervention. Research Sponsor: None.

Local and state paid sick leave policies and timeliness of treatment initiation among working-age patients with early-stage breast cancer.

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Background: Local and state paid sick leave (PSL) mandates have been associated with increased use of preventive services, including cancer screening, and reduced emergency care utilization. Little research has examined PSL policies and cancer after diagnosis. This study evaluates associations of PSL policies and timely treatment initiation among women with early-stage breast cancer. **Methods:** We identified patients aged 18–64 years newly diagnosed with stages 0–II breast cancer from the National Cancer Database in 2004–2023 and linked then to area-level policy implementation, measured as the month and year the state, county, or city required PSL. Primary outcomes were receipt of definitive surgery or neoadjuvant therapy within 30, 60, and 90 days of diagnosis. We compared changes in treatment initiation between patients residing in areas with and without PSL policies during and after the month and year of diagnosis. We used a staggered difference-in-differences design to account for differential timing of implementation, adjusting for patient demographics, clinical, and area-level characteristics. Random errors were clustered at the state level. Supplemental analyses stratified by county-level unemployment rates and individual insurance coverage. **Results:** The study included 1,891,411 patients, of whom 249,313 (13.2%) resided in an area with PSL policies at diagnosis. Patients in areas with PSL policies were more likely to have Medicaid, reside in higher-income and metropolitan areas. PSL policy implementation was significantly associated with a 3.4 percentage point (PPT) increase in the probability of treatment ≤30 days (95% CI: 1.1–5.7), 3.0 PPT increase ≤60 days (95% CI: 1.6–4.3), 1.3 PPT increase ≤90 days (95% CI: 0.5–2.1) (Table). Improvements in timely treatment were concentrated in low-unemployment areas; no significant improvements were observed in high-unemployment areas. The magnitude of associations between PSL policies and treatment initiation was stronger among patients without private insurance than with private insurance. **Conclusions:** Local and state PSL mandates were associated with earlier treatment initiation among working-age patients with early-stage breast cancer, especially in areas with low female unemployment rate. Findings suggest that PSL policies play an important role in timely cancer treatment for employed women who may not have PSL through their jobs. Research Sponsor: None.

Association of paid sick leave policies and breast cancer treatment initiation.					
	Time from diagnosis to surgery/neoadjuvant therapy (days)	DID PPT	Lower 95% CI	Upper 95% CI	P-value
Overall	≤30	3.4	1.1	5.7	0.004
	≤60	3.0	1.6	4.3	0.000
	≤90	1.3	0.5	2.1	0.001
Low female unemployment	≤30	2.2	-0.7	5.0	0.136
	≤60	3.8	1.8	5.8	0.000
	≤90	1.2	0.3	2.2	0.012
High female unemployment	≤30	1.8	-0.6	4.2	0.145
	≤60	-1.2	-4.5	2.0	0.459
	≤90	-1.4	-3.7	0.9	0.232

Association of facility type and metastatic burden with survival in gastric adenocarcinoma: A National Cancer Database study.

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Background: While we know metastatic burden dictates survival in gastric adenocarcinoma (GA), how this intersects with where a patient receives care remains less clear. Academic centers (AC) often report better outcomes, but we haven't fully determined if this "academic advantage" holds true once you account for the sheer extent of disease at the time of diagnosis. We set out to test whether AC care offers a survival benefit that persists regardless of a patient's baseline metastatic burden. **Methods:** We retrospectively analyzed the National Cancer Database (2016–2023), identifying 102,869 patients with GA. We grouped patients by facility type (AC vs. community). We mapped metastatic burden at diagnosis across six specific sites: bone, brain, liver, lung, distant lymph nodes, and other. After comparing baseline characteristics, we estimated 3-year overall survival (OS) using Kaplan–Meier methods. Our primary tool was a multivariable Cox model, adjusting for age, Charlson–Deyo score, clinical stage, and metastatic burden to isolate the link between facility type and mortality. **Results:** Of the 102,869 patients, 58.4% (n = 60,064) were treated at ACs and 41.6% (n = 42,805) at community sites. Interestingly, community patients arrived with a higher burden of disease (33.8% vs. 30.4%; $p < 0.001$), and 11.7% of the total cohort had multi-site metastasis (≥ 2 sites). The liver was the most frequent site of spread, appearing more often in community settings (18.4% vs 15.4%; $p < 0.001$). Three-year OS was significantly higher at ACs (45.2% vs 35.8%; $p < 0.001$). After adjusting for site count, comorbidity, age, and stage, AC treatment remained independently associated with lower mortality (HR 0.81; 95% CI 0.80–0.83; $p < 0.001$). Notably, this academic survival advantage was not driven by any single metastatic site; the benefit persisted across all individual sites of involvement, including brain and lung, with no site showing a loss of AC advantage. **Conclusions:** Survival differed by treatment facility even after accounting for metastatic burden. Patients treated at academic centers had better outcomes across metastatic sites, including those with extensive disease. These findings point to differences in care delivery and access to specialized expertise. Expanding academic practices, such as multidisciplinary tumor boards and referral pathways, into community settings may help reduce these gaps. Research Sponsor: None.

Shifting drivers of hospitalization in endometrial cancer: Toxicity-like organ failure phenotypes in the modern treatment era.

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Background: Frontline endometrial cancer care has rapidly shifted toward immune-based regimens. Whether inpatient admissions have concurrently shifted toward toxicity-like organ failure syndromes, with changing ICU use and rescue outcomes, remains unknown. **Methods:** We performed a survey-weighted analysis of the National Inpatient Sample (NIS) 2016–2023. Adult hospitalizations with endometrial cancer in any diagnosis position (C54/C55) were included; admissions with palliative care coding (Z51.5) were excluded. Eras were defined as 2016–2017 versus 2018–2023. Toxicity-like organ failure phenotypes were identified using ICD-10-CM proxies including pneumonitis or respiratory toxicity, colitis or diarrhea, myocarditis or pericarditis, hepatitis or liver failure, neutropenic sepsis, acute kidney injury, and electrolyte collapse. A broader sensitivity phenotype additionally included endocrine crises. ICU escalation was proxied by mechanical ventilation or shock. Major complications were defined using a composite bundle, and failure-to-rescue was defined as death among complication admissions. Outcomes included in-hospital mortality, ICU escalation, complications, length of stay (LOS), cost, and routine discharge. **Results:** Among 74,895 unweighted endometrial cancer hospitalizations, 25.8% occurred in 2016–2017 and 74.2% in 2018–2023. Overall inpatient mortality was 1.86% (95% CI 1.66%–2.07%) in 2016–2017 and 2.09% (95% CI 1.96%–2.22%) in 2018–2023. Hospitalizations involving any toxicity-like organ failure phenotype increased from 34.3% (95% CI 33.4%–35.1%) in 2016–2017 to 45.2% (95% CI 44.7%–45.7%) in 2018–2023. Pneumonitis or respiratory toxicity increased from 6.23% to 9.91%, acute kidney injury from 14.9% to 21.0%, and electrolyte collapse from 23.7% to 31.7%. ICU proxy use increased from 2.50% (95% CI 2.27%–2.73%) to 3.30% (95% CI 3.15%–3.45%), driven by higher shock coding (0.82% to 1.61%). Major complications increased from 36.1% (95% CI 35.3%–36.9%) to 46.5% (95% CI 46.0%–47.1%). Mortality among admissions with toxicity-like organ failure decreased modestly from 4.75% (95% CI 4.25%–5.30%) to 4.25% (95% CI 4.00%–4.52%), while mortality among ICU-level admissions remained high and unchanged (29.7% vs 29.2%). Routine discharge declined from 66.6% (95% CI 65.6%–67.6%) to 62.2% (95% CI 61.7%–62.7%), and LOS increased in the modern era (mean 5.22 days, 95% CI 5.16–5.28). **Conclusions:** From 2016–2023, endometrial cancer hospitalizations increasingly involved toxicity-like organ failure phenotypes with rising ICU escalation and complication burden, while inpatient mortality changed minimally. These findings highlight a growing disconnect between outpatient therapeutic advances and inpatient recognition and rescue capacity. Research Sponsor: None.

Early-phase operational readiness gaps in oncology cell and gene therapy trials and implications for scalable trial infrastructure.

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Background: First-in-human (FIH) and Phase 1 oncology cell and gene therapy (CGT) trials have highlighted that operational readiness, rather than scientific feasibility, is often the primary constraint on trial execution and patient access. Many clinical sites lack the infrastructure, staffing, and process maturity required to support CGT trials, limiting enrollment and scalability. **Methods:** Operational lessons were analyzed across multiple early-phase oncology CGT programs, including autologous and allogeneic platforms. Assessments focused on trial execution during FIH and Phase 1 activation, site readiness, vector and cellular product handling, storage and chain-of-custody requirements, coordination among manufacturing, sites, and couriers, staffing and training needs, and turnaround times from leukapheresis or biopsy to dosing. **Results:** Consistent site readiness gaps were identified in apheresis coordination, vector storage and handling, chain-of-custody documentation, and real-time cross-functional communication. Autologous programs showed increased operational complexity driven by patient-specific manufacturing, narrow scheduling windows, and variable vein-to-vein turnaround times. Allogeneic programs had reduced scheduling constraints but introduced challenges related to centralized manufacturing oversight and site-level accountability. Across platforms, CGT trials required specialized staffing and training beyond standard oncology research models. Insufficient early operational enablement resulted in delayed dosing and reduced patient access by ~1–3 months. **Conclusions:** Lessons from early-phase oncology CGT trials demonstrate that proactive operational readiness, particularly at the site level, is essential to enable scalable trial infrastructure and equitable patient access. Early readiness assessments, targeted workforce training, and integrated manufacturing–logistics coordination are critical to support efficient CGT trial execution and future expansion. **Learning Objectives:** Recognize common operational readiness gaps identified during FIH and Phase 1 oncology CGT trials. Understand how manufacturing, logistics, and site coordination impact early-phase trial execution. Apply early operational learnings to inform scalable CGT trial infrastructure. **Key Takeaways:** Operational readiness is a primary determinant of early CGT trial success. Many sites require significant enablement to conduct CGT trials effectively. Early investment in readiness improves turnaround times and patient access. **Research Sponsor:** None.

Prevalence and trends in rural patient enrollment in SWOG cancer clinical trials, 1992-2022.

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Background: A recent ASCO report highlighted improving patient access to cancer clinical trials as a fundamental priority. Although prior research found that 19% of participants in NCI-sponsored trials reside in rural areas, there is substantial heterogeneity in the classification of rurality. In addition, sociodemographic characteristics across different levels of rurality are unknown. In this analysis, we evaluated the prevalence and trends over time in trial enrollment by categories of rurality. **Methods:** We analyzed pooled data from phase II, II/III, and III trials conducted by the SWOG Cancer Research Network from 1992–2022. Rurality was defined by linking patient zip code to the Rural–Urban Continuum Codes, and categorized into four groups (large urban, small urban, rural, frontier). Baseline and patient demographic data were obtained from trial registration forms. Neighborhood deprivation, based on the Area Deprivation Index, was derived from patient zip code. The associations between rurality and patient characteristics were evaluated using multivariate logistic regression with covariate adjustments. Rurality enrollment was compared to corresponding overall US rurality estimates during the same period. **Results:** In total, N = 39,729 patients enrolled in 69 trials in brain, breast, GI, GU, gynecological, head and neck, lung, sarcoma, melanoma, and hematologic cancers were examined. Across the geographic groups, 52.2% lived in large urban, 30.9% lived in small urban, 11.6% lived in rural, and 5.4% lived in frontier areas, compared to corresponding US population estimates of 56.0% large urban, 28.6% small urban, 10.3% rural, and 5.0% frontier. Patients residing in frontier areas were nearly 80 times as likely to live in the highest versus lowest deprivation areas (OR = 78.37, 95% CI, 64.71–94.92, $p < .0001$). Similar though less pronounced associations were found among patients from rural and small urban areas ($p < .0001$). Frontier patients were more likely to be on Medicare (OR = 1.96, 95% CI, 1.66–2.30, $p < .0001$). Over the 30-year study period, trial enrollment among patients from frontier areas has decreased over time relative to the US population, whereas trial enrollment of patients from large urban areas has increased. **Conclusions:** Patients from rural and frontier areas are well-represented in SWOG clinical trials, however, enrollment among patients from frontier areas has shown a declining trend. Strong representation of patients with cancer from rural areas enhances the generalizability of trial findings. Given ongoing changes to healthcare, declining representation from frontier areas is likely to continue without targeted interventions. Further research is needed to expand access to care in these vulnerable areas and guide efforts that ensure adequate socioeconomic support for all patients, regardless of their geographic locale. Research Sponsor: National Cancer Institute/U.S. National Institutes of Health; U10CA180888, U10CA180819, UG1CA189974; The Hope Foundation for Cancer Research; AHRQ; K01HS028730.

Body mass index and mortality in immune checkpoint inhibitor–treated cancers: A real-world propensity-matched analysis.

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Background: Immune checkpoint inhibitors (ICIs) are a cornerstone of treatment for multiple solid tumors, including lung cancer and melanoma. Emerging evidence suggests that body mass index (BMI) may influence outcomes with immunotherapy, though findings remain inconsistent and largely derived from clinical trial populations. We evaluated the association between BMI and mortality among patients with cancers treated with ICIs using real-world data. **Methods:** We conducted a retrospective observational study using data from TriNetX, a global real-world research platform based on de-identified electronic health records. Adult patients with lung cancer or melanoma who received immune checkpoint inhibitor therapy, including durvalumab, pembrolizumab, nivolumab, ipilimumab, or atezolizumab, were identified. Patients were stratified by documented baseline body mass index into two groups: BMI 19–24.9 (Normal) and BMI 30–49.9 (Obese). To address baseline differences, 1:1 propensity score matching (PSM) was performed using demographics and major comorbidities. The primary endpoint was all-cause mortality; secondary endpoints included inpatient hospitalization frequency. **Results:** Before matching, the cohorts consisted of 7,951 patients (BMI 30–49.9) and 4,651 patients (BMI 19–24.9). After PSM, 4,152 patients were included in each cohort. Baseline characteristics, including age (mean 67 years), sex (59% male), and comorbidities (hypertension, diabetes, CKD), were well-balanced ($p > 0.05$). All-cause mortality was significantly higher in the BMI 19–24.9 group compared to the BMI 30–49.9 group (49.2% vs 43.4%), with a risk ratio of 0.88 (95% CI, 0.84–0.92; $p < 0.001$). Overall survival was significantly longer in the obese cohort, with a median survival of 1,043 days compared to 579 days in the normal BMI cohort. High BMI was associated with a 27.5% reduction in the hazard of death (HR 0.725, 95% CI 0.68–0.77; $p < 0.001$). Conversely, the high BMI cohort had a higher risk of inpatient encounters (57.6% vs 55.3%; $p = 0.032$) and a higher mean number of hospitalizations (5.4 vs 4.6; $p < 0.001$). **Conclusions:** In this large real-world study, higher BMI was associated with significantly lower mortality and nearly double the median survival time in patients treated with ICIs. While higher BMI was also associated with increased hospitalization frequency, the overall survival benefit remains robust. These findings support the "obesity paradox" in immunotherapy and suggest that nutritional status is a critical determinant of long-term ICI efficacy and healthcare utilization. Research Sponsor: None.

Burden and site-specific spectrum of second primary malignancies after adult acute myeloid leukemia: A population-based SEER standardized incidence ratio study with latency-stratified risk profiling (2000–2022).

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Background: As survival after acute myeloid leukemia (AML) improves, second primary malignancies (SPMs) represent an increasingly relevant survivorship outcome. We quantified overall and site-specific SPM risk following adult AML and characterized latency-dependent patterns and demographic heterogeneity. **Methods:** We performed a population-based cohort analysis using SEER 17 registries (2000–2022). Adults (≥ 18 years) with AML were followed for incident SPMs occurring ≥ 2 months after AML diagnosis. Risk was summarized using standardized incidence ratios (SIRs; observed/expected) with 95% confidence intervals (CIs), overall and by cancer site, and stratified by latency (2–11, 12–59, 60–119, ≥ 120 months), age, sex, and race. **Results:** Overall, 751 SPMs were observed versus 563.87 expected (SIR 1.33; 95% CI 1.24–1.43). Solid tumors overall were not significantly increased (SIR 1.03; 0.94–1.12), but select sites showed excess risk: oral cavity/pharynx (SIR 2.35; 1.64–3.27), skin excluding basal/squamous (SIR 1.42; 1.04–1.90), kidney (SIR 1.88; 1.31–2.60), and eye/orbit (SIR 4.32; 1.18–11.06), while breast cancer was reduced (SIR 0.65; 0.47–0.86). Hematologic SPMs were markedly elevated (lymphatic/hematopoietic SIR 2.48; 2.06–2.96), including leukemia overall (SIR 4.42; 3.45–5.59) and acute lymphoblastic leukemia (SIR 21.51; 11.76–36.08). All-site risk remained elevated across latency windows (SIR range 1.30–1.38), while solid-tumor risk increased after 5 years (SIR 1.27 at 60–119 months and ≥ 120 months). Risk was highest in ages 0–59 (SIR 1.91), and remained elevated in males (1.37) and females (1.27). **Conclusions:** Adult AML survivors experience a sustained excess risk of SPMs, driven primarily by secondary hematologic malignancies with additional site-specific solid-tumor excesses emerging in longer-term follow-up, supporting risk-adapted survivorship surveillance. Research Sponsor: None.

Site-specific risk of second primary malignancies after adult AML (SEER 17, 2000–2022).

Site	Observed	Expected	O/E	CI Lower	CI Upper
All Sites	751	563.87	1.33#	1.24	1.43
All Solid Tumors	506	491.44	1.03	0.94	1.12
All Lymphatic and Hematopoietic Diseases	123	49.66	2.48#	2.06	2.96
Lymphoma	42	24.97	1.68#	1.21	2.27
Leukemia	70	15.83	4.42#	3.45	5.59
Acute Lymphocytic Leukemia	14	0.65	21.51#	11.76	36.08
Acute Myeloid Leukemia	13	4.71	2.76#	1.47	4.72
Chronic Myeloid Leukemia	22	2.11	10.40#	6.52	15.75

Concordance of tissue and plasma NGS in early-stage non–small cell lung cancer.

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Background: Comprehensive molecular profiling is standard of care for patients with advanced non–small cell lung cancer (NSCLC), and plasma-based next generation sequencing (NGS) demonstrates high concordance with tissue testing in metastatic disease. However, the performance of liquid biopsy in early-stage NSCLC remains poorly defined. In early stage, tissue-based NGS may be limited by inadequate sample quantity, low tumor cellularity, or DNA degradation. We evaluated the concordance of tissue and plasma NGS in patients with stage I to III NSCLC to determine whether liquid biopsy can reliably complement tissue-testing in this setting. **Methods:** We conducted a retrospective analysis of patients diagnosed with stage I to III NSCLC from 2021 to 2025 at the University of Illinois Cancer Center. Clinical and demographic data were abstracted through chart review. Paired NGS results were obtained from the Tempus Hub, including tissue-based sequencing (Tempus xT) and plasma-based sequencing (Tempus xF+). Actionable genomic alterations were assessed for concordance using 2x2 contingency tables, with calculation of overall concordance and positive percentage agreement (PPA). **Results:** A total of 71 patients with early-stage NSCLC were identified. The cohort was 52% male and 48% female; 61% Black, 23% White, 14% Asian and 3% other; 9% Hispanic and 88% non-Hispanic. 52% were 65 years or older at diagnosis. Disease stage included stage I (20%), stage II (10.6%), stage III (41%), with stage unknown 29%. No NTRK2/3, ROS1, RET, and MET alterations were detected on liquid or tissue. PPA for actionable mutations was low overall: BRAF V600E 66.7%, KRAS G12C 40%, EGFR 16.7%, HER2 0%, and EML4-ALK 0%. Despite low PPA, overall concordance exceeded 80% for all genes, driven by high negative percent agreement. **Conclusions:** In early-stage NSCLC, plasma-based NGS demonstrates limited sensitivity for detecting actionable driver alterations, despite high overall concordance driven by negative agreement. Reliance on liquid biopsy alone may miss clinically meaningful oncogenic drivers, even in potentially curable disease. While plasma NGS may be useful as a complementary or rule-out tool when tissue is inadequate, tissue-based molecular profiling remains essential for accurate genomic characterization in early-stage NSCLC. Research Sponsor: None.

Concordance and PPA analysis.		
	Concordance	PPA
BRAF V600E	91.2%	66.7%
EGFR	86.0%	16.7%
HER2	98.6%	0%
KRAS G12C	84.5%	40%
EML4-ALK	98.6%	0%

Clinical-stage AI-enabled therapeutic assets: An industry-wide analysis of scale, clinical progression, and company characteristics.

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Background: Artificial intelligence (AI) is increasingly applied in therapeutic discovery and has driven substantial investment in AI-native biotechnology firms. However, the extent to which AI-enabled assets have progressed into and through clinical development remains incompletely characterized. We performed an industry-wide descriptive analysis of AI-enabled therapeutic assets that have entered interventional clinical trials. **Methods:** We identified AI-enabled therapeutic assets that entered at least one Phase 1–3 interventional clinical trial through July 1, 2025. Assets were manually curated using industry databases, public disclosures, and trial registries. AI enablement was defined at the asset level and required evidence of AI contribution to discovery or design. Drug-, trial-, and company-level characteristics were summarized using descriptive statistics. Company characteristics were obtained from PitchBook and public sources. **Results:** A total of 117 AI-enabled therapeutic assets across 63 companies entered interventional clinical trials. Oncology accounted for 69 assets (59.0%), and most assets were small molecules (96/117; 82.1%). As of December 1, 2025, 60 assets (51.3%) had completed Phase 1 and 8 (6.8%) had completed Phase 2. Among assets with reported Phase 1 enrollment ($n = 103$), the median sample size was 50 participants (IQR, 24–76.5). Approximately 35.9% of assets targeted a novel biological target. At the company level, the median time from founding to Phase 1 entry was 6.5 years (IQR, 4.0–9.2; $n = 44$). Median total funding was \$186.7 million (IQR, \$48.1M–\$595.0M; $n = 57$), and median employee count at clinical entry was 73 (IQR, 32–129; $n = 35$). Median operational intensity was \$2.72 million per employee (IQR, \$1.71M–\$5.83M; $n = 47$). **Conclusions:** AI-enabled therapeutic assets are increasingly entering clinical development, particularly in oncology, but most remain early in the clinical pipeline, with few having completed Phase 2. AI-native biotechnology companies that have reached the clinic typically do so within several years of founding with relatively small employee counts and high operational intensity. These findings provide a transparent baseline for evaluating the clinical impact of AI-enabled drug discovery as this cohort matures. Research Sponsor: None.

Impact of market entry of biosimilars in the US on cancer biologics’ pricing strategies, market share, and payer costs.

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Background: Biosimilars have been anticipated to lower the financial burden of cancer for payors as well as patients. As of 2025, 42% (n=13 from three product lines: bevacizumab, rituximab, and trastuzumab) of physician-administered biosimilars launched in the US were indicated for cancer. These three product lines accounted for approximately \$5.35 billion healthcare expenditure at clinics and nonfederal hospitals in 2024. **Methods:** Using MarketScan claims data and Average Sales Price (ASP) data from the Centers for Medicare & Medicaid Services, we calculated quarterly ASP of reference products to compare the pricing strategies of reference biologics for cancer vs. non-cancer treatment. We also compared the market share between cancer vs. non-cancer biologics and estimated the average monthly payor costs of the three cancer product lines 12 months before biosimilar entry versus 2023. We identified biologics using Healthcare Common Procedure Coding System codes and adjusted costs to 2025 USD using the prescription drugs Consumer Price Index. **Results:** Analyses included 8,252,400 claims of 8 reference products and 27 biosimilars. All three cancer biologics experienced biosimilar market entry starting late 2019. On average, the ASP of reference biologics for cancer decreased by 4.3% annually after biosimilar entry, contrasting to 17.2% decrease for non-cancer reference biologics. Meanwhile, the market share of reference biologics decreased on average 39.3%, 34.2%, and 35.4% annually for bevacizumab, rituximab, and trastuzumab, respectively, contrasting to 15.4% decrease for non-cancer reference biologics. Compared to monthly payor costs averaging over 12 months before the first biosimilar launch, monthly payor costs of biologics (including reference and biosimilars) in 2023 fell for all three cancer biologics in the commercial and Medicare market. The annual decrease rate in monthly payor costs was on average 45.1%, 52.0%, and 34.6% for bevacizumab, rituximab, and trastuzumab, respectively. **Conclusions:** After biosimilar entry, reference biologics for cancer reduced prices at a slower pace than non-cancer reference biologics, this pricing strategy led to a much faster decrease in their market share. Biosimilars for cancer, by gaining larger market share over time, has significantly reduced payor costs of cancer biologics for commercial and Medicare insurers. Research Sponsor: None.

Drug	Reference product ASP annual change	Reference product market share annual change	Commercial insurance mean monthly payor costs			Medicare Part B mean monthly payor costs		
			Before biosimilar entry	2023	Change	Before biosimilar entry	2023	Change
bevacizumab	-2.1%	-39.3%	\$5,261.9	\$2,823.0	-46.4%	\$2,720.0	\$1,526.8	-43.9%
rituximab	-4.4%	-34.2%	\$7,187.4	\$3,799.2	-47.1%	\$3,977.7	\$1,717.1	-56.8%
trastuzumab	-6.5%	-35.4%	\$4,781.6	\$3,302.7	-30.9%	\$2,401.6	\$1,485.0	-38.2%

Heart failure in hospitalizations for hematologic malignancies versus solid tumors: National burden and inpatient outcomes, 2018-2022.

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Background: Heart failure (HF) is a common and morbid comorbidity in oncology. Whether HF burden and prognosis differ between hospitalizations for hematologic malignancies and solid tumors remains incompletely characterized at a national level. This study compared HF prevalence and HF-associated outcomes across these cancer groups. **Methods:** A serial cross-sectional analysis was conducted using adult hospitalizations in the 2018 to 2022 Healthcare Cost and Utilization Project National Inpatient Sample with discharge-level survey weighting. Cancer hospitalizations were classified by principal diagnosis as hematologic malignancy or solid tumor. HF was identified using ICD-10-CM I50* in any diagnosis field. Outcomes included HF prevalence, in-hospital mortality, intensive care unit utilization, shock, length of stay, and hospitalization cost. Survey-weighted multivariable regression adjusted for demographics, comorbidities, hospital characteristics, and admission factors. Models restricted to HF admissions evaluated associations between cancer type and outcomes within the HF subgroup. **Results:** Among an estimated 4.81 million cancer hospitalizations nationally, HF prevalence was higher in hematologic malignancies than in solid tumors (13.2% vs 8.0%, $p < 0.001$). After adjustment, hematologic malignancy was associated with higher odds of HF (adjusted odds ratio (aOR) 1.53, 95% CI 1.50 to 1.57). Among HF hospitalizations, hematologic malignancies had higher mortality (11.7% vs 8.0%), intensive care unit utilization (8.5% vs 7.3%), and shock (3.8% vs 3.4%) (all $p < 0.001$). In adjusted models restricted to HF admissions, hematologic malignancy remained associated with higher mortality (adjusted odds ratio 1.34, 95% CI 1.26 to 1.42) and intensive care unit utilization (aOR 1.15, 95% CI 1.07 to 1.23). Resource utilization was greater in hematologic malignancy HF admissions, including longer length of stay (12.1 vs 8.3 days) and higher costs (\$50,518 vs \$30,906; both $p < 0.001$). Interaction modeling showed no significant effect modification of HF-associated mortality by cancer type. **Conclusions:** Hospitalizations for hematologic malignancies have higher HF prevalence than solid tumor hospitalizations and demonstrate higher mortality, intensive care utilization, shock, length of stay, and costs among admissions with HF. These findings identify hematologic malignancy hospitalizations as a high-risk context for HF-associated inpatient deterioration and resource use. Research Sponsor: None.

Closing the information gap in oncology: A retrieval-augmented generation multi-modal AI platform for personalized patient education and physician efficiency.

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Background: Effective patient education is critical in oncology but hindered by the complexity of treatment guidelines and the time constraints of clinicians. Traditional static materials often fail to address the personalized needs of diverse demographics, particularly the elderly. We developed an Intelligent Medical Science Popularization Platform integrating Multimodal Large Language Models (MLLM) with Retrieval-Augmented Generation (RAG) to automate the production of reliable, guideline-based oncology educational content. **Methods:** The platform utilizes a three-tier architecture deployed at a tertiary cancer center. The core engine combines a self-developed MLLM with RAG, anchoring content generation to authoritative sources (e.g., CSCO/NCCN guidelines and peer-reviewed journals) to ensure clinical accuracy. The system features: (1) Physician Portal: Automates the conversion of clinical protocols into patient-friendly text, layouts, and animations; (2) Multimodal Synthesis: Generates virtual avatar videos explaining diagnoses and treatments; (3) Patient Interface: Delivers personalized, accessible content via mobile apps, supporting voice interaction for elderly adherence. **Results:** Implementation data demonstrated significant efficiency and engagement gains. The MLLM+RAG model achieved > 98% accuracy in content generation as verified by expert oncologists. The production time for educational videos was reduced from 72 hours to ~10 minutes (> 99% reduction), enabling rapid updates aligned with new trial data. Animation production costs decreased by 10-fold. Daily content output exceeded 15 units. Notably, in a cohort of elderly cancer patients, the platform increased user retention rates by 40% and extended average session duration by 50 seconds, indicating improved engagement with health information. **Conclusions:** This policy-compliant AI platform validates the utility of RAG-based MLLMs in oncology. By shifting from passive information supply to active, personalized intelligent services, it significantly reduces the workload for oncologists while bridging the digital divide for vulnerable patient populations. This model offers a scalable solution for enhancing health literacy and treatment adherence in cancer care. Research Sponsor: None.

The 2026 primary care oncology toolkit: An evolving shared-care framework for the implementation of prospective survivorship evidence.

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Background: As cancer survivorship transitions into a chronic disease model, a significant "implementation gap" exists between landmark 2025 clinical data and frontline primary care. Survivors face a 2.39-fold higher risk of cardiovascular mortality, yet standardized protocols for PCP-led surveillance remain in development. This review identifies an evolving "Shared-Care Framework" designed to integrate prospective 2025 evidence into the internal medicine setting, anticipating a shift toward decentralized, longitudinal survivorship care. **Methods:** A narrative synthesis was performed to develop a pilot-ready framework for primary care. We analyzed practice-changing evidence published between January 2025 and January 2026, including the Barac Risk Model, the Bhalraam et al. SGLT2i meta-analysis, and emerging cervical screening strategies. Findings were synthesized into thematic surveillance blocks to identify opportunities for prospective guideline-concordant implementation. **Results:** Synthesis of recent landmark data identified several opportunities for prospective adoption in the internal medicine setting. The framework evaluates evolving cardio-metabolic surveillance strategies, including the integration of the Barac Model (2025) for 10-year heart failure (HF) risk prediction and the proactive use of SGLT2 inhibitors, which have demonstrated a 51% reduction in HF hospitalizations among survivors. Furthermore, the review identifies prospective clinical blocks for PCP-led surveillance of stable survivors, emphasizing proactive bone health monitoring for patients on aromatase inhibitors and metabolic screening for those on androgen deprivation therapy (ADT). This includes the potential adoption of low-dose oxybutynin as a new standard for managing ADT-induced hot flashes. Finally, the framework addresses health equity paradigms by evaluating the transition to in-office HPV self-sampling and automated EMR alerts for age 45 colorectal screening to mitigate the rising incidence of early-onset disease. **Conclusions:** This evolving shared-care framework offers a scalable model for the future of survivorship. By aligning primary care protocols with prospective 2025 landmark data, clinicians can optimize long-term coordination and address health disparities ahead of formal guideline updates. Research Sponsor: None.

Inpatient burden and outcomes across gastrointestinal cancer subtypes among younger adults in the United States, 2018–2022.

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Background: Early-onset gastrointestinal (GI) cancers are increasingly recognized, yet national data describing inpatient burden and outcomes across GI cancer subtypes in younger adults remain limited. **Methods:** A serial cross-sectional analysis was performed using the 2018–2022 Healthcare Cost and Utilization Project National Inpatient Sample. Adult hospitalizations among younger adults (age 18–49 years) with a principal diagnosis of GI malignancy were identified and categorized by cancer subtype. Outcomes included in-hospital mortality (primary), length of stay (LOS), and hospitalization cost estimated using cost-to-charge ratios. National estimates accounted for survey weighting, clustering, and stratification. Survey-weighted multivariable logistic regression evaluated associations between cancer subtype and in-hospital mortality, adjusting for age, sex, race/ethnicity, payer, neighborhood income quartile, elective admission, APR-DRG severity, hospital teaching status, geographic region, and calendar year. Sensitivity analyses were performed restricting the cohort to age < 45 years. **Results:** Across 2018–2022, principal GI cancer hospitalizations among younger adults were dominated by colorectal cancer, followed by stomach, pancreatic, liver or intrahepatic biliary, and esophageal cancers. In-hospital mortality varied by cancer subtype and year, with higher crude mortality observed for pancreatic, stomach, esophageal, and liver or intrahepatic biliary cancers compared with colorectal cancer. Resource utilization increased markedly during 2020 across subtypes, with corresponding increases in LOS and hospitalization costs. In adjusted analyses using colorectal cancer as the reference, odds of in-hospital mortality were higher for stomach (adjusted odds ratio [aOR] 3.01, 95% CI 1.78–5.10), esophageal (aOR 2.12, 95% CI 1.03–4.37), and liver or intrahepatic biliary cancers (aOR 2.56, 95% CI 1.36–4.79). Pancreatic cancer demonstrated a borderline increase in mortality (aOR 1.79, 95% CI 0.96–3.36). Higher APR-DRG severity was strongly associated with mortality (aOR 5.20, 95% CI 3.50–7.72). Sensitivity analyses demonstrated similar subtype ordering and mortality patterns. **Conclusions:** Among younger adults hospitalized with GI malignancies, inpatient mortality and resource utilization varied substantially by cancer subtype. Colorectal cancer accounted for the largest share of hospitalizations, while stomach, esophageal, and liver or intrahepatic biliary cancers were associated with higher adjusted inpatient mortality. These nationally representative findings provide benchmarking data on inpatient outcomes across early-onset GI cancer subtypes. Research Sponsor: None.

Enhanced financial assistance intervention for unmet essential needs: A prospective pilot study to improve timely cancer treatment completion.

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Background: Unmet essential needs, such as food, transportation, and housing insecurity, can create barriers to timely cancer treatment. Delayed or prolonged courses of definitive radiotherapy (RT) can compromise cancer outcomes like recurrence and survival. There are limited prospective data testing interventions to improve timely cancer treatment completion by meeting essential needs. **Methods:** We conducted a pragmatic single-arm pilot study testing an enhanced financial assistance intervention for unmet needs during RT. Eligibility criteria included adults with a cancer diagnosis and unmet social needs (via social risk screening and/or social worker evaluation) who were prescribed or undergoing a course of RT with > 10 fractions remaining. Participants received standard institutional assistance (e.g., limited support for travel/lodging with strict eligibility criteria) plus the enhanced assistance intervention, including needs assessments prior to and during RT and up to \$2000/patient of tailored unconditional monetary transfer via gift cards for all essential needs identified. The primary outcome was delay-free completion of RT (DFC: completing all prescribed RT fractions and delaying < 5 fractions). The study was powered (power = 80%, 1-sided alpha = 0.2 for this pilot study) to detect a 10-percentage point increase in % DFC relative to a historic benchmark of 83% (based on similar patients from our institution), with required sample size of N = 33. Due to delays in gift card administration (on average ~2 weeks after consent), we also present per protocol analysis, limited to patients who had > 10 fractions remaining after first receiving financial assistance. Post-hoc analyses using generalized linear mixed models evaluated percentages of delayed fractions prior to and after an individual's receipt of financial assistance. **Results:** 35 met inclusion criteria and were approached, 33/35 enrolled. Participants received median assistance of \$1800 (\$700–2000) and had a median of 27 RT fractions after consent (range: 12–35) and 17 (3–34) after receiving assistance. In the overall cohort, 1 patient did not complete RT and 2 patients had ≥5 delayed fractions, leading to 30/33 achieving DFC (90.9%, 80% CI = 83.9 – 100), significantly higher than the 83% benchmark. In the per protocol analysis, 27/28 achieved DFC (96.4%, 80% CI = 89.7–100, P = .037). Among the 27 patients who started RT prior to receiving assistance, mixed model analysis showed more delayed fractions prior to (7.1%) vs. after (3.0%) receiving assistance (OR 2.84, 95% CI = 1.43–5.80, P = .003). **Conclusions:** In this prospective pilot study, a tailored enhanced financial assistance intervention for unmet essential needs led to improved delay-free completion of RT over a historic benchmark. Further analysis on patient-reported quality of life and financial toxicity will be reported in the future. Clinical trial information: NCT06582849. Research Sponsor: Conquer Cancer, the ASCO Foundation; WashU, Siteman Cancer Center.

Has racial and ethnic representation in oncology clinical trials changed?: A 30-year systematic analysis using artificial intelligence.

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Background: Despite societal emphasis on racial and ethnic representation in oncology trials, it remains unclear whether participant diversity has meaningfully changed over time. Recent advances in large language models (LLMs) enable scalable extraction of data from PDF documents, facilitating high-throughput research. **Methods:** We identified all oncology clinical trials published in The Lancet and The New England Journal of Medicine (NEJM) between 1995 and 2025, and retrieved full-text PDFs from the journals’ websites. Using an LLM (Gemini-2.5-Flash), structured variables, including trial phase, cancer type, enrollment countries, and participant race and/or ethnicity, were automatically extracted from texts, tables, and figures. Trials were stratified by decade (1995–2005, 2006–2015, and 2016–2025) to evaluate temporal trends. **Results:** We identified 1,385 oncology trials between 1995 and 2025, including 334, 448, and 603 for the three decades, respectively. The proportion of phase III trials increased steadily over time (68%, 72%, and 76%). Trials also became more globally distributed, with multi-continental studies rising from 27% to 46% and 58%. Most notably, Asian countries were increasingly involved among trial enrollment sites, rising from 14% to 25% and 45%. Reporting of race/ethnicity increased over time, from 16% to 29% and 47% of publications across decades. Among studies that reported race, non-White enrollment increased, with the median percentage per study rising from 10% in both earlier decades to 21% in 2016–2025. However, after excluding Asian participants, the median non-White percentage declined across decades (7.5%, 5.3%, and 4.3%). In pooled analyses across all trials, non-White patients comprised 15%, 11%, and 15% of total enrollment, respectively; excluding Asian patients, this decreased from 13.2% to 6.2% and 6.9%. Black enrollment declined over time, with the median percentage falling from 6.8% to 2.4% and 1.5%. Among trials reporting ethnicity, Hispanic enrollment remained consistently low (5.4%, 4.0%, and 4.6%). **Conclusions:** Globalization and race/ethnicity reporting in oncology trials improved, but the observed increases in diversity were largely attributable to the expansion of trial enrollment in Asia. In contrast, Black and Hispanic representation remained low or declined across decades. Research Sponsor: None.

	1995-2005, n (%)	2006-2015, n (%)	2016-2025, n (%)
Total Studies	334	448	603
Clinical Trial Phase			
Phase 1	78 (23)	86 (19)	55 (9)
Phase 2	25 (7)	38 (8)	87 (14)
Phase 3	228 (68)	323 (72)	460 (76)
Major Cancer Types			
Breast	55 (17)	64 (14)	78 (13)
Hematologic	54 (16)	77 (17)	114 (19)
Colorectal	49 (15)	40 (9)	29 (5)
Lung	17 (5)	37 (8)	66 (11)
Continents			
Africa	16 (5)	29 (6)	16 (3)
Asia	47 (14)	113 (25)	274 (45)
Europe	158 (47)	272 (61)	403 (67)
North America	102 (31)	219 (49)	361 (60)
South America	0 (0)	5 (1)	19 (3)
Oceania	43 (13)	134 (30)	203 (34)

The Bermuda model: Achieving world-class, equitable, and efficient cancer care in a small island nation.

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Background: Bermuda is a small island nation that historically faced significant challenges in provision of local cancer care. Between 2000–2017, 100% of patients requiring radiation therapy (RT) had to travel abroad, causing prohibitive financial toxicity. In 2017, Bermuda Cancer and Health Centre (BCHC) evolved to deliver an integrated and comprehensive national cancer solution, including RT. The "Bermuda Model" represents a national approach to address critical gaps in cancer care by leveraging innovative partnership models to enable access, efficiency, health equity and international quality standards. **Methods:** We conducted a retrospective descriptive cohort study. Data for cancer incidence/outcomes were collected from the Bermuda National Tumour Registry; treatment/quality data and patient satisfaction surveys were collected from BCHC clinical records. Timeframes for travel reduction data were between 2015–2020. Outcomes measures included percentage of overseas referrals for RT and chemotherapy, international quality assurance, patient satisfaction scores from 2025, access measures such as interval from diagnosis to treatment, cancer-specific overseas insurance claims, and selected clinical outcomes, including early breast cancer detection and survival rates. **Results:** The Bermuda Model has eliminated the need for overseas RT, ensuring access for the 70–90% who previously went abroad and the remainder who went without. Through an international strategic partnership with Brigham and Women's Hospital, high quality and consistent peer-review of radiation treatment plans by Harvard faculty specialists was ensured for 100% of all patients receiving RT at BCHC. Patient satisfaction rates for RT were 100% positive for multiple months in 2025. Between 2017–2019, Bermuda achieved excellent clinical outcomes including an 87% early detection rate for localized (Stage 1–2) breast cancer and a lower breast cancer mortality rate than either the USA or Europe. Care timelines were efficient; average time from diagnosis to first treatment was as low as 16 days in 2025. The model was associated with an approximately 24% reduction in cancer-specific overseas insurance claims between 2017–2020 (\$6.2 million and \$4.7 million respectively). **Conclusions:** The "Bermuda Model" demonstrates that with strategic investment and international partnerships, a small island nation can locally establish world-class, equitable, and efficient cancer care services. Eliminating overseas treatment, high satisfaction, and excellent outcomes evidence its success. The reduction in claims has been particularly impactful for Bermudian residents with government-level insurance, helping to advance, access-to-all cancer care. This model serves as a valuable blueprint for other small nations or isolated regions seeking to improve their delivery of cancer care. Research Sponsor: None.

Integrating AI-derived lung cancer risk and social determinants of health to improve risk stratification in a safety net lung cancer screening program.

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Background: Lung cancer screening (LCS) outcomes remain inequitable, with social and environmental determinants of health (SDOH) influencing lung cancer risk, screening adherence, and cancer detection. Sybil is a validated deep learning model that predicts future lung cancer risk from a single low-dose CT (LDCT) scan using imaging features alone, without demographic or clinical inputs created by MIT/MGH. Its relationship to SDOH in real-world, safety-net screening populations has not been well characterized. **Methods:** We analyzed 2,645 individuals enrolled in the UI Health LCS program with baseline LDCT imaging and available Sybil risk scores. Scores were generated using the publicly available model applied exclusively to volumetric LDCT images, without retraining or incorporation of demographic, clinical, or SDOH variables. Individual-level clinical data were linked to census- and community-level SDOH measures. Sybil scores were log₁₀-transformed and analyzed as continuous and categorical variables. Associations between Sybil risk, SDOH, and lung cancer diagnosis were assessed using multivariable logistic regression. **Results:** Mean baseline Sybil score was 0.014 (median 0.002). Ninety-six individuals (3.6%) were diagnosed with lung cancer. Sybil scores were significantly higher among individuals later diagnosed with cancer (mean log score -1.52 vs -2.48; $p < 0.001$). In multivariable models, Sybil risk was the strongest independent predictor of lung cancer diagnosis (OR 6.12 per log-unit increase, 95% CI 4.31–8.83; $p < 0.001$), independent of BMI and SDOH. High Sybil risk remained strongly associated with cancer diagnosis across multiple thresholds (all $p < 0.001$). Census-level area deprivation and community-level measures of food insecurity, vehicle access, and neighborhood conditions were also independently associated with cancer diagnosis (Table 1). **Conclusions:** In a large safety-net LCS cohort, AI-derived Sybil risk robustly predicted lung cancer diagnosis and remained informative despite relying solely on imaging data. Integrating AI-based risk prediction with SDOH context may support more equitable, precision-guided lung cancer screening strategies. Research Sponsor: None.

Association of Sybil AI-risk scores and social determinants of health with lung cancer diagnosis in the UI Health lung cancer screening cohort.

Predictor	Comparison / Scale	Adjusted OR (95% CI)	P value
Sybil score	Log10 continuous	6.12 (4.31–8.83)	<0.001
Sybil score	High vs Low (median cutoff)	4.18 (2.38–7.79)	<0.001
Sybil score	High vs Low (75th percentile)	5.10 (3.08–8.57)	<0.001
Sybil score	High vs Low (tertiles)	8.02 (3.90–18.72)	<0.001
BMI	Per unit increase	0.93 (0.89–0.96)	<0.001
Area Deprivation Index	Census-level	1.02 (1.00–1.04)	0.02
Food insecurity	Community-level (%)	1.08 (1.02–1.15)	0.01
No vehicle access	Community-level (%)	1.05 (1.02–1.09)	0.003

Closing the distance and the Specialist Nursing Optimal Placement Tool (SN-OPT): Strategic placement of specialist cancer nurses to achieve resource and geographic equity in Australia.

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Background: Cancer workforce planning that enables effective specialist nurse placement is critical for delivering high-quality, patient-centered care. Inequitable access to specialist nursing represents a significant gap in cancer care delivery. No standardized tools assess specialist cancer nursing resource needs across national healthcare systems. We developed SN-OPT, an innovative resource allocation tool, using 30 new centrally funded specialist melanoma nurse positions for Australia as a case study. **Methods:** A multidisciplinary panel developed SN-OPT via expert consensus, incorporating three data domains: Clinical Infrastructure Assessment: Analysis of facility capabilities including multidisciplinary team (MDT) structures, clinical trial programs, and existing nursing and support services Demand Assessment: Quantitative analysis of case load, treatment complexity, and nursing workload benchmarks Health Equity: Population-level analysis incorporating geographic accessibility and socioeconomic disadvantage SN-OPT combines cancer incidence data with facility metrics to allocate nursing resources operating within a MDT framework. Equity assessment utilized Australian Statistical Geography Standard, Index of Relative Socio-Economic Disadvantage and Travel Time to Hospitals in Australia dataset. **Results:** SN-OPT evaluated 46 Australian facilities for melanoma nursing allocation. The weighted scoring algorithm ranked 33 sites for nurse allocation, with a mean allocation of 0.87 full time equivalent (FTE) positions per metro facility and 0.64 FTE per regional facility. The tool achieved equitable geographic distribution of specialist nursing expertise: regional facilities, treating 25% of patients, received 36% of nursing FTE (167 patients/FTE/year). Metro facilities, managing 75% of patients, received 64% of FTE (212 patients/FTE/year). Allocations largely aligned with facility-determined resource need, with 58% receiving their requested FTE. Among the remaining facilities, median allocation variance was -0.4 FTE (range -0.1 -1.0). On a population level, 89% of Australians would have geographic access to specialist melanoma nursing care within 2-hours of travel, including 81% of the most socioeconomically disadvantaged regions. **Conclusions:** SN-OPT offers a reproducible framework for data-driven allocation of specialist cancer nurses. While implemented using melanoma nurses as a case study, SN-OPT's framework has the potential to be adapted across cancer streams and countries, providing a scalable approach to equitable cancer workforce planning. Early implementation balances clinical service delivery and demand requirements within a MDT framework, while allowing adequate geographical access including socioeconomically disadvantaged regions. Research Sponsor: None.

Equity in breast cancer research authorship: Country, gender, and income representation in phase III trials presented at the ASCO Annual Meeting (2015–2025).

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Background: Equitable representation in global oncology research is essential for scientific validity, generalizability, and ethical trial conduct. However, leadership in clinical research remains concentrated in high-income countries (HICs), with persistent gender inequities. We evaluated longitudinal trends in geographic, economic, and gender representation among authors of Phase III breast cancer trials presented at the ASCO Annual Meeting. **Methods:** We conducted a retrospective analysis of abstracts accepted to the ASCO Annual Meeting from 2015–2025 within breast cancer tracks, including metastatic and local/regional/adjuvant categories. Abstracts were identified using keyword searches for “phase” and included if they reported Phase III clinical trial data. For each eligible abstract, data were extracted for first and senior (last) authors, including institutional affiliation, country, World Bank region, and World Bank income classification. Author gender was assigned using a hierarchical approach incorporating culturally associated names, publicly available professional profiles, and genderize.io. Differences in authorship distribution by country were assessed using a univariate generalized linear model with country as a fixed effect. **Results:** Of 1,199 screened abstracts, 420 met inclusion criteria. Authorship was dominated by North America (44%) and Europe/Central Asia (40%), with representation from Latin America/Caribbean and Middle East/North Africa/Afghanistan/Pakistan each < 1%. The United States accounted for 40.7% of all authorship. East Asia representation increased from 2.8% (2015) to 19.1% (2025), driven by China, South Korea, and Japan. Country effect on authorship share was significant ($F = 3.381$, $p = 0.001$), while year was not ($F = 0.000$, $p = 1.000$), indicating persistent structural hierarchies. Overall, 93% of authors were affiliated with HICs, ~7% with upper-middle-income countries, and < 1% with lower-middle-income countries; no senior authors were from lower-middle-income countries. Gender distribution was 61.7% male and 37.7% female. Only Germany demonstrated female predominance in senior authorship among top contributing countries, while Japan exhibited 100% male senior authorship. **Conclusions:** Phase III breast cancer research presented at ASCO remains structurally concentrated in high-income countries with persistent geographic, economic, and gender inequities. Low- and middle-income countries remain largely excluded from academic leadership, and senior authorship remains male-dominated. These findings demonstrate enduring structural imbalances in global oncology research production and leadership, underscoring the need for equity-focused funding models, inclusive trial governance, and capacity-building research partnerships. Research Sponsor: None.

Evaluating value in the age of accelerated approval: A pembrolizumab case study.

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Background: The FDA accelerated approval (AA) program was established to expedite approval of promising drugs that meet unfulfilled clinical needs. AA is granted on the basis of surrogate endpoints, decreases time to market, and increases access to therapies. Pursuing multiple AA and label expansions can also be a significant component of a drug's lifecycle strategy. Among 322 anticancer drug approvals (2009–2020), 59% were label expansions, with only 16% granted to new drugs with a novel mechanism of action. Our goal was to understand changes in value across multiple label-expanding AAs for high-cost anticancer medications. We studied pembrolizumab, a highly successful immune checkpoint inhibitor, evaluating value from its initial approval through multiple label expansions. **Methods:** We calculated value scores for different indications of pembrolizumab using the ASCO Value Framework Net Health Benefit Worksheet (2020) and ESMO-MCBS v2.0. The value calculations require mature survival outcomes, so we could not calculate scores for AA indications awaiting data maturity (2) or those eventually withdrawn from the market (2). We utilized the FDA drug database and primary literature to gather safety and efficacy outcomes for each indication. Analysis generated descriptive statistics about how the value of pembrolizumab evolved from 2014 to 2025. **Results:** We calculated value scores for 28 pembrolizumab indications, 12 with AA. Value scores varied widely across indications, with ASCO Net Health Benefit Score (NHBS) ranging from 17 (biliary tract cancer) to 59 (MSI/dMMR colorectal cancer) and ESMO MCBS scores ranging from 1 to 5. NHBS was not perfectly collinear with OS gains. The rolling average of NHBS across all indications over time remained fairly stable with a mean score of 37.67 (range: 30–41). We also compared the NHBS for each AA indication to the cumulative NHBS average at the time each AA was granted. The NHBS for HCC, HNSCC, and cervical cancer were lower than respective pre-AA NHBS averages. The other 9 AAs yielded a final NHBS higher than each's pre-AA average NHBS. **Conclusions:** The NHBS formula generated varying values for different pembrolizumab indications, distinct from simple measures such as OS-rank order. Although the average NHBS remained fairly constant over time, it was lower than the maximum NHBS (59) and less than the NHBS of other breakthrough approvals (osimertinib for NSCLC: 110, nivolumab for melanoma: 53). If the average value of multiple indications in a drug's indication portfolio is significantly lower than a few blockbuster successes, clinicians could be vulnerable to an availability heuristic and overestimate the value of new AAs, based on anecdotal understanding of prior successes. In an environment of fast-paced AAs and label expansions, clinicians, patients, and payers should develop and deploy rapid value assessment tools in order to sustainably maintain access to high-yield cancer therapies. Research Sponsor: None.

Dysphagia-associated inpatient risk phenotypes and mortality in hospitalized head and neck cancer: A national analysis.

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Background: Dysphagia is common in patients with head and neck cancer (HNC) but is often viewed as a quality-of-life issue rather than a driver of acute inpatient outcomes. Its contribution to airway failure, mortality, and resource utilization is poorly defined, particularly when dysphagia is uncoded. We evaluated whether dysphagia-associated clinical signals define inpatient risk phenotypes, including a high-risk subgroup with silent dysphagia. **Methods:** We conducted a survey-weighted analysis of the National Inpatient Sample (NIS), 2016 to 2023, including adults hospitalized with HNC identified using ICD-10-CM codes C00 to C14 and C30 to C32. Tumors were categorized by first-hit anatomic site, and palliative admissions (Z51.5) were excluded. Dysphagia-associated signals included dysphagia (R13*), aspiration pneumonia (J69*), and feeding tube placement (ICD-10-PCS 0DH6*), which were combined into mutually exclusive dysphagia phenotypes. Silent dysphagia was defined as aspiration pneumonia or feeding tube placement without dysphagia coding. The primary outcome was in-hospital mortality. Secondary outcomes included mechanical ventilation, tracheostomy, shock, length of stay (LOS), and hospitalization cost. Survey-weighted regression models adjusted for demographics, payer, socioeconomic status, admission characteristics, hospital factors, tumor site, comorbidity burden, and year. **Results:** Among 112,495 unweighted HNC hospitalizations (weighted national estimate approximately 562,000), 26.6% had coded dysphagia, 8.7% aspiration pneumonia, and 16.3% underwent feeding tube placement; 11.4% met criteria for silent dysphagia. Mortality increased stepwise across phenotypes, from 1.82% (95% CI 1.72 to 1.93) in patients without dysphagia-associated signals to 8.59% (95% CI 7.80 to 9.47) with aspiration alone. Aspiration plus feeding tube placement was associated with the longest LOS (20.2 days, 95% CI 18.9 to 21.6) and highest mean cost (\$77,615, 95% CI \$70,531 to \$84,700). In adjusted analyses, aspiration alone was associated with higher mortality (OR 3.77, 95% CI 3.26 to 4.36), as was aspiration with feeding tube placement (OR 2.40, 95% CI 1.70 to 3.40). Dysphagia coding alone was not associated with increased mortality (OR 0.71, 95% CI 0.60 to 0.83). Silent dysphagia was independently associated with mortality (OR 2.31, 95% CI 2.04 to 2.61), mechanical ventilation (OR 3.77, 95% CI 3.51 to 4.03), and tracheostomy (OR 4.69, 95% CI 4.40 to 4.99). **Conclusions:** Dysphagia-associated clinical signals define inpatient risk phenotypes in hospitalized patients with HNC. While dysphagia coding alone does not confer excess mortality risk, aspiration pneumonia and feeding tube placement when dysphagia is uncoded identify a high-risk population with increased mortality, airway failure, LOS, and cost, supporting earlier inpatient recognition and intervention. Research Sponsor: None.

PRIME-ROSE: A blueprint for implementing precision cancer medicine in Europe.

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Background: Precision Cancer Medicine (PCM) is limited by increasingly small patient sub-groups defined by tumor type and biomarker, producing rare cohorts even within common cancers. This is demonstrated by several European national PCM platform trials like DRUP (NL), IMPRESS-Norway (NO) and ProTarget (DK). From our experiences, we identify four essential requirements for successful, scalable PCM implementation: i) integration of platform trials with national healthcare systems via molecular tumor boards for efficient screening by comprehensive molecular profiling and accrual; ii) cross-national data merging; iii) scalable networks to onboard new countries; and iv) clear decision pathways linked to outcome data for reimbursement. **Methods:** PRIME-ROSE links national PCM implementation platforms through a robust data sharing framework that retains national/regional data governance while enabling harmonised statistical analyses and standardised endpoints for decision-makers. Predictable implementation pathways provide multiple, pre-defined decision points for industry, health technology assessment (HTA) bodies and payers, and integrate risk-sharing and responder-only reimbursement options with existing data collection. A scalable, transparent network facilitates rapid expansion to additional European partners. **Results:** We have developed and tested an operational data-sharing framework, with defined protocols for minimal datasets and harmonised merging procedures. Patient-level data from multiple national cohorts (1100 patients in 400 cohorts) have been aggregated, and analyses of five filled cohorts are in progress. PRIME-ROSE uses a staged implementation model to detect initial efficacy signals (industry-financed drugs) to confirm and expand on prior evidence, facilitating predictable scale-up. Risk-sharing is operationalised via responder-only reimbursement after 16 weeks of treatment and a defined transition from trial to commercial supply. In 2025, PRIME-ROSE expanded partnerships, secured the first and second multi-trial industry access contracts, and expanded payer commitment to make reimbursement decisions after Stage III. **Conclusions:** PRIME-ROSE translates lessons from platform trials into a practical, scalable blueprint that preserves national governance, accelerates evidence generation and reduces payer uncertainty – thereby lowering barriers to equitable, continent-wide PCM adoption. Aligned with initiatives such as Basket of Baskets and ROME, PRIME-ROSE is positioned for further scale-up through member state collaboration under the Joint Action on Personalised Cancer Medicine. Research Sponsor: Funded by the European Union; Grant no. 101104269.

Weekend admission and early in-hospital mortality among patients with hematologic malignancies admitted for febrile neutropenia.

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Background: Weekend admissions have been associated with worse health outcomes compared with weekday admissions, a phenomenon known as the ‘weekend effect’. While predictors of in-hospital outcomes among patients with febrile neutropenia (FN) and hematologic malignancies are well described, the impact of the ‘weekend effect’ in this population remains unclear. Our study assessed the association between weekend admission, 3- and 7-day mortality. We further evaluated whether septic shock mediates the relationship between weekend admission and inpatient mortality, regardless of length of inpatient stay. **Methods:** We conducted a retrospective analysis of the National Inpatient Sample (2016 to 2020). Using ICD-10 codes, we identified patients with hematologic malignancies admitted for FN (D70.X, R50.81 and R50.9). Weekend admission was the primary exposure, while 3- and 7-day in-hospital mortality were the outcomes assessed. Generalized linear models were used to assess the association between weekend admission and each outcome, adjusting for sociodemographic characteristics, Charlson Comorbidity Index, mechanical ventilation, acute renal failure, protein energy malnutrition, cancer type, and length of stay. We performed a mediation analysis to assess whether septic shock mediated the association between weekend admission and overall mortality, estimating natural direct, indirect, and marginal total effects. **Results:** Among 45,540 patients in this study, 57% were male, 65% were white (mean age was 51 years). Patients had lymphoma (27%), leukemia (54%), multiple myeloma (10%), and multiple/other hematologic malignancies (9%). Weekend admission was associated with a higher risk of 3-day (adjusted risk ratio [adj RR] 1.48; 95% CI: 1.21–1.83) and 7-day mortality (adj RR 1.32; 95% CI: 1.12–1.56). When outcomes were assessed across the entire inpatient stay, weekend admission was associated with higher risk of septic shock (adj RR 1.14; 95% CI, 1.05–1.25). Further mediation analysis demonstrated that septic shock significantly mediated the association between weekend admission and overall inpatient mortality – indirect effect (adj RR 1.03; 95% CI 1.01–1.04), whereas the direct effect (adj RR 1.06; 95% CI 0.94–1.20) and overall effect (adj RR 1.09; 95% CI: 0.96–1.23) of weekend admission on mortality were not statistically significant. **Conclusions:** Weekend admission was associated with a higher risk of 3- and 7-day mortality. Septic shock partially mediated the relationship between weekend admission and mortality when assessed across the entire inpatient stay. The absence of a direct weekend effect suggests that health system-level factors contributing to septic shock such as delays in recognition, escalation, or time to antibiotics, may represent key intervention targets to improve mortality outcomes in this high-risk population. Research Sponsor: None.

Reporting of sex-related data in landmark phase III solid tumor trials presented at ASCO 2025.

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Background: Sex-related differences may influence cancer biology, treatment efficacy, and toxicity. Although consideration of sex as a biologically relevant variable is increasingly encouraged in oncology research, the extent to which sex-specific information is visible at the time of initial presentation of practice-changing clinical trial results remains unclear. **Methods:** We conducted a cross-sectional review of phase III solid tumor trial abstracts enrolling mixed-sex populations presented at the ASCO Annual Meeting 2025. Plenary, oral, and rapid oral abstracts representing practice-changing studies across tumor types and treatment modalities were included. Abstracts were systematically assessed for reporting of sex distribution and for sex-stratified efficacy or toxicity outcomes. **Results:** Ten landmark phase III trials across gastrointestinal, lung, genitourinary, head and neck, and melanoma cancers were included. Female representation was reported in 1 of 10 abstracts (10%). None of the abstracts reported sex-stratified efficacy analyses, and none reported sex-stratified toxicity outcomes. The absence of sex-specific reporting was consistent across tumor types, therapeutic classes, and session formats, including plenary presentations. **Conclusions:** Among landmark phase III solid tumor trials presented at ASCO 2025, sex-specific reporting was largely absent at the abstract level, including in practice-changing studies. Limited visibility of sex-specific data at abstract presentation may constrain clinical interpretation and highlights an opportunity to improve reporting practices in oncology trials. Research Sponsor: None.

Center-level delivery patterns and capacity during rapid CAR-T expansion in the United States (2021-2023).

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Background: Chimeric antigen receptor T-cell (CAR-T) therapy has rapidly expanded in the United States, accompanied by substantial growth in utilization and expenditures. However, whether this expansion has been matched by proportional growth in delivery capacity and how CAR-T workload is distributed across centers remains unclear. **Methods:** We conducted a national retrospective analysis using publicly available Medicare administrative data from 2021-2023 obtained from the Medicare Inpatient Hospitals dataset on data.cms.gov. CAR-T hospitalizations were identified using the diagnosis-related group (DRG) descriptions for CAR-T therapy and other immunotherapies. Active CAR-T centers were defined annually based on inpatient discharges. This DRG-based approach may include non-CAR-T immunotherapies, and Medicare data captures primarily older adults, potentially missing younger patients with acute lymphoblastic leukemia and lymphoma. Center-level CAR-T volume and expenditures were aggregated annually. Per-center delivery burden was assessed by strain (total CAR-T discharges divided by number of active centers). Concentration of CAR-T delivery across centers was evaluated using cumulative contribution analyses. **Results:** From 2021 to 2023, active CAR-T centers increased from 23 to 46, while total CAR-T discharges rose from 544 to 1,303. Total annual CAR-T expenditure increased substantially over the same period, from \$728 million in 2021 to \$2.56 billion in 2023. Despite this expansion, median annual discharges per center remained relatively stable (24 in 2021 vs 25.5 in 2023), while mean discharges increased from 23.7 to 28.3, indicating that growth was driven disproportionately by higher-volume centers. Correspondingly, the center-level strain increased from 23.6 to 28.3, reflecting rising per-center delivery burden. CAR-T delivery remained moderately concentrated across years, with top quartile of centers (approximately 21.7% of centers) accounting for 37.3% of CAR-T discharges in 2021, increasing to 39.5% of discharges in 2023. **Conclusions:** Despite rapid expansion in CAR-T centers and substantial growth in utilization and expenditures, delivery is increasingly concentrated among higher-volume centers. Stable median per-center volumes alongside increasing mean volumes and persistent concentration patterns suggest that growth has outpaced effective distribution of delivery capacity. While the relationship between center volume and patient outcomes remains incompletely characterized, these findings highlight the need for workforce development, infrastructure investment, and policy strategies to support both high-volume centers experiencing rising delivery burden and lower-volume centers developing expertise, ensuring sustainable and equitable CAR-T delivery as utilization continues to expand. Research Sponsor: None.

Safety-net coverage instability during cancer care and association with overall survival.

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Background: Means-tested (contingent on income) financial programs for uninsured individuals, such as Medicaid and county charity/indigent care, require periodic eligibility re-verification. A recent systematic review found that insurance coverage disruptions are associated with worse cancer stage and survival, but also highlighted that studies suffered from a limited ability to distinguish administrative lapses from eligibility-driven disruptions, and relied on single time-point measures to define longitudinal coverage. Consequently, the dynamics and clinical implications of coverage instability during cancer care are incompletely characterized. We investigated the coverage portions of the electronic health record (EHR) to overcome these issues and characterize coverage instability. **Methods:** We conducted a retrospective cohort study linking tumor registry records (2010–2022) to coverage verification fields from the EHR of a large county safety-net health system (2010–2024). Renewal limbo was defined as any gap between verified coverage intervals occurring > 365 days after a first verification. Multivariable logistic regression estimated odds of renewal-limbo within two years after diagnosis. Cox models estimated time to first renewal limbo and negative-binomial models for limbo duration; Prentice–Williams–Peterson models examined recurrent limbo. Two-year overall survival was estimated using a 12-month landmark design, with survival follow-up beginning at 12 months after diagnosis to ensure comparable risk windows across coverage instability groups. **Results:** Among 24,186 patients (56% female; 78% < age 65; 6% Medicaid, 50% County charity care; 15% breast, 8% colorectal, and 8% lung cancer), 26% experienced renewal limbo in the first year after diagnosis and 36% by the second year. Among patients with charity coverage at diagnosis who experienced renewal limbo, nearly 90% returned to charity coverage, and over two-thirds of Medicaid enrollees returned to Medicaid. Median limbo duration was 32 days (IQR, 3–220). Compared to diagnoses in 2010–2019, those diagnosed in 2020–2022 had substantially reduced odds of renewal limbo (aOR 0.29, 95% CI: 0.25–0.32) in Medicaid. In landmark analyses, uninterrupted coverage during the first year was associated with the highest survival, while patients in limbo at the time of diagnosis and at renewal limbo had the lowest survival (Table 1). **Conclusions:** Coverage lapses at annual renewal were common among safety-net patients treated for cancer and was largely temporary, suggesting administrative rather than eligibility-driven disruptions. Although lapses were brief, they were associated with measurably lower overall survival even 2 years after cancer diagnosis. Strong calendar-year effects in 2020–2022 suggests the influence of suspended re-verification during the COVID19 public health emergency. Research Sponsor: American Cancer Society; DBG-25-1374401-01-HOPS.

Real-world EGFR, ALK, and PD-L1 testing performance and end-to-end intervals in Colombian patients with non–small cell lung cancer.

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Background: Timely and comprehensive EGFR, ALK, and PD-L1 testing underpins effective precision oncology care in NSCLC, yet real-world data on testing completeness and integration into care pathways remain scarce in Latin America. **Methods:** We conducted a retrospective cohort study of adults with pathologically confirmed NSCLC treated at Fundación Santa Fe de Bogotá (2018–2025). EGFR/ALK/PD-L1 testing completeness, complete-panel availability, biomarker distributions, and turnaround times (order-to-report and diagnosis-to-report) were assessed. Stage III–IV sub analysis was performed. **Results:** A total of 242 patients were included. Most were female (53.3%), never-smokers (45.0%), and had adenocarcinoma histology (82.2%). EGFR, ALK, and PD-L1 results were available in 84.3%, 80.6%, and 80.6% of cases, respectively. Complete-panel availability was 74.4% and improved over time (adjusted OR per year, 1.28; 95% CI, 1.10–1.50; p=0.002). Turnaround times were favorable, with a median order-to-report time of 5 days (IQR, 2–8), and 68.0% completed within 7 days. The median diagnosis-to-report time was 12 days (IQR, 6–28.5), with 54.3% completed within 14 days. Activating EGFR mutations occurred in 38.7%, ALK fusions in 9.7%, and PD-L1 TPS ≥50% in 21.0%. In exploratory multivariable models, EGFR positivity was less frequent in ever-smokers (OR 0.26; 95% CI 0.13–0.51) and non-adenocarcinoma histology (OR 0.26; 95% CI 0.07–0.96). Guideline-concordant first-line targeted therapy was used in >80% of systemically treated patients with actionable alterations. In the stage III–IV subset (median age, 71.3 years; 53.8% female), median intervals were 13 days for imaging-to-diagnosis and 27 days for diagnosis-to-treatment (IQR, 16–52), with 33% exceeding 30 days and higher rates among patients referred after extra-institutional diagnosis. Median diagnosis-to-molecular report and report-to-treatment intervals were 11 days (IQR, 5–21) and 14 days, respectively. Requirement for EBUS was associated with longer imaging-to-diagnosis delays (75% >30 days; p=0.01). **Conclusions:** This study provides Latin American benchmarks for precision oncology delivery in NSCLC, showing high and improving molecular testing completeness with rapid turnaround. While molecular readiness was favorable, treatment initiation—especially for referred patients—represented the principal optimization gap. Standardized diagnosis-initiated testing and navigation workflows may improve end-to-end pathway performance. Research Sponsor: None.

Temporal trends in biomarker testing completeness in NSCLC (2018–2025).				
Metric	2018–2020 (n=87)	2021–2023 (n=93)	2024–2025 (n=59)	Overall (N=242)
EGFR available, %	77.0	86.0	93.2	84.3
ALK available, %	73.6	80.6	91.5	80.6
PD-L1 available, %	71.3	83.9	89.8	80.6
Complete panel available, %	65.5	74.2	88.1	74.4

Investigating reasons patients do not join a cancer clinical trial.

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Background: The perennial challenge to cancer clinical trials is accrual. To date, the focus to improve accruals rested on addressing patient knowledge, attitudes and beliefs rooted in patient reluctance to be experimented on, financial and practical barriers and issues of mistrust. We undertook this study to describe the impact of an educational intervention to democratize recruitment and improve understanding of and information about cancer clinical trials.

Methods: We implemented a time series intervention (INT) identifying cancer patients at treatment decision points at 3 participating Cancer Centers, educating consented breast, liver and lung cancer patients about clinical trials in general and providing clinical trial match lists to oncologists and patients prior to treatment decision-making. We defined a treatment decision point as a new, recurrent or progressing cancer. We surveyed patients and their oncologists pre- and post-intervention about their knowledge, attitudes and beliefs (KABs) of clinical trials. We compared pre & post KABs using Chi Sq and Fisher's Exact T tests. **Results:** Of 523 consented patients at treatment decision points, 514 completed pre & 368, post-INT surveys; 60% were non-white with no racial ethnic difference in response rates (70% BIPOC v 79% White; $p = 0.07$). Following an educational intervention, there was no significant change in positive attitude towards clinical trials (CT): 71% pre-intervention vs 77% post-intervention; $p = 0.55$, regardless of race-ethnicity (RE) ($p = 0.5025$). Black patients as compared to white patients, reported greater barriers to CT including: transportation (60% vs 37%; $p < 0.001$) and family responsibilities (46% vs 25%; $p = 0.001$). There was no RE difference in other barriers: patient report of physicians talking with them about clinical trials (89% vs 65%; $p = .36$), insurance (77% vs 74%; $p = 0.6051$); out of pocket expenses (64% vs 53%; $p = 0.12$); time off work (41% vs 37%; $p = 0.5457$). 25/28 (89%) treating oncologists of consented patients responded. Oncologists reported being less likely to offer CTs to patients who they perceived were reluctant to: get placebo (48%), be randomized (48%), have increased family responsibilities (52%), would have difficulty getting time off work (45%) or had comorbidities (40%). **Conclusions:** More than $\frac{3}{4}$ of patients have a positive attitude towards clinical trials with no racial-ethnic difference. Black patients reported more barriers to trial enrollment than white patients. Despite Black patients having more barriers that would reduce oncologists' likelihood of offering CTs to patients, there was no RE in patients' report of oncologists talking with them about CTs. Clinical trial information: NCT05146297. Research Sponsor: Stand Upto Cancer.

Health shocks and advance care planning among U.S. older adults: Evidence from HRS 2012-2022.

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Background: Advance care planning (ACP) allows individuals to discuss and document preferences for future medical care under serious illness, yet engagement among older adults remains limited. Experiences of a health shock, such as a diagnosis of cancer, major illnesses, or hospitalization, may prompt participation in ACP. This study aimed to examine the association between health shocks and subsequent ACP engagement and variation by key sociodemographic characteristics. **Methods:** We conducted a longitudinal cohort study using data from the Health and Retirement Study (HRS), a nationally representative survey of U.S. adults aged ≥ 65 years. Adults from 2012–2022 HRS with no baseline ACP who completed at least one follow-up wave were included. The exposure was a new health shock, defined as a new diagnosis of cancer, stroke, heart disease, or hospitalization. The outcome was new ACP engagement in subsequent waves. Generalized estimating equation models estimated adjusted odds ratios (ORs) of experiencing a health shock due to cancer diagnosis and due to other causes (vs. no health shock) on new ACP; and how such associations varied by respondents' characteristics. **Results:** Among 8,553 person-wave observations (4,426 unique respondents), median age was 74 years (IQR 69–79); 52.9% were women, 24.3% lived alone, 27.6% experienced a health shock, and 3.11% reported a health shock from new cancer diagnosis. Health shocks were associated with higher odds of ACP engagement (OR = 1.41; 95% CI, 1.28–1.56). In the three-level shock model, both non-cancer shock (OR = 1.43; 95% CI, 1.28–1.59) and cancer shock (OR = 1.31; 95% CI, 1.01–1.70) were associated with higher odds of ACP compared with no shock. Older age, female gender, and higher education were associated with greater ACP engagement overall. Compared with non-Hispanic Whites, non-Hispanic Black (OR = 0.73; 95% CI, 0.64–0.84) and Hispanic (OR = 0.55; 95% CI, 0.47–0.65) had lower odds of ACP. Living alone was associated with higher ACP engagement (OR = 1.29; 95% CI, 1.14–1.45). However, when stratified by patient socio-demographic characteristics, the associations between health shock and ACP were similar across groups, except that for those living alone who showed larger odds of initiating a new ACP following health shock (OR = 1.76; 95% CI, 1.45–2.14) than those not living alone (OR = 1.31; 95% CI, 1.16–1.47). **Conclusions:** Health shocks were associated with new ACP engagement among older adults, with similar associations observed for cancer-specific and non-cancer health shocks. Although disparities in ACP by sociodemographic characteristics persisted, health shocks were associated with similarly odds of initiating ACP across population subgroups. This highlights the importance of leveraging health shocks as clinical touchpoints for ACP discussions, and the need for targeted strategies to reduce inequities in ACP engagement outside of acute health events. Research Sponsor: None.

Insights from initial scoring in the Health Equity Report Card (HERC) pilot in community oncology settings.

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Background: The Health Equity Report Card (HERC) is an innovative tool designed to assess and promote equity in cancer care. Standardized scoring is performed in four domains: Community Engagement, Accessibility of Care and Social Determinants of Health, Addressing Bias in Care Delivery, and Quality and Comprehensiveness of Care. Initial scoring is reported. **Methods:** Five diverse community oncology sites were recruited to evaluate the HERC's feasibility and usability in this setting. The primary objective is to evaluate the feasibility of implementing the HERC with scoring at community oncology sites. Key metrics include the ability to collect HERC data and complete self- and third-party scores. Baseline scores were calculated using data from prior six months. Quantitative and qualitative feedback was collected via surveys and semi-structured interviews. Results were summarized using descriptive statistics. This study was granted Institutional Review Board exemption by Pearl IRB and sites received funding support.

Results: All sites completed self- and third-party scores (Table 1). Average self-scores and third-party scores were similar, with third party scores slightly lower across all domains. There was a wide range in scores across all domains. All sites felt the HERC was easy to understand. Sites requested clarification on four measures and expect the final round of scoring to be easier and faster. 4/5 sites stated collecting sources of evidence was feasible. Key challenges included: a lack of formal documentation and processes not implemented consistently across the practice. Best practices included: 5/5 used tracking logs, 5/5 used a team approach, and 4/5 utilized provided materials to orient staff to the project. All sites stated the HERC was a helpful resource for community practices, was useful to learn about health equity initiatives across the site, and was helpful to identify or prioritize quality improvement projects. All sites felt the HERC would inform changes to site processes and plan to identify improvement strategies based on their baseline scores. **Conclusions:** Initial implementation of the HERC in community oncology practices was feasible with completion of scoring across all practices. Score variation across sites and domains highlight differences in resources, documentation, and practice. Sites confirmed the HERC is a helpful resource and catalyst for quality improvement. The project remains ongoing. The HERC is a promising tool to foster equitable care delivery for all cancer patients. Research Sponsor: Merck Foundation through the Alliance for Equity in Cancer Care; Pfizer, Inc.; Lilly; GlaxoSmithKline, LLC; Bristol Myers Squibb Company.

Summary statistics of baseline self- and third-party scores.

Domain	Max Score	Self-Score			Third-Party Score		
		Mean	SD	Range (Max-Min)	Mean	SD	Range (Max-Min)
Community Engagement	4	3	1.1	3 (1-4)	2.2	1.5	4 (0-4)
Accessibility	6	3.9	1.7	4.5 (1-5.5)	3.7	1.5	4.5 (1-5.5)
Bias	5	1.9	1.3	3 (0.5-3.5)	1.5	1.2	3.5 (0-3.5)
Quality of Care	4	2.6	1.7	4 (0-4)	2.4	1.6	4 (0-4)

Same day/next day cancer care program: An early access program for patients with aggressive malignancies.

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Background: Rapid referral of patients with suspected malignant disease to an oncology specialist is associated with improved earlier-stage diagnosis and survival benefits. The advantage of such rapid care transition can be especially pronounced in aggressive malignancies, where early interventions are critical in reducing mortality. Patients with already established cancer diagnosis may also benefit from such programs. Same Day/Next Day Cancer Care (SDND) is a Jefferson Health enterprise designated referral system allowing patients with newly diagnosed cancers to be seen by an advanced practice clinicians via telemedicine within 48 hours at the Sidney Kimmel Comprehensive Cancer Center (SKCC). **Methods:** Adult patients with an established diagnosis of aggressive types of malignancies were referred through SDND to SKCCC in the Greater Philadelphia Area if they had concerning symptoms related to disease. The following malignancies were selected: acute leukemias, T-cell lymphomas, diffused large B-cell lymphomas, Burkitt lymphomas, melanomas, glioblastoma multiforme, pancreatic adenocarcinoma, esophageal or gastric carcinoma, small cell lung carcinoma, biliary tract malignancy, anaplastic thyroid cancer. Socio-demographics, time to appointment with an oncologist and treatment were analyzed. **Results:** Between July 2024 and December 2025, 209 patients with aggressive malignancies, of which 49% were female with a median age of 67 years, were referred to oncology specialists. Only 19% were new patients, while 81% had already established care. Medical providers made 78.3% of referrals, while other 21.7% were self-referred. Average SDND schedule lag days was 1.04 days. About 85% of patients had medical oncologist consultation appointments, of which 68.8% completed the planned visit. Thirty-four patients (16%) were referred for infusion therapy, of which 64.7% successfully initiated infusion therapy within 50 days. Similarly, 76 patients (36%) had scheduled a surgical specialty consultation, of which 77.9% completed the appointment. Importantly, 53.7% of the patients underwent surgery within 30 days of the SDND referral. **Conclusions:** SDND is a centralized access program aimed at reducing time to first appointments for newly diagnosed cancer patients. It led to accelerated assessment by oncology providers with high adherence to the management plan. It can ensure faster diagnostic workups and symptom management related to aggressive malignancies by advanced care clinicians, with the potential to improve survival rates, patient satisfaction, reduce treatment-related anxiety and cancer-related morbidity. Further research is needed to determine if this early clinical evaluation by advanced practice providers via telemedicine may reduce complications warranting high-cost care, such as emergency department visits or hospitalizations in high-risk cancer population. Research Sponsor: None.

Empowering multidisciplinary teams in cancer survivorship: Results from the ASCO Project ECHO survivorship program in Brazil.

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Background: As the number of cancer survivors increases in Brazil, access to structured survivorship education for health professionals remains limited. ASCO Project ECHO Survivorship Program was implemented to strengthen survivorship knowledge and care coordination among multidisciplinary teams. **Methods:** This longitudinal, virtual, case-based education series was conducted from September to December 2025. Intended audience included oncologists, general physicians, nurses, psychologists, and other professionals involved in survivorship care. Program consisted of 08 distinct, self-contained sessions, beginning with an introductory session on core survivorship principles, followed by cancer-specific survivorship topics delivered through short didactics and case discussions. Participants were encouraged to attend all sessions; however, each session was designed to be independent. Attendance was tracked, and final post-program survey assessed satisfaction and self-reported impact on clinical practice. Analyses focused on participants attending ≥ 4 sessions ($\geq 50\%$), which was the criterion for certification and a pragmatic threshold to ensure meaningful engagement. **Results:** 161 health professionals attended at least one session, and 65 (40.4%) participated in ≥ 4 sessions. Participants represented diverse disciplines, including physicians and oncologists (31%), psychologists (13.7%), nutritionists (8.7%), pharmacists (6.2%), nurses (11.2%), and other professionals. Subsequent analyses were limited to participants attending ≥ 4 sessions. Among these, final survey response rate was 66.2%. Reported practice changes and satisfaction outcomes were collected through the post-program survey. Respondents described increased confidence in identifying and managing late and long-term physical effects, addressing psychosocial and sexual health concerns, improving interdisciplinary collaboration, and supporting transitions to post-treatment care. Overall satisfaction was high, with 97.7% reporting being satisfied or very satisfied. Despite high satisfaction, attendance declined across sessions, highlighting the need to better understand factors influencing sustained participation in longitudinal virtual education programs. **Conclusions:** ASCO Project ECHO Survivorship Program in Brazil demonstrated strong engagement and meaningful self-reported integration of survivorship principles into clinical practice among a multidisciplinary workforce. This flexible, scalable educational model supports survivorship capacity-building across diverse professional roles in middle-income settings. Further evaluation is needed to better understand factors associated with decreased attendance over time and to inform strategies that optimize sustained engagement in longitudinal survivorship education programs. Research Sponsor: None.

Admission acuity and inpatient outcomes across major gastrointestinal malignancies in the United States, 2018–2022.

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Background: Hospitalization for gastrointestinal (GI) malignancies frequently occurs in the setting of acute decompensation or unplanned admission. National data quantifying the association between admission acuity and inpatient outcomes across major GI cancer subtypes remain limited. **Methods:** A serial cross-sectional analysis was conducted using the 2018–2022 Healthcare Cost and Utilization Project National Inpatient Sample. Adult hospitalizations with a principal diagnosis of esophageal (C15), gastric (C16), colorectal (C18–C20), liver or intrahepatic bile duct (C22), or pancreatic cancer (C25) were identified. Admission acuity was classified as elective or non-elective. Outcomes included in-hospital mortality (primary), length of stay (LOS), and hospitalization cost estimated using cost-to-charge ratios. National estimates accounted for survey weighting, clustering, and stratification. Survey-weighted multivariable logistic regression evaluated factors independently associated with in-hospital mortality, adjusting for admission type, cancer subtype, demographics, payer, neighborhood income quartile, hospital characteristics, and calendar year. **Results:** From 2018–2022, 214,740 unweighted GI cancer hospitalizations represented an estimated 1.07 million hospitalizations nationally. Colorectal cancer accounted for 56.7% of admissions, followed by pancreatic (17.6%), liver or intrahepatic bile duct (10.5%), gastric (8.6%), and esophageal cancer (6.6%). Overall, 52.9% of hospitalizations were non-elective. In-hospital mortality was higher for non-elective than elective admissions (5.92% vs 1.89%), with longer LOS (7.61 vs 6.15 days) and lower mean hospitalization costs (\$25,644 vs \$32,166). In adjusted analyses, elective admission was associated with substantially lower odds of in-hospital mortality compared with non-elective admission (adjusted odds ratio [aOR] 0.395; 95% CI 0.328–0.476). Relative to esophageal cancer, adjusted mortality odds were lower for colorectal, gastric, and pancreatic cancers, while no significant difference was observed for liver or intrahepatic bile duct cancers. **Conclusions:** Across major gastrointestinal malignancies, non-elective admission was associated with substantially higher inpatient mortality and longer length of stay independent of cancer subtype and sociodemographic factors. These nationally representative findings provide benchmarking data for admission acuity as a marker of inpatient risk in gastrointestinal oncology. Research Sponsor: None.

Survival outcomes in individuals with cancer and pre-existing autoimmune disease receiving immune checkpoint inhibitors: A multicenter, propensity-matched real-world survival analysis.

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Background: Autoimmune disease (AID) affects approximately 5–10% of individuals with cancer. Although immune checkpoint inhibitors (ICIs) have transformed cancer therapy, individuals with pre-existing AID are routinely excluded from clinical trials due to concerns about immune-related adverse events. Consequently, long-term real-world survival outcomes in this population remain incompletely defined, limiting evidence-based risk-benefit assessment.

Methods: We conducted a retrospective, multicenter cohort study using a large U.S.-based real-world oncology network derived from harmonized electronic health records across academic and community cancer centers. Adults (≥ 18 years) with solid tumors who received at least one immune checkpoint inhibitor (PD-1, PD-L1, or CTLA-4) were included. Individuals were classified by the presence or absence of documented pre-existing AID prior to ICI initiation. Cohorts were matched 1:1 using propensity scores based on age, sex, race, and baseline comorbidities, including cardiovascular disease, diabetes, chronic kidney disease, chronic obstructive pulmonary disease, cerebrovascular disease, and heart failure. Survival outcomes at 1, 3, and 5 years from ICI initiation were evaluated using Kaplan–Meier methods and Cox proportional hazards models. **Results:** After propensity score matching, 13,800 adults were included (6,900 with AID and 6,900 without), with excellent balance across baseline covariates. All-cause mortality was higher among individuals with pre-existing AID at 1 year (36.7% vs 32.6%), 3 years (48.3% vs 44.7%), and 5 years (50.1% vs 47.0%). Pre-existing AID was independently associated with worse overall survival at all time points (HR 1.15; 95% CI 1.09–1.22 at 1 year; HR 1.15; 95% CI 1.10–1.21 at 3 years; HR 1.15; 95% CI 1.09–1.20 at 5 years; all $P < 0.001$). Kaplan–Meier analyses demonstrated early separation of survival curves that persisted through long-term follow-up (log-rank $P < 0.001$). **Conclusions:** In this large, multicenter, real-world cohort, pre-existing autoimmune disease was associated with a modest but durable reduction in survival among individuals treated with immune checkpoint inhibitors, persisting through 5 years of follow-up. These findings do not contraindicate ICI use but highlight the need for individualized risk stratification, multidisciplinary collaboration, proactive toxicity surveillance, and informed shared decision-making when initiating immunotherapy in this population. Research Sponsor: None.

Racial and payer-based disparities in inpatient resource utilization and mortality among patients hospitalized with head and neck cancer in the United States, 2018 to 2022.

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Background: Inpatient hospitalizations for head and neck cancer (HNC) reflect advanced disease, treatment-related complications, and high healthcare utilization. National data on racial and payer-based disparities in inpatient length of stay (LOS), costs, and mortality remain limited. **Methods:** A survey-weighted cohort analysis of the Healthcare Cost and Utilization Project National Inpatient Sample (NIS), 2018 to 2022, was performed. Hospitalizations with a principal diagnosis of HNC were identified using ICD-10-CM codes C00 to C06, C07 to C08, C09 to C14, C30 to C32, and C76.0; thyroid cancer (C73) was excluded. Outcomes included in-hospital mortality, LOS, and hospitalization cost. Survey-weighted mean LOS and cost were estimated by race and primary payer. A survey-weighted multivariable logistic regression evaluated predictors of in-hospital mortality, adjusting for age, sex, year, anatomic subsite, race, payer, ZIP-code income quartile, elective admission status, and hospital teaching and location characteristics. **Results:** The weighted national estimate included 166,020 inpatient HNC hospitalizations (95% CI 158,702 to 173,338). Mean LOS ranged from 7.43 days among White patients (95% CI 7.29 to 7.56) to 10.21 days among Black patients (95% CI 9.81 to 10.60), with intermediate LOS among Hispanic (9.22 days), Asian or Pacific Islander (8.41 days), Native American (8.86 days), and Other race groups (8.25 days). Mean hospitalization costs were highest among Asian or Pacific Islander patients (\$46,577, 95% CI \$41,648 to \$51,506) and Hispanic patients (\$42,384, 95% CI \$39,129 to \$45,640), compared with White patients (\$36,887, 95% CI \$35,197 to \$38,577). Medicaid hospitalizations had the longest LOS (10.58 days, 95% CI 10.16 to 10.99) and high costs (\$42,217, 95% CI \$40,126 to \$44,308), whereas privately insured hospitalizations had the shortest LOS (6.54 days, 95% CI 6.37 to 6.72). In adjusted analyses, mortality increased with age (OR 1.02 per year, 95% CI 1.01 to 1.03). Asian or Pacific Islander (OR 1.51, 95% CI 1.07 to 2.13) and Other race patients (OR 1.59, 95% CI 1.09 to 2.32) had higher mortality than White patients. Non-Medicare other insurance was associated with higher mortality than Medicare (OR 2.56, 95% CI 1.89 to 3.46). Elective admissions (OR 0.21, 95% CI 0.16 to 0.27) and care at urban teaching hospitals (OR 0.34, 95% CI 0.25 to 0.47) were associated with lower mortality. **Conclusions:** Racial and payer-based disparities persist in inpatient LOS, costs, and mortality among patients hospitalized with HNC. Black and Medicaid-insured patients experience longer hospitalizations, while Asian or Pacific Islander and Hispanic patients incur higher costs. Persistent mortality differences after adjustment highlight structural and health-system contributors and support targeted equity-focused interventions. Research Sponsor: None.

Consumer wearables and medical care utilization in gastrointestinal cancers: A Fitbit data analysis in NIH All of Us Research Program.

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Background: Patients with gastrointestinal (GI) cancers may experience delayed or forgone care due to cost, travel, or health system barriers. Wearable devices are widely used and capture physical activity that may reflect health status, mobility, and social factors. Whether wearable activity data can help identify patients at risk for delayed care is not well understood. We examined associations between activity levels and delayed or forgone care among adults with GI cancers in the NIH All of Us Research Program. **Methods:** Adults with GI cancers who contributed wearable activity data and healthcare utilization surveys were included; ≥ 30 valid Fitbit days were required. Mean daily step counts were calculated and categorized into cohort-specific quartiles: Q1 ($\leq 3,621$ steps/day), Q2 (3,621–5,591), Q3 (5,591–8,272), and Q4 ($> 8,272$). Delayed or forgone care was determined from survey items asking whether participants postponed or avoided medical care due to financial or access barriers. Analyses were performed in the overall GI cohort ($n = 407$) and stratified by cancer site (colorectal, pancreatic, upper GI, hepatobiliary, and other). Logistic regression evaluated associations between activity and delayed care using categorical quartiles, continuous log-transformed steps, and age-adjusted models. **Results:** The analytic cohort included 407 participants with GI cancers. After age adjustment, higher daily step counts—analyzed continuously and across ordered quartiles—were associated with lower odds of delayed or forgone care. Age itself was independently associated with fewer delays (OR per 10 years 0.62, $p = 0.001$ – 0.002). In categorical models using Q3 as the reference, participants in Q1 had higher odds of delayed care (OR 3.57, 95% CI 1.06–12.10, $p = 0.041$), while Q2 and Q4 did not differ significantly from Q3, supporting a non-linear association. Site-stratified analyses showed similar non-linear patterns; for example, pancreatic cancer ($n = 60$) had delayed care prevalences of Q1 11.1%, Q2 0%, Q3 5.0%, Q4 9.1%, and upper GI cancers ($n = 59$) had Q1 9.1%, Q2 0%, Q3 6.3%, Q4 13.3%. In colorectal cancer ($n = 210$), Q3 had the lowest delayed care vs Q1 (OR 0.25, 95% CI 0.05–1.32), although other quartile estimates were less precise due to small event counts. **Conclusions:** Among patients with GI cancers who contributed wearable and survey data, delayed or forgone care showed a non-linear association with activity, with the lowest odds in the moderate–high activity range. Participants in Q1 had higher odds of delayed care compared with Q3 after age adjustment. Wearable activity data may help identify patients who face barriers to timely care, although this cross-sectional study cannot show cause and effect. Longitudinal studies are needed to determine whether passive wearable data can support care navigation and healthcare utilization in oncology. Research Sponsor: None.

Recent trends in utilization of outpatient medical oncology services.

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Background: Health systems face escalating demand from rising cancer incidence and treatment complexity. Effective health human resource planning is critical to accommodate these trends. Limited data are available on longitudinal utilization of medical oncology services, especially volumes and complexity of care. We sought to characterize real-world longitudinal utilization of outpatient medical oncology services across common solid tumors to inform workforce planning and policy. **Methods:** We conducted a retrospective, population-based retrospective cohort study using linked administrative health data from Ontario, Canada. Adults diagnosed between 2015 and 2022 with lung, colon, rectal, pancreatic, breast, melanoma, or prostate cancer were identified through the Ontario Cancer Registry. Medical oncology consultations, clinic visits, and systemic treatment encounters were captured from the provincial Activity Level Reporting database. Primary outcomes included consultation and systemic therapy initiation trend, and mean clinic and treatment visits during the first year following medical oncology consultation. **Results:** The cohort consisted of 332,604 patients (median age 68 years; 48.7% male), with new cases increasing from 39,688 in 2015 to 45,011 in 2022. Medical oncology consultation and systemic treatment initiation were encountered by 57.8% (range: 17.2% prostate to 92.8% breast) and 71.2% respectively (range: 45.1% melanoma to 82.8% breast). The proportion of patients with medical oncology consultation increased appreciably for pancreatic (59.8% to 79.0%), colon (55.8% to 60.2%), rectal (64.4% to 69.6%), and lung cancers (57.3% to 61.4%), with resultant growth in consultation volumes except for melanoma, colon and lung cancers. Total clinic visits increased from 131,950 in 2015 to 174,630 in 2022. Mean clinic visits per patient increased significantly for all cancers except prostate ($p < 0.001$), with the greatest increase observed in melanoma (+0.33 visits/year). Systemic therapy exposure increased across most cancers, most notably melanoma (25.7% to 47.2%) and prostate cancer (61.2% to 73.9%). Total systemic treatment visits increased from 129,380 in 2015 to 165,149 in 2022 with total and mean per patient trends exhibiting mixed, disease-specific patterns. **Conclusions:** Outpatient medical oncology service utilization per patient has expanded substantially over time, driven by rising volumes of consultations, systemic therapy and clinic visits. Taken with the rising complexity of care, these data suggest that consultation-based workload metrics likely underestimate service demand. Workforce planning models should incorporate follow-up care, treatment monitoring, and disease-specific trajectories to ensure sustainable, high-quality oncology care delivery. Research Sponsor: None.

Hidden advanced physiology in non-metastatic gastrointestinal cancer: Malnutrition/cachexia and in-patient failure-to-rescue.

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Background: Cancer stage is often used as a proxy for inpatient risk, yet physiologic reserve may better determine outcomes. It was hypothesized that among gastrointestinal (GI) cancer hospitalizations without coded metastasis, malnutrition/cachexia identifies a vulnerable subgroup with complication burden, ICU escalation, and post-complication mortality approaching that of metastatic disease. **Methods:** A survey-weighted analysis of the National Inpatient Sample (NIS), 2016–2023, was conducted. Adult hospitalizations with any GI malignancy (ICD-10–CM C15–C20, C22–C25) were included; encounters with palliative care coding (Z51.5) were excluded. Metastatic disease was defined by C77–C79. Vulnerability was defined as malnutrition/cachexia (E43, E44, E46, R64). Major complications included sepsis, bleeding/transfusion, venous thromboembolism, acute kidney injury (AKI), bowel injury/peritonitis, and respiratory failure. ICU escalation proxies included mechanical ventilation and/or shock. Outcomes were compared across three groups: non-metastatic/no vulnerability, non-metastatic/vulnerable, and metastatic. Failure-to-rescue was defined among non-metastatic surgical hospitalizations as death following ≥ 1 major complication. **Results:** The cohort included 748,734 weighted hospitalizations; 39.6% had coded metastasis. Among non-metastatic admissions, vulnerability prevalence increased from 15.6% in 2016 to 21.9% in 2023. In-hospital mortality in the non-metastatic/vulnerable group (4.14% [95% CI, 4.00–4.29]) approximated metastatic mortality (3.96%) and exceeded non-metastatic/no vulnerability mortality (1.86% [95% CI, 1.81–1.91]). Compared with non-metastatic/no vulnerability, vulnerable admissions demonstrated higher ICU escalation (7.75% [95% CI, 7.56–7.94] vs 3.54%), AKI (27.30% [95% CI, 26.98–27.62] vs 17.25%), and any major complication (59.31% [95% CI, 58.95–59.67] vs 42.93%). Resource utilization was higher in the vulnerable group (LOS 9.33 vs 5.49 days; cost \$33,156 vs \$22,879). Among non-metastatic admissions with complications, mortality was higher with vulnerability (6.46% [95% CI, 6.24–6.69] vs 3.88%). In the non-metastatic surgical subcohort, failure-to-rescue mortality was 5.90% (95% CI, 5.59–6.22) with vulnerability versus 2.65%. **Conclusions:** Among U.S. GI cancer hospitalizations without coded metastasis, malnutrition/cachexia identifies a high-risk inpatient phenotype with complication burden, ICU escalation, and post-complication mortality closely resembling metastatic disease. These findings suggest physiologic vulnerability, rather than stage alone, drives inpatient risk and failure-to-rescue, supporting targeted inpatient risk stratification and earlier supportive interventions. Research Sponsor: None.

Quality of life among caregivers of patients with breast cancer in Mexico: A multicenter cross-sectional survey using the Caregiver Quality of Life Index–Cancer (CQOLI-C).

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Background: Family caregivers of patients with breast cancer (BC) often experience emotional, physical, social, and financial strain that can compromise their quality of life (QoL). The Caregiver Quality of Life Index–Cancer (CQOLI-C) is a validated cancer-specific instrument, however data on factors associated with caregiver QoL across healthcare settings in Mexico remain limited. **Methods:** We conducted a multicenter, cross-sectional survey of primary caregivers of patients with BC in Mexico. Consecutive eligible caregivers were recruited across public and private care settings (Sep 2025 – Jan 2026) and completed an online questionnaire. QoL was measured using the CQOLI-C (35 items scored 0–4; total score range 0–140; higher scores = greater caregiver burden (CB)); positively worded items were reverse-coded and summed to generate the total score. We summarized caregiver/patient characteristics and CQOLI-C scores with descriptive statistics and compared them across key groups (metastatic status, caregiving hours/week, additional helpers, self-reported unsustainable caregiving (yes/no), and care setting (public vs private)). We evaluated associations between CQOLI-C total score and prespecified predictors using multivariable OLS linear regression with robust standard errors (two-sided $p < 0.05$). **Results:** Seventy-three caregivers completed the survey (mean age 46.9 ± 15.5 years; 54.8% male). Caregivers were most commonly partners (43.8%) or adult children (32.9%). 53.4% of patients received care in the private sector; 26% had metastatic disease. The most common numbers of additional caregivers were 2 (27.4%) and 0 (21.9%). Over half of caregivers (52.1%) reported providing 0–10 hours/week of care, while 16.4% reported > 50 hours/week. Median caregiver burden measured by CQOLI-C was 45 (IQR 29.5–62). 41% reported caregiving became too difficult to sustain. High burden items most frequently endorsed (score 3–4) included fear of patient death (54.8%), concern about treatment adverse effects (42.5%), and anger to see loved one deteriorating (41.1%). In adjusted regression ($n = 73$), compared with no helpers, reporting two helpers ($\beta = 16.5$; $p = 0.020$) and five helpers ($\beta = 24.4$; $p = 0.016$) was associated with higher scores, while six or more helpers was associated with substantially lower scores ($\beta = -42.0$; $p = 0.002$). Metastatic disease ($\beta = 16.7$; $p = 0.043$) and public vs private sector ($\beta = 24.2$; $p = 0.009$) were associated with worse scores; caregiving hours showed no consistent independent association. **Conclusions:** Caregiver burden was substantial and clustered around unsustainable caregiving demands, metastatic disease, and public care settings. These factors can help identify caregivers most in need of support and should guide systematic caregiver screening and targeted supportive-care interventions in Mexico. Research Sponsor: None.

Patient-perceived caregiver burden after intense oncology treatment.

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Background: Although oncology caregiver burden is well-known (e.g. Alam, *JCO*, 2020), less is understood about how patients themselves perceive their caregivers' quality of life (QOL) after intensive cancer treatment such as hematopoietic cell transplantation (HCT). **Methods:** Patients undergoing allogeneic HCT at Dana-Farber Cancer Institute (12/2017 to 12/2021) were surveyed approximately 100 and 180 days post-HCT. We utilized a questionnaire adapted from the Caregiver Quality of Life Index-Cancer Scale (Weitzner, *Qual Life Res*, 1999), redesigned to be administered to patients themselves. Caregiver stress was assessed with the question "My caregiver seems more stressed than before my transplant" (0: not at all to 4: very much), dichotomized into lower (0-2) versus higher (3-4) stress. Familial financial burden was measured with the question "How satisfied are you with your family's present financial situation?" (1: not satisfied at all to 5: completely satisfied), dichotomized into higher (1-3) versus lower (4-5) burden. Paired McNemar tests assessed changes in caregiver stress between Day 100 and Day 180, and multivariable logistic regression modeled the relationship between financial burden and caregiver stress, adjusting for age and gender. **Results:** At Day 100 and Day 180, 165 and 142 patient surveys were analyzed (overall response rates were 60.5% and 70.0% among patients alive at each time); 89 patients completed surveys at both times. The mean age was 61.5, 38.2% were female, and 61.8% received reduced-intensity HCT conditioning. Most respondents (86.1%) identified their caregiver as a family member (as compared to a friend or paid professional). Approximately half reported their caregiver was working at both Day 100 (51.2%) and Day 180 (53.2%). The majority felt that the HCT process had not negatively impacted their relationship with their caregiver (93.3% at Day 100; 96.5% at Day 180). At Day 100, 30.9% of respondents perceived their caregiver as being more stressed than prior to HCT, compared with 33.3% at Day 180 (comparing the two time point proportions: $\chi^2 = 0.80$, $p = 0.37$). Lower financial burden was significantly associated with lower odds of reporting increased caregiver stress at both Day 100 (OR = 0.49, 95% CI: 0.24-0.99) and at Day 180 (OR = 0.17, 95% CI: 0.07-0.39). **Conclusions:** In this cohort of patients undergoing intense oncology treatment, most had caregivers who were working family members. A minority perceived increased caregiver stress due to their treatment, with similar perceptions at both Day 100 and Day 180. This relatively modest perception of stress potentially reflects caregivers' successful efforts to lower patients' self-perceived burden. Moreover, lower familial financial burden was strongly protective against patient-perceived caregiver stress, particularly at Day 180, suggesting that financial circumstances meaningfully influence how patients interpret and perceive caregiver burden. Research Sponsor: None.

Patient trust in oncologists versus artificial intelligence for cancer-related questions.

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Background: Artificial intelligence tools, including the recent introduction of ChatGPT Health, are increasingly accessible to patients seeking medical information. In oncology, where discussions surrounding prognosis and treatment are highly sensitive, trust in the source of information is critical. However, patient perspectives on AI tools compared with oncologists for cancer-related questions remain poorly characterized. **Methods:** We conducted a cross-sectional survey of 75 adult cancer patients at an academic safety-net oncology clinic. The survey assessed patients' perspectives on technology use and their trust in AI tools like ChatGPT compared with oncologists for cancer-related questions. The primary outcome was patients' preferred source of trust when asked who they would rely on most to answer a serious question about their cancer. Secondary outcomes assessed attitudes toward physician versus AI trust using Likert-scale items and comfort engaging with AI for cancer-related questions. Binomial proportions are reported with 95% confidence intervals. Spearman correlation and Fisher's exact tests were used for secondary exploratory analyses. **Results:** Among 75 respondents, the median age group was 55–64 years; 42.7% were male and 57.3% female. English was the primary language for 53.4% and Spanish for 43.8%. The most common cancer types were gastrointestinal (24.0%), breast (20.0%), and hematologic malignancies (17.3%). For the primary outcome, when asked who they would trust most to answer a serious question about their cancer's future, an overwhelming majority selected their oncologist (97.3%; 73/75; 95% CI 90.7–99.7). No respondents selected ChatGPT/AI (0%; 95% CI 0–4.8), while 2.7% were unsure (95% CI 0.3–9.3). In secondary analyses, greater self-reported comfort with technology was associated with greater comfort engaging with AI tools for cancer-related questions (Spearman $\rho = 0.40$, $p < 0.001$). In exploratory subgroup analyses, Spanish speakers showed a trend toward less agreement that they would trust a doctor's answer more than AI (71.9% vs 87.2%). This may reflect increased trust when medical information is delivered in a patient's primary language. In addition, a similar directional signal was observed among younger patients (73.3% vs 84.4%). **Conclusions:** Cancer patients currently demonstrate a strong preference for oncologists over AI tools when addressing serious cancer-related questions, underscoring the central role of physician trust in oncology care. However, comfort engaging with AI varies by technological familiarity, suggesting that this preference may evolve over time as younger, more digitally fluent generations enter care and AI becomes increasingly integrated into healthcare. This study highlights the potential of AI tools to support oncologists in providing more accurate and individualized prognostic estimates for patients with advanced malignancies. Research Sponsor: None.

Latent transitions of distress risk during cancer treatment and their concordance with anxiety, depression, and quality of life in a large multicenter cohort.

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Background: Distress is prevalent in patients with cancer and may change throughout treatment. However, longitudinal transitions between distress-risk states and their relationship with psychosocial outcomes in real-world oncology settings remain poorly characterized. We sought to identify latent distress-risk states, describe transitions during cancer treatment, and evaluate their clinical determinants and concordance with anxiety/depression and health-related quality of life (HRQOL). **Methods:** This longitudinal multicenter cohort study included adult patients with cancer treated across all Brazilian states. Distress was assessed at baseline (prior to treatment initiation), mid-treatment, and end of treatment using the Distress Thermometer (DT). Symptoms of anxiety/depression and HRQOL were assessed using the Hospital Anxiety and Depression Scale (HADS) and FACT-G. Latent Transition Analysis (LTA) identified distress-risk states and transition probabilities over time; model selection was based on Bayesian Information Criterion, entropy, and clinical interpretability. Multinomial logistic regression evaluated clinical predictors of baseline distress-risk states. Directional concordance between changes in DT and changes in HADS and FACT-G was assessed using concordance matrices and chi-square tests. **Results:** A total of 2197 patients were included. Median age was 58 years, 72.3% were female, and most were diagnosed with breast (40.1%) or gastrointestinal (18.8%) cancer, with 40.0% presenting with advanced-stage disease (III-IV). A four-state LTA model with optimal fit identified high critical, moderate persistent, low vulnerable, and low stable distress-risk profiles. The low stable state was the most prevalent and highly stable, with 94.5% remaining in the same state across assessments, whereas the high critical and low vulnerable states were more dynamic. Among high critical patients, 22.8% transitioned to moderate risk and 19.6% to low risk, while 28.6% of moderate persistent patients transitioned to the low stable state. Worsening occurred in up to 12.6% of patients. Male sex (OR = 1.8, 95% CI 1.08-3.09) and stage IV disease (OR = 1.8, 95% CI 1.09-2.97) were independently associated with higher-risk distress states (Ps = 0.02). Changes in distress states showed high directional concordance with psychosocial outcomes (HADS 82.9%; FACT-G 77.0%; χ^2 p < 0.001). **Conclusions:** Distinct and clinically meaningful distress-risk states and dynamic transitions were observed during cancer treatment. While most patients remained stable or improved, a relevant subgroup experienced worsening distress. These findings support repeated distress screening and adaptive, risk-based psychosocial interventions integrated into routine oncology care. Research Sponsor: None.

Clinical efficiency of remote symptom monitoring using electronic patient-reported outcome (ePRO) in lung cancer: Results of the prospective, multicenter REAL-MOOV-LUNG trial.

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Background: Remote symptom monitoring using electronic patient-reported outcome (ePRO) has been shown to provide clinical benefits and is being implemented for routine care in cancer patients (pts). It may represent a significant operational burden for healthcare providers, that has to be balanced with its actual efficiency in generating clinically meaningful alerts leading to modify pts management. **Methods:** REAL-MOOV-LUNG is a prospective, multicenter, phase IV trial evaluating the MOOVCARE system in patients (pts) ≥ 18 yo with non-progressive lung cancer, any histology, any stage, who had completed anticancer treatment for < 8 weeks (cohort 1), or who were receiving adjuvant, consolidation or maintenance anticancer treatment for ≥ 8 weeks (cohort 2). Primary endpoint was the proportion of patients who had a clinically meaningful modification of the management, predefined as unplanned consultation at the hospital or CT-scan imaging following a MOOVCARE alert. Secondary endpoints included management of alerts, patients and healthcare providers satisfaction, observance, quality-of-life, and survival. **Results:** From October 2021 to October 2024, 188 pts were enrolled, including 107 men, 81 women, 155 pts with non-small cell lung cancer, 36 with other histologies; 36 pts had oncogene-addicted tumors; 70 pts had metastatic disease, 58 locally-advanced disease, and 60 had early-stage disease. 92% of pts filled at least 1 ePRO questionnaire, median number of questionnaires was 56/pts; 81% of pts had at least 1 alert, median number of alerts was 11, and total number of alerts was 2294. After a median follow-up of 23.9 mo, 39 (21%) pts had a modification of management between 2 scheduled visits, 29 (74%) of which related to preplanned visit, not to an alert; among the remaining 10 (26%) pts, only 5 (13%) pts had clinically meaningful modifications as per the predefined definition. 18-month overall survival was 79.6% [IC95% 73.6%-86.1%]. **Conclusions:** While adoption of remote symptom monitoring on ePRO was high, with frequent alerts generated from surveys, the actual impact on clinical management of patients with lung cancer was limited in the context of frequent preplanned visits at the hospital as per clinical guidelines. Clinical trial information: NCT04934865. Research Sponsor: SIVAN.

Impact of remote therapeutic monitoring on time to discontinuation and acute care events among patients treated with immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICI) are used to treat several solid tumors but can cause serious toxicities which may lead to early discontinuation of therapy. This study describes the effect of the Canopy electronic patient-reported outcomes (ePROs)-based remote therapeutic monitoring (RTM) platform on time to treatment discontinuation, acute care events, and steroid prescribing in patients receiving ICI therapy. **Methods:** We studied patients with metastatic cancer from four oncology clinics who started ICI treatment from Jan 1, 2024 to July 20, 2025. An RTM group was defined by submission of two ePRO reports in the first 45 days after first ICI treatment. The control group was never enrolled or did not submit ePRO reports within 45 days. Time to discontinuation (TTD) of ICI, acute care events, and steroid prescribing were assessed using propensity score weighting to account for potential differences in cohort characteristics; costs were taken as rate differences multiplied by average acute care event cost. TTD was assessed by Kaplan-Meier estimation, Cox proportional hazards modeling, and restricted mean survival time at 90 days (RMST). Descriptive statistics were taken about symptoms in the RTM group versus the control group. **Results:** The study included 363 patients using RTM and 1,199 in the control group. Lung cancer, melanoma, and kidney cancer were the most frequent diagnoses. In the RTM group time to treatment discontinuation was significantly greater and prescriptions for steroids were more frequent (Table 1). Additionally, RTM use was associated with about a 51% risk of hospitalization (95% CI: 0.29, 0.88, p: 0.015) and 82% risk of ER visits (95% CI: 0.49, 1.39, p: 0.458) compared to the control group. Estimated cost savings in hospitalization associated with RTM use were \$11,733,933 per 1000 patients treated for one year. Symptoms were detected more frequently in the RTM group compared to the control group, including potentially ICI-related symptoms such as rash (18% vs 3.2%), diarrhea (28% vs 4.7%), and difficulty breathing (28% vs 4.8%). **Conclusions:** Active ePRO-based RTM with Canopy is associated with increased time to ICI discontinuation and decreased acute care events. Increased use of steroids in patients reporting symptoms suggesting ICI toxicity may explain the beneficial effect of RTM. Research Sponsor: None.

Weighted analysis outcomes.				
Outcome	RTM group	Control group	Risk or Hazard Ratio RTM / Control (95% CI)	Risk or RMST difference RTM - Control (95% CI)
Time to discontinuation	Median: 7.5 mos (95% CI: 6.7, 8.8)	Median: 4.1 mos (95% CI: 3.6, 4.6)	0.55 (95% CI: 0.47 to 0.64, p < 0.001)	19 days (16, 22)
Hospitalization	6.9%	14%	0.51 (0.29, 0.88, p: 0.015)	-6.66 (-11.02, -2.13, p: 0.008)
Emergency room visit	9.9%	12%	0.82 (0.49, 1.39, p: 0.458)	-2.46 (-8.05, 2.95, p: 0.366)
Steroid use	53%	31%	1.69 (1.41, 2.02, p < 0.001)	21.67 (13.90, 29.13, p < 0.001)

E-PROs in oncology: Improving treatment adherence to treatment while reducing emergency care and costs for patients with gastrointestinal malignancies receiving systemic therapy.

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Background: Patients with cancer undergoing systemic therapy are prone to experience symptom-related complications which may lead to emergency room visits (ERV) and non-planned inpatient admissions (NIA), resulting in increased costs to health systems. Symptom monitoring and proactive management based on ePRO protocols have been shown to reduce acute care utilization; however, the economic impact of this intervention remains incompletely characterized. In addition, patients monitored through ePRO systems tend to remain on active anticancer treatment for longer periods, with fewer unplanned treatment interruptions. Our aim was to evaluate the economic impact of a remote Comprehensive Companion Program (CCP) in a private health system. **Methods:** We conducted a retrospective study within the AUNA oncological network in Lima, Peru. Adult patients with GI malignancies receiving systemic therapy who experienced at least one ERV or NIA between June 2021 and July 2022 were included. Patients were grouped according to enrollment in a remote CCP or receipt of usual care. Costs related to ERV and NIA were analyzed from a payer's perspective and adjusted by time on treatment to estimate average monthly cost per-patient. Data were analyzed using descriptive and comparative statistical methods. **Results:** A total of 97 patients with comparable baseline clinical characteristics were included (50 in the CCP group and 47 with usual care). Patients in the CCP group had a significantly longer time on treatment (median 235.5 vs 151 days; $p = 0.0009$), driven primarily by patients with metastatic disease. When costs associated with ERV and NIA were normalized by treatment duration, the CCP group was associated with significantly lower monthly acute care costs. Median monthly variable costs per patient were USD \$147.14 versus \$449.70 ($p = 0.0137$), representing an 67% of costs reduction in monthly variable costs per patient. Similarly, median monthly prorated expenses per patient were \$220.33 versus \$636.66 ($p = 0.0151$), corresponding to an approximate 65% reduction in monthly prorated expenses. **Conclusions:** Our study showed that patients enrolled in a CCP incorporating e-PRO based symptom monitoring remained on treatment for longer; however, this was associated with significantly lower time-adjusted acute care costs. These findings highlight the potential value of the CCP in reducing cancer care-related costs, while acknowledging that the results are limited to a private health care setting. Research Sponsor: None.

Determinants of cervical cancer awareness, procedural knowledge, and information sources among Nepali women undergoing HPV screening.

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Background: Successful implementation of cervical cancer screening in low- and middle-income countries (LMICs) depends on community acceptance. Although general awareness of cancer is rising, limited understanding of screening procedures continues to hinder participation. This study examined the factors influencing cervical cancer awareness, procedural knowledge, and sources of screening information among Nepali women undergoing HPV-based screening. **Methods:** HPV screening was conducted through two community health fairs in Janakpur, Nepal, in 2025. Clinician-collected samples were tested using an isothermal amplification assay. Survey data collected included participants' age, education level, cervical cancer awareness, procedural knowledge on vaginal sampling, sources of screening information, and health decision-making practices. Multivariate logistic regression was used to identify factors associated with cervical cancer awareness, procedural knowledge, and information sources. **Results:** Valid survey data from 274 Nepali women, including 32 HrHPV-positive cases, were analyzed. Cervical cancer awareness was significantly associated with education. Women with secondary education or higher were more likely to have heard of cervical cancer (aOR 4.45; 95% CI 1.81-10.95, $p = 0.001$), compared to those with less education. However, education was not associated with specific knowledge of vaginal sampling. Procedural knowledge was instead hindered by low health autonomy (husband or in-laws as decision-maker: aOR 0.42, 95% CI 0.25-0.72, $p = 0.002$, vs. self-decision making). Women who tested HrHPV-positive were significantly less likely to understand the sampling procedure prior to testing than those who tested negative (aOR 0.33, 95% CI 0.14-0.78, $p = 0.01$). Regarding information sources, women aged 30-44 years relied more on community networks, i.e., female community health volunteers (FCHVs) than medical providers, compared to women < 30 years (aOR 1.89, 95% CI 1.01-3.53, $p = 0.048$). **Conclusions:** Cervical cancer awareness in Nepali women is driven by education, but procedural knowledge is limited by low health autonomy. Middle-aged and older women rely on FCHVs or their community networks to acquire information about cervical screening. Future implementation strategies should address interventions that empower women and improve understanding of screening procedures, as well as tailored training on FCHVs to promote cervical screening among middle-aged women. **Keywords:** Cervical Cancer, Procedural Knowledge, Awareness, Implementation Science, Health Literacy, Global Health Research Sponsor: None.

Digital oncology navigation based on ePROs: Effects on acute healthcare utilization and cost savings in a middle-income country setting.

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Background: Oncologic treatment is associated with a high clinical and economic burden. Traditional patient navigation models often lack real-time symptom monitoring, increasing the risk of clinical deterioration. Digital navigation models incorporating ePROs have emerged as a promising strategy to address this gap. However, evidence on their implementation in low- and middle-income settings remains limited. This study aimed to assess the healthcare utilization and economic impact of an ePRO-based digital oncology navigation program in a real-world Brazilian healthcare setting. **Methods:** We conducted a prospective, single-arm, before-and-after study between February and November 2025 at a private healthcare provider in southern Brazil. Adult patients (pts) with any cancer type undergoing intravenous chemotherapy and/or immunotherapy were enrolled in a digital oncology navigation program integrating app-based ePRO monitoring, automated symptom triage, and proactive nurse-led follow-up. The primary outcome was estimated cost avoidance (from the healthcare provider perspective), calculated as the difference between pre- and post-implementation costs associated with acute healthcare utilization (hospitalizations and emergency room [ER] visits). Secondary outcomes included hospitalization and ER utilization rates, patterns of digital health service use (program adherence and daily and overall volume of symptom reports), and the clinical profile of pts who required hospitalization. Descriptive statistics were applied. **Results:** A total of 55 pts were included. The mean age was 54 years, and 63.5% were female. Breast cancer (25.5%; n = 14), non-Hodgkin lymphoma (12.7%; n = 7), and lung cancer (10.9%; n = 6) were the most frequent tumor types. Most pts had stage II–III disease (63.9%) and were receiving chemotherapy (54.8%). Hospitalization rates decreased from 29% to 22% after program implementation, while ER utilization declined from 80% to 35%. Patient adherence was high (90.8%), with consistent engagement in symptom reporting throughout follow-up (600 total symptom reports; mean of 5.4 daily reports). Most reported symptoms were managed remotely by the nursing team (95%), with minimal need for physician escalation. Among pts who required hospitalization, lung cancer was the most frequent primary tumor (50.1%). The estimated total cost avoidance was R\$332,769 (≈US\$66,500), corresponding to a mean saving of R\$6,050 (≈US\$1,210) per pt. Avoided hospitalizations accounted for most of the economic benefit. **Conclusions:** Implementation of an ePRO-driven digital oncology navigation program may reduce acute healthcare utilization and meaningful short-term cost avoidance in a real-world healthcare setting. These findings support the integration of digital symptom monitoring as scalable, cost-saving strategie in oncological care delivery. Research Sponsor: None.

PROgress Tracker Breast Cancer Registry: Reporting worry of illness from a longitudinal peer-led, national patient-reported outcomes (PRO) registry.

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Background: PROgress Tracker Breast Cancer Registry is a national, ethics approved non-interventional patient-reported outcome measure (PROMs) registry, using a peer-to-peer model directed by patient advocacy group Breast Cancer Canada. Here, initial results report breast cancer survivors nature of cancer illness worry and intensity based on age, stage and molecular subtype at diagnosis. **Methods:** PROgress Tracker was launched in 2023, with enrollment over 10 years of Canadians with Stage 0-IV breast cancer. Participants self-refer and complete a series of validated PROMs (demographic, socioeconomic, clinical, global wellbeing) via a digital platform, capturing current status on a quarterly basis for up to 10 years. Real-world analysis assisted by AI (*January 2026; Claude [Opus 4.5], manufacturer: Anthropic; data extraction, statistical analysis with means, percentages, patient-level aggregation, stratification by clinical variables, longitudinal pattern analysis and visualization; all outputs validated against source data*) of FACT-B PROM data capture and analysis methodology was used. **Results:** To date, 823 participants have enrolled with 186 participating for ≥ 2 years. From participation start, longitudinal worry is reported using 3 factors from FACT-B PROM; hereditary risk of family members (HR), if stress impacts illness (SI), and if participant's condition will worsen (CW). Highest degree of reported worry scores was in HR 40.4% (n = 74), SI 31.7% (n = 59) and CW at 17.4% (n = 32). Worry intensity varied by age, stage and molecular subtype. Participants diagnosed < 50 years reported higher levels in all 3 factors (HR 51% mean 2.53; SI 46.9% mean 2.24; CW 24.5% mean 1.78) to those at > 50 years (HR 37.1% mean 1.92; SI 25.9% mean 1.63; CW 14.3% mean 1.32). Stage IV participants show 66.7% high worry (CW and HR) compared to stage I at 8.5% (CW). Molecular subpopulations show higher worry in HR- / HER2- (TNBC) n = 34 (HR 48.5% mean 2.24; SI 38.2% mean 2.00; CW 17.6% mean 1.59) compared to HR+ / HER2- n = 81 (HR 37.5% mean 2.04; SI 35.4% mean 1.90; CW 17.3% mean 1.41) and HR+ / HER2+ n = 13 (HR 30.8% mean 2.08; SI 23.1% mean 1.77; CW 7.7% mean 1.38). Non-linear trajectory over time shows 24% (n = 183) experienced high worry at registry entry, declining at 12 months to 15.8% with a secondary peak at 18 months in 21.7% of participants. **Conclusions:** Patient-reported outcomes show the burden of worry by breast cancer survivors for hereditary risk to family and individuals' illness. These findings offer directional insights for psychosocial screening, care resources and tailored education throughout survivorship. Research Sponsor: Breast Cancer Canada; Astra Zeneca Canada, Gilead Sciences Canada, Novartis Canada; The Hecht Foundation.

Text-based electronic patient-reported outcome monitoring in oncology: A 180-day longitudinal analysis of symptom burden changes in 701 cancer patients.

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Background: Digital electronic patient-reported outcome (ePRO) systems promise to improve symptom management in oncology, yet evidence demonstrating sustained clinical benefit across diverse cancer populations remains limited. This study evaluated the longitudinal effectiveness of a text-based ePRO platform delivering weekly validated symptom assessments in reducing overall symptom burden among cancer patients over 180 days. **Methods:** This retrospective study consisted of 701 patients with cancer recruited between 2022–2025. The patients were eligible if they were on the platform for at least 90 days, completed the baseline survey within 14 days of enrollment, and had a survey completion rate of at least 30%. ePRO responses triggered review by a virtual care team that provided protocolized symptom management outreach and triage in collaboration with treating oncology practices. The primary outcome was the change in overall symptom burden over 180 days, measured by the Edmonton Symptom Assessment System (ESAS; total score 0–90). Secondary outcomes included physical symptoms (0–60), emotional symptoms (0–20), and well-being (0–10). Stratified analyses were done using paired t-tests. **Results:** The final cohort (mean age 64.6 years; 57.2% female; 20.5% metastatic; mean adherence 66.1%) demonstrated significant reduction in total symptom burden (20.99 to 18.11 points; -2.89 points, -13.7%, $p < 0.001$) and physical symptoms (14.86 to 12.18 points; -2.68 points, -17.0%, $p < 0.001$). Emotional symptoms and well-being showed no significant change. Efficacy was engagement-dependent: high-engagement patients ($N = 465$) achieved -2.80-point reduction ($p < 0.001$) versus non-significant changes in medium/low-engagement groups. Stratified analyses revealed heterogeneity: breast cancer patients demonstrated exceptional response (-8.96 points, -46.3%, $p = 0.008$), while GI cancer patients showed resistance (-0.43 points, $p = 0.915$). Non-metastatic patients (-3.06 points, $p < 0.001$), females (-3.27 points, $p < 0.001$), and patients aged < 50 years (-4.28 points, $p = 0.011$) demonstrated superior outcomes compared to metastatic, male, and elderly (≥ 75 years) patients. **Conclusions:** Text-based digital ePRO monitoring significantly reduced symptom burden in cancer patients over 180 days, with physical symptom improvement as the primary driver. Clinical benefit was engagement-dependent and varied substantially by cancer type, metastatic status, age, and gender. These findings validate the clinical utility of SMS-delivered ePRO systems while identifying highly responsive populations (breast cancer, non-metastatic, younger patients) and vulnerable subgroups requiring enhanced symptom management support. Research Sponsor: None.

Advancing value-based breast cancer screening in a safety-net health system: A multimodal approach to improving population health and system sustainability.

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Background: Evaluation of breast cancer screening (BCS) adherence in our large safety-net health system revealed wide variability and late-stage diagnosis rates that exceeded national benchmarks. A multidisciplinary taskforce (primary care, radiology, cancer center, and patient advocates) identified barriers, co-designed, and implemented a multi-pronged intervention to address screening uptake and adherence. **Methods:** Mixed-methods evaluation across 18 primary care sites revealed wide variability in BCS rates (60–82%); lack of systematic management of screening bottlenecks (ordering, scheduling, no-shows/cancellations); and unmet patient needs (transportation, screening hesitancy). We co-developed and implemented a phased intervention from March–December 2025 to address identified barriers through: (1) radiology navigator outreach to primary care patients at low-performing sites (March), (2) electronic medical record patient portal self-scheduling (July), (3) AI-assisted rescheduling after no-shows/cancellations (December), and (4) assessment and navigation of social needs and screening hesitancy (March). Outcomes measured were outreach, engagement, and screening completion. We performed multivariate regression to examine demographic predictors of screening. **Results:** Of 57,041 HEDIS-eligible patients, 15,971 (28%) were overdue at baseline (mean age 58 yo, 77% Hispanic or non-Hispanic Black, 74% Medicaid or Dual). Overall, the intervention resulted in 1,610 additional screens over 9 months, improving systemwide BCS rates from 72 to 76%. Of the additional screens, radiology navigator achieved 452 screens (29%), patient portal self-scheduling achieved 1,097 screens (70%), and AI-assisted outreach of no-show/cancelled achieved 61 screens (4%). Engagement and show rates varied: navigator outreach had the highest scheduling engagement (74%) but lower show rates (46%); patient portal self-scheduling showed moderate engagement (44%) with higher show rates (76%); and AI-assisted outreach had low engagement (4%) with moderate show rates (56%). Demographics did not predict screening outcomes. Screening hesitancy (37%) and transportation (10%) were the most common barriers, addressed through social and peer navigation, respectively. Revenue from additional screenings fully offset navigator costs. **Conclusions:** A coordinated, resource-efficient screening outreach strategy combining digital tools, human navigation, and AI assistance—co-designed with patients and clinical stakeholders—improved BCS adherence, addressed unmet needs of underserved populations, and proved itself financially sustainable across a safety net health system. Future efforts will focus on further scaling of population health approaches to cancer screening programs. Research Sponsor: None.

Proactive response initiative for symptom management (PRISM): A multi-institutional symptom monitoring program for veterans receiving systemic cancer therapy.

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Background: Symptom assessment and management in cancer care are challenging. Within the Veterans Health Administration (VHA), gaps remain in widescale implementation of standardized symptom assessment, technology support, and adaptable workflows. PRISM was developed as a multi-institutional, technology-enabled clinical program to improve early identification and treatment of cancer-related symptoms for Veterans with the ultimate goal of system-wide implementation. **Methods:** We adapted an evidence-based proactive symptom intervention for the Long Beach VA with a working group of clinicians, pharmacists, social workers, case managers, and ancillary staff. The intervention involved a peer specialist conducting weekly telephone-based assessments using a modified Veteran Symptom Assessment System (VSAS) for Veterans initiating systemic anti-cancer treatment. Symptom scores ≥ 4 on a scale of 0-10 or a score increase by 2 points automatically triggered Nurse Practitioner (NP) review and follow up. We conducted an evaluation of our first PRISM site and assessed Veteran retention, symptom burden, interventions, and process metrics to inform scale and spread for two future VHA sites this quarter. **Results:** From May 22, 2025 to December 1, 2025, 30 patients (pts) enrolled in PRISM; 4 (13%) withdrew < 1 month, 2 (6.7%) withdrew > 1 month, 2 (6.7%) completed the program, and 1 (3.3%) died. Frequently reported symptoms of any score were fatigue ($n = 14$; 61%), dyspnea on exertion ($n = 6$; 26%), and pain ($n = 6$; 26%). Of the 412 times symptoms were reported as ≥ 4 on a scale of 0-10, the most frequent were fatigue (22%), dyspnea with exertion (13%), and drowsiness (13%). For the 23 pts who remained in the program for > 1 month there were 308 peer specialist encounters and 205 NP encounters. NPs intervened in 91% (186/205) of encounters with a total of 961 interventions. The mean number of interventions per NP encounter was 3.67. The most frequent intervention was pt education 86% (827/961), medication prescriptions 13% (123/961), and alerting the primary oncology team 4.2% (41/961). The mean time interval between a VSAS survey and indicated NP follow up was 1.06 days. The call duration was a mean 9.25 minutes per encounter with the peer specialist and 17.3 minutes per encounter with the NP. Documentation and chart review took a mean of 10.5 minutes per peer specialist encounter and a mean of 14.4 minutes per NP encounter. **Conclusions:** Early results from our first real world PRISM implementation in the VHA demonstrate feasibility, retention, and frequent early identification of and intervention for symptoms using this proactive symptom management program embedded within existing pt oncology care. The process metrics regarding capacity for peer support and NP effort will inform our expansion to two implementation sites by June 2026 and an additional 10 sites by 2027. Research Sponsor: None.

Factors associated with clinical trial failure and termination in non-small cell lung cancer immunotherapy: A ten-year review.

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Background: Immunotherapy (IO) has transformed NSCLC management, yet trial efficiency and strategy-level success patterns across settings remain incompletely described. We evaluated NSCLC IO trials for termination trends, outcome accessibility, shifts in strategies over time, and factors associated with endpoint success and failure to inform future trial designs.

Methods: We identified interventional NSCLC IO trials from ClinicalTrials.gov from 2015–2024 with completed/terminated status. Trials were categorized by setting (metastatic 1L and beyond 1L; perioperative; other/mixed), intervention strategy (PD-(L)1 monotherapy; PD-(L)1+chemotherapy; PD-(L)1+CTLA-4; PD-(L)1+targeted/VEGF/ADC; RT/CRT+ICI; other IO), phase group, sponsor type (industry vs non-industry), and disease stage. Statistic analysis was done using chi-square/Fisher tests and multivariable logistic regression. Among completed trials, success/failure was defined as meeting/not meeting the primary endpoint when outcomes were assessable. **Results:** Among 198 NSCLC IO trials, 67 (33.8%) were terminated, 131 (66.2%) completed. Termination increased over time (24.0% 2015–2017, 48.1% 2018–2019, 57.1% 2020–2022; $p = 0.0005$) and persisted after accounting for setting, phase, sponsor type (2018–2019 vs 2015–2017: OR 2.87, $p = 0.0037$; 2020–2022 vs 2015–2017: OR 3.22, $p = 0.0277$). Metastatic disease trials shifted from late (56.0%, 2015–2017; 42.9%, 2020–2022) to 1L (28.8% – 47.6%). Endpoint outcomes were assessable in 72/131 (55.0%) completed trials – more in metastatic 1L vs later-line (75.0% vs 42.3%, $p = 0.0086$; OR 0.30, $p = 0.013$) and in industry vs non-industry trials (71.9% vs 41.9%; $p = 0.0012$, OR 0.38, $p = 0.030$). Among these, 47 (65.3%) met primary endpoints. Success varied by strategy: PD-(L)1+chemo 73.1%, PD-(L)1 mono 60.9%, PD-(L)1+CTLA-4 50.0%, PD-(L)1+targeted 20.0%, RT+ICI 85.7%; PD-(L)1+chemo outperformed PD-(L)1+targeted (Fisher $p = 0.0416$). Strategy shifted over time ($p = 0.034$), with decreased PD-(L)1 mono and increased RT+ICI and PD-(L)1+targeted combinations in later years. Proportion of PD-(L)1 monotherapy was higher for perioperative trials (47.4%) vs metastatic 1L (16.7%) and later-line settings (26.7%). Cell-($n = 8$) and vaccine/virus-based ($n = 12$) approaches were uncommon (term. 25% and 50%) with limited assessable outcomes. **Conclusions:** Treatment strategies shifted away from PD-(L)1 monotherapy toward combination approaches and, in metastatic disease, from late-line to 1st line settings. PD-(L)1+chemotherapy and RT+ICI showed higher success rates than PD-(L)1+targeted combinations, though some subgroups were small. Other IO agents are rarely used in NSCLC and have insufficient reporting. Incorporating predictive risk models into trial planning may reduce low-yield studies and accelerate identification of effective treatments. Research Sponsor: None.

Evaluating the role of informal caregivers in metastatic cancer patients treated with oral anticancer therapy: A prospective observational study.

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Background: The increasing use of oral anticancer agents (OAAs) in metastatic cancer has shifted treatment management from hospital to home, transferring responsibility for adherence and symptom monitoring to patients and informal caregivers. Evidence on caregiver burden and its impact on patient-reported outcomes in this setting remains limited. **Methods:** This prospective observational study evaluated patients with metastatic cancer receiving OAAs and their informal caregivers. At baseline and three months, patients completed the EORTC QLQ-C30, MMAS-8, TEMPS-A, and the G8 geriatric screening tool; caregivers completed the Zarit Burden Interview (ZBI), Caregiver Reaction Assessment (CRA), TEMPS-A, and an ad hoc caregiving questionnaire. Statistical analyses were performed using IBM SPSS Statistics ($p < 0.05$). **Results:** Sixty-eight patients (median age 67 years; 50% female) were enrolled; among patients aged >70 years, the G8 score indicated a predominance of non-frail patients (68.2%). 66.1% had a caregiver, most commonly a spouse (46.5%) or child (41.9%). Caregivers (mean age 56 years) were involved for >2 years in 76.7% of cases and attended outpatient visits in 69.8%. ZBI showed minimal/no burden in 60.5% and mild-to-moderate burden in 32.6%. CRA scores were highest for self-esteem (4.13 ± 0.62), followed by schedule (3.31 ± 1.36) and health (3.10 ± 0.66). Patients with caregivers reported worse quality of life, physical, role, and emotional functioning, higher symptom burden (fatigue, pain, dyspnea, appetite loss, financial difficulties), and lower adherence compared with those without caregivers (all $p < 0.05$). Caregiver presence was associated with cyclothymic, depressive, and anxious temperaments. Patients cared for by a child showed better role functioning, while spousal caregiving was associated with irritable temperament. At three months ($n=22$), patients showed significant improvements in adherence, quality of life, physical and role functioning, and symptom burden, suggesting early adaptation to oral therapy despite high baseline caregiving demands. **Conclusions:** Informal caregivers play a central role in OAA-treated metastatic cancer. Caregiver involvement appears to reflect greater patient vulnerability rather than a causal determinant of poorer outcomes, supporting the need for systematic caregiver assessment and targeted supportive interventions. Research Sponsor: None.

Caregiver characteristics and associated patient outcomes.

Variable	Caregiver present	No caregiver
Patients, %	66.1	33.9
Relationship, %	Spouse 46.5 / Child 41.9	—
Care duration >2 yrs, %	76.7	—
Presence at visits, %	69.8	—
ZBI burden, %	None/min 60.5; Mild-mod 32.6	—
CRA self-esteem (mean $\pm$ SD)	4.13 ± 0.62	—
Quality of life	↓	↑
Physical functioning	↓	↑
Symptom burden	↑	↓
Therapy adherence	↓	↑

Real-world utilization patterns and adverse events among patients receiving antibody–drug conjugates (ADCs) across the University of California health system.

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Background: Antibody–drug conjugates (ADCs) have rapidly expanded across oncology indications, yet real-world safety profiles remain incompletely characterized. Pivotal trials may not fully capture adverse events (AEs) associated with real-world treatment patterns, such as cumulative exposure or sequential ADC therapy. **Methods:** We performed a retrospective cohort study across six UC medical centers using de-identified structured EHR data from the University of California Health Data Warehouse (UCHDW). We included adult patients who received at least 1 dose of ADC between Jan 2015 and Feb 2025. Observational period for safety surveillance is at least 8 months. Key safety outcomes were the incidence and timing of key AEs following ADC initiation. Secondary outcomes included duration of ADC therapy and the frequency of sequential ADC. Descriptive statistics were used to analyze toxicity and time to AE of special interest. **Results:** Across the UC system, 4,531 patients received at least one ADC and had a documented cancer-related diagnosis, 82.7% of patients had metastatic cancer at initiation of ADC. Breast cancer was the most frequently observed cancer type (38.8%), followed by hematologic malignancies (28.5%) and bladder/urothelial cancers (11.2%). Mean dose number was 10.1 (standard deviation: 11.3). Among 4,531 ADC-treated patients, 10.6% transitioned to a second ADC, and 78.9% received concomitant anticancer therapy, including immune checkpoint inhibitors (38.0%), ICI plus chemotherapy (21.8%), or chemotherapy alone (18.7%). Incident neurotoxicity was the most frequent AE (728 patients, 16.1%), followed by hematologic (15.0%) and cardiotoxicity (14.6%) AEs. Incident ocular toxicity was observed in 343 patients (7.5%) with a median time to onset of 84 days, and incident mononeuritis in 480 patients (10.6%) with a median onset of 105 days following ADC initiation. **Conclusions:** In this large, multi-center real-world cohort, ADC treatment was associated with substantial rates of neurologic, hematologic, and cardiac toxicities. The frequent use of concomitant anticancer treatments and observed transitions between ADCs underscore the complexity of real-world exposure and highlight the need for proactive toxicity monitoring and optimized safety management strategies in routine oncology practice. Research Sponsor: None.

Inpatient palliative care utilization and outcomes among decedent patients with metastatic cancer in the U.S.

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Background: Palliative care (PC) is a key component of high quality cancer care, especially at the end of life. However, real world national data describing inpatient PC utilization remain limited. We evaluated patterns of PC use and associated outcomes among decedent patients with metastatic cancer in the U.S. **Methods:** We conducted a cross-sectional analysis of the 2021–2023 National Inpatient Sample of decedent patients with metastatic cancer. Palliative care, cancer type, and metastatic status were identified using ICD-10 codes. Patient characteristics included age, sex, race, comorbidity burden, insurance status, and household income. Hospital characteristics included location (urban vs rural) and ownership (public, private not-profit, and private invest-own). Outcomes included length of stay (LOS), inpatient procedures, and total costs. Factors associated with palliative care use and adjusted mean differences in outcomes were estimated. **Results:** An estimated 52,841 hospitalizations of decedent patients with metastatic cancer were identified, with 34,955 (66.2%) involving palliative care. PC utilization varied by cancer type (Table) and increased over time (aOR per year 1.15; 95% CI 1.12–1.18). PC use was independently associated with older age, female sex, private insurance, higher neighborhood income, and care at private not-for-profit hospitals (all $p < 0.001$). PC was associated with fewer inpatient procedures (adjusted mean difference -1.38 ; 95% CI -1.45 to -1.31), shorter LOS (-1.25 days; 95% CI -1.45 to -1.06), and lower total costs ($-\$10,557$; 95% CI $-\$11,421$ to $-\$9,694$). Reductions in procedures, LOS and costs were significant across most cancer types. (Table). **Conclusions:** Inpatient PC was associated with lower care intensity and costs across cancer types among decedent patients with metastatic cancer. Yet, about one third never received PC, highlighting a major end-of-life care gap and the need for earlier, more equitable integration to improve value based oncology care. Research Sponsor: None.

Palliative care utilization and outcomes by major cancer type.

Cancer Type	PC use	Adjusted Procedures difference	Adjusted Cost difference (\$)	Adjusted LOS difference (days)
Breast	2646 (66.7%)	-1.47 (-1.70,-1.24)	-12512 (-16301,-8722)	-1.90 (-2.63,-1.17)
Colorectal	2932 (65.8%)	-1.75 (-1.49,-2.00)	-12231 (-15261,-9201)	-1.09 (-1.83,-0.35)
Lung	8942 (67.9%)	-1.14 (-1.28,-1.00)	-6341 (-7894,-4968)	-0.90 (-1.24,-0.56)
Prostate	1897 (62.3%)	-1.24 (-1.52,-0.97)	-9736 (-12915,-6558)	-0.88 (-1.82,0.05)*
Pancreas	2574 (68.4%)	-1.46 (-1.72,-1.21)	-7396 (-9525,-5266)	-0.39 (-0.94,0.17)*
Kidney	936 (66.3%)	-1.72 (-2.20,-1.23)	-12353 (-17623,-7082)	-1.93 (-3.11,-0.75)
Liver	1362 (67.8%)	-0.87 (-1.24,-0.51)	-8896 (-13426,-4367)	-1.27 (-0.33,-2.20)

All $p < 0.001$ unless noted with *.

Risk of immune-related adverse events from checkpoint inhibitors in cancer patients with autoimmune disease: An emulated target trial.

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Background: Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment by activating the immune system to target and eliminate cancer cells, leading to durable responses and improved survival. However, patients with preexisting autoimmune diseases are excluded from ICI clinical trials due to concerns about triggering immune-related adverse events (irAEs). Consequently, there is limited real-world data comparing the risk of irAEs between ICIs and other systemic cancer therapies in this high-risk population. **Methods:** We conducted a target trial emulation using a new-user, active-comparator design to compare the risk of developing de novo irAEs following ICI initiation compared to chemotherapy or targeted therapy. Using Merative MarketScan data (2014–2023), we identified adults with cancer and a preexisting autoimmune disease who initiated treatment with ICIs, chemotherapy, or targeted therapy. Propensity score matching (1:1) was performed for two comparisons: ICI versus chemotherapy and ICI versus targeted therapy. The primary outcome was de novo irAEs affecting organ systems distinct from the patient's baseline autoimmune disease. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), with subgroup analyses by age, sex, cancer type, preexisting autoimmune disease category, and ICI class. **Results:** A total of 3,601 matched patient pairs were included in the ICI–chemotherapy comparison and 1,479 matched pairs in the ICI–targeted therapy comparison. Patients receiving ICI had a significantly higher risk of developing de novo irAEs compared to those receiving chemotherapy (HR=1.71; 95% CI, 1.49–1.97) or targeted therapy (HR=1.43; 95% CI, 1.20–1.70). This increased risk was consistent across age and sex. By ICI class, CTLA-4 inhibitors were associated with the highest risk (HR=2.64; 95% CI, 1.97–3.53 vs chemotherapy; HR=1.72; 95% CI, 1.18–2.50 vs targeted therapy), followed by ICI combination therapy (HR=2.46; 95% CI, 1.80–3.37 vs chemotherapy). By cancer type, patients with liver cancer had the greatest risk (HR=2.75; 95% CI, 1.96–3.85 vs chemotherapy; HR=2.67; 95% CI, 1.68–4.24 vs targeted therapy), followed by breast cancer (HR=2.11; 95% CI, 1.31–3.42 vs chemotherapy; HR=1.97; 95% CI, 1.06–3.68 vs targeted therapy). By baseline autoimmune disease category, patients with endocrine autoimmune diseases consistently showed elevated risk across both comparisons (HR=1.74; 95% CI, 1.42–2.14 vs chemotherapy; HR=1.92; 95% CI, 1.43–2.58 vs targeted therapy). **Conclusions:** ICI use in cancer patients with preexisting autoimmune diseases is associated with a higher risk of de novo irAEs than chemotherapy or targeted therapy, with risk varying by ICI type, cancer type, and underlying autoimmune condition, highlighting the need for individualized risk assessment and close monitoring. Research Sponsor: None.

Trends in ivermectin medication records with cancer as the primary diagnosis following public attention: A national EHR analysis.

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Background: Ivermectin, an antiparasitic agent not indicated for cancer treatment, has received public attention since early January 2025 due to widespread discussion on social media and other non-clinical forums. Little is known about whether the increased visibility may influence medication use or reporting among patients with cancer in real-world clinical data.

Methods: We conducted a retrospective descriptive analysis using the EPIC COSMOS, a large, multi-institutional U.S. electronic health record network. We identified all ivermectin medication records from quarter (Q)1 2024 to Q3 2025, including prescribed/administered and patient-reported medications linked to clinical encounters. Our primary outcome was the quarterly trend in the percentage of ivermectin records where cancer was listed as the primary diagnosis for the encounter. Secondary measures included other diagnosis associated with the encounter (e.g., parasitic) and patient demographics. **Results:** We identified 96,525 ivermectin medication records, increasing from 11,854 in Q1 2024 to 15,223 in Q3 2025. The proportion of records with cancer as the primary diagnosis increased modestly during 2024 (from 2.3% to 3.1%; average quarterly increase=0.2 percentage points [ppts]), followed by a larger increase in Q1 2025 (from 3.1% to 4.2%, adjusted increase=1.0 ppts, relative increase=32%, $p<.001$), which stabilized in Q2 and declined slightly in Q3 2025. The surge from Q4 2024 to Q1 2025 was larger for patient-reported ivermectin (from 156 to 231 records, 48% increase) than prescribed/administered medications (292 to 347 records, 19% increase). In contrast, the proportion of ivermectin records associated with strongyloidiasis, onchocerciasis, or scabies ranged from 18.5%–19.5% in 2024 and declined to 17.1% in Q1 2025, while records associated with other infectious conditions remained stable (~4.9%). Among records with cancer as the primary diagnosis ($n=3,157$), mean patient age was 62 years, with 4.6% female, 76% White, 8% Black, and 10% Hispanic; the proportion prescribed to White patients increased from 71% in Q4 2024 to 81% in Q1 2025. Physician specialty distribution associated with prescribed/administered ivermectin was 35% oncologists, 20% primary care, 22% dermatologists, 4.2% advanced practice providers, and 19% other specialties. **Conclusions:** Although ivermectin use in cancer care remained uncommon overall, real-world data show a rapid, largely patient-driven increase during Q1 2025. This rise is distinct from the stable or declining proportions of records linked to approved parasitic indications. These findings suggest that social trends may shape medication use, highlighting the importance of careful medication reconciliation and patient counseling in oncology settings to address non-evidence-based use. Research Sponsor: U.S. National Institutes of Health; K12AR084234.

Machine learning–based prognostic models for mortality prediction after unplanned hospitalization in cancer patients.

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Background: Unplanned hospitalizations in oncology patients often indicate acute clinical deterioration and are associated with high mortality. Prognostic assessment at admission remains a challenge, particularly in resource-limited settings. Machine learning (ML) methods can integrate clinical and laboratory features to generate individualized mortality predictions, although the data is scarce. We aimed to develop and validate ML-based models to predict in-hospital, 30-day, and 90-day all-cause mortality in adult cancer patients with unplanned hospitalizations. **Methods:** We retrospectively analyzed patients with cancer who were admitted for unplanned hospitalizations at Hacettepe University Oncology Hospital between January 2018 and August 2024. Class imbalance was addressed using SMOTE, and ANOVA-based feature selection retained the top 20 predictors. Nine ML algorithms were tested, including SVM, kNN, decision trees, neural networks, and ensemble models. Model performance was assessed via 5-fold cross-validation using accuracy, precision, recall, F1-score, and AUC. **Results:** A total of 1646 cancer patients with unplanned hospitalizations were included. The most common cancers were gastrointestinal malignancies (32.8%), lung cancer (17.4%), and breast cancer (9.8%). For in-hospital mortality prediction, Random Forest achieved the best performance on the original dataset (AUC-ROC: 0.89; accuracy: 84.6%). After SMOTE, SVM yielded the superior results (AUC-ROC: 0.98; accuracy: 93.6%). For 30-day mortality prediction, Random Forest was optimal pre-SMOTE (AUC-ROC:0.85; accuracy:83.6%), whereas LightGBM reached the highest post-SMOTE performance (AUC-ROC:0.97; accuracy:91.8). For 90-day mortality prediction, XGBoost demonstrated the best performance on the original dataset (AUC-ROC: 0.84; accuracy: 80.4%). Following the application of SMOTE, LightGBM outperformed the other models (AUC-ROC:0.90; accuracy:82.3%). **Conclusions:** This first study focusing on predicting in-hospital mortality in cancer patients with unplanned admissions shows that ML models based on routine admission data can reliably predict early- and long-term mortality. Incorporating such models into workflows may support early risk stratification, shared decision-making, and individualized care planning. Research Sponsor: None.

Mortality caused by coexisting malignant neoplasms and type 2 diabetes mellitus in U.S. adults: A CDC WONDER analysis (1999–2020).

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Background: Type 2 diabetes mellitus (T2DM) and malignant neoplasms are among the most prevalent chronic diseases worldwide. When coexisting, they substantially increase morbidity and mortality. However, national trends in cancer-related mortality among patients with T2DM in the United States remain underexplored. **Methods:** We analyzed CDC WONDER mortality data (1999–2020) to identify deaths among U.S. middle-aged (55–74 years) and older adults (≥ 75 years) in which both malignant neoplasms (ICD-10 C00–C97) and T2DM (ICD-10 E11.0–E11.9) were listed as causes of death on death certificates. Age-adjusted mortality rate (AAMR) per 100,000 were calculated and stratified by sex, age group, race/ethnicity, and urbanization status. Trends in overall AAMRs were analyzed using the Joinpoint Regression Program to calculate the average annual percentage change (APC), with statistical significance set at ≤ 0.05 . **Results:** From 1999 to 2020, a total of 255,154 U.S. adult deaths involved both T2DM and malignant neoplasms. The AAMR increased significantly over the study period (APC 2.91%; 95% CI 2.32–3.50; $p < 0.01$). Joinpoint regression identified an inflection point around 2011, after which mortality accelerated markedly (APC 6.67%; 95% CI 4.94–8.42). Mortality rates were consistently higher in men compared with women (overall AAMR 13.4 vs. 7.28; $p < 0.01$). Older adults experienced the highest mortality burden (overall AAMR 23.4; APC 2.83%; 95% CI 2.25–3.41), while middle-aged adults demonstrated a steeper relative increase (2.14; 3.40%; 2.72–4.07). Marked racial and ethnic disparities were observed. Asian or Pacific Islanders (API) showed the steepest rise (APC 5.96%; 95% CI 5.35–6.58), followed by Hispanics (5.12%; 4.61–5.63), non-Hispanic (NH) Whites (2.66%; 2.03–3.28), NH Blacks (2.47%; 1.87–3.07), and American Indian/Alaska Natives (AI/AN) (3.15%; 1.03–5.32). Overall AAMRs were highest among AI/AN (15.2) and NH Black adults (11.5), followed by Hispanics (10.5), NH Whites (9.39), and API (7.34). Rural populations consistently had higher mortality rate (overall AAMR 12.9; APC 1.20%; $p < 0.01$), whereas urban populations demonstrated a greater relative increase (8.98; 3.24%; $p < 0.01$). Regionally, the West experienced the most rapid increase in mortality, while the highest overall rates were observed in Nebraska, West Virginia, and Minnesota. **Conclusions:** Mortality among U.S. adults with concomitant T2DM and malignant neoplasms increased markedly from 1999 to 2020, significant disparities by sex, age, race/ethnicity, region, and urbanization. Integrated public health strategies linking diabetes management with cancer prevention, targeted screening, and equity-focused interventions are urgently needed. Research Sponsor: None.

Timing and prognostic impact of thromboembolic events in lung cancer patients treated with immune checkpoint inhibitors: A time-dependent real-world analysis.

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Background: Thromboembolic events (TEEs) are complications associated with malignancy, and emerging evidence suggests immune checkpoint inhibitors may further increase thrombotic risk; however, the prognostic impact of thromboembolic events in the era of immune checkpoint inhibitors, where inflammation and vascular toxicity may be amplified, remains unclear. We analyzed the incidence, timing, and impact on survival of thromboembolic complications in lung cancer patients treated with immunotherapy at a single tertiary academic institution. **Methods:** We conducted a retrospective study of adult lung cancer patients treated with immunotherapy at a single rural academic center (2015–2025). Thromboembolic events were classified as arterial (myocardial infarction, stroke) or venous (deep vein thrombosis, pulmonary embolism). Clinical characteristics and VAN Index scores were compared by TEE status, and overall survival was assessed using Kaplan-Meier and time-dependent Cox regression to address immortal time bias. **Results:** Altogether, 505 lung cancer patients received immunotherapy during the study period; patients were predominantly White (76.6%) and male (56.4%), with 21.4% identifying as Black. 22.8% experienced at least one TEE. Histologic subtypes included 59% with non-small cell lung cancer and 41% with small cell lung cancer. The mean age at diagnosis was 65 years. Among patients with TEE, 63.5% experienced arterial and 40.0% venous events. Some patients experienced both venous and arterial events during follow-up. The mean time to first TEE was 404 days, with venous events occurring earlier in the disease course. Patients with TEE had significantly higher comorbidity burden (9.28 vs 6.51) and thrombotic risk by VAN Index (31.99 vs 23.69; both $p < 0.001$). While unadjusted Kaplan-Meier analysis showed no survival difference (22 vs 19 months; $p = 0.126$) and multivariable Cox models treating TEE as a baseline exposure showed no independent association with survival (aHR 1.05, 95% CI 0.80–1.38), time-dependent Cox modeling demonstrated a significantly increased mortality risk following TEE (aHR 2.45, 95% CI 1.85–3.26; $p < 0.001$). **Conclusions:** Thromboembolic events occurred in nearly one-quarter of lung cancer patients treated with immunotherapy and were associated with higher comorbidity and thrombotic risk. Although standard analyses showed no survival difference, time-dependent modeling demonstrated significantly increased mortality following TEE. These findings demonstrate that failure to account for TEE as a time-varying exposure may substantially underestimate its prognostic impact, underscoring the need for prospective dynamic risk assessment and thromboprophylaxis strategies during immunotherapy. Research Sponsor: None.

Natural language processing–assisted chart review to assess documented cannabis use in electronic medical records (EMR) of adults undergoing cancer infusion therapy.

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Background: Patients' consumption of cannabis for symptom management is well-documented, yet prevalence of cannabis use, and its documentation among patients undergoing active cancer treatment is understudied. Our goal was to assess the prevalence of documented cannabis use in the EMR of patients undergoing infusion cancer therapy. **Methods:** We conducted a cross-sectional analysis of adult members of Kaiser Permanente Southern California undergoing infusion therapy between February 16 to 28, 2025. Natural language processing (NLP) of search terms indicative of cannabis use was used to identify any EMR documentation of such use in unstructured clinical notes in the past year. Each matched query included 15–20 words before and after the keyword and was manually reviewed for clinical context and confirm cannabis use. **Results:** We identified N = 690 cancer survivors undergoing infusion therapy during the two-week period. Of these, N = 354 (51%) had a cannabis notation in their EMR after applying the NLP program. Half were female. Altogether 1,010 snippets from N = 354 patients were output into a spreadsheet for manual review; each snippet required about 30 seconds to determine cannabis use status. Of the N = 354 patients, overall prevalence of cannabis use was 29% (N = 101). The highest prevalence was in patients undergoing first line palliative treatment (38%); followed by palliative after first line (25%); adjuvant (16%); then curative first line therapy (13%). Cannabis use was lower in among those undergoing curative after first line therapy (6%) and neoadjuvant therapy (3%). Highest cannabis use was observed in those with cancer of the breast (15%); lung (14%); prostate (10%); colorectal (10%) and gynecologic (8%). Regarding demographics, odds of cannabis use was greater in males (OR = 1.34, 95% CI: 0.82–2.21) vs. females (ref). Compared with Asians (ref), odds of cannabis use was about two-fold greater in Hispanic (OR = 1.95, 95% CI: 0.78–5.35), Black (OR = 2.47, 95% CI: 0.80–7.87), and White (OR = 2.30, 95% CI: 0.95–6.15) patients. Odds of cannabis use was 24% greater in younger individuals (< 50 years, OR = 1.76, 95% CI: 0.84–3.61), but all confidence intervals crossed the null. **Conclusions:** NLP-assisted manual review of chart notes is a time-efficient method to collect information on unstructured data. This methodology determined prevalence of cannabis use in patients undergoing cancer infusion therapy is 29%. Cannabis use was greater among patients being treated in palliative settings compared to adjuvant/curative settings. A limitation of this study is that cannabis use may be underestimated because we assume that not all discussions were recorded in the EMR. Information garnered from this cross-sectional data exploration will be used to plan a prospective study of cancer survivors to examine the risks and benefits of cannabis use. Research Sponsor: National Cancer Institute/U.S. National Institutes of Health.

Breast cancer screening and detection after the 2024 USPSTF recommendation for women aged 40–49.

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Background: In April 2024, the US Preventive Services Task Force (USPSTF) expanded its biennial screening mammography recommendations to include women aged 40–49, citing rising breast cancer incidence in this age group and persistent disparities in outcomes. How this expansion has influenced diagnosis and stage at diagnosis in real-world practice is not yet well characterized. **Methods:** Using a subset of de-identified electronic health record data from Truveta, we identified women aged 40–74 who underwent screening mammography between 2018 and 2025, had no prior breast cancer diagnosis and who had evidence of outpatient care 6–18 months before and 1–12 months after screening. For patients with multiple eligible screening mammograms, only the first was retained for analysis. Analyses were restricted to health systems with available cancer stage data. April 30, 2024, was used as the cut point (pre- vs. post-guideline). Outcomes included: (1) screening uptake by age group, (2) breast cancers diagnosed within 180 days of screening, (3) stage at diagnosis (early [AJCC 0–I] vs. later [II–IV]). Diagnosis and stage were derived from clinical notes and categorized as early- (AJCC stage 0–I) versus later-stage (II–IV). Logistic regression, adjusted for race, ethnicity, rural–urban residence, and family history, was used to evaluate differences by age group and guideline period. **Results:** Among 985,687 women aged 40–74 who received a screening mammogram, 880,685 (89.3%) occurred pre-guideline and 105,002 (10.7%) occurred post-guideline. Women aged 40–49 comprised a substantially larger share of screenings post-guideline (53,227/105,002, 50.7% vs. 262,330/880,685, 29.8% pre-guideline $p < .001$). The likelihood of a breast cancer diagnosis within 180 days did not differ between the pre- and post-guideline periods for women aged 40–49 (OR 1.03, 95% CI 0.79–1.34) or 50–74 (OR 0.87, 95% CI 0.75–1.01). Among women diagnosed within 180 days with cancer stage information available ($n = 3,866$), the likelihood of early- versus later-stage diagnosis did not differ between the pre- and post-guideline periods for women aged 40–49 (early-stage: 63.6% vs. 68.3%; OR 1.26, 95% CI 0.72–2.21) or 50–74 (OR 0.91, 95% CI 0.67–1.24). **Conclusions:** Following the April 2024 USPSTF guideline expansion, screening mammography uptake among women aged 40–49 increased substantially, however the likelihood of a breast cancer diagnosis within 180 days did not significantly differ between the pre- and post-guideline periods. Stage at diagnosis did not differ significantly in the short post-guideline period; longer follow-up is needed to assess whether earlier detection translates to stage-shift benefits over time. These findings provide early real-world evidence to inform the ongoing risk-benefit discussion surrounding breast cancer screening in younger women. Research Sponsor: Truveta.

Safety and efficacy of immunotherapy rechallenge in solid tumors after discontinuation of immune checkpoint inhibitors for immune-related adverse events: A systematic review and meta-analysis.

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Background: Immune-related adverse events (irAEs) often require treatment discontinuation in patients with cancer receiving immune checkpoint inhibitors (ICIs). Given limited subsequent treatment options, ICI rechallenge is frequently considered. We aimed to estimate the incidence of recurrent irAEs and objective response rates (ORR) in patients receiving ICI rechallenge following prior irAEs. **Methods:** PubMed, Web of Science, and Embase were searched for studies evaluating ICI rechallenge in patients with advanced solid tumors who previously suspended treatment due to irAEs. Outcomes included the incidence of grade 1–5 (Gr1–5), Gr1–2, and Gr3–5 irAEs, recurrent irAEs, new irAEs, ORR, and disease control rate (DCR). Random-effects meta-analyses and subgroup analyses by cancer type were performed. Meta-regression analysis was conducted to evaluate the impact of the grade and type of initial irAEs on response outcomes. Heterogeneity was assessed using I^2 statistics ($\geq 50\%$ considered high). **Results:** Thirty-seven studies comprising 1,126 patients with initial irAEs (Gr1–2: 62.8%, Gr3–4: 37.2%) leading to suspension of ICIs were included. The most common initial irAEs in the pooled cohort were hepatitis/liver enzyme elevations (20.5%), pneumonitis (16.1%), and nephritis/acute kidney injury (14.8%). Pooled incidences of Gr1–5, Gr1–2, and Gr3–5 irAEs after ICI rechallenge were 42.2% (95% confidence interval [CI]: 35.3–49.3), 27.1% (95% CI: 22.9–31.7), and 18.8% (95% CI: 14.7–23.8), respectively. Subgroup analysis showed overall higher incidences of irAEs in melanoma (Gr1–5: 54.6%, Gr1–2: 23.2%, Gr3–5: 26.4%) than those in lung cancer (Gr1–5: 39.7%, Gr1–2: 27.4%, Gr3–5: 14.0%) and solid tumors (Gr1–5: 36.7%, Gr1–2: 22.8%, Gr3–5: 20.1%). The same type of irAEs recurred in 23.8% (95% CI: 20.1–28.0) of patients, while new types of irAEs developed in 29.3% (95% CI: 25.2–33.7) of patients undergoing ICI rechallenge. The overall ORR was 45.2% (95% CI: 34.5–56.4), with cancer type-specific ORRs of 60.5% (95% CI: 47.9–71.9) in melanoma, 39.1% (95% CI: 17.4–66.2) in lung cancer, and 39.5% (95% CI: 27.7–52.6) from studies investigating solid tumors. DCR was high across cancer types: 77.3% (95% CI: 67.7–84.7) overall, 68.2% (95% CI: 41.3–86.8) in melanoma, 91.2% (95% CI: 67.7–98.1) in lung cancer, and 72.5% (95% CI: 63.3–80.1) in solid tumors. Meta-regression analysis showed that commonly observed initial irAE types or grades of initial irAEs (Gr1–2 vs. Gr3–4) did not significantly impact ORR or DCR. **Conclusions:** ICI rechallenge after discontinuation due to irAEs demonstrates clinical activity but carries a substantial risk of both recurrent and new irAEs. These findings highlight the need for predictive biomarkers to optimize patient selection and maximize survival without compromising safety. Research Sponsor: None.

Overall survival after intravenous iron use in patients with cancer and iron deficiency: A propensity-matched real-world study.

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Background: Iron deficiency affects up to two-thirds of patients with cancer and frequently coexists with anemia, with the highest prevalence in pancreatic, colorectal, and lung cancers. Functional iron deficiency driven by cancer-related inflammation predominates. Although intravenous (IV) iron is recommended to improve hematologic outcomes and reduce transfusion requirements, its impact on survival remains uncertain. We evaluated the association between IV iron use and overall survival (OS) in patients with advanced solid tumors using large real-world data. **Methods:** We conducted a retrospective cohort study using a TriNetX, a federated electronic health record network. Adults with solid malignancies and laboratory-defined iron deficiency (TSAT $\leq$ 20% and ferritin $\leq$ 500 ng/mL) were identified and categorized by IV iron exposure. Cohorts were matched 1:1 using propensity score matching for demographics, comorbidities, cancer site, iron indices (ferritin, transferrin saturation), hemoglobin, and treatment-related variables. OS was assessed using Kaplan–Meier analysis (5-year cap) and Cox proportional hazards modeling. **Results:** After propensity matching, 4,802 patients receiving IV iron were compared with 4,751 patients who did not receive IV iron, with a good balance across baseline characteristics. In Kaplan–Meier analysis (capped at 5 years), median overall survival (OS) was 875 days in the IV iron group and 858 days in the no IV iron group, with similar 5-year survival probabilities (38.6% vs 37.5%) and no significant difference by log-rank testing ($p=0.53$). On multivariable Cox proportional hazards modeling, IV iron exposure was not independently associated with mortality (HR 1.04, 95% CI 0.996–1.094; $p=0.075$). Male sex (HR 1.09, $p<0.0001$) and increasing age (HR 1.013 per year, $p<0.0001$) were associated with higher mortality. Iron indices demonstrated strong prognostic associations, with low transferrin saturation ($<10\%$: HR 1.48; 10–20%: HR 1.24; both $p<0.0001$) and anemia diagnoses including iron deficiency anemia (HR 1.05, $p=0.0048$) and anemia of chronic disease (HR 1.23, $p<0.0001$) independently associated with increased mortality, while lower ferritin levels were associated with improved survival (<100 ng/mL: HR 0.53; 100–200 ng/mL: HR 0.78; both $p<0.0001$). Cancer site was also independently associated with OS, with higher mortality observed in digestive, respiratory, urinary tract, and central nervous system malignancies, and improved survival in breast and thyroid/endocrine cancers. **Conclusions:** In this large propensity-matched real-world cohort, IV iron was not associated with worse overall survival in patients with cancer and iron deficiency, supporting its survival safety while highlighting iron indices, anemia, and cancer type as key prognostic markers. Research Sponsor: None.

Impact of facility type and surgical management on survival outcomes in colon adenocarcinoma stratified by metastatic burden.

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Background: Survival for colon cancer varies by facility type, yet the impact of granular metastatic burden and surgical intervention on this disparity remains poorly defined. We examined whether academic survival advantages persist after stratifying by disease extent and evaluated how surgical management contributes to these outcomes. **Methods:** Using the NCDB (2016–2023), we identified 438,590 adults with colon adenocarcinoma. We compared academic vs. community settings, quantifying metastatic burden by involved organ site count at diagnosis (liver, lung, bone, brain, lymph nodes, viscera; 0–6). Overall survival (OS) was the primary endpoint. Multivariable Cox models adjusted for age, Charlson–Deyo score, clinical stage, and site count. Sequential adjustment for primary tumor resection and metastatic-site surgery was performed to assess potential mediation. **Results:** Of 438,590 patients, 49.2% were treated at academic centers. Academic cohorts presented with more complex disease, including higher metastatic rates (22.4% vs 20.1%; $p < 0.001$) and frequent liver involvement (16.9% vs 15.1%; $p < 0.001$). In stage IV cases, metastatic-site surgery occurred more often at academic facilities (19.1% vs 14.0%). While primary resection rates were high in both cohorts, academic centers achieved superior Ro rates (95.0% vs 94.3%). Adjusted for age, comorbidity, and site count, academic care was associated with a survival benefit (HR 0.93; 95% CI 0.92–0.94). Primary tumor resection strongly predicted OS (HR 0.29; 95% CI 0.29–0.30). Adjusting for primary resection strengthened the academic effect (HR 0.91; 95% CI 0.90–0.92), indicating that surgical management partially mediates this advantage. Conversely, metastatic-site surgery was associated with higher mortality (HR 1.32; 95% CI 1.29–1.34) and did not explain the facility-based survival gap. **Conclusions:** The survival advantage at academic centers persists regardless of initial metastatic burden and is driven more by primary tumor surgical management than by metastatic-site interventions. These data suggest that improving community outcomes requires broader access to academic-level surgical standards and multidisciplinary care. Ensuring specialized surgical evaluation for high-burden patients is critical, regardless of their initial point of entry into the healthcare system. Research Sponsor: None.

Integrated tumor-informed and tumor-agnostic ctDNA molecular residual disease (MRD) assessment with imaging in early breast cancer.

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Background: Accurate ctDNA-based MRD detection in early breast cancer is limited by tumor heterogeneity, clonal evolution and methodological issues, limiting tumor-informed (TI) assays reliant on predefined variants. Tumor-agnostic (TA) approaches, while broader, are susceptible to false positives from clonal hematopoiesis and reduced sensitivity in low-tumor burden settings. **Methods:** We analyzed a single-center cohort of 74 female patients with stage I–III breast cancer undergoing post-treatment surveillance after completion of curative-intent therapy (surgery, radiation, and adjuvant systemic therapy as appropriate). Plasma samples collected post-treatment were analyzed using an integrated MRD assay combining TI ddPCR and TA NGS ctDNA detection strategies. CHIP filtering was incorporated to improve analytical robustness. MRD status was correlated with clinicopathologic features and contemporaneous imaging. MRD positivity was defined as detection by either TI or TA component. **Results:** At the time of ctDNA assessment, which was performed during standard post-treatment surveillance following completion of curative-intent therapy, 94.6% (70/74) of patients were imaging-negative. MRD was detected in 31.1% (23/74) of patients overall. All imaging-positive patients (4/4) were MRD-positive. Notably, among imaging-negative patients, 27.1% (19/70) were MRD-positive, indicating molecular residual disease not captured by conventional imaging. No imaging-positive cases were MRD-negative. MRD positivity was observed across all stages, including early-stage disease (I–II: 26%, 14/54), with the highest prevalence in stage III (47.4%, 9/19); one case had unknown staging. MRD was detected in 33.3% (18/54) of HR⁺/HER2[−], 25% (2/8) of TNBC, and 25% (3/12) of HER2⁺ tumors, demonstrating applicability across biological subtypes. Importantly, the hybrid approach increased detection sensitivity significantly. Among MRD-positive patients (n=23), 47.8% were detected exclusively by TA component, 43.5% by the TI component alone, and only 8.7% were detected by both. Reliance on a single MRD strategy would have failed to identify 91.3% (21/23) of MRD-positive cases, highlighting substantial biological complementarity between the two approaches. At early follow-up (median 113.5 days), MRD was detected in 23 patients, including 19 who were imaging-negative; among those with subsequent imaging-confirmed recurrence (n=4), the median MRD–imaging interval was 9.75 months. **Conclusions:** A hybrid TI and TA ctDNA MRD platform detects clinically occult molecular disease beyond imaging in stage I–III breast cancer. The complementary performance of TI and TA approaches substantially improves MRD detection and supports the use of hybrid MRD testing for early risk stratification and MRD-guided clinical trials. Research Sponsor: None.

Role of iron supplementation in the efficacy of immune checkpoint inhibitors (ICIs): A real-world propensity-matched analysis.

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Background: Iron plays a crucial role in the induction of ferroptosis mediated by immune checkpoint inhibitors (ICIs) in cancer. However, it plays a complex role in T-cell and macrophage function in the tumor immune microenvironment, which could influence anti-cancer immunity. Currently, the role of iron supplementation in affecting the therapeutic outcomes in patients receiving ICIs is unknown. **Methods:** A retrospective analysis utilizing TriNetX, a global federated health research network database, of patients receiving ICIs from January 2006 to January 2026, was conducted. Patients were divided into 3 cohorts based on whether they received intravenous (IV) iron (cohort A), oral (PO) iron (cohort B), or no iron supplementation (cohort C), 1 month prior to or up to 3 months after receiving ICIs. Propensity score matching (PSM) was used to balance the cohorts based on age, race, ethnicity, hemoglobin (Hb), ferritin, CRP, albumin, metastatic disease, line of treatment and underlying comorbidities. Kaplan-Meier analyses were used to analyze overall survival (OS). **Results:** A total of 4464, 5299, and 201,014 patients were identified across cohorts A, B and C, respectively. The most common primary sites of malignancies were the lung and/or bronchus, the gastrointestinal tract (and associated glands), and the urinary tract. Although IV iron recipients had better survival outcomes than PO iron recipients, both groups had worse outcomes than patients receiving no supplementation (Table 1). Similar trends were seen in subgroups receiving anti-PD1 and anti-PDL1. In the subgroup of patients with likely true iron deficiency ($Hb \leq 11g/dl$ and ferritin $< 100ng/ml$) ($n=508$ after PSM), IV iron recipients had better outcomes than PO iron recipients (2Yr OS HR (95% CI): 0.822 (0.691,0.978) $p=0.027$). In the subgroup of patients having $Hb \leq 11g/dl$ and ferritin $\geq 300ng/ml$, likely anemia of chronic disease ($n=2483$ after PSM), iron supplement recipients, whether IV or PO, had worse survival outcomes than patients receiving no supplementation (2Yr OS HR (95% CI): 1.22 (1.137,1.308) $p<0.0001$). **Conclusions:** Our study highlights the adverse impact of concurrent iron supplementation in patients receiving ICIs, especially in those without true iron deficiency. When clinically indicated, the IV route is preferred. Clinical studies are planned or ongoing to determine the role of iron supplementation in patients receiving ICIs, given its potential to induce ferroptosis. We suggest careful reconsideration or appropriate stratification of the cohort based on iron deficiency and/or type of iron supplementation in such studies. Research Sponsor: None.

2-year overall survival (OS).

Comparison groups	Number of patients after PSM	2-Year OS HR (95% CI) p-value (log-rank test)
IV Iron v/s PO Iron	2762	0.898 (0.83,0.97) $p=0.006$
IV Iron v/s No Iron	3808	1.199 (1.121,1.283) $p<0.0001$
PO Iron v/s No Iron	5210	1.405 (1.327,1.488) $p<0.0001$

Pan-cancer discovery of clinical and genomic determinants of immune-related adverse events.

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Background: Immune-related adverse events (irAEs) from immune checkpoint inhibitors (ICIs) can be lifelong, fatal, or require treatment discontinuation, substantially limiting the clinical benefit of immunotherapy. Despite their impact, predictors of irAE susceptibility remain poorly defined, largely due to the lack of scalable approaches for toxicity phenotyping. Here, we leverage large language models and integrated clinico-genomic data to identify determinants of irAEs. **Methods:** We developed a custom retrieval augmented generation and large language model (RAG-LLM) pipeline to automatically annotate 6 key adverse events (adrenal insufficiency, hepatotoxicity, hyperthyroidism, hypothyroidism, colitis, and pneumonitis) using free text from clinical notes across Memorial Sloan Kettering Cancer Center. We first validated RAG-LLM predictions using a gold standard prospectively collected adverse event dataset from 8,119 patients across 1,057 individual clinical trials. RAG-LLM imputations were then scaled to 55,406 (12,291 ICI-treated) patients. All patients had associated somatic and germline MSK-IMPACT panel sequencing data. Single nucleotide polymorphism (SNP) imputation was performed using GLIMPSE and time-to-event genome-wide association studies (GWAS) were performed using SPACox. HLA class I genotypes were imputed using HLA-HD. Random Survival Forest (RSF) models were trained to predict irAE occurrence. **Results:** The custom RAG-LLM pipeline had strong performance across all 6 irAEs (area under the ROC curve of 0.77-1.00). In the RAG-LLM imputed data, 799 (1.4%) patients had adrenal insufficiency, 2,803 colitis (5.1%), 7,130 hypothyroidism (12.9%), 448 hyperthyroidism (0.8%), 15,627 hepatotoxicity (28.2%), and 3,730 pneumonitis (6.7%). Among ICI-treated patients, pneumonitis (HR 1.4; 95% CI 1.1-1.8; $p < 0.01$) and hepatotoxicity (HR 1.4; 95% CI 1.2-1.6; $p < 0.01$) were associated with worse overall survival. The GWAS found two genome-wide significant hits that predicted adrenal insufficiency (rs115003145, HLA region) and hypothyroidism (rs7864322, FOXE1 gene enhancer region) with $p < 5 \times 10^{-8}$. Fine mapping of the HLA SNP showed that HLA-C*06:02 was specifically associated with increased risk of adrenal insufficiency in ICI-treated patients only (HR 1.6; 95% CI 1.2-2.2; $p < 0.01$). RSF model performance for irAE occurrence had F1 scores of 0.67-0.85. For pneumonitis, patients with the highest risk quartile by RSF model had 7.1% risk of pneumonitis at 1 year compared to 0.4% for the lowest risk quartile (HR 14.9; 95% CI 10.4-21.3; $p < 0.01$). **Conclusions:** We developed and validated a novel custom RAG-LLM pipeline that allows automatic annotation of irAEs using clinical notes. Using this pipeline, we identified novel biomarkers of ICI-related adrenal insufficiency and hypothyroidism. Finally, we developed predictive models for irAE prediction that can be used at the point of care. Research Sponsor: Fund for Innovation in Cancer Informatics; National Cancer Institute; P30-CA008748; Memorial Sloan Kettering Cancer Center.

Estimating survival in advanced cancer: A prospective single-center study on the accuracy of oncologists' prognostic accuracy (Pre-Sur).

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Background: The ability to estimate survival is a cornerstone of care for patients (pts) with advanced cancer, influencing therapeutic strategies, access to clinical trials, and timing of palliative care referral. Existing evidence on clinical prediction of survival (CPS) largely derives from end-of-life pts. The Pre-Sur study addresses this gap by evaluating oncologists' prognostic accuracy in pts with metastatic solid tumors starting first-line therapy and investigating discordance-related factors. **Methods:** Pre-Sur is a prospective, observational, monocentric study enrolling pts with advanced tumors prior to first-line therapy (hormonal therapy was excluded). During the baseline consultation, clinicians provided an estimated survival time-frame using categorical intervals (0-4 to >36 months). The primary endpoint was concordance between CPS and overall survival (OS). Survival estimates and outcomes were analyzed descriptively and through cross-tabulation. Secondary analyses explored factors potentially influencing accuracy, including ECOG-PS, age, comorbidities, and clinician characteristics, using Chi-square tests and multivariable models. **Results:** From October 2022 to December 2025, 183 pts were enrolled; 135 completed the required follow-up. 58% of pts were male and 49% were ≥75 years. Gastrointestinal (45%) and thoracic (35%) cancers were the most prevalent. Median CPS (mCPS) was 18.0 months (95%CI: 15.9-20.0), median OS (mOS) of 8.0 months (95%CI: 5.9-10.0). Prognostic estimates were accurate in 17% of cases, optimistic in two-thirds, and underestimated in less than one-quarter. No significant associations emerged for sex, tumor site, PS or target therapy use. mCPS were often more consistent with the mOS reported in randomized clinical trials (RCT); the observed real-world OS were inferior to that expected from RCT (Table 1). **Conclusions:** This study highlights the difficulty of predicting OS in pts with metastatic solid tumors. CPS may be influenced by expectations derived from RCT outcomes, which may not fully capture the complexity of real-world pts. Prognostic evaluation in clinical practice should integrate features such as age, PS, comorbidities, and disease burden, to improve prognostic accuracy and support informed decision-making. Research Sponsor: None.

Overall survival and clinical prediction of survival by disease sites.

Site	Patients, n (%)	mOS, months (CI 95%)	mCPS, months (CI 95%)	mOS trend in registrative RCTs, months
Lung	44 (32.2)	7 (2-12)	12 (11-13)	12-26
Colorectal	24 (17.8)	9 (5-13)	18 (13-23)	25-30
Pancreas	15 (11.1)	8 (2-14)	24 (21-27)	11
Gastric	11 (8.1)	5 (2-8)	12 (7-17)	14
Head and neck	6 (4.4)	6 (0-13)	30 (NA-NA)	15
Kidney	6 (4.4)	6 (4-8)	18 (5-30)	45
Biliary ducts	5 (3.7)	2 (1-3)	18 (13-23)	12
Pleural	4 (3.0)	2 (NA-NA)	8 (NA-NA)	12
Skin	4 (3.0)	22 (NA-NA)	12 (NA-NA)	33
Bladder	3 (2.2)	11 (0-27)	18 (8-28)	21

Trends and disparities in mortality from malignant neoplasms of male genital organs in the United States, 1999–2023.

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Background: Genital malignant neoplasms remain an important cause of mortality among males living in the United States. Tumor progression and organ-specific compromise contribute to increased risk and disease severity. Although recent data show overall declines in mortality over time, disparities persist, highlighting the need to analyze and interpret trends across demographic and geographic factors. **Methods:** The mortality data from the CDC WONDER underlying cause of death files for men aged ≥ 25 years were used to analyze age-adjusted and crude mortality rates (AAMRs and CMRs) per 100,000 for male genital neoplasms (ICD-10 Codes: C60–C63.9), stratified by year, gender, race/ethnicity, place of death, and geography. Joinpoint regression was used to estimate average annual percent change (AAPC) and annual percent change (APC) with 95% confidence intervals (CIs). Statistical significance was defined as $p < 0.05$. **Results:** From 1999 to 2023, a total of 765,516 deaths were reported among patients of male genital malignant neoplasms, with most occurring at the decedent’s home. The overall AAMR decreased from 18.29 in 1999 to 12.51 in 2023 (AAPC: -1.55; 95% CI: -1.71 to -1.39; $p < 0.001$), with the most significant decline observed between 1999–2013 (APC: -2.73; $p < 0.001$). Men aged 65 years and older experienced the greatest annual decline (-2.50%; $p < 0.001$), but had the highest CMR (63.84), whereas mortality among men aged 25–44 years increased notably between 2013–2023 (APC: 3.65; $p < 0.001$). The highest AAMR was observed among non-Hispanic (NH) Blacks (26.98), while the lowest AAMR was noted among NH Asians (6.30). Geographic disparities were evident, with the West having the highest AAMR (14.48) and the Northeast having the lowest (13.02). Non-metropolitan areas showed a higher AAMR (14.94 vs 13.79) and a slightly steeper decline in mortality than non-metropolitan areas (AAPC: -1.81 vs -1.80). At the state level, the District of Columbia ranked the highest, placed in the top 90th percentile, between 1999 and 2023. **Conclusions:** Despite a significant decline in mortality related to malignant neoplasms of male genitals over the past two decades, disparities persist, especially among older men, NH Black individuals, those living in non-metropolitan areas, and the West region. This underscores the need for targeted prevention, early detection, and equitable integrated care. Research Sponsor: None.

Average annual percent change (AAPC) of age-adjusted mortality rates for male genital malignant neoplasms in the United States, 1999 to 2023.		
Variable	Deaths	AAPC (95%CI)
Overall (Male)	765,516	-1.55 (-1.71 to -1.39)
Non-metropolitan areas	126,009	-1.80 (-2.05 to -1.55)
Metropolitan areas	537,718	-1.81 (-2.00 to -1.62)

Trends and disparities in mortality from malignant neoplasms of digestive system and renal failure in the United States, 1999-2023.

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Background: Malignancies of the digestive system represent a substantial global health burden, often exacerbated by coexisting renal failure, which complicates therapeutic interventions and significantly elevates mortality risk. This study aims to analyze and interpret annual mortality trends and disparities among adults in the United States from 1999 to 2023, for various demographic and geographic factors. **Methods:** The mortality data from the CDC WONDER multiple cause of death files for adults aged ≥ 25 years were used to analyze age-adjusted and crude mortality rates (AAMRs and CMRs) per 1,000,000 through ICD 10 code: C15-C26 (digestive system malignant neoplasms) and ICD 10 code: N17-N19 (renal failure), stratified by year, gender, race/ethnicity, place of death and geography. Joinpoint regression was used to estimate average annual percent change (AAPC) and annual percent change (APC) with 95% confidence intervals (CIs). Statistical significance was defined as $p < 0.05$. **Results:** From 1999 to 2023, a total of 164,004 deaths were reported due to malignant neoplasms of the digestive system and renal failure, mostly occurring in medical facility inpatient settings. The overall AAMR increased from 27.58 in 1999 to 36.84 in 2023 (AAPC: 1.17; 95% CI: -0.01 to 2.36; $p = 0.05$), with an initial decline observed between 2011 and 2017 (APC: -4.91; $p < 0.001$), followed by a notable increase through 2023 (APC: 8.26; $p < 0.001$). Men are noted to have higher AAMR than women (42.40 vs 19.19). Adults aged 65 and above experienced the highest CMR (110.96), whereas adults aged 45-64 years exhibited the greatest annual increase (3.19%; $p < 0.001$). By race, the highest AAMR was among non-Hispanic (NH) Black individuals (53.41), and the lowest was among NH White individuals (25.73). Geographic disparities were evident, with the West region having the highest AAMR (31.80) and the Northeast region having the lowest AAMR (27.77). Non-metropolitan areas showed higher AAMR than metropolitan areas (29.42 vs 27.91). At the state level, the District of Columbia and South Dakota ranked highest, placed in the top 90th percentile during 1999-2020 and 2021-2023, respectively. **Conclusions:** Mortality related to malignant neoplasms of the digestive system and renal failure has increased over the past two decades, with disproportionate burden among older adults, men, NH Black individuals, those living in non-metropolitan areas, and the West region, underscoring the need for targeted prevention, early detection, and equitable, integrated care. Research Sponsor: None.

Average annual percent change (AAPC) of neoplasms of digestive system and renal failure related age-adjusted mortality rates in the United States, 1999 to 2023.

Variable	Deaths	AAPC (95%CI)
Overall	164,004	1.17 (-0.01 to 2.36)

Hospitalized oncology patients with diarrhea: Clinical outcomes and prognostic factors.

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Background: Diarrhea is a frequent cause of hospitalization in oncology patients and may lead to substantial morbidity and mortality. However, data on short-term outcomes and prognostic factors in hospitalized cancer patients with diarrhea are limited. This study aimed to evaluate clinical outcomes and identify factors associated with poor prognosis in this population.

Methods: Medical records of 6,349 oncology patients hospitalized over a 3-year period were retrospectively reviewed. A total of 163 adult patients hospitalized primarily for diarrhea were included; patients with immune checkpoint inhibitor-related diarrhea were excluded. Collected variables included demographic characteristics, disease stage, Eastern Cooperative Oncology Group (ECOG) performance status, febrile neutropenia at admission, systemic anticancer therapy, serum albumin level, and diarrhea grade. Primary outcomes were intensive care unit (ICU) admission and 30-day mortality. Logistic regression analysis was used to identify independent predictors of mortality. **Results:** Diarrhea accounted for 2.6% of all oncology-related hospitalizations, and 83.4% of patients had grade ≥ 3 diarrhea. ICU admission was more frequent in patients with ECOG ≥ 2 compared with those with ECOG < 2 (42.4% vs 14.4%, $p < 0.001$) and in patients with grade ≥ 3 diarrhea (27.9% vs 7.4%, $p = 0.024$). The overall 30-day mortality rate was 16.0% and was higher in patients with ECOG ≥ 2 (39.0% vs 2.9%, $p < 0.001$), metastatic disease (23.5% vs 7.7%, $p = 0.006$), and grade ≥ 3 diarrhea (19.1% vs 0%, $p = 0.009$). Febrile neutropenia was not associated with ICU admission or mortality. In multivariable analysis, ECOG ≥ 2 (OR: 17.1, $p < 0.001$) and lower serum albumin level (OR: 0.42, $p = 0.049$) were independent predictors of 30-day mortality. Diarrhea grade was excluded from the multivariable model due to complete separation. **Conclusions:** Diarrhea in hospitalized oncology patients is associated with substantial ICU utilization and short-term mortality, independent of febrile neutropenia. Poor functional status and low serum albumin are key prognostic factors, highlighting that diarrhea should be regarded as a potentially life-threatening condition requiring early risk stratification and prompt supportive care. Research Sponsor: None.

Beyond geography: The intersecting impact of rurality, race, and depression on breast cancer survival.

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Background: Rural–urban disparities in breast cancer outcomes are well-documented, with rural populations typically experiencing worse survival due to limited access to screening and specialty care. However, the role of integrated healthcare systems in mitigating these disparities and the impact of psychosocial factors, such as depression, on survival remain underexplored. This study evaluated the survival outcomes of breast cancer patients treated within an integrated, academic health system, focusing on the intersecting effects of geographic residence, race, and antidepressant therapy. **Methods:** We conducted a retrospective cohort study of 6,788 female breast cancer patients diagnosed between 2014 and 2024 at MUSC-affiliated facilities in urban and rural South Carolina. Data on patient demographics, cancer stage, hormone receptor status, depression diagnosis, and antidepressant use were extracted from electronic medical records. We used Kaplan–Meier survival analysis with log-rank tests and multivariable Cox proportional hazards models to assess the association of geographic location, race, and antidepressant use with overall survival, while adjusting for clinical and demographic confounders. **Results:** Contrary to national trends, rural patients demonstrated superior overall survival compared to urban patients (5-year survival: 92.1% vs. 85.3%, $p < 0.001$). In a multivariable model, rural residence was an independent protective factor (HR = 0.72, 95% CI: 0.61–0.85, $p < 0.001$). Antidepressant treatment was also associated with significantly improved survival (HR = 0.78, 95% CI: 0.65–0.93, $p = 0.006$). This survival benefit was consistent across urban and rural subgroups. While African American race showed a borderline increased risk of mortality (HR = 1.18, 95% CI: 0.98–1.42, $p = 0.081$), the rural survival advantage was maintained within both African American and non-African American subgroups. Triple-negative breast cancer (TNBC) was an independent and significant predictor of mortality (HR = 1.34, 95% CI: 1.15–1.57, $p < 0.001$), and was more prevalent in the urban cohort. **Conclusions:** Our findings suggest that a coordinated, academic-affiliated care model can effectively address geographic barriers to care. The study also highlights the critical role of psychosocial health, demonstrating that antidepressant therapy is an independent predictor of improved survival, reinforcing the need for integrated mental health support in oncology. Furthermore, the higher prevalence of aggressive triple-negative breast cancer in the urban cohort, coupled with the potential for the urban facilities to receive more complicated referrals, may contribute to the observed urban survival disadvantage, underscoring the interplay of tumor biology and patient referral patterns within integrated systems. Research Sponsor: None.

A risk stratification schema for patients with non-small cell lung cancer with multiple organ metastases.

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Background: The majority of patients with non-small cell lung cancer (NSCLC) will have multiple organ sites of metastasis and poor overall survival (rwOS). Specific organ involvement influences patient outcomes, but the impact of overarching patterns of metastasis on rwOS and response to systemic therapy (ST) is poorly understood. Prior studies have been limited in their scale, availability of detailed data on sites of metastasis, and inclusion of patients receiving immunotherapy (IO) or targeted therapy (TT). We leveraged a large-scale, real-world database to characterize and assess the prognostic value of patterns of metastasis on rwOS and time to next therapy (rwTTNT) in patients with metastatic NSCLC receiving ST. **Methods:** This retrospective study utilized the Flatiron Health Research Database of patients with NSCLC treated with first-line (1L) ST (n = 327,044). Patient, tumor, and treatment variables were summarized descriptively and compared across patterns of metastasis. rwOS and rwTTNT from 1L start were estimated via Kaplan Meier method and compared with logrank test. Bernoulli mixture models were used to cluster patients by metastatic sites at 1L start. **Results:** Sites of disease were evaluated for 75,304 patients. Data from 5 metastatic sites revealed 6 clusters reflective of real-world patterns of metastasis: bone (n = 33,882), pleural (n = 12,123), liver (n = 6,133), brain (n = 11,441), adrenal avid (n = 6,975), and high metastatic burden (HMB, ≥ 3 sites with frequency ≥ 0.5 , n = 4,750). While HMB (7.2 months median rwOS, 4.8 months median rwTTNT) and liver avid disease (9.4, 5.2 months) had poor outcomes as expected, we also found that bone (11.0, 5.9 months) and adrenal (11.8, 6.0 months) avid clusters had worse median rwOS and shorter rwTTNT compared to pleural (15.7, 7.6 months) and brain (15.3, 7.4 months, $p < 0.001$). Outcomes associated with a specific site of metastasis varied based on patient cluster assignment. Compared to the cluster equivalent (e.g., brain avid), individual metastatic site (e.g., brain) as a prognostic factor was associated with worse median rwOS by 1.0–2.9 months and shorter median rwTTNT by 0.1–0.9 months. Compared to individual sites and site-avid clusters, HMB more often had EGFR mutations (20.7% vs 13.6% overall). IO was associated with greater median rwOS over TT in the adrenal cluster (17.7 vs 15.6 months), and IO + CTX had better rwOS vs IO alone in pleural (15.7 vs 12.9 months) and liver clusters (10.7 vs 9.4 months, $p < 0.001$). **Conclusions:** The survival outcomes and treatment response associated with defined clusters of metastases are distinct from those associated with individual organ sites or widespread disease alone. A risk-stratification framework that uses “risk phenotypes” representative of real-world patterns of metastasis may have better prognostic and predictive significance in patients with multiple sites or higher burden of disease. Research Sponsor: U.S. National Institutes of Health.

Safety of glucagon-like peptide-1 receptor agonists in patients with breast cancer: A real-world multicenter cohort study.

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are increasingly prescribed for patients with breast cancer and coexisting type 2 diabetes mellitus (T2DM). While GLP-1RAs have demonstrated metabolic and cardiovascular benefits in the general population, data regarding their safety in patients with breast cancer remain limited. **Methods:** We conducted a retrospective cohort study using the TriNetX Research Network, which aggregates de-identified electronic health record data from over 140 international healthcare organizations. Adult patients (≥ 18 years) with breast cancer who received breast cancer-directed systemic therapy and antidiabetic medications were included. The exposed cohort comprised patients who received a GLP-1RA within 90 days of systemic therapy initiation, while the comparator cohort included patients who received non-GLP-1RA antidiabetic agents. To minimize confounding, 1:1 propensity score matching was performed using demographics, body mass index, hemoglobin A1c, metastatic disease, breast cancer-directed therapy, and comorbidities. Outcomes were evaluated over 12 months using Cox proportional hazards models. Primary safety outcomes included adverse events commonly associated with GLP-1RA use: pancreatitis, biliary disease, and gastrointestinal adverse events (gastroesophageal reflux disease [GERD], bowel obstruction, and nausea/vomiting). Secondary outcomes included all-cause mortality and major adverse cardiovascular events (MACE), defined as a composite of myocardial infarction, ischemic stroke, and cardiovascular death. **Results:** A total of 29,380 patients with breast cancer and T2DM were identified. After propensity score matching, 3,796 patients were included in each cohort. Over 12 months of follow-up, GLP-1RA use was not associated with an increased risk of pancreatitis compared with non-GLP-1RA use (hazard ratio [HR], 1.20; 95% confidence interval [CI], 0.53–2.71). No significant differences were observed in biliary disease (HR, 0.93; 95% CI, 0.60–1.45) or bowel obstruction (HR, 0.70; 95% CI, 0.40–1.23). GLP-1RA use was associated with higher risks of GERD (HR, 1.48; 95% CI, 1.14–1.92) and nausea/vomiting (HR, 1.59; 95% CI, 1.26–2.00). Importantly, GLP-1RA use was associated with a lower risk of MACE (HR, 0.76; 95% CI, 0.59–0.99) and all-cause mortality (HR, 0.51; 95% CI, 0.37–0.69). **Conclusions:** In this study, GLP-1RA use was not associated with increased risks of serious gastrointestinal or biliary adverse events among patients with breast cancer receiving systemic therapy. While nausea/vomiting and GERD were more frequent, GLP-1RA use was associated with significant reductions in major adverse cardiovascular events and all-cause mortality. Prospective studies are warranted to confirm long-term safety and oncologic outcomes. Research Sponsor: None.

The corticosteroid timing paradox in immune checkpoint inhibitor–treated solid tumors and its association with overall survival: A TriNetX retrospective cohort study.

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Background: Systemic corticosteroids are frequently used in patients receiving immune checkpoint inhibitors (ICIs) for symptom control and management of immune-related adverse events (irAEs). However, corticosteroids may impair antitumor immunity, and the impact of timing of corticosteroid exposure relative to ICI initiation on survival outcomes remains incompletely defined. We evaluated the association between corticosteroid timing and overall survival (OS) in a large real-world cohort of ICI-treated solid tumor patients. **Methods:** We conducted a retrospective cohort study using the TriNetX Global Collaborative Network, including adult patients (≥ 18 years) with solid tumors treated with ICIs. Patients were stratified based on systemic corticosteroid exposure into three groups: baseline use (-30 to 0 days before ICI initiation), early intercurrent use ($1-56$ days after ICI initiation), and late intercurrent use ($57-180$ days after ICI initiation). Patients without corticosteroid exposure served as controls. The primary outcome was overall survival (OS). Kaplan–Meier analysis and Cox proportional hazards models were used to estimate survival outcomes and hazard ratios (HRs) with 95% confidence intervals (CIs). **Results:** A total of 43,282 ICI-treated solid tumor patients were included. Baseline corticosteroid use was associated with significantly worse OS compared with no corticosteroid exposure (median OS 564 vs 900 days; HR 1.32, 95% CI 1.28–1.35; $p < 0.0001$). Similarly, early intercurrent corticosteroid use was associated with inferior OS (median OS 543 vs 907 days; HR 1.35, 95% CI 1.32–1.39; $p < 0.0001$). In contrast, late intercurrent corticosteroid use was not associated with a survival detriment compared with controls (median OS 617 vs 650 days; HR 0.99, 95% CI 0.97–1.02; $p = 0.60$). **Conclusions:** In this large real-world analysis, systemic corticosteroid exposure prior to or early during ICI therapy was associated with significantly worse overall survival, whereas corticosteroid use later during treatment did not adversely impact survival. These findings support a corticosteroid timing paradox, suggesting that early immunosuppression may impair ICI efficacy, while later corticosteroid use—often for irAE management—may be oncologically safe. Prospective studies are needed to further define optimal corticosteroid timing and indications in ICI-treated patients. Research Sponsor: None.

New-onset inflammatory bowel disease associated with immune checkpoint inhibitor therapy: A real-world multicenter analysis.

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Background: Immune checkpoint inhibitors (ICIs) are increasingly used across a broad range of malignancies and are known to cause immune-mediated gastrointestinal toxicity. While acute colitis is a recognized adverse effect, the potential for ICIs to trigger de novo inflammatory bowel disease (IBD), a chronic immune-mediated condition with long-term treatment implications, has not been well studied, as ICIs enhance immune activation in ways that may also affect normal intestinal immune balance. With the expanding use of ICIs across cancer types and earlier lines of therapy, we examined the association between ICI exposure and the risk of developing incident IBD compared with chemotherapy. **Methods:** We conducted a retrospective cohort study using the TriNetX global federated research network, including adults (≥ 18 years) diagnosed with malignancy between 2020 and 2024. Patients with pre-existing Crohn's disease, ulcerative colitis, or prior IBD-directed biologic or targeted therapy were excluded. Two cohorts were defined: patients treated with PD-1/PD-L1 or CTLA-4 inhibitors and patients treated with chemotherapy without ICI exposure. Propensity score matching (1:1) was performed to balance demographics, cancer type, and comorbidities, yielding 63,190 patients per cohort. Outcomes assessed within 365 days included incident IBD diagnoses, initiation of first-line IBD therapies, and escalation to biologic or targeted IBD agents. Risk estimates, hazard ratios (HRs), and Kaplan-Meier analyses were performed. **Results:** After propensity score matching, baseline characteristics were well balanced between cohorts. The risk of developing incident IBD was significantly higher among ICI-treated patients compared with chemotherapy-treated patients (risk ratio [RR] 2.96, 95% CI 1.86–4.70). Time-to-event analysis demonstrated a significantly increased hazard of IBD following ICI exposure (HR 3.37, 95% CI 2.12–5.35; log-rank $p < 0.001$). Escalation to biologic or targeted IBD therapies was also more common in the ICI cohort (RR, 3.04; 95% CI, 1.90–4.87; HR, 3.46; 95% CI, 2.16–5.55). In contrast, initiation of first-line therapies (mesalamine or budesonide) did not differ significantly between groups (RR 0.97, 95% CI 0.93–1.01). **Conclusions:** Among cancer patients without pre-existing IBD, immune checkpoint inhibitor therapy was associated with a significantly increased risk of de novo IBD and a greater likelihood of requiring advanced IBD therapies compared with chemotherapy alone. These findings suggest that, in a subset of patients, immune checkpoint inhibition may be associated with the development of chronic intestinal immune disease, highlighting the need for increased awareness and longitudinal gastrointestinal monitoring as ICI use continues to expand. Research Sponsor: None.

The impact of the COVID-19 pandemic on breast cancer stage at time of diagnosis at a major health system in New Jersey.

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Background: The COVID-19 pandemic led to strict social distancing protocols in all aspects of daily life creating barriers to healthcare access. This resulted in a decrease in cancer screening, including mammography, which in turn led to higher stage of breast cancer at the time of diagnosis. This is reflected in the current literature¹. We completed a study at our institution to evaluate the impact of the COVID-19 pandemic on breast cancer screening and stage at diagnosis. **Methods:** We performed a retrospective chart review of patients aged 18 and older in a large New Jersey health system. IRB approval was obtained. Clinical and pathologic stage at time of breast cancer diagnosis as well as number of screening mammograms ordered and completed in the pre-COVID era (January 1, 2016 – December 31, 2019) and post-COVID era (January 1, 2020 – December 31, 2023) were evaluated. Chi-square hypothesis testing was used for data analysis. Of the 5613 patients identified, 4279 patients had clinical staging data documented. **Results:** Between 2016–2019, 80.1% of ordered screening mammograms were completed in our health system. As expected, the percentage of completed screening mammograms decreased to 63.7% during the peak of the COVID-19 pandemic from 2020–2021. However, this percentage further decreased to 61.8% between 2022–2023; p-value < 0.001 (Table 1). We also noted an increase in stage 0 and 1 breast cancers and a decline in stage 2–4 breast cancers during these time periods; p-value < 0.001. **Conclusions:** Our study demonstrates an expected decline in screening mammogram rates during the peak of the COVID-19 pandemic (2020–2021). This can be explained by the uncertainties around health care and social distancing recommendations. Despite participation in a national cancer screening campaign led by the American Cancer Society from May to December 2021, the completion rates of screening mammograms unfortunately continued to decline in the post-COVID years. Contrary to what has been reported, this study found that patients were diagnosed at an earlier stage in the post-COVID era. Our study demonstrates that completion rates of screening mammogram dropped during the COVID-19 pandemic and have not improved in the post-COVID times. We hypothesize that with longer-term studies an increase in late-stage breast cancers may be identified due to missed screening mammograms. 1. Pintican, Roxana et al. "COVID-19 pandemic resulted in more metastatic breast cancer cases at diagnosis." *Scientific reports* 15,1 29296. 11 Aug. 2025, doi:10.1038/s41598-025-14582-z. Research Sponsor: None.

Number and percentage of mammography orders completed and canceled by year.

	Orders Completed	Orders Canceled	Total
2016 – 2019	157,507 80.1%	39,054 19.9%	196,561 100%
2020 – 2021	99,571 63.7%	56,766 36.3%	156,337 100%
2022 – 2023	129,722 61.8%	80,330 38.2%	210,052 100%
Total	386,800 68.7%	176,150 31.3%	562,950 100%

Clinical associations of cannabis use among patients receiving immune checkpoint inhibitors: A real-world analysis.

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Background: Cannabis use is common in patients with cancer, yet its clinical associations during immune checkpoint inhibitor (ICI) therapy is poorly defined. We evaluated the association between documented cannabis use and clinical outcomes among patients receiving ICIs.

Methods: We conducted a retrospective cohort study of adults ≥ 18 years in the TriNetX US Collaborative Network with advanced or metastatic solid tumors treated with ICIs since January 1, 2019. Cannabis exposure was defined by diagnostic codes for cannabis-related disorders or prescriptions for cannabis-derived products documented 3 months prior to 2 years after ICI start. Patients who died in 60 days were excluded. Primary outcome was 3-year overall survival (OS); secondary outcomes included 2-year inpatient and emergency department (ED) visit, with joint sprain as a negative control outcome. Propensity matching adjusted for demographics, comorbidities, cancer type and stage, and tobacco and alcohol use. Hazard ratios (HR) and risk ratios (RR) with 95% confidence intervals (CI) and Kaplan–Meier analyses were calculated.

Results: After matching, 3,634 patients were included in the OS cohort. Patients with no documented cannabis use had significantly higher 3-year OS and median survival versus cannabis users (HR 0.67; 95% CI 0.63–0.72; median OS 34.8 vs 18.7 months). This association was observed across all tumor subgroups except head and neck squamous cell carcinoma (HNSCC) (Table 1). Among 2,855 matched patients in the healthcare utilization cohort, patients without cannabis use had lower healthcare utilization within 2 years, including fewer ED visits (RR 0.83; 95% CI 0.79–0.87) and inpatient admissions (RR=0.82; 95% CI 0.79–0.84). These findings were consistent across subgroups except for ED visits in HNSCC (Table 1). Joint sprain showed no association with cannabis exposure (RR 0.93, 95% CI 0.64–1.35). **Conclusions:** Cannabis use during ICI therapy was associated with lower survival and higher healthcare utilization in multiple solid tumors. This may reflect unmeasured symptom burden or clinical vulnerability but also raises the hypothesis of a potential interaction between cannabis exposure and ICI therapy. Prospective studies incorporating symptom severity, dose, timing, and route of exposure are needed to clarify these relationships. Research Sponsor: None.

Clinical outcomes by cannabis exposure.

Group	Overall survival HR (95% CI)	OS p-value	ED Visit RR (95% CI)	ED p-value	Inpatient visit RR (95% CI)	Inpatient visit p-value
Overall	0.67 (0.63–0.72)	<0.01*	0.83 (0.79–0.87)	<0.01*	0.82 (0.79–0.84)	<0.01*
NSCLC	0.73 (0.68–0.79)	<0.01*	0.85 (0.81–0.90)	<0.01*	0.85 (0.82–0.89)	<0.01*
RCC	0.60 (0.50–0.73)	<0.01*	0.81 (0.73–0.91)	<0.01*	0.78 (0.72–0.85)	<0.01*
Melanoma	0.52 (0.40–0.69)	<0.01*	0.70 (0.59–0.83)	<0.01*	0.73 (0.65–0.82)	<0.01*
HNSCC	0.93 (0.74–1.16)	0.52	1.05 (0.89–1.25)	0.56	0.87 (0.77–0.98)	0.02*

*Statistically significant ($p < 0.05$).

Relationship between immune-mediated adverse events and clinical outcomes in patients with metastatic melanoma treated with immune checkpoint inhibitors (ICIs): A retrospective real-world analysis.

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Background: ICIs targeting programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) revolutionized the treatment landscape for advanced melanoma. However, these agents can cause immune-related adverse events (AEs). Several studies have demonstrated a correlation between AEs and improved clinical outcomes. Understanding the co-occurrence patterns and prognostic implications of immune-related adverse events, as well as the impact of concomitant medications such as antibiotics (ATB), immunosuppressants (IS) and/or corticosteroids (CS), and proton pump inhibitors (PPIs), is crucial for immunotherapy management. In this study, we evaluated the relationship between immune-related toxicity, the use of IS and/or CS and ATB, and progression-free survival (PFS) and overall survival (OS) in patients with advanced melanoma treated with ICIs. **Methods:** Retrospective, analytical, multicenter study of patients (pts) with stage IV melanoma treated with ICIs (ipilimumab/nivolumab, nivolumab or pembrolizumab), between 2014 and 2025. Immune-related adverse events were graded according to CTCAE criteria and categorized as none, grade 1-2 or 3-4, demographic characteristics, use of IS and/or CS, ATB and number of toxicities were obtained from medical records. PFS and OS were estimated using the Kaplan-Meier method and compared using Cox proportional hazards models, with statistical significance set at $p < 0.05$. **Results:** Among 364 pts included, 275 (77,4%) experienced AEs. Dermatologic and endocrine toxicities, including rash, pruritus, vitiligo, hypothyroidism and hypophysitis were associated with improved survival outcomes. The results regarding PFS in relation to the presence, grade, and number of toxicities, as well as the use of IS and/or CS and ATB, are described in the table below. OS showed a statistically significant association with toxicity grade, with better OS observed among patients with grade 1-2 toxicity (HR 0.55; 95% CI, 0.35-0.87; $P = 0.010$), as well as who did not use IS and/or CS (HR 1.84; 95% CI, 1.20-2.82; $P = 0.005$). PFS showed a trend toward improved outcomes in patients who did not use PPI, without statistical significance due to the small number of pts. **Conclusions:** Our data show that pts who developed grade 1-2 toxicity and did not receive IS and/or CS experienced improved OS and PFS when treated with ICIs. Pts with a greater number of different toxicities and those who did not use ATB experienced better PFS. Research Sponsor: None.

Parameter	HR for PFS	95% CI	p-value
Toxicity vs. No Toxicity	0.39	0.29-0.52	<0.001
Degree of toxicity			
0 vs. Grade 1+2	0.38	0.28-0.51	<0.001
0 vs. Grade 3+4	0.50	0.35-0.73	<0.001
Number of toxicities			
0 vs. 1-2	0.50	0.38-0.67	<0.001
0 vs. 3 or +	0.26	0.17-0.38	<0.001
IS and/or CS vs. No IS and/or CS	1.43	1.05-1.95	<0.022
ATB vs. No ATB	1.53	1.11-2.12	<0.010

Real-world outcomes with atezolizumab versus durvalumab plus chemotherapy for extensive-stage small cell lung cancer: A TriNetX propensity-matched analysis.

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Background: First-line treatment for extensive-stage small cell lung cancer (ES-SCLC) consists of platinum-etoposide plus an immune checkpoint inhibitor (ICI), either atezolizumab or durvalumab. No head-to-head randomized trials have compared these regimens. We evaluated real-world outcomes associated with these ICIs using a large multi-institutional database.

Methods: We performed a retrospective cohort study using the TriNetX Global Collaborative Network. Adults with ES-SCLC treated with platinum-etoposide plus atezolizumab or durvalumab were included. The index date was initiation of platinum, etoposide, and ICI therapy. Cohorts were matched 1:1 using propensity scores based on age, sex, race, tobacco use, and comorbidities. The primary outcomes were overall survival (OS) and real-world progression-free survival (rwPFS), defined as time to second-line therapy or death. Survival was analyzed using the Kaplan-Meier method and cox proportional hazards models. Secondary endpoints were immune-related adverse events (irAEs) and hospitalization rates and evaluated by z-test. The study protocol was created and reviewed by the authors prior to implementation and did not require IRB approval.

Results: Among 750 eligible patients (677 atezolizumab, 73 durvalumab), 69 matched pairs were identified. Median follow-up was 13.4 months for atezolizumab and 8.6 months for durvalumab. Median OS was significantly longer with durvalumab compared with atezolizumab (23.2 vs 9.1 months; Hazard Ratio [HR] 0.58, 95% CI 0.47–0.93; $p=0.021$). No significant difference in rwPFS was observed (8.6 vs 6.7 months; HR 0.72, 95% CI 0.47–1.11; $p=0.14$) as shown in Table 1. Atezolizumab was associated with higher rates of hematologic adverse events (35 vs 22 events; $p=0.025$) and a trend toward increased hospitalizations (34 vs 24; $p=0.085$). No significant differences were observed in other irAE categories. **Conclusions:** This retrospective real-world analysis found that durvalumab-based first-line therapy was associated with longer OS compared to atezolizumab in patients with ES-SCLC, although no significant difference in rwPFS was observed. Interpretation is limited by shorter follow-up duration in the durvalumab cohort, which may contribute to observed survival differences. Due to the observational study design, potential residual confounding, and limited sample size, these results should be regarded as hypothesis-generating. These findings underscore the need for additional comparative effectiveness research to clarify optimal immunotherapy selection in ES-SCLC. Research Sponsor: None.

Outcomes in propensity-matched cohort.

Outcomes	Atezolizumab	Durvalumab	Effect Estimate
Patients (n)	69	69	
Median OS (months)	9.1	23.2	HR 0.58 (95% CI 0.47–0.93)
Median rwPFS (months)	6.7	8.6	HR 0.72 (95% CI 0.47–1.11)

Sinonasal adverse events of immune checkpoint inhibitors: Pharmacovigilance using FAERS.

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Background: Immune checkpoint inhibitors (ICIs) are cancer therapies with diverse toxicities, known as immune-related adverse events (irAEs). Sinonasal irAEs have been described primarily in case reports, and their population-level characteristics remain poorly defined. To date, no statistical analysis of the FDA Adverse Events Reporting System Database (FAERS) has evaluated sinonasal adverse events (sNAEs) associated with ICIs. **Methods:** We investigated sNAEs associated with FDA-approved ICIs in FAERS between 1/1/2011 and 10/1/2025. ICIs were grouped by therapeutic target (PD-1, PD-L1, or CTLA-4). Analyses were conducted in R using Bioconductor package “faers”. Data were standardized using preferred term in the Medical Dictionary for Regulatory Activities and deduplicated based on concordance across drug, adverse event, and demographics. Disproportionality analysis used reporting odds ratio (RORs) in comparison with the overall FAERS database. We excluded adverse events with <2 reports. The study was created and reviewed by the authors prior to implementation. **Results:** 17 million FAERS reports were identified, of which 2,476 ICI-associated reports included sNAEs. Two rare events demonstrated significant disproportionality among PD-1 inhibitors: chronic eosinophilic rhinosinusitis (n=3; ROR 7.71, 95% CI 2.34–25.42) and nasal mucosal hypertrophy (n=2; ROR 8.67, 95% CI 1.99–37.73). In contrast, more frequently reported sNAEs including sinusitis, rhinorrhea, nasal congestion, anosmia, nasal polyps, paranasal sinus inflammation, parosmia, and rhinitis, were not overreported (Overall ROR_{2.5} ≤1). **Conclusions:** In this large pharmacovigilance analysis sNAEs were not broadly overreported after ICI therapy. Rare inflammatory phenotypes were disproportionately reported with PD-1 inhibition, suggesting an immune-mediated mechanism. Given the limitations of spontaneous reporting data and small event counts, these findings should be interpreted cautiously but highlight the need for increased clinical awareness and prospective studies to better characterize sinonasal immune-related toxicities. Research Sponsor: None.

Sinonasal adverse events reported after ICI therapy.

Adverse event	Overall Freq	Overall ROR (95% CI ROR _{2.5} – ROR _{97.5})	CTLA 4 Freq	CTLA4 ROR	PD-1 Freq	PD-1 ROR	PD-L1 Freq	PD-L1 ROR
Anosmia	31	0.22 (0.15-0.32)	4	0.17	23	0.23	4	0.13
Chronic eosinophilic rhinosinusitis	3	7.71 (2.34-25.42)	0	0	3	10.56	0	0
Nasal congestion	157	0.2 (0.17-0.24)	15	0.12	122	0.23	20	0.13
Nasal mucosal hypertrophy	2	8.67 (1.99-37.73)	0	0	2	11.88	0	0.00
Nasal polyps	12	0.17 (0.09-0.33)	3	0.33	8	0.21	1	0.09
Paranasal sinus inflammation	4	1.96 (0.87-4.42)	0	3.69	3	2.23	1	1.44
Parosmia	48	0.52 (0.38-0.7)	9	0.64	37	0.63	2	0.11
Rhinitis	50	0.51 (0.39-0.68)	2	0.12	34	0.50	14	0.67
Rhinorrhoea	267	0.3 (0.27-0.35)	32	0.24	215	0.37	20	0.11
Sinusitis	300	0.21 (0.19-0.24)	56	0.27	204	0.22	40	0.14

Bold denotes statistical significance (ROR_{2.5}>1).

National trends in opioid-related hospitalizations among adult cancer patients: 2000-2022.

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Background: Opioid use disorder is increasingly prevalent among cancer patients. Since mid-2010s, heightened attention to the opioid crisis has led to restrictive opioid prescribing policies; however, national trends in opioid-related hospitalizations (ORH) among cancer patients following these policies remain underreported. This study examines ORH trends from 2000 to 2022 and associated factors among adult cancer patients. **Methods:** We identified hospitalizations among adult patients (age ≥ 18 years) with any cancer in the National Inpatient Sample (2000–2022). Outcomes included: 1) primary ORH (PORH), defined as admissions with a primary diagnosis indicating opioid poisoning, dependence or abuse, and 2) any ORH (AORH), capturing these conditions in any diagnostic field. The risks of PORH and AORH were calculated as the number of cases per 10,000 hospitalizations, respectively. Join-point regression assessed trends in risks of PORH and AORH, reporting annual percentage changes (APCs). Multivariable logistic regression identified factors associated with PORH and AORH, with adjusted odds ratio (aORs) reported. **Results:** Overall, among 59,682,271 weighted hospitalizations in cancer patients (median age 66.8 years, IQR 56.5–76.3), PORH occurred in 5.5 per 10,000 hospitalizations ($n = 32,641$) and AORH in 200 per 10,000 hospitalizations ($n = 1,192,358$). The risk of PORH increased non-significantly from 2.2 per 10,000 hospitalizations in 2000 to 4.8 in 2014 (APC = 5.6, $p > 0.05$), then rose sharply to 10.6 in 2017 (APC = 25.1, $p < .001$), before declining significantly to 6.8 in 2022 (APC = -9.7, $p < .001$). The risk of AORH also increased non-significantly from 45 per 10,000 hospitalizations in 2000 to 60.8 in 2014 (APC = 0.2, $p > 0.05$), then rose to 594.4 in 2019 (APC = 118.2 for 2013–2016 and 11.7 for 2016–2019; both $p < .001$), before decreasing non-significantly to 476.8 in 2022 (APC = -7.8, $p > .05$). Higher PORH risk was associated with younger age (< 65 vs. ≥ 65 : aOR = 2.53, $p < .001$), race and ethnicity (Native American: aOR = 2.07, Black: aOR = 1.85, White: aOR = 1.79, relative to Asian/Pacific Islanders; all $p < .001$), public or no health insurance, lower income, co-occurring substance use disorders (SUD) (e.g., sedative aOR = 35.19, cocaine aOR = 3.57, both $p < .001$), depression (aOR = 2.46, $p < .001$), anxiety, chronic pain, metastases, and care in small, non-teaching, rural hospitals and the West region. Similarly, AORH were associated with younger age, race and ethnicity, insurance, low income, co-occurring SUD, mental health condition, chronic pain, metastases, comorbidity burden, and the West region. **Conclusions:** Opioid-related hospitalizations decreased substantially in recent years following heightened attention and clinical/policy efforts in the mid-2010s. Elevated risks were primarily associated with patient demographics, co-occurring substance use disorder, mental health conditions, and chronic pain. Research Sponsor: NIH, Clinical and Translational Science Award (CTSA) program, The TRANSFORM KL2 Mentored Career Development Award.

Long-term incidence of hypothyroidism and thyroiditis after CAR T-cell therapy versus standard chemotherapy in hematologic malignancies: A propensity-matched multi-institutional cohort study.

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Background: Thyroid dysfunction is a common endocrine immune-related adverse event with modern cancer immunotherapies. Chimeric antigen receptor T-cell (CAR T) therapy is an adoptive cellular immunotherapy with expanding use in relapsed/refractory hematologic malignancies; its toxicity profile of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome are well described, whereas endocrine sequelae are comparatively less characterized. Large-scale population analysis regarding the effect of CAR T therapy on thyroid function remains limited. As CAR T survivorship increases and indications broaden, defining long-term thyroid-related outcomes is essential in optimizing care.

Methods: We performed a propensity-matched cohort study using the TriNetX Research Network (Jan 1, 2018–Jan 24, 2026). Adult, non-pregnant patients with DLBCL, PMBCL, follicular lymphoma, mantle cell lymphoma, multiple myeloma, or ALL were included. Patients receiving CAR T in addition to chemotherapy were compared with chemotherapy alone. Exclusions included prior thyroid disease/malignancy, central endocrine disorders, radiation therapy, bone marrow transplant, and baseline exposure to thyroid-active/thyroid-disrupting therapies (e.g., amiodarone, immune checkpoint inhibitors, tyrosine kinase inhibitors, interferons, immunomodulatory agents like lenalidomide). Propensity score matching balanced age, sex, race, malignancy type, baseline comorbidities, steroid exposure, and antipsychotic exposure. The primary outcome was new-onset hypothyroidism or thyroiditis; effect estimates are reported as ORs with 95% CIs. **Results:** Before propensity-score matching, there were 921 patients in the CAR T group and 24,426 in the chemo-only group. Post-matching, there were 878 CAR T patients and 879 chemo-only patients. Hypothyroidism or thyroiditis occurred in 16 patients in the CAR T group (1.822%) and in 21 patients in the chemo-only group (2.389%). Absolute risk difference was -0.567% (95% CI -1.909% , 0.776% ; $p = 0.4081$) and the OR was 0.758 (95% CI 0.393, 1.463). No statistically significant difference in incidence was observed. Mean follow-up for CAR T after chemo and chemo-only groups were 670 and 964 days, respectively. **Conclusions:** In this large, multi-institutional propensity-matched real-world analysis with long-term follow-up, CAR T therapy after chemotherapy was not associated with increased incidence of hypothyroidism/thyroiditis compared with chemotherapy alone. These findings provide reassuring thyroid safety data, supporting the expanding use of CAR T as indications broaden. Future studies should evaluate thyroid outcomes by CAR T construct/target and characterize timing and severity to inform monitoring strategies. Research Sponsor: None.

Risk of renal adverse events (RE-AE) and electrolyte changes with immunotherapy (IT) in a real-world cohort.

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Background: IT is used across multiple tumor types but is linked to immune-related AE (irAE), including RE-AEs. Acute kidney injury (AKI) is the most common renal irAE (1–2%); however, real-world comparative data on RE-AE & electrolyte trends across tumor types remain limited. We evaluated RE-AE incidence & longitudinal electrolyte & urine trends following IT. **Methods:** We conducted a retrospective cohort study of 5,556 adult cancer patients treated at Cleveland Clinic Ohio between 2010–2022. Included cancers were advanced-stage (III–IV) bladder, endometrial, esophageal, gastric, head & neck, renal, & lung cancers (NSCLC/SCLC), & metastatic melanoma. We compared IT ($\pm$ chemo/radiation) vs non-IT regimens. Follow-up began at systemic therapy initiation & continued until RE-AE, death, or last encounter. Outcomes included AKI, AKI progressing to chronic kidney disease (CKD), & clinically significant proteinuria. Poisson regression estimated incidence rates, Kaplan–Meier methods cumulative incidence (CIR), & time-dependent Cox models assessed risk with IT as a time-varying exposure. Longitudinal serum electrolytes & urine parameters were extracted electronically & analyzed via mixed-effects & generalized linear models over a one-year post-initiation period. **Results:** Among the cohort, 1,291 (23%) received first-line IT & 4,265 (77%) later-line IT. Median age was 66 years; 38% were female. During median follow-up of 14 months (CI 6–34), 195 RE-AEs occurred (IT: 46; non-IT: 149). The incidence rates per 100 person years were 0.18 (0.13, 0.24) in IT group & 0.13 (0.11, 0.15) in non-IT group. 2-year CIR was 4.6% with IT & 3.9% without IT ($P = 0.6$). Adjusted time-dependent Cox models demonstrated no significantly increased risk for AKI, CKD, or composite RE-AEs associated with IT exposure: [AKI HR 0.99 (0.7–1.5); CKD HR 1.5 (0.97–2.4); RE-AE HR 1.3 (0.9–1.7)]. Most RE-AEs were CTCAE grade II–III. Immunomodulatory therapy was used in 15%, primarily steroids, with a 50% response rate. Longitudinal analyses showed IT was associated with higher mean CO_2 & calcium compared with non-IT ($P < 0.05$), but not other labs (Table 1). While on therapy, IT was associated with lower urine pH ($\beta = -0.37$, CI $-0.69 - 0.04$) but no other UA parameter changes were noted. **Conclusions:** In this large real-world cohort, IT was not associated with an increased incidence of RE-AE compared with non-IT therapy, suggesting that stringent trial exclusion criteria for baseline renal impairment may be unnecessarily restrictive. IT was associated with statistically significant changes in calcium, CO_2 , & urine pH, the clinical significance of which remains uncertain. Research Sponsor: None.

Laboratory parameter	Estimate	95% CI
Sodium	0.14	-0.04 – 0.32
Potassium	0.02	-0.001 – 0.04
BUN	-0.03	-0.59 – 0.54
Creatinine	0.02	-0.003 – 0.05
CO_2 / Bicarbonate	0.16	0.001 – 0.32
Calcium	0.10	0.067 – 0.14
Chloride	0.18	-0.038 – 0.4
GFR	-1.59	-4.73 – 1.55
Phosphorus	-0.11	-0.25 – 0.04

Immune checkpoint inhibitors and respiratory outcomes in cancer patients with pre-existing asthma: A TriNetX propensity-matched cohort study.

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Background: Immune checkpoint inhibitors (ICIs) are associated with immune-related pulmonary toxicity. Real-world data on outcomes in patients with pre-existing asthma across malignancies remain limited. **Methods:** We conducted a retrospective cohort study using the TriNetX Global Collaborative Network (170 HCOs). Adults (≥ 18 years) with asthma (ICD-10 J45) and malignancy (ICD-10 C00–C96) were identified. The ICI cohort included patients receiving ICIs (HCPCS J9271, J9299, J9119, J9272, J9345, J9022, J9173, J9023, J9228, J9347) after cancer diagnosis (first ICI within 3 years of first malignancy). The comparator cohort included patients receiving non-ICI systemic therapy (TNX:1002 chemotherapy, TNX:1003 targeted therapy, TNX:1004 hormone therapy, and/or Z51.11) and excluded ICI exposure. Outcomes were assessed from day 1 through day 1095 after index. Propensity score matching (1:1) was performed (final N = 4,074 per cohort). **Results:** In the matched cohorts (N = 4,074 each), ICI exposure was associated with higher risks of inpatient admissions (41.65% vs 32.78%; RR 1.27; HR 1.22), all-cause mortality (47.62% vs 38.76%; RR 1.23; HR 1.44), respiratory failure (J96) (25.01% vs 15.13%; RR 1.65; HR 1.66), and drug-induced interstitial lung disorders (1.91% vs 0.87%; RR 2.20; HR 4.26). ICI exposure was also associated with increased risk of mechanical ventilation (4.00% vs 2.93%; RR 1.36; HR 1.45), emergency intubation (2.55% vs 2.00%; RR 1.27; HR 1.32), and ED visits (38.98% vs 31.56%; RR 1.24; HR 1.74). Asthma exacerbation (J45.901) showed a modest increase in risk (RR 1.23), with survival analysis not reaching statistical significance (HR 1.15; p = 0.078). **Conclusions:** Among adults with asthma and cancer, ICI exposure was associated with increased risks of hospitalization, respiratory failure, drug-induced interstitial lung disorders, and mortality compared with non-ICI systemic therapy. These findings support close pulmonary monitoring and risk mitigation when initiating ICIs in patients with asthma. Research Sponsor: None.

Real-world data on clinical profile of immune-related adverse events (irAEs) associated with immune checkpoint inhibitors (ICIs) in oncology.

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Background: Immune checkpoint inhibitors (ICIs) are widely used in cancer, and are associated with immune-related adverse events (irAEs) in many organs. Real-world data on the spectrum, timing, severity, and outcomes of irAEs is limited. In this study, we aimed to gather real world data on the immune toxicity of ICIs. **Methods:** We conducted a retrospective cohort study on adult oncology patients on ICI therapy between Jan 2018-Dec 2024. IrAEs were categorized by organ system, time to onset (early < 12 weeks, intermediate 12-24 weeks, and late > 24 weeks), and severity (standard toxicity criteria CTCAEv6.0). Management strategies, therapy discontinuations, hospitalizations, and survival were assessed. **Results:** We screened 652 patients who received ICIs across different cancer types -169 (26%) were identified with irAEs. Sixty-four percent patients had received ICI alone, and the remainder had received ICIs in combination with other agents. The most common organ affected was thyroid (43%), followed by skin (28.4%), and lung (11.8%), more than one organ was affected in 22.5% patients. IrAEs occurred across a broad time frame following treatment- cumulative incidence before 12 weeks was 41.4%, between 12-24 weeks was 44.4%, and beyond 24 weeks was 91.3%. Musculoskeletal, hepatic, pulmonary, gastrointestinal, dermatologic, and pancreatic irAEs generally presented early, with median onset around 10-14 weeks. Renal, ophthalmologic, infusional, and dermatologic irAEs generally occurred across early, and intermediate time frames, while neurological irAEs tended to occur late. Endocrine irAEs, had a median onset of 20.1 weeks, and frequently occurred beyond 24 weeks. Hepatitis, pneumonitis, colitis, CNS and pancreatic toxicity were among the more severe irAEs, with a median CTCAE grade of 3, while renal, endocrine, ophthalmologic, infusional, and dermatologic irAEs were generally of lower severity (grade 1 or 2). IrAE grade > 2 was associated with increased risk of death (HR 2.7, 95% CI 1.1-6.5). Management of irAEs comprised supportive care alone (62%), systemic corticosteroids (31%), or observation alone (8%). Patients with higher grades of irAEs were more likely to receive steroids. Hospitalization was required in 29%, and ICIs were permanently discontinued in 25%. Complete resolution of irAEs was seen in 40%, 5% died attributable to the irAE, and the remainder had partial resolution of irAE with need for continued replacement therapy (as with endocrine irAEs). **Conclusions:** In our real-world practice, oncology patients receiving ICIs had irAEs across a broad range of organ systems, with heterogeneous timing and severity. Several clinically meaningful toxicities presented late in the treatment course, underscoring the importance of long-term monitoring. Occurrence of grade 2 or higher irAEs was associated with higher mortality. Research Sponsor: None.

Association of β -blocker selectivity with survival and immune-related outcomes in melanoma and lung cancer patients treated with immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICIs) are standard of care for advanced melanoma and lung cancer. Retrospective studies suggest that non-selective β -blocker use correlates with improved overall survival, potentially through modulation of the tumor immune microenvironment. However, real-world evidence comparing the effect of selective versus non-selective beta-blockers remains limited. **Methods:** We conducted a multicenter retrospective study using the TriNetX Global Collaborative Network. Adult patients (≥ 18 years) with melanoma or lung cancer treated with immune checkpoint inhibitors (pembrolizumab, nivolumab, ipilimumab, atezolizumab, durvalumab, cemiplimab, or avelumab) were identified. Patients were categorized based on exposure to non-selective β -blockers (carvedilol, propranolol, nadolol, labetalol, timolol) or selective β -blockers (metoprolol, atenolol, bisoprolol, nebivolol, acebutolol) within two months before or at ICI initiation. The index date was first ICI exposure. One-to-one propensity score matching was performed using covariates selected based on baseline imbalance, including demographics, cardiovascular and cerebrovascular comorbidities, and prior procedures. The primary outcome was overall survival. Secondary outcomes included hospitalization and immune-related adverse events (irAEs), defined using a composite endpoint of organ-specific immune-mediated toxicities based on prior published methodology. **Results:** After matching, 3,720 patients with melanoma and 11,160 patients with lung cancer were included in the analysis. Among melanoma patients treated with ICIs, non-selective β -blocker use was associated with lower mortality (HR 0.799; 95% CI 0.652–0.980) and decreased hospitalization (HR 0.865; 95% CI 0.759–0.984) compared with selective β -blockers. Most immune-related adverse events did not differ between groups, except for higher hepatic toxicity with non-selective β -blockers (HR 1.382; 95% CI 1.064–1.796). In lung cancer patients, non-selective β -blocker use was associated with lower mortality (HR 0.847; 95% CI 0.797–0.900), reduced ICU admission (HR 0.87; 95% CI 0.800–0.946), and decreased hospitalization (HR 0.912; 95% CI 0.864–0.963). Additionally, fewer cardiovascular (RR 0.811; 95% CI 0.711–0.925) and respiratory (RR 0.842; 95% CI 0.772–0.918) immune-related adverse events compared with selective β -blockers. **Conclusions:** In this real-world, propensity-matched analysis, non-selective β -blocker use was associated with improved early survival and reduced healthcare utilization among melanoma and lung cancer patients treated with ICIs. These findings suggest that non-selective β -blockers represent a low-cost and available adjunct to immunotherapy and warrants prospective validation. Research Sponsor: None.

Second-generation H1 antihistamine use with survival and immune-related outcomes in lung cancer and melanoma patients receiving immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICIs) are standard of care for melanoma and lung cancer but are associated with immune-related adverse events and variable outcomes. Previous studies suggest that H1 antihistamine use may be associated with improved outcomes, potentially through histamine-mediated modulation of the tumor microenvironment. However, real-world evidence is limited. **Methods:** We conducted a multicenter retrospective study using the TriNetX Global Collaborative Network. Adult patients (≥ 18 years) with melanoma or lung cancer receiving ICIs (pembrolizumab, nivolumab, ipilimumab, atezolizumab, durvalumab, cemiplimab, or avelumab) were identified. Patients were categorized by exposure to second-generation H1 antihistamines (cetirizine, loratadine, fexofenadine, desloratadine, or levocetirizine) within 3 months before or during ICI initiation. One-to-one propensity score matching was performed based on demographics, baseline comorbidities, cancer characteristics, prior treatments, and conditions commonly associated with antihistamine use, including allergic and atopic disorders. The index date was defined as first ICI exposure, and outcomes were assessed from day 1 to day 180. The primary outcome was overall survival. Secondary outcomes included hospitalization and immune-related adverse events (irAEs), defined using a composite endpoint of organ-specific immune-mediated toxicities based on prior published methodology. **Results:** After matching, 2,141 melanoma and 11,812 lung cancer patients were included. In lung cancer patients, H1 antihistamine use was associated with reduced all-cause mortality (HR 0.769, 95% CI 0.727–0.815), lower hospitalization rates (HR 0.862, 95% CI 0.821–0.906), fewer intensive care unit admissions (HR 0.867, 95% CI 0.797–0.943) and reduced emergency department use (HR 0.940, 95% CI 0.899–0.984). 6-month overall survival was 80.93% in antihistamine users vs 75.98% in non-users. It was also associated with decreased endocrine (HR 0.843, 95% CI 0.776–0.916), and musculoskeletal irAEs (HR 0.840, 95% CI 0.752–0.938). In patients with melanoma, H1 antihistamine use was associated with reduced all-cause mortality (HR 0.685, 95% CI 0.581–0.808), lower hospitalization rates (HR 0.837, 95% CI 0.734–0.955), and reduced neutropenia (HR 0.441, 95% CI 0.266–0.729). 6-month overall survival was 88.15% vs 83.20%, respectively. No statistically significant differences were observed across other major immune-related organ systems. **Conclusions:** Second-generation H1 antihistamine use was associated with improved early survival and reduced healthcare utilization among melanoma and lung cancer patients treated with ICIs, without a significant increase in irAEs. Despite the retrospective design and potential confounding, prospective validation is warranted. Research Sponsor: None.

Trends in ischemic stroke and ischemic heart disease-related mortality among patients with malignancies in the United States: A 25-year CDC-WONDER analysis (1999-2023).

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Background: Substantial advances in cancer screening, diagnostics, and therapeutic strategies have improved survival and quality of life. Despite these efforts, cancer-related complications continue to contribute significantly to morbidity and mortality. Malignancies induce a pro-thrombotic state and substantially increase the risk of venous and arterial thromboembolism. As a result, the patients with cancer have a higher incidence of Ischemic stroke (IS) and ischemic heart disease (IHD) compared to the general population. The greatest risk of these thromboembolic diseases is greatest during the first six months of cancer diagnosis, but remains elevated thereafter. In this study, we sought to assess temporal trends and socio-demographic differences in ischemic stroke and ischemic heart disease related mortality among patients with neoplasms. **Methods:** We analyzed deidentified CDC WONDER death certificate data to assess malignant neoplasm, (ICD = C00-C97) and ischemic heart disease (ICD = I20-I25) and ischemic stroke (ICD = I63) related mortality in patients of all ages. Age-adjusted mortality rates (AAMR) per 100,000 persons and average annual percent change (AAPC) were calculated and stratified by year, gender, state, urban-rural status, census region, place of death (POD), and age group. **Results:** From 1999 to 2023, 1235844 deaths were attributed to Ischemic stroke and ischemic heart disease-related deaths in cancer patients. Overall, AAMR decreased from 19.7 in 1999 to 12.9 in 2023 (APC -1.74*, 95% CI: -1.88 to -1.63). Males had higher mortality rates than females throughout the period (23.26 vs 8.88, respectively). Racial analysis showed that non-Hispanic whites had the highest mortality (AAMR: 15.064), followed by Blacks or African Americans (AAMR: 14.24); in contrast, Asians or pacific islanders had the lowest mortality (AAMR: 7.48, data available till 2020). The Midwest region had the highest mortality of all census regions (AAMR: 15.92). Lastly, non-metropolitan areas had higher mortality rates than metropolitan areas (AAMR of 15.75 vs 14.04, respectively). **Conclusions:** Overall mortality rates in cancer patients with co-morbid ischemic stroke and ischemic heart diseases declined from 1999 to 2023. However, higher mortality rates were observed among men, non-Hispanic Whites, residents of the Midwest, and those living in non-metropolitan areas of the U.S., underscoring the need for targeted public health efforts, and equitable access to cardio-oncology preventive care in these high-risk groups. Research Sponsor: None.

Five-year survival disparities in two population-based cohorts of adults with early-onset colorectal cancer.

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Background: Early-onset colorectal cancer (EO-CRC) is now the leading cause of cancer-related death in those under the age of 50 despite advances in treatment. However, the impact of specific sociodemographic and clinical factors on long-term survival remains poorly characterized. We evaluated 5-year survival patterns and risk factors across two diverse, population-based cohorts to optimize risk reduction strategies and survivorship care delivery.

Methods: We constructed two cohorts of adults < 50 years of age with newly diagnosed EO-CRC from 2015 to 2018 (stages I-III) and treated with curative-intent surgery. One cohort was derived from three SEER registries (Georgia, Los Angeles County, Kentucky; n = 2995) and one cohort was derived from the Veteran's Health Administration (VHA) (n = 295). Pathologic-confirmed recurrence was identified in the follow-up period 6 months to five years after curative-intent surgery via human review of electronic pathology reports. Five-year survival was estimated from the date of curative-intent surgery to five years post-surgery. Adjusted risk of CRC-specific mortality was estimated in both populations using multivariable proportional hazards regression, adjusting for key demographic and clinical characteristics. **Results:** The proportion of patients surviving 5 years was 86% in the SEER cohort and 92% in the VHA cohort. Overall, 14% experienced recurrence in SEER and 18% in VHA, and recurrence was strongly associated with reduced survival in both cohorts (both p < 0.01). Five-year survival varied by clinical stage and was higher in the VHA across all stages (SEER: 93% stage I, 87% stage II, and 76% stage III vs. VHA: 97% stage I, 93% stage II, and 88% stage III). Mortality risk varied by race/ethnicity in the SEER cohort only: Hispanic patients (adjusted HR 1.6, 95% CI: 1.1–2.2) and Black patients (adjusted HR 1.9, 95% CI: 1.5–2.5) had a greater risk of 5-year mortality vs. white patients. Age at diagnosis, sex, and living in a rural area were not significantly associated with mortality in either cohort. Rectal tumors (vs. colon) were associated with an increased risk of mortality in VHA (adjusted HR: 2.5, 95% CI: 1.0–6.4), but not in SEER. Lymphovascular invasion was associated with an increased risk of mortality in both cohorts.

Conclusions: There are critical sociodemographic and clinical disparities in survival among adults with stage I-III EO-CRC. These distinct patterns observed between the two cohorts underscore the influence of varying population-level risk profiles. Tailoring survivorship care to identify and support these high-risk subgroups is essential to mitigate disparities and improve long-term outcomes in this growing patient population. Research Sponsor: National Cancer Institute; R37CA275907.

Assessment of the role of rapid drug desensitization to treat cancer patient with infusion-related allergic reactions.

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Background: Rapid Drug Desensitization (RDD) as The Castells protocol is based on progressively increasing concentrations and infusion rates of the drug under close monitoring, inducing temporary drug tolerance. To assess the role of Rapid Drug Desensitization (RDD) to treat cancer patient with infusion-related allergic reactions (IRRs) we planned an observational trial in 2021. **Methods:** From 2021 to 2025 all patients experiencing IRRs at the Rimini Oncology Unit, after an allergological evaluation, were treated according to the Castells desensitization protocol. We analyzed the safety of this approach as well as the treatment discontinuation rate. The IRR severity was classified (grade 1-3) using the Brown classification from 2004. **Results:** A total of 155 patients were treated with RDD. Among drugs administered using a desensitization protocol, drugs administered with the RDD were paclitaxel (38.06%), oxaliplatin (25.80%), docetaxel (14.10%), and carboplatin (12.9%), irinotecan (1.94%), etoposide (1.94%), liposomal doxorubicin (1.29%), trastuzumab (1.29%), atezolizumab (0.65%), cetuximab (0.65%), cyclophosphamide (0.65%), and cisplatin (0.65%). Grade 3 reactions occurred in 1.29% of patients during RDD, while grade 2 and grade 1 reactions were observed in 3.87% and 2.58%, respectively. No deaths associated with desensitization treatment occurred. The IRRs were managed with treatment interruption and administration of steroids and antihistamines. Notably, 3.22% of patients experienced an allergic reaction during RDD but were able to complete treatment. In total 132 patients completed the planned treatment (85.2%) using the RDD approach. Among those who discontinued, 7 patients (4.5%) stopped due to allergic reactions during the first desensitization cycle. The remaining treatment discontinuations were due to clinical deterioration, patient decision or transfer to another institution (1.9% each), progressive disease (3.9%), or other causes (0.7%). We summarized the characteristics in the table. **Conclusions:** The RDD protocol is safe and permits to maintain the original schedule in the most part of cancer patients that present a major allergic reaction during chemotherapy. Further trials are probably needed to better define the role of RDD and the drugs primarily candidate to the desensitization protocol. Research Sponsor: None.

	Number of patients	% of the total (155 patients)
Treatment completed	132	85.2%
Discontinuation for infusional reaction	7	4.5%
Discontinuation for clinical deterioration	3	1.9%
Discontinuation for patient decision	3	1.9%
Discontinuation for progressive disease	6	3.9%
Discontinuation for transfer to another institution	3	1.9%
Discontinuation for other causes	1	0.7%

Trends and racial disparities in pulmonary embolism–related mortality among older adults with neoplasms: A population-based retrospective study in the United States from 1999-2020.

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Background: Pulmonary embolism (PE) remains a major cause of preventable mortality, particularly among older adults with cancer who face heightened thrombotic risk. Understanding temporal trends in PE-related deaths is essential for guiding prevention and early detection. This study evaluates national patterns and racial disparities in PE-related mortality among older adults with neoplasms. **Methods:** We performed a retrospective cross-sectional analysis of the national death certificate data from the CDC's WONDER database. We included persons ≥ 65 years of age with neoplasms (ICD-10 code C00-D48) as the underlying cause of death and PE (ICD-10 code I26) as a contributing cause of death. The exposure variable was the year of death, and the outcome was PE-related age-adjusted mortality rate (AAMR) stratified by sex, race, rural-urban status, and census region. We calculated the PE-related AAMR in neoplasm per 100,000 population. Trends were evaluated with Joinpoint regression and expressed as an average annual percentage change (AAPC) with a 95% confidence interval (CI). $P < 0.05$ defined statistical significance. **Results:** Of 928 million people, 104,743 PE-related deaths occurred in older adults with neoplasms (AAMR 11.4). The AAMR was higher in males (13.3 vs 10.1 in females; $P < 0.01$), Black (17.0 vs 11.2 in White, $P < 0.000001$), and the Midwest census region (12.3 vs 11.7 in NorthEast, the Midwest, and 10.4 in the South; $P < 0.0001$). The AAMR was similar in rural areas (11.4 vs 11.3 in urban areas, $P < 0.000001$). The overall PE-related AAMR in neoplasms increased from 8.7 to 14.1 (AAPC 4.03%; CI: 3.12– 5.23). Furthermore, the AAMR increased in males (AAPC 3.37%; CI: 1.61–6.6) and females (AAPC 4.53%; CI: 3.15–6.20). Similarly, it increased in Black (AAPC 3.14%; CI: 2.42–4.07), White (AAPC 3.98%; CI: 3.07–5.14), rural (AAPC 3.70%; CI: 2.69–5.39), urban (AAPC 4.24; CI: 3.44–5.23), and across all geographic census regions. **Conclusions:** Pulmonary embolism related mortality among older adults with neoplasms has risen steadily over the past two decades across all demographic and geographic groups. Given that cancer-associated thrombosis is a well-recognized and largely preventable complication, these findings suggest important gaps in the prevention, recognition, and management of PE in oncology populations at the health-system level. The consistent upward trend highlights an urgent need to strengthen thromboprophylaxis strategies, risk stratification, and early detection efforts in older adults with cancer to reduce avoidable mortality. Research Sponsor: None.

Safety of immune checkpoint inhibitors in solid tumor patients with hepatitis C: A real-world analysis.

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Background: Patients with hepatitis C virus (HCV) infection are commonly excluded from immune checkpoint inhibitor (ICI) trials. We evaluated hepatotoxicity and outcomes after ICI therapy in patients with versus without HCV. **Methods:** Retrospective cohort study using the TriNetX Research Network (2014–2024). Adults with solid tumors initiating ICIs were classified as HCV if they had detectable HCV RNA and/or ICD-10 B18.2 (chronic viral hepatitis C) within 1 year prior to ICI start. Cohorts were 1:1 propensity-score matched on demographics, comorbidities, cancer type, metastatic site, and baseline liver tests. Outcomes from day 1–90 after ICI started were ALT ≥ 150 U/L, total bilirubin ≥ 3 mg/dL, diagnosis-coded hepatotoxicity, and diagnosis-coded hepatic failure. Overall survival (OS) was assessed for up to 5 years. A sensitivity analysis restricted HCV definition to lab-confirmed HCV RNA (no ICD-10 inclusion). **Results:** In the primary analysis, 1,157 HCV and 109,309 non-HCV ICI-treated patients were identified; 1,137 patients remained per group after matching. Patients with Hep C had a higher risk of ALT ≥ 150 U/L, although this did not reach statistical significance (7% vs 5%; $p = 0.066$). There was no difference in the risk of bilirubin ≥ 3 mg/dL (5.0% vs 5.0%; $p = 1.0$). Diagnosis-coded hepatotoxicity was similar (1.8% vs 1.8%; $p = 0.875$), while diagnosis-coded hepatic failure was higher in the HCV cohort (4.7% vs 2.5%; $p = 0.005$). Median OS was 20.1 vs 17.2 months ($p = 0.0595$). In the RNA-only sensitivity analysis (308 matched patients), there was no significant difference in overall survival between patients with and without HCV prior to treatment (27% vs 32%; $p = 0.7489$). However, the risk of ALT ≥ 150 U/L was significantly higher in the HCV group (10% vs 5%; $p = 0.0058$). There was no significant difference in mean bilirubin values after treatment ($p = 0.0636$). **Conclusions:** Pre-existing HCV was associated with an increased risk of transaminitis in patients receiving immunotherapy, but there was no statistically significant difference in biliary toxicity or median overall survival. There is also an approximate two-fold increased risk of hepatic failure. These real-world data highlight the importance of closely monitoring for hepatotoxicity in patients receiving immunotherapy and support ICI use in patients with HCV. Research Sponsor: None.

Real-world resource use and cost in patients treated with originator or biosimilar rituximab in a large U.S. insurance claims database.

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Background: Rituximab-pvvr, Rituximab-arrx, and Rituximab-abbs are monoclonal antibodies approved by the FDA as biosimilars to originator rituximab. All are approved for treatment of non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL). Biosimilars are intended to deliver equal clinical outcomes to originators at a lower cost, but there remains limited ‘real-world’ investigation of these outcomes. This study describes and compares resource use and cost for patients receiving originator or biosimilar rituximab in the Carelon Research Healthcare Integrated Research Database (HIRD). **Methods:** We conducted a retrospective cohort study of adults with newly diagnosed NHL and CLL identified by ICD-10 codes between 1/1/2018 and 7/31/2024 in the Carelon Research HIRD and treated with rituximab. Included patients had ≥1 claim for originator or biosimilar rituximab after NHL or CLL diagnosis. Baseline demographics were assessed at rituximab initiation (*index date*). Inpatient, outpatient, and emergency department (ED) resource use and medication cost were assessed over one year following rituximab initiation. Costs were inflation-adjusted to 2024 USD. Originator and biosimilar rituximab groups were compared using t-test or ANOVA to assess mean differences in resource use and cost. **Results:** A total of 11,525 patients met inclusion criteria with mean age of 64.4 years, 57.2% male, and 76.9% reporting white non-Hispanic race/ethnicity. Most of the cohort (89.8%) were diagnosed with NHL. There were no significant differences in mean follow-up duration (p=0.960), rituximab infusions (p=0.987), treatment duration (p=0.106), inpatient hospitalizations (p=0.241), or ED visits between groups (p=0.702) (*see table*). Mean overall medication costs were significantly lower in all biosimilar groups vs. originator (p<0.001). **Conclusions:** In this large real-world cohort of NHL and CLL patients, resource use was similar in patients treated with originator and biosimilar rituximab, but medications costs were significantly lower in the biosimilar groups. Our findings demonstrate how biosimilar therapies in cancer can deliver similar clinical outcomes to originators, while generating meaningful cost savings for the U.S. healthcare system. Research Sponsor: Pfizer.

Mean 1-Year Outcomes	Originator Rituximab (n=7,123)	Biosimilar Rituximab-pvvr (n=1,846)	Other Rituximab Biosimilars (n=2,556)
Follow-Up Duration, Months (SD)	10.8 (2.7)	10.8 (2.7)	10.8 (2.7)
Count of Rituximab Infusions (SD)	5.7 (2.5)	5.7 (2.6)	5.7 (2.5)
Rituximab Treatment Duration, Months (SD)	4.2 (3.3)	4.1 (3.3)	4.1 (3.3)
Count of All-Cause Inpatient Stays (SD)	1.6 (3.1)	1.6 (3.2)	1.5 (2.9)
Count of All-Cause ED Visits	0.6 (1.4)	0.6 (1.3)	0.6 (1.2)
Medication & Related Costs (SD)*	\$123,499 (\$145,374)	\$77,728 (\$96,377)	\$90,868 (\$122,510)

*Includes all medications paid under medical benefit, including rituximab.

Impact of concomitant antibiotic exposure on overall survival in patients with esophagogastric cancer treated with immune checkpoint inhibitors: A real-world cohort study.

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Background: Gut microbiota composition plays a critical role in mediating response to immune checkpoint inhibitors (ICIs). Antibiotic exposure has been associated with impaired ICI efficacy across tumor types; however, data specific to esophagogastric cancers remain limited. We evaluated the association between peritreatment antibiotic exposure and overall survival (OS) among patients with advanced esophagogastric cancer receiving ICIs in routine clinical practice. **Methods:** We conducted a retrospective cohort study using the TriNetX Global Collaborative Network. Adult patients with advanced or metastatic esophageal or gastric adenocarcinoma who received nivolumab- or pembrolizumab-based therapy between 2016 and 2024 were identified. Patients were categorized as antibiotic-exposed (receipt of systemic antibiotics within 60 days before or after ICI initiation) and non-exposed (no documented antibiotic exposure during the same period). Cohorts were 1:1 propensity score matched for age, sex, cancer subtype, Charlson comorbidity index, infection-related diagnoses, baseline corticosteroid use, and hospitalization within 30 days prior to ICI initiation. The primary endpoint was OS. Kaplan–Meier and Cox proportional hazards models were used for analysis. Sensitivity analyses evaluated the timing and duration of antibiotic exposure. **Results:** After matching, 3,024 patients were included (1,512 per cohort). Baseline characteristics were well balanced (mean age 63.7 years; 34% female; median Charlson comorbidity index 5). At a median follow-up of 19.8 months, antibiotic exposure was associated with significantly worse overall survival compared with non-exposure. Median OS was 10.6 months in antibiotic-exposed patients versus 14.3 months in non-exposed patients (log-rank $p < 0.001$). Antibiotic exposure was independently associated with inferior OS (HR 1.34, 95% CI 1.22–1.47). The negative association was most pronounced among patients with broad-spectrum antibiotic exposure (HR 1.41) and among those with antibiotic exposure within 30 days prior to ICI initiation (HR 1.38). Findings remained robust in sensitivity analyses excluding patients with documented sepsis or prolonged hospitalization. **Conclusions:** In this large real-world cohort of patients with esophagogastric cancer treated with ICIs, peritreatment antibiotic exposure was associated with significantly worse overall survival. These findings further support the role of the gut microbiome in modulating immunotherapy response and underscore the importance of judicious antibiotic use during ICI therapy. Research Sponsor: None.

EU-OPEN: A novel approach for generating European oncology real-world evidence at scale.

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Background: The European Oncology Platform for Evidence Needs (EU-OPEN) is a strategic initiative to generate high-quality oncology real-world evidence (RWE) in Europe. It focuses on establishing multi-study partnerships with access to clinically rich data, regional medical expertise and to enable adoption of novel approaches to conduct research on cohorts of interest efficiently at scale. **Methods:** For each tumor area (*e.g.*, *EU-OPEN Breast*), master protocols aligned to specific patient populations (*e.g.*, *ER+/HER2- earlier stage breast cancer or triple negative metastatic breast cancer*) are developed alongside a fit-for-purpose data assessment at prospective data partners (primarily hospital sites and registries). Data partners are selected based on their data availability, data quality and operational aspects of collaboration. After finalizing the master protocol, supporting documentation (including common data models and statistical analysis plans) are prepared and shared with partner sites for consistent execution. Data partners then curate, harmonize and analyze data in accordance with the study requirements. Studies and patient cohorts can be efficiently refreshed to capture longer-term outcomes. **Results:** The initiative began in 2024 with a multi-tumor assessment of prospective data partners and an early breast cancer pilot study (completed and published in 2025). EU-OPEN has since expanded to metastatic breast, endometrial, ovarian and esophageal cancers. Collectively these studies encompass 11 cohorts and plan to include > 2,200 patients. Future plans include expanding to additional tumor areas and data partner types, adopting advanced capabilities such as natural language processing (NLP) to maintain 'live cohorts' for rapid analyses, and strengthening governance through clinical and data committees across partners. **Conclusions:** EU-OPEN demonstrates a scalable, efficient approach to generating research-grade European Oncology RWE at scale. As the initiative grows, adoption of novel technologies and deeper collaboration with data and clinical experts will further accelerate insight generation. Research Sponsor: None.

Midday immune checkpoint inhibitor (ICI) infusion influence on survival in patients with metastatic cancer: A real-world chrono-immunotherapy study.

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Background: Circadian rhythms regulate immune activity, and earlier ICI dosing has been linked to better survival. However, prior findings remain inconsistent, often relying on pre-defined time categories. To address this, we clustered actual infusion times to assess survival associations in a real-world cohort. **Methods:** This retrospective study included metastatic cancer patients treated with ICIs. Mean dosing times (up to 24 infusions/patient) were analyzed using circular statistics and clustered via k-means. Overall survival (OS) was defined from ICI initiation to progression, death, or last follow-up, and analyzed via Kaplan-Meier and multivariable Cox regression adjusted for cancer and ICI type. **Results:** A total of 640 patients (median age 61 years [range 23–87]; 78% male) were included. The most common tumor types were non-small cell lung cancer (52%), renal cell carcinoma (19%), and malignant melanoma (12%), followed by urothelial (5.5%) and small cell lung cancer (4.8%). The majority of patients received nivolumab (74%) or pembrolizumab (11%), while a smaller proportion were treated with other ICIs including atezolizumab (6.3%), avelumab (2%), or ipilimumab-based combinations (5.4%). ECOG performance status was 0–1 in 80% of patients. The most frequent metastatic sites were lymph nodes or soft tissue (78.6%), lungs (48.1%), bones (32.8%), liver (17.7%), and central nervous system (14.2%). Based on mean ICI infusion times, patients were grouped into three clusters: cluster 1 (2:15 PM, n = 76), cluster 2 (1:31 PM, n = 151), and cluster 3 (11:04 AM, n = 413). Median OS was 50.4, 28.2, and 15.7 months in Clusters 2, 1, and 3, respectively (log-rank p = 0.003). In multivariable analysis, Cluster 2 showed improved OS compared to Cluster 1 (Hazard Ratio [HR] 0.52, 95% Confidence Interval [CI] 0.31–0.86, p = 0.01), while no difference was seen between Clusters 3 and 1 (HR 1.13, 95% CI 0.75–1.70, p = 0.59). **Conclusions:** ICI administration around midday was associated with the longest survival, aligning with circadian peaks in T-cell infiltration, dendritic cell migration, and immune responsiveness. These findings support a personalized chrono-immunotherapy approach based on intrinsic biological rhythms. Research Sponsor: None.

Ischemic heart disease as a competing cause of death among patients with lung cancer in the United States: A multiple cause-of-death analysis, 1999–2023.

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Background: Despite improvement in lung cancer prevention, early diagnosis & management, Ischemic heart disease (IHD) has become a major concurrent cause of mortality in lung cancer. Population level evidence on long term deaths due to IHD & lung cancer especially across sex & racial groups are lacking. Identification of these trends is necessary for cardio-oncology risk stratification & promote equitable survivorship care. **Methods:** We used the CDC WONDER Online Database to obtain mortality data for IHD & Lung Cancer from 1999–2023 from patients aged 45–85 & above. We used current final multiple cause of death data from 1999–2020 & 2018–2023. We used ICD-10 codes I20–I25 for IHD & C33–34 for Lung cancer. Data were stratified by Race (Non-Hispanic [NH] American Indian or Alaska Native, NH Asian or Pacific Islander, NH Black or African American, NH White, Hispanic or Latino), sex (male & female) and age groups (45–85+). We calculated age-adjusted mortality rates (AAMR) per 100,000 population based on the 2000 US standard population. Temporal mortality trends were analyzed using Joinpoint regression. ($P < 0.05$). **Results:** From 1999–2023, AAMR from lung cancer & IHD decreased in most demographic groups. Males had higher AAMR than females, with mortality decreasing from 20.3 to 10.6 per 100,000, compared with a decline from 6.8 to 4.6 per 100,000 among females. Joinpoint regression identified substantial reduction among males from 1999–2010 (annual percent change [APC] -2.35% , $p < 0.05$) & 2010–2016 (APC -5.45% , $p < 0.05$), followed by stabilization. Among females, declines were observed from 2005–2012 (APC -2.76% , $p < 0.05$) & 2012–2015 (APC -7.35% , $p < 0.05$), with a nonsignificant plateau thereafter. NH Black exhibited higher AAMRs despite significant declines from 2005–2018 (APC -4.11% , $p < 0.05$). NH White showed persistent declines from 1999–2017, followed by a marginal increase during 2017–2021. Hispanic & Asian or Pacific Islander individuals maintained the lowest AAMRs, with decreasing trends & brief late-2010s increases in select subgroups, while American Indian or Alaska Native individuals exhibited greater year-to-year variability without statistically significant joinpoints. **Conclusions:** During 1999–2023, mortality from IHD & lung cancer decreased significantly in the US. Males & NH Black experienced a major disease burden. Recent improvement in death trends among the select patient population showed appropriate cardiovascular risk management in survivors with lung cancer. This analysis highlighted the importance of cardio-oncology care models & precision-guided, equity-driven interventions to decrease cardiovascular mortality among patients with lung cancer. Research Sponsor: None.

Real-world cost effectiveness of androgen receptor pathway inhibitors for metastatic hormone sensitive prostate cancer: An economic evaluation utilizing data from the International Registry for Men with Advanced Prostate Cancer (IRONMAN).

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Background: Several therapies are approved for metastatic hormone sensitive prostate cancer (mHSPC), with differing efficacy and costs. While many cost-effectiveness analyses (CEAs) rely on randomized trial data, such analyses lack generalizability to real-world practice. We evaluated the real-world cost effectiveness (CE) of adding androgen receptor pathway inhibitors (ARPIs) to androgen deprivation therapy (ADT) for first-line (1L) mHSPC using the IRONMAN registry (NCT03151629). **Methods:** We conducted a US public payer perspective CEA using individual patient-level IRONMAN data. Eligible patients (pts) received 1L ADT alone, ADT + enzalutamide (ENZ), or ADT + apalutamide (APA) with ≥ 1 follow-up visit. A 3-state Markov model with 1-month cycles and a 10-year horizon was used. Progression-free survival (PFS) was proxied by time-to-next-treatment (TTNT); overall survival (OS) was time from 1L initiation to death or last follow-up. Costs and outcomes were discounted at 3% per year. Outcomes were measured in life-years gained (LYG) and incremental cost-effectiveness ratios (ICER) were reported. Uncertainty was assessed via one-way sensitivity analysis and probabilistic sensitivity analysis. A scenario analysis evaluated hypothetical ENZ price reductions aligned with planned Inflation Reduction Act negotiations. **Results:** 1187 pts with mHSPC met inclusion (ADT: n=405, ENZ: n=412, APA: n=370; Table 1). In the base case, both ARPI strategies improved OS versus ADT alone, though only APA provided a statistically significant reduction in risk (ENZ: HR 0.78, 95% CI 0.58–1.03, p=0.08; APA: HR 0.50, 95% CI 0.36–0.70, p<0.001). Using TTNT as a proxy for PFS, ADT alone had a reduced risk compared to either ARPI (ENZ: HR 1.97, 95% CI 1.39–2.77, p<0.001; APA: HR 1.51, 95% CI 1.05–2.18, p=0.028); underreporting of subsequent therapies in the ADT alone group may have contributed to this finding. Median follow-up was 26.7 months; median TTNT and OS were not reached. Neither ARPI strategy was CE at conventional US thresholds (ENZ: ICER = \$444,947/LYG; APA: ICER = \$669,530/LYG), and ENZ would require a 79% price discount to meet CE thresholds. Sensitivity analyses supported the base case results. **Conclusions:** Adding ENZ or APA to ADT for 1L mHSPC improved OS but was not found to be to be cost-effective at current US prices over a 10-year horizon. Substantial ENZ price reductions would be required to reach commonly used CE thresholds. Research Sponsor: Movember Foundation; Amgen; Astellas; AstraZeneca; Bayer; Johnson & Johnson Innovative Medicine; Merck; Novartis; Sanofi.

Baseline characteristics.

	ADT (N = 405)	ENZ (N = 412)	APA (N = 370)
Median age at study entry (IQR)	71 (64, 78)	71 (65, 76)	71 (65, 76)
PSA at study entry (ng/mL)			
Median (IQR)	9 (1, 53)	4 (1, 21)	3 (0, 13)
Range	0, 5430	0, 3560	0, 5530
Missing (%)	137 (34)	62 (15)	56 (15)
Duration of follow-up (months)			
Median (IQR)	24 (10, 41)	28 (17, 41)	28 (17, 40)
Range	3, 80	3, 67	2, 64

Neurological immune-related adverse events and overall survival in patients with advanced solid tumors treated with immune checkpoint inhibitors in a global real-world analysis.

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Background: Immune checkpoint inhibitors (ICIs) have transformed the treatment of advanced malignancies, and many immune-related adverse events have been associated with improved treatment outcomes. Neurological immune-related adverse events, however, are uncommon, often severe, and poorly characterized in large real-world populations. Whether the development of neurological toxicity during ICI therapy is associated with long-term survival remains unclear. We examined the relationship between neurological immune-related adverse events and overall survival in a large real-world cohort of patients treated with ICIs. **Methods:** We performed a retrospective cohort study using data from the TriNetX Global Collaborative Network. Adult patients with advanced solid tumors treated with immune checkpoint inhibitors, including pembrolizumab, nivolumab, ipilimumab, atezolizumab, or durvalumab, were identified. Patients who developed neurological immune-related adverse events (such as encephalitis, meningitis, Guillain-Barré syndrome, myasthenia gravis, or immune-mediated polyneuropathy) within six months of treatment initiation were compared with patients who did not experience neurological toxicity. One-to-one propensity score matching was used to balance age, sex, race, ethnicity, and major medical comorbidities. Overall survival was assessed in the matched cohorts. **Results:** After matching, 9,744 patients were included (4,872 per cohort) with well-balanced baseline characteristics. Patients who developed neurological immune-related adverse events experienced significantly worse overall survival compared with matched controls. Median overall survival was 473 days in the neurological toxicity cohort versus 1,083 days among patients without neurological events ($p < 0.001$). Development of neurological immune-related adverse events was associated with a 57% higher risk of death (hazard ratio 1.57; 95% CI, 1.48–1.67). At five years, survival probability was 30.9% in the neurological toxicity group compared with 41.7% in the control group. **Conclusions:** In this large real-world analysis, neurological immune-related adverse events were associated with substantially worse overall survival in patients treated with immune checkpoint inhibitors. In contrast to other immune-related toxicities that may reflect effective immune activation, neurological complications appear to confer significant morbidity and mortality that outweigh potential treatment benefit. These findings highlight the need for early recognition, multi-disciplinary management, and careful risk-benefit assessment when neurological toxicity develops during immunotherapy. Research Sponsor: None.

Pulmonary immune-related adverse events post-immune checkpoint inhibitors (ICI): Real-world experience.

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Background: Immunotherapy (IT) has transformed cancer treatment and is often better tolerated than chemotherapy; however, immune-related pulmonary adverse events (Pulm-AE) have emerged as clinically significant and potentially treatment-limiting toxicities that may impact morbidity, treatment continuity, and survival. Real-world *comparative data* on Pulm-AE risk remain limited. We evaluated the incidence, cumulative risk, severity, and clinical outcomes of Pulm-AEs in patients receiving IT versus non-IT systemic therapies. **Methods:** We conducted a retrospective cohort study of 5,556 adult cancer patients treated at the Cleveland Clinic between 2010–2022. Included cancers were bladder (stage II–IIIA n = 476; IV n = 158), endometrial IV (n = 157), esophageal/gastric (II–III n = 797; IV n = 590), head & neck IV (n = 36), renal (III n = 88; IV n = 223), metastatic melanoma (n = 45), and lung cancers: non-squamous NSCLC (IIIB n = 206; IV n = 1,609), squamous NSCLC (IIIB n = 182; IV n = 366), and SCLC IIIB–IV (n = 623). Patients receiving IT ($\pm$ chemotherapy or radiation) were compared with non-IT regimens and followed from treatment initiation to Pulm-AE, death, or last encounter. Pulm-AEs included pneumonitis, pleural effusion $\pm$ pleuritis, and interstitial lung disease. Data were collected on demographics, CTCAE grade, timing, management, and outcomes. Incidence rates per 100 person-years (py) were estimated using Poisson regression, cumulative incidence (CIR) using Kaplan–Meier methods, and adjusted hazard ratios (HRs) using time-dependent Cox models. **Results:** Of 5,556 patients, 2,133 (38%) received IT, including 1,291 (60%) as first-line therapy; 99.9% of IT exposure was ICI. The cohort was 38% female, 87% White, with a median age of 66 years. Over a median follow up of 14 months (CI: 6–35), 127 Pulm-AEs occurred, including 51 among first-line IT recipients. Pulm-AE incidence was higher with IT than non-IT (0.2 vs 0.06 per 100 py; $P < 0.05$), driven primarily by pneumonitis (0.16 vs 0.04 per 100 py; $P < 0.05$). At 24 months, CIR for Pulm-AEs was 5.5% with first-line IT versus 2.0% without (HR 3.50, $P < 0.001$); pneumonitis CIR was 4.3% versus 1.3% (HR 5.21, $P < 0.001$). Among pneumonitis cases, 86% were CTCAE grade 2–4, 81% required steroid therapy, and 28% resulted in permanent IT discontinuation, frequently necessitating long-term immunosuppression. Other Pulm-AEs in the IT & non-IT groups were pleural effusion (n = 10, 24), pleuritis without effusion (n = 0, 2), and interstitial lung disease (n = 0, 2). **Conclusions:** Receipt of IT was associated with a significantly increased risk of Pulm-AEs, primarily clinically significant pneumonitis. These toxicities were common (~7% by 24 months), frequently severe, and often led to irreversible damage and treatment cessation, underscoring the need for vigilant monitoring, early recognition, multidisciplinary management, and prompt intervention to minimize morbidity. Research Sponsor: None.

Comparative real-world survival outcomes of ribociclib and abemaciclib in breast cancer.

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Background: Cyclin-dependent kinase 4/6 inhibitors (CDK4/6i), including ribociclib and abemaciclib, are widely used in hormone receptor-positive, HER2-negative high-risk early-stage breast cancer in combination with endocrine therapy. While randomized trials have demonstrated survival benefits, comparative real-world outcomes between these agents remain limited. This study evaluates all-cause mortality among patients treated with ribociclib versus abemaciclib using a large real-world database. **Methods:** We conducted a retrospective cohort study using the TriNetX US Collaborative Network, a global federated health research network, including adult patients with breast cancer treated with ribociclib ($n = 7,697$) or abemaciclib ($n = 12,626$) within the past 20 years. Two cohorts were constructed and balanced using 1:1 propensity score matching (PSM) based on age at diagnosis, sex, and race. The primary outcome was all-cause mortality at 1, 3, and 5 years. Kaplan-Meier survival curves and Cox proportional hazards models were used to estimate survival probabilities and hazard ratios. **Results:** After PSM, a total of 15,374 patients were included (7,687 per cohort). Mean age was 60.2 ± 13.5 years in the ribociclib cohort and 60.2 ± 13.4 years in the abemaciclib cohort. Most patients were female (99%) and White (72%). At 1 year, survival probability for ribociclib was 91.5% compared with 89.0% for abemaciclib (hazard ratio 0.74, 95% CI 0.66–0.84; log-rank $p < 0.001$). There was no significant difference in survival probabilities at 3 years (70.1% vs 72.1%) or 5 years (56.6% vs 55.1%), with hazard ratios not significantly different from 1.0. **Conclusions:** In this real-world analysis, ribociclib use was associated with lower all-cause mortality at 1 year compared with abemaciclib; however, this difference did not persist at longer follow-up. These findings should be interpreted cautiously given potential residual confounding and differences in clinical indications between agents. Further studies accounting for disease stage and treatment context are warranted. Research Sponsor: None.

When autoimmunity meets immunotherapy: Immune checkpoint inhibitors in cancer patients with rheumatoid arthritis.

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Background: Immune checkpoint inhibitors (ICIs) improve outcomes across multiple malignancies but are associated with immune-related adverse events (irAEs). Patients with rheumatoid arthritis (RA) have been largely excluded from clinical trials, and disease-specific real-world data remain limited. We evaluated irAEs and survival outcomes in cancer patients with and without preexisting RA treated with ICIs. **Methods:** We conducted a retrospective cohort study using the TriNetX Research Network. Patients with RA diagnosed prior to ICI initiation were compared with patients without RA. Propensity score matching (1:1) was performed on age, sex, race, ethnicity, cancer type, ICI type, comorbidities, metastatic disease, other autoimmune conditions, and preexisting irAE codes. Outcomes were measured beginning 1 day after ICI initiation. Overall survival (OS) and organ-specific irAEs were assessed. Sensitivity analyses were conducted excluding patients with baseline glucocorticoid or disease-modifying anti-rheumatic drug (DMARD) exposure to account for differences in preexisting autoimmune treatment. **Results:** Before matching, 3,172 patients with RA and 156,543 without RA were identified. After matching, 3,162 patients were included in each cohort with balanced baseline characteristics and laboratory values. OS was numerically lower in the RA cohort but not statistically significant (29% vs 30%; median 21.9 vs 23.7 months; $p = 0.1861$). Early survival differed within 6 months (76% vs 78%; $p = 0.0415$) but not at 1 year. RA patients experienced higher rates of gastrointestinal (8.4% vs 6.9%; $p = 0.0234$) and pulmonary irAEs (5.4% vs 4.0%; $p = 0.0106$), with no significant differences in hepatic, dermatologic, or endocrine irAEs. Glucocorticoid and DMARD use were more frequent in RA patients. In sensitivity analyses excluding prior exposure, new DMARD use remained significantly higher in RA patients (4.5% vs 1.0%; $p < 0.0001$), while other differences attenuated. **Conclusions:** Cancer patients with preexisting RA treated with ICIs experience higher rates of select irAEs without a significant long-term OS disadvantage. These findings suggest increased immune toxicity risk with preserved anticancer efficacy, supporting cautious but feasible ICI use in RA patients with appropriate monitoring. Research Sponsor: None.

Sex differences in immune-related adverse events requiring hospitalization among patients with checkpoint inhibitor-sensitive malignancies: A national analysis.

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Background: Immune checkpoint inhibitors (ICIs) can cause immune-related adverse events (irAEs) with significant morbidity/mortality. Sex influences immunity, yet sex-specific irAE patterns and outcomes in hospitalized patients remain underexplored. We investigated sex differences in irAE hospitalizations and mortality in ICI-sensitive cancers. **Methods:** Retrospective cohort study using the National Inpatient Sample (2019–2022) identified adults with ICI-sensitive malignancies (lung, melanoma, renal cell carcinoma [RCC], bladder, hepatocellular carcinoma [HCC]) and high-specificity irAEs (colitis, pneumonitis, cardiac, hepatic, dermatologic, neurologic) at academic centers. Primary outcome was in-hospital mortality. Secondary outcome was irAE distribution by sex. Multivariable logistic regression adjusted for demographics, cancer type, comorbidities, irAE type, discharge weights for national estimates. **Results:** Among 203,990 weighted hospitalizations (62.8% male; mean age 68), women had lower mortality (13.7% vs 15.0%; aOR 0.91, 95% CI 0.88–0.93, $p < 0.0001$), consistent across models. Women had higher odds of neurologic (aOR 1.76, 95% CI 1.68–1.85), dermatologic (1.24, 1.20–1.29), hepatic (1.08, 1.05–1.11), and pneumonitis (1.05, 1.01–1.08) irAEs; men had higher GI colitis (aOR 0.51 for women, 0.48–0.53) and cardiac (0.81, 0.79–0.83) risks. Within irAEs, women had lower mortality for neurologic (6.0% vs 10.0%), pneumonitis (11.5% vs 14.2%), colitis (4.7% vs 6.5%), and dermatologic (4.5% vs 6.2%). Female survival advantage persisted across cancers (e.g., lung aOR 0.91, 0.87–0.94; HCC 0.95, 0.91–1.00) and after excluding autoimmune disease (aOR 0.93, 0.91–0.96). Temporal analysis showed widening sex gap (2019 aOR 0.99 to 2022 0.86; year $\times$ sex interaction $p = 0.0002$). **Conclusions:** Women experience distinct irAE patterns (more neurologic/dermatologic) but lower overall and subtype-specific mortality versus men, with differences amplifying over time. Sex-stratified irAE surveillance and personalized ICI strategies can be implemented to optimize outcomes. Research Sponsor: None.

In-hospital mortality by sex in irAE hospitalizations.

Characteristic / Subgroup	N (weighted)	Male In-Hospital Mortality (%)	Female In-Hospital Mortality (%)	Adjusted OR (Female vs Male)	95% CI	p-value
Overall (Fully adjusted model ¹)	203990	15	13.6	0.93	0.91–0.96	<0.0001
Overall (Fully adjusted + irAE type ²)	203990	15	13.6	0.91	0.88–0.93	<0.0001
Lung Cancer	93135	16.2	14.2	0.91	0.87–0.94	<0.0001
Melanoma	6725	11.2	9.6	0.72	0.60–0.87	0.0006
Bladder Cancer	16795	10.3	8.4	0.74	0.64–0.85	<0.0001
GI Colitis irAE	17610	6.5	4.7	0.65	0.56–0.74	<0.0001
Pneumonitis irAE	21075	14.2	11.5	0.76	0.70–0.83	<0.0001
Dermatologic irAE	15215	6.2	4.5	0.62	0.54–0.73	<0.0001
Neurologic irAE	8695	10	6	0.66	0.55–0.79	<0.0001

Prevalence and fracture burden of osteoporosis among patients with colorectal cancer: A real-world analysis.

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Background: Osteoporosis is a common age-related skeletal disorder that may be underrecognized among patients with colorectal cancer (CRC), despite shared risk factors including advanced age, systemic inflammation, nutritional deficiencies, and cancer-related treatments. Population-level data describing the prevalence, demographic distribution, and fracture burden of osteoporosis in CRC remain limited, particularly in real-world clinical settings. **Methods:** We conducted a retrospective, cross-sectional cohort study using the TriNetX Global Collaborative Network comprising over 180 million patients across 165 healthcare organizations using R. Adult patients aged 18–85 years with colorectal cancer were identified using ICD-10-CM codes C18–C20. Two cohorts were constructed: CRC patients with osteoporosis (defined by ICD-10-CM codes M80–M81) and CRC patients without osteoporosis. Osteoporosis subtypes were further categorized into osteoporosis with current pathological fracture (M80) and osteoporosis without current pathological fracture (M81). Cohorts were compared using aggregate-level demographic data, including age, sex, race, ethnicity, and fracture status. **Results:** Among 696,434 patients with colorectal cancer, 40,051 (5.7%) had a documented diagnosis of osteoporosis. CRC patients with osteoporosis were significantly older than those without osteoporosis (mean age 74 vs 68 years) and were predominantly female (79.2% vs 43.9%). Racial distribution among CRC patients with osteoporosis included White (56.7%), Black or African American (6.0%), Asian (6.8%), and other or unknown race (30.5%). Age-stratified analyses demonstrated a marked increase in osteoporosis prevalence with advancing age, particularly among patients aged ≥ 75 years. Among the CRC with osteoporosis cohort, 13% had documented osteoporosis with current pathological fracture (M80), while 87% had osteoporosis without fracture (M81), indicating a substantial fracture burden in this population. Age-related osteoporosis accounted for the majority of cases, with multiple fracture-related subcodes reflecting clinically significant skeletal fragility. Patient arrival rate analyses demonstrated sustained real-world healthcare utilization across participating institutions. **Conclusions:** In this large real-world cohort, osteoporosis was prevalent among patients with colorectal cancer and was strongly associated with advanced age and female sex. A clinically meaningful proportion of CRC patients with osteoporosis had documented pathological fractures, highlighting an underappreciated source of morbidity. These findings underscore the importance of routine bone health assessment and fracture risk evaluation in colorectal cancer care, particularly among older adults. Research Sponsor: None.

Body mass index (BMI) and overall survival (OS) among Hispanic patients treated with immune checkpoint inhibitors (ICIs).

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Background: Prior studies have suggested improved OS among cancer patients receiving ICIs with higher BMI, despite obesity being a known cancer risk factor; however, these findings are largely derived from predominantly non-Hispanic cohorts. In Austin, Texas, Hispanic individuals comprise approximately 30% of the population, limiting the external validity of prior studies. We evaluated whether the previously described association between BMI and OS extends to Hispanic patients treated with ICIs. **Methods:** We retrospectively identified Hispanic patients with solid tumors treated with ICIs at Ascension/UT Health Austin between November 2013 and December 2025 using Research Electronic Data Capture (REDCap) data. BMI at ICI initiation was categorized as normal (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), or obese (≥ 30 kg/m²); underweight patients were excluded. Overall survival (OS) was defined as time from ICI initiation to death, with censoring at last follow-up or 5 years. Missing 5-year survival status was addressed using single stochastic regression imputation. Stabilized inverse probability of treatment weighting from a multinomial propensity score model was used to adjust for baseline differences, including age, sex, ECOG status, cancer type and stage, ICI agent, steroid exposure, and antibiotic exposure. Weighted Cox proportional hazards models estimated associations between BMI and OS, with prespecified subgroup analyses by sex and stage. **Results:** Among 177 Hispanic patients included, average age was 54 years and 53% were male; 32% had normal BMI, 31% were overweight, and 37% were obese. Median overall survival (OS) was 497 days. After inverse probability weighting, BMI was not associated with OS ($p = 0.90$). Compared with normal BMI, overweight patients had a hazard ratio (HR) of 0.94 (95% CI 0.49–1.80) and obese patients an HR of 1.09 (95% CI 0.60–2.00). No significant differences were observed between obese and overweight patients (HR 1.16; 95% CI 0.64–2.09). Subgroup analyses by sex and cancer stage showed no survival advantage associated with higher BMI. Among women, obese patients had an HR of 1.58 (95% CI 0.49–5.13), while among men the HR was 1.30 (95% CI 0.66–2.58). When stratified by stage, obese patients had an HR of 1.68 (95% CI 0.44–6.40) in stages I–III and 1.13 (95% CI 0.53–2.40) in stage IV. **Conclusions:** In this cohort of Hispanic patients with solid tumors treated with immune checkpoint inhibitors, we did not find a survival advantage for those with higher BMI. These findings raise the possibility that BMI associated survival advantages reported in predominantly non-Hispanic cohorts may not extend to the Hispanic population. Larger studies are needed to determine whether these findings represent true population-specific differences. Research Sponsor: None.

Insurance and racial disparities in CAR T-cell therapy outcomes: A National Inpatient analysis.

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Background: To understand equity gaps for Chimeric antigen receptor T-cell (CAR-T) therapy, we conducted an analysis examining insurance-based and racial disparities in CAR-T cell therapy. **Methods:** Using the National Inpatient Sample (2020–2022), we identified CAR-T recipients via ICD-10-PCS procedure codes (XW0 series) with FDA-approved indications including diffuse large B-cell lymphoma (DLBCL), B-cell acute lymphoblastic leukemia (B-ALL), multiple myeloma, follicular lymphoma, and mantle cell lymphoma. The primary outcome was in-hospital mortality. Secondary outcomes included cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and ICU utilization. Multivariable logistic regression estimated adjusted odds ratios (aOR) controlling for age, sex, race, insurance status, and disease indication. Access disparities were assessed by comparing racial composition of CAR-T recipients to US Census population estimates. **Results:** Among 10,610 weighted CAR-T hospitalizations (mean age 59.4 years; 62.1% male; 97% at academic centers), the most common indications were DLBCL (46.9%), multiple myeloma (25.0%), and B-ALL (12.7%). Overall in-hospital mortality was 8.6%, CRS occurred in 42.3%, and ICANS in 19.7%. Compared to privately insured patients (mortality 5.5%), both Medicare (11.5%; aOR 1.59, 95% CI 1.32–1.92, $p < 0.0001$) and Medicaid patients (10.7%; aOR 1.89, 95% CI 1.45–2.47, $p < 0.0001$) experienced significantly higher mortality after adjustment for demographics, comorbidities, and indication. This disparity persisted across the study period, with the Medicare-to-Private mortality ratio increasing from 1.9x (2020) to 2.2x (2022). Black (9.1% of CAR-T recipients vs 13.6% US population) and Hispanic patients (13.7% vs 18.9%) were significantly underrepresented, receiving CAR-T at only 67% and 72% of expected rates based on population demographics, respectively. Black patients demonstrated significantly higher ICANS risk (aOR 1.38, 95% CI 1.16–1.64, $p = 0.0003$) but lower CRS risk (aOR 0.79, 95% CI 0.68–0.91, $p = 0.001$) compared to White patients. Black patients also experienced higher rates of ICU-level care (23.8% vs 16.6%) and mechanical ventilation (12.4% vs 8.1%). No significant sex-based disparities were observed in mortality (aOR 0.90, 95% CI 0.78–1.04, $p = 0.17$). **Conclusions:** We identified insurance-based mortality gaps with 60–90% higher adjusted mortality compared to privately insured patients. Concurrent access disparities result in Black and Hispanic patients being underrepresented by approximately one-third. Black patients who do receive CAR-T demonstrate distinct toxicity phenotypes with higher neurotoxicity and ICU utilization. These findings support the need to address barriers to CAR-T access and optimize outcomes across all patient populations. Research Sponsor: None.

Mental health and malignancy: Real-world associations between early-onset hormone-related cancers and mental illness.

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Background: Although progress has been made in reducing overall cancer incidence, early-onset cancers have continued their troublesome rise. Similarly, the incidence and/or prevalence of psychiatric disorders has increased, particularly among young adults. Mental illness may influence cancer development, however, real-world evidence linking mental illness to early-onset hormone-related cancers is limited. **Methods:** We conducted a real-world, retrospective cohort study using the TriNetX United States Research Database, a federated network of de-identified electronic health records from over 70 healthcare organizations, to examine this association. Adults aged 18–50 years with at least one of five pre-determined core mental illnesses, including generalized anxiety disorder (GAD), major depressive disorder (MDD), obsessive-compulsive disorder (OCD), bipolar disorder, and schizophrenia, were compared with same-aged individuals without any of the core mental illnesses. A five-year lookback period was used from January 25th, 2021 to January 25th 2026 and propensity score matching was used to adjust for confounders. Incidence of early-onset cancers diagnosed were then assessed during five-year follow-up. Sensitivity analyses required a ≥ 1 -year lag between mental illness diagnosis and cancer onset. **Results:** 2,911,432 patients were identified as having a core mental illness, whereas 21,439,614 patients were identified as not having any core mental illness. All-cause mental illness was associated with an increased risk of developing early-onset breast cancer (RR 2.253, CI 2.149–2.362, $p < 0.0001$), uterine cancer (RR 1.711, CI 1.515–1.934, $p < 0.0001$), and ovarian cancer (RR 1.984, CI 1.790–2.198, $p < 0.0001$). Associations with early-onset prostate cancer and testicular cancer did not meet thresholds for statistical significance. Within the subgroup analysis, GAD was associated with an increased risk of developing early-onset breast cancer (RR 2.565, CI 2.398–2.742, $p < 0.0001$), uterine cancer (RR 1.534, CI 1.278–1.841, $p < 0.0001$) and ovarian cancer (RR 1.736, CI 1.492–2.019, $p < 0.0001$). MDD was associated with early-onset breast cancer (RR 2.380, CI 2.161–2.622, $p < 0.0001$), uterine cancer (RR 2.089, CI 1.625–2.685, $p < 0.0001$), and ovarian cancer (RR 1.983, CI 1.591–2.472, $p < 0.0001$). Bipolar disorder was associated only with early-onset breast cancer (RR 1.415, CI 1.244–1.610, $p < 0.0001$). OCD and schizophrenia had no statistically significant associations. **Conclusions:** In this large, real-world cohort study, all-cause mental illness, GAD, and MDD were associated with an increased risk of early-onset hormonal cancers more commonly affecting female patients. These findings suggest that mental health represents a potential modifiable risk factor in early-onset, hormone-related cancers and warrants further investigation. Research Sponsor: None.

Mental health and malignancy: Real-world associations between early-onset gastrointestinal cancers and mental illness.

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Background: Although progress has been made in reducing overall cancer incidence, early-onset cancers have continued their troublesome rise. Similarly, the incidence and/or prevalence of psychiatric disorders has increased, particularly among young adults. Mental illness may influence cancer development, however, real-world evidence linking mental illness to early-onset gastrointestinal cancers is limited. **Methods:** We sought to conduct a real-world, retrospective cohort study using the TriNetX United States Research Database, a federated network of de-identified electronic health records from over 70 healthcare organizations, to examine this association. Adults aged 18–50 years with at least one of five pre-determined core mental illnesses, including generalized anxiety disorder (GAD), major depressive disorder (MDD), obsessive-compulsive disorder (OCD), bipolar disorder, and/or schizophrenia, were compared with same-aged individuals without any of the core mental illnesses. A five-year lookback period was used from January 25th, 2021 to January 25th 2026. Propensity score matching adjusted for demographic and clinical confounders. Incidence of early-onset cancers diagnosed were then assessed during five-year follow-up. Sensitivity analyses required a ≥ 1 -year lag between mental illness diagnosis and cancer onset. **Results:** 2,911,432 patients ages 18–50 were identified as having a core mental illness, whereas 21,439,614 patients ages 18–50 were identified as not having any core mental illness. All-cause mental illness was associated with an increased risk of developing early-onset gastric cancer (RR 1.451, CI 1.189–1.771, $p < 0.0001$), pancreatic cancer (RR 1.566, CI 1.328–1.822, $p < 0.0001$) and colorectal cancer (RR 1.407, CI 1.313–1.506, $p < 0.0001$). Associations with early-onset esophageal cancer, biliary tract cancer, and small intestine cancer did not meet thresholds for statistical significance. In addition, subgroup analysis was completed for each core mental illness. GAD was associated with an increased risk of developing early-onset pancreatic cancer (RR 1.627, CI 1.220–2.169, $p < 0.0001$), small intestine cancer (RR 2.435, CI 1.498–3.956, $p < 0.0001$), and colorectal cancer (RR 1.625, CI 1.441–1.833, $p < 0.0001$). MDD was only associated with an increased risk of developing early-onset colorectal cancer (RR 1.425, CI 1.213–1.674, $p < 0.0001$). OCD, bipolar disorder, and schizophrenia had no statistically significant association with the development of the early-onset cancers noted above. **Conclusions:** In this large, real-world cohort study, all-cause mental illness, GAD, and MDD were associated with an increased risk of several early-onset gastrointestinal cancers. These findings suggest that one's mental health represents a potentially modifiable risk factor in early-onset gastrointestinal cancers and warrants further investigation. Research Sponsor: None.

Patterns and determinants of radiotherapy treatment default in a rural cancer centre: A retrospective observational study.

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Background: Radiotherapy requires uninterrupted daily treatment over several weeks, making treatment adherence challenging, particularly in rural and resource-limited settings. Treatment default adversely affects outcomes and reflects underlying socioeconomic, access-related and clinical barriers. There is limited real-world data from rural India evaluating the magnitude and determinants of treatment default. This study aimed to determine the radiotherapy default rate and identify the associated factors. **Methods:** This retrospective observational study included patients enrolled for definitive, adjuvant, and palliative radiotherapy over a 2 year period at a rural tertiary cancer centre. Radiotherapy default was defined as missing 3 or more consecutive fractions after initiation of treatment or failure to complete the planned prescribed dose. Descriptive statistics were used to summarise patient demographics, socioeconomic characteristics and clinical variables. The radiotherapy default rate was expressed as a percentage. Associations between radiotherapy default and categorical variables were analysed using Chi-square or Fisher's exact test, as appropriate. Variables significant on univariate analysis were included in a multivariate logistic regression model to identify independent predictors of radiotherapy default. A p-value < 0.05 was considered statistically significant. **Results:** Among 2755 patients enrolled for radiotherapy during the study period, 363 patients defaulted, resulting in an overall default rate of ~13.2%. Higher default rates were significantly associated with longer daily travel distance, financial constraints, lower educational status, inadequate family support, poor baseline general condition, treatment related toxicities, diet-related difficulties—particularly among head and neck cancer patients ($p < 0.05$). On multivariate logistic regression analysis, long travel distance, financial constraints, poor general condition, inadequate family support and diet-related difficulties remained independent predictors of radiotherapy default. **Conclusions:** Radiotherapy default remains a clinically significant challenge in rural practice and is driven by a combination of socioeconomic, access-related and clinical factors. Long travel distance, financial constraints, inadequate family support, poor general condition and diet-related difficulties independently contribute to treatment default. Early identification of high-risk patients and targeted interventions—including patient and caregiver counselling, nutritional optimisation, financial and travel assistance, symptom control, and multidisciplinary supportive care—have the potential to reduce radiotherapy default rates and improve treatment completion in resource-limited settings. Research Sponsor: None.

Assessing burden and outcomes: Colon cancer survival across the U.S. safety-net spectrum.

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Background: Safety-net hospitals (SNHs) provide essential care for uninsured and underinsured patients but often face systemic constraints that may affect cancer outcomes. Colon cancer, a leading cause of cancer-related death in the United States, requires complex multidisciplinary management. This study assessed the association between hospital safety-net burden and clinical outcomes in colon cancer across a national dataset. We also identified patient-level factors contributing to disparities in care delivery. **Methods:** Using the National Cancer Database (NCDB), we identified approximately 1.2 million adult patients diagnosed with colon cancer in the United States between 2004 and 2020. Facilities were stratified by safety-net burden into Non-Safety-Net Hospitals (NSNH; < 25% Medicaid/uninsured cases), Safety-Net Hospitals (SNH; 25–75%), and Extreme Safety-Net Hospitals (Extreme-SNH; > 75%). This safety-net spectrum provided a novel framework for capturing both facility- and patient-level disparities that influence colon cancer care and outcomes. Multivariable logistic and Cox regression models were used to evaluate differences in disease stage, treatment timelines, and survival, adjusting for age, comorbidity, and AJCC stage. Kruskal-Wallis and chi-square tests were used for descriptive analyses. **Results:** SNHs and Extreme-SNHs cared for a greater proportion of patients with advanced-stage disease, lower rates of chemotherapy, immunotherapy, and palliative care utilization, and higher short-term mortality when compared with NSNH. Thirty-day readmission rates after surgery were similar across groups. Survival analyses demonstrated a graded decline in outcomes with increasing safety-net burden: median overall survival was 91.2 months in NSNH, 83.6 months in SNH, and 70.9 months in Extreme-SNH ($p < 0.001$). One-year survival exceeded 95% across all facilities, but five-year survival declined to 68.9% for NSNH vs 59.4% for Extreme-SNH. Additional disparities in colon cancer outcomes were observed by health literacy level, residential setting (urban, metropolitan, rural), race, age, and sex. **Conclusions:** Colon cancer patients treated at hospitals with higher safety-net burden experience substantially poorer long-term survival despite comparable short-term outcomes. These findings highlight the need for targeted policy, resource allocation, and quality-improvement efforts to reduce disparities and strengthen oncology care delivery in high-burden safety-net systems. A Plan-Do-Check-Act (PDCA) approach tailored to individual hospital settings and regional contexts may help identify gaps in colon cancer care and guide targeted interventions to improve patient outcomes. Research Sponsor: None.

Prognostic value of circulating tumor DNA (ctDNA) for recurrence detection across solid tumors: A real-world meta-analysis.

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Background: Early detection of recurrence after curative-intent treatment is a critical priority, traditional imaging often detects relapse when disease burden is high, potentially limiting treatment efficacy. ctDNA has emerged as an established prognostic biomarker for molecular residual disease (MRD) detection and early relapse. We performed a real-world meta-analysis on published datasets that utilized personalized, tumor-informed ctDNA testing to assess its performance across tumor types and clinical management approaches. **Methods:** Real-world studies published from December 2022 to December 2025 using the personalized, tumor-informed Signatera ctDNA assay (Natera, Inc.) were included. Eligibility required ctDNA assessment in the MRD (2–16 weeks post-surgery (histology dependent)/pre adjuvant therapy (ACT)) and/or surveillance (post-ACT/end of the MRD window if no ACT was given) settings, with outcomes stratified by ctDNA status and hazard ratios (HR) reported from univariable or time-dependent Cox regression analysis. Exclusions included: clinical trials, biobanks, metastatic disease treated with palliative intent, case reports, reviews, editorials, or commentaries. Clinical outcomes were harmonized into a composite event-free survival (EFS) endpoint (time to recurrence, progression, or death). Pooled HRs and 95% CIs were estimated using random and fixed effects models and heterogeneity between studies was assessed using the I^2 and Cochran's Q test. Median lead time from ctDNA-positivity to radiographic or clinical recurrence was summarized when available. **Results:** We identified 18 eligible publications comprising 3,004 unique patients across 15 solid tumor types. During the MRD window, ctDNA positivity was associated with a significantly increased risk of an EFS event compared with ctDNA negativity (pooled HR: 8.15; 95% CI: 6.12–10.85, $I^2 = 0.00\%$, $P = 0.844$, $n = 13$). During the surveillance window, inclusive of post-definitive treatment, ctDNA positivity conferred an even greater EFS risk (pooled HR: 18.30; 95% CI: 14.17–23.65, $I^2 = 0\%$, $P = 0.911$ for heterogeneity, $n = 16$). Across studies, ctDNA detection during surveillance preceded radiographic or clinical recurrence by a median of 3.20 months (95% CI: 2.50–4.10, $P < 0.0001$, $n = 10$), although this varied substantially by study/tumor type ($I^2 = 80.9\%$). **Conclusions:** In this pan-cancer real-world meta-analysis, ctDNA positivity assessed using a tumor-informed assay was highly prognostic following curative-intent therapy at all timepoints evaluated with low heterogeneity between studies. These findings support the broad clinical utility of tumor-informed ctDNA testing for post-treatment risk stratification and longitudinal disease monitoring across solid tumors. Research Sponsor: None.

Predictors of tumor lysis syndrome in non-Hodgkin lymphoma hospitalizations.

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Background: Tumor lysis syndrome (TLS) is a life-threatening oncologic emergency in non-Hodgkin lymphoma (NHL) caused by rapid tumor cell breakdown and severe metabolic derangements. Although TLS is well recognized, most risk data derive from small cohorts or trials, limiting generalizability. We used a nationally representative inpatient dataset to identify predictors of TLS in hospitalized NHL patients. **Methods:** We performed a cross-sectional analysis of the National Inpatient Sample (2016–2020). Adult NHL hospitalizations were identified using ICD-10 codes. Survey-weighted chi-square tests and multivariable logistic regression evaluated demographic, clinical, and treatment predictors. Analyses accounted for the complex survey design. Statistical significance was defined as $p < 0.05$. **Results:** An estimated 350,400 NHL hospitalizations were identified, of which 0.79% had TLS. TLS patients were younger (65.7 vs 69.5 years, $p < 0.001$) and demonstrated different racial distributions, with lower proportions of White patients (67.8% vs 76.9%) and higher proportions of Black (12.7% vs 9.2%) and Hispanic patients (11.6% vs 8.6%) ($p < 0.001$). TLS occurred more frequently in hospitals in the West and Northeast ($p = 0.036$). TLS admissions had significantly longer stays (10.48 vs 5.91 days) and higher charges (\$174,972 vs \$76,884; $p < 0.001$). Survey-weighted regression identified several strong predictors of TLS. Bone marrow involvement was one of the strongest independent predictors (OR 13.78 [95% CI 5.45–34.84]). Electrolyte derangements were also powerful predictors: hyperkalemia (OR 8.20 [95% CI 6.82–9.86]), hyperphosphatemia (OR 8.28 [95% CI 6.62–10.36]), and hypocalcemia (OR 7.02 [95% CI 5.67–8.69]). Additional predictors included sepsis (OR 2.29 [95% CI 1.89–2.77]), neutropenia (OR 1.71 [95% CI 1.27–2.31]), HIV infection (OR 1.73 [95% CI 1.05–2.84]), and receipt of inpatient chemotherapy (OR 1.38 [95% CI 1.01–1.87]). Prior chemotherapy (OR 0.44 [95% CI 0.30–0.63]) and radiation therapy (OR 0.61 [95% CI 0.38–0.99]) were protective, suggesting TLS risk is greatest in chemo-naïve or high-tumor burden presentations. **Conclusions:** TLS in hospitalized NHL patients is associated with distinct demographic patterns and substantial increases in healthcare utilization. Early risk stratification incorporating clinical, laboratory, and treatment factors may improve prevention strategies and outcomes. Research Sponsor: None.

Predictors of TLS among hospitalized patients with NHL.

Predictor	Adjusted OR	95% CI	p-value
Bone marrow involvement	13.78	5.45–34.84	<0.001
Hyperkalemia	8.20	6.82–9.86	<0.001
Hyperphosphatemia	8.28	6.62–10.36	<0.001
Hypocalcemia	7.02	5.67–8.69	<0.001
Sepsis	2.29	1.89–2.77	<0.001
Neutropenia	1.71	1.27–2.31	<0.001
HIV infection	1.73	1.05–2.84	0.031
Inpatient chemotherapy	1.38	1.01–1.87	0.041
Prior chemotherapy	0.44	0.30–0.63	<0.001
Radiation therapy	0.61	0.38–0.99	0.046

Direct oral anticoagulants versus low-molecular-weight heparin in patients with liver metastases and cancer-associated thrombosis: A multi-center real-world analysis.

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Background: Patients with liver metastases are at high risk for cancer-associated thrombosis (CAT) and require therapeutic anticoagulation. Although direct oral anticoagulants (DOACs) are increasingly used, their safety relative to low-molecular-weight heparin (LMWH) in this high-risk population, particularly regarding gastrointestinal (GI) bleeding, remains uncertain.

Methods: We conducted a retrospective, federated cohort study using the TriNetX Global Collaborative Network, including adult patients with liver metastases and CAT who initiated a DOAC or LMWH within 10 days of CAT diagnosis. The index date was defined as the first qualifying anticoagulant exposure. Propensity score matching was performed to balance measured demographics, comorbidities, and concomitant medications, yielding 19,380 patients per cohort. Outcomes were assessed from 1 to 365 days after the index date and included GI bleeding, thrombotic recurrence by DVT/PE or stroke, intensive care unit (ICU) admission, and all-cause mortality. GI bleeding was identified using diagnosis-based coding algorithms, with exclusion of patients who had GI bleeding prior to anticoagulation initiation. Risk estimates were calculated and time-to-event analyses. **Results:** GI bleeding occurred more frequently among patients treated with DOACs compared with LMWH (9.7% vs 8.3%; hazard ratio [HR] 1.11, 95% CI 1.02–1.19). Thrombotic recurrence was common in both groups (61.4% with DOACs vs 60.0% with LMWH); however, time-to-event analysis demonstrated a modestly lower hazard of recurrence among DOAC-treated patients (HR 0.94, 95% CI 0.92–0.97). ICU admission was infrequent but occurred more often in the DOAC cohort (0.6% vs 0.3%; HR 1.80, 95% CI 1.33–2.46). DOAC use was associated with significantly lower all-cause mortality compared with LMWH (50.8% vs 55.7%; HR 0.84, 95% CI 0.82–0.86). **Conclusions:** In patients with liver metastases and CAT, DOAC therapy was associated with a modestly increased risk of GI bleeding but improved overall survival compared with LMWH. Given the small absolute differences in bleeding risk and the potential for residual confounding from unmeasured factors such as cancer burden, performance status, life expectancy, and hospice referral, these findings may support clinical equipoise between anticoagulation strategies. Individualized treatment decisions remain essential in this vulnerable population. Research Sponsor: None.

Clinical outcomes in propensity-score matched patients with liver metastasis and cancer associated thrombosis.

Outcome	DOAC (n=19,380)	LMWH (n=19,380)	HR	CI
GI bleeding	9.7%	8.3%	1.11	1.02-1.19
Thromboembolic recurrence	61.4%	60.0%	0.94	0.92-0.97
ICU admission	0.6%	0.3%	1.80	1.33-2.46
All-cause mortality	50.8%	55.7%	0.84	0.82-0.86

Arrhythmia phenotype and 30-day readmission in selected cancers: Propensity-matched NRD study.

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Background: Cardiac arrhythmias are common in oncology and may increase rehospitalization and resource use, but arrhythmia-type and cancer-specific readmission risk is incompletely characterized. **Methods:** Retrospective cohort of adult index hospitalizations for colorectal, breast, lung, prostate, kidney, or melanoma in the HCUP Nationwide Readmissions Database. Arrhythmias coded during the index stay (atrial fibrillation [AF], atrial flutter [AFL], ventricular tachycardia [VT], supraventricular tachycardia [SVT]) were identified using ICD-10-CM codes. Primary outcome was all-cause 30-day readmission. For each phenotype, propensity-score matching (caliper 0.05) created arrhythmia and no-arrhythmia cohorts balanced on demographics, payer, income quartile, and comorbidity. Multilevel logistic regression with hospital clustering estimated adjusted odds ratios (aOR) with 95% CI and tested arrhythmia-by-cancer interactions. Secondary outcomes were index length of stay (LOS) and total charges, analyzed with mixed-effects models; results are reported as adjusted mean differences (days) and incremental charges (USD). Two-sided $p < 0.05$ was significant. **Results:** Among 1,562,919 index hospitalizations, AF was present in 214,475 (13.7%), AFL 27,545 (1.8%), VT 5,184 (0.3%), and SVT 25,714 (1.6%). After matching/adjustment, AFL was associated with higher 30-day readmission (aOR 1.095, 95% CI 1.03-1.17; $p = 0.005$). AF (aOR 1.001, 0.98-1.03; $p = 0.940$), VT (aOR 1.128, 0.99-1.29; $p = 0.078$), and SVT (aOR 1.018, 0.95-1.09; $p = 0.598$) were not significant overall. AF demonstrated cancer-specific heterogeneity: lung aOR 1.092 (1.043-1.144; $p < 0.001$) and melanoma aOR 1.143 (1.019-1.283; $p = 0.023$), while breast was not increased (aOR 0.964, 0.908-1.025; $p = 0.242$). In the AF model, older age was inversely associated with readmission (aOR 0.974 per year, 95% CI 0.972-0.976; $p < 0.001$). In the AF model, highest income quartile was associated with higher readmission (aOR 1.409, 95% CI 1.275-1.557; $p < 0.001$). AF/VT/SVT increased LOS: AF +0.658 days, VT +1.419 days, SVT +1.146 days ($p < 0.001$); charges increased: AF +\$12,399 (95% CI 8,231-16,569), VT +\$48,114 (36,846-59,382), SVT +\$26,656 (19,822-33,489) (all $p < 0.001$). **Conclusions:** In selected cancers, AFL was independently associated with higher 30-day readmission, while AF readmission risk varied by cancer type. AF/VT/SVT were linked to increased LOS and charges, with the largest resource impact in VT. Prospective studies incorporating cancer stage and therapy exposures should test phenotype-guided cardio-oncology transitional care to reduce readmissions and costs. Limitations include ICD-coded phenotyping, inability to distinguish incident vs prevalent arrhythmias, and unavailable outpatient therapy/anticoagulation; residual confounding is possible. Misclassification may bias estimates toward null, particularly for VT. Research Sponsor: None.

Trends and factors associated with glucagon-like peptide 1 receptor agonists prescription for cancer populations with type 2 diabetes.

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are increasingly used in cancer survivors with Type 2 Diabetes (T2D) given its efficacy, yet concerns regarding treatment tolerance, weight loss, and limited oncology-specific guidance during active treatment and survivorship may influence prescribing patterns. To date, little evidence exists regarding the trends and factors associated with GLP-1RA use in cancer populations with T2D. **Methods:** We conducted a retrospective cohort study using SEER-Medicare data to identify patients newly diagnosed with seven most common cancers in 2010-2021 with pre-existing T2D. Pre-existing T2D was defined by relevant diagnosis codes within 12 months prior to cancer diagnosis. Patients with continuous Medicare Parts A & B and Part D enrollment were followed annually from diagnosis until death or end of follow-up (12/31/2022) to assess GLP-1RA use. A non-cancer cohort with T2D was identified using a 5% random sample of Medicare beneficiaries without cancer. We calculated annual proportions of beneficiaries with any GLP-1RA use, stratified by Traditional Medicare (TM) and Medicare Advantage (MA, data available in 2016-2021). Multivariable logistic regression models evaluated patient sociodemographic and clinical characteristics associated with GLP-1RA use in 2021. **Results:** We included 482,878 and 542,285 Medicare beneficiaries with T2D in the cancer and non-cancer cohort respectively (1,927,771 and 3,265,774 person-years in 2010-2022). Among TM beneficiaries, GLP-1RA use in the cancer cohort increased from 0.5% to 8.2% in 2010-2022, compared to an increase from 0.4% to 6.4% among non-cancer cohort; similarly higher GLP-1RA use was observed in cancer than non-cancer cohort among MA beneficiaries in 2016-2021 (1.8% to 6.8% vs. 1.3% to 5.7%; unadjusted p-values < 0.001). Rapid uptake was observed for dulaglutide and semaglutide from 2015, while liraglutide use declined modestly after peaking in 2018. In adjusted analyses within the cancer cohort, patients with breast (0.87 percentage points [ppts], $p < 0.001$), female genital (1.08 ppts, $p < 0.001$), and prostate cancers (0.62 ppts, $p = 0.001$) were more likely to receive GLP-1RAs than those with colorectal cancer. More advanced cancer stage was associated with lower likelihoods of GLP-1RA use; Non-Hispanic White, higher socioeconomic neighborhoods, and dual eligibility were associated with higher likelihoods of GLP-1RAs use. **Conclusions:** GLP-1RA use increased substantially among Medicare beneficiaries with cancer and T2D, and was consistently higher than those without cancer, which may reflect greater clinical engagement and cardiometabolic risk burden following a cancer diagnosis. Variation by cancer site, stage, and socioeconomic factors suggest that both clinical complexity and structural determinants shape GLP-1RA use in cancer survivors. Research Sponsor: National Cancer Institute; 3P30CA138292.

Organ-specific metastatic progression in non-small cell lung cancer treated with pembrolizumab versus atezolizumab: A TrinetX network analysis.

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Background: Immune checkpoint inhibitors (ICIs) targeting the PD-1 (Pembrolizumab) and PD-L1 (Atezolizumab) have revolutionized the first-line management of metastatic non-small cell lung cancer (mNSCLC). While these agents are often considered clinically interchangeable, the differences in molecular binding mechanism and tissue-specific penetration may lead to distinct therapeutic patterns. Since the real-world evidence on the propensity for organ-specific metastatic spread remains limited, we aim to compare organ-specific metastatic progression patterns between the two therapies. **Methods:** We conducted a retrospective cohort study utilizing the TriNetX US Collaborative Network. After identifying adults with stage IV mNSCLC on initial Pembrolizumab or Atezolizumab monotherapy, patients with pre-existing metastases at the specific organ site of interest were excluded. Propensity score matching (1:1) was performed to balance cohorts across demographic and clinical variables. Our endpoints were metastases to the CNS, mediastinum, bone, liver, adrenal glands, and skin over 365 days. Hazard ratios (HR) were estimated using Cox proportional hazards models. **Results:** Atezolizumab was associated with a significantly higher risk of CNS metastases compared with Pembrolizumab (1-year incidence: 16.9% vs 6.1%; HR 3.08, 95%CI: 2.73–3.46; $p < 0.001$). A similar pattern was seen in the mediastinum (HR 1.62, 95% CI: 1.32–1.99), bone (HR 1.53, 95% CI: 1.38–1.70), liver (11.5% vs 7.8%; HR 1.55, 95% CI: 1.37–1.75), and adrenal glands (HR 1.43, 95% CI: 1.20–1.75). In contrast, an inverse relationship was observed in the skin where Atezolizumab showed a significantly lower risk of metastases (1.0% vs 1.7%; HR 0.59, 95% CI: 0.44 – 0.79; $p = 0.01$). **Conclusions:** Markedly distinct patterns of organ-specific metastasis were seen, where Atezolizumab consistently demonstrated an elevated risk of progression in the CNS and visceral organs, whereas Pembrolizumab showed a greater propensity for cutaneous progression. These observations indicate that the selection between PD-1 and PD-L1 inhibition may influence the location of the subsequent site of disease progression. Research Sponsor: None.

Metastatic Site	Atezolizumab Cohort (Events / N)	Pembrolizumab Cohort (Events / N)	Hazard Ratio* (95% CI)	P-Value
CNS	994 / 5,890	376 / 6,138	3.08 (2.73 – 3.46)	<0.001
Mediastinum	228 / 7,043	150 / 7,153	1.62 (1.32 – 1.99)	0.02
Bone	824 / 4,997	624 / 5,374	1.53 (1.38 – 1.70)	0.43
Liver	602 / 5,250	490 / 6,262	1.55 (1.37 – 1.75)	0.35
Adrenal Gland	287 / 6,821	213 / 6,912	1.43 (1.20 – 1.75)	0.068
Skin	71 / 7,306	123 / 7,177	0.59 (0.44 – 0.79)	0.01

Note: N varies by organ site due to the exclusion of patients with pre-existing metastases at that specific site.

*Hazard Ratio > 1.0 indicates increased risk with Atezolizumab; HR < 1.0 indicates increased risk with Pembrolizumab.

Frailty among hospitalized patients with pancreatic cancer: A National Inpatient analysis.

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Background: Frailty is increasingly recognized as a key determinant of outcomes in older adults with cancer; however, its prevalence and inpatient correlates among hospitalizations for pancreatic cancer remain incompletely characterized. We examined the national inpatient burden of frailty among adults hospitalized with pancreatic cancer and compared demographics, comorbidities, and healthcare utilization between frail and non-frail patients. **Methods:** We analyzed National Inpatient Sample data (2016–2020) to identify adult pancreatic cancer hospitalizations using ICD-10 codes. Frailty was defined by ICD-10 R54. Survey-weighted analyses accounted for complex sampling, with statistical significance set at $p < 0.05$. **Results:** Among an estimated 775,510 weighted adult hospitalizations with pancreatic cancer, frailty was identified in 0.39%. Frail patients were significantly older (74.96 vs 68.32 years, $p < 0.001$) and more often female (56.4% vs 47.7%, $p < 0.001$). Frailty was more prevalent among patients from lower-income neighborhoods and varied by hospital region (both $p < 0.01$). Frail patients experienced longer hospital stays (7.16 vs 6.16 days, $p < 0.001$), with similar total hospitalization charges (\$77,978 vs \$75,477). Frailty was associated with higher burdens of congestive heart failure (15.9% vs 10.3%) and sepsis (22.8% vs 17.0%) (both $p < 0.001$). Frail patients demonstrated marked nutritional and functional vulnerability, including underweight status (24.6% vs 9.1%), anemia (52.5% vs 44.0%), malnutrition (46.2% vs 28.8%), chronic pain (24.4% vs 19.5%), and falls or mobility impairment (8.5% vs 3.6%) (all $p < 0.01$). In multi-variable analysis, advanced age, female sex, underweight status, malnutrition, anemia, chronic pain, sepsis, congestive heart failure, functional impairment, and lower socioeconomic status remained independently associated with frailty. **Conclusions:** Frailty was uncommon but clinically meaningful among adults hospitalized with pancreatic cancer and was associated with advanced age, nutritional and functional vulnerability, acute illness severity, and socioeconomic disadvantage. These findings underscore the need for improved inpatient frailty recognition and targeted supportive care strategies. Research Sponsor: None.

Predictor of frailty in pancreatic cancer.

Predictors	Frail (%)	Non-frail (%)	p-value
Congestive heart failure	15.9	10.3	<0.001
Sepsis	22.8	17.0	<0.001
Underweight	24.6	9.1	<0.001
Anemia	52.5	44.0	<0.001
Malnutrition	46.2	28.8	<0.001
Chronic pain	24.4	19.5	<0.001
Falls/mobility impairment	8.5	3.6	<0.001
Obesity	4.4	8.6	0.0002
Smoking	9.3	12.2	0.034
Chronic kidney disease	16.2	12.8	0.012

Baseline corticosteroid use and outcomes in non–small cell lung cancer patients receiving immune checkpoint inhibitors, stratified by indication.

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Background: Baseline systemic corticosteroids are often prescribed to patients with non-small cell lung cancer (NSCLC) initiating immune checkpoint inhibitors (ICIs). Prior studies associating steroids with reduced ICI efficacy have largely treated steroid exposure as binary without accounting for indication. We evaluated outcomes following baseline steroid use by indication. **Methods:** We conducted a retrospective cohort study using TriNetX, a federated research network of de-identified electronic medical records. Using approximately 7,000–12,000 patients per stratum, NSCLC patients initiating ICIs were stratified by presence of systemic steroid prescriptions within 30 days prior to ICI initiation by indication: brain metastases (BM), pulmonary disease (PD), autoimmune disease (AI), and palliative indications (PI). In each stratum, steroid-exposed patients were compared with propensity-matched steroid-naïve controls adjusting for demographics, non-brain metastases, comorbidities, substance use, and prior cancer treatments. Outcomes included mortality, ICU admission, and infection at 1 month. **Results:** Baseline steroid use was associated with worse 1 month outcomes in an indication dependent manner. Among patients receiving steroids for BM, mortality was higher compared with controls (8.75% vs 5.46%; HR 1.62, 95% CI 1.44–1.82; $p < 0.001$), as were ICU admission (5.06% vs 2.80%; RR 1.81, 95% CI 1.53–2.14; $p < 0.001$) and infection (6.81% vs 4.20%; RR 1.62, 95% CI 1.40–1.88; $p < 0.001$). Similarly, among patients receiving steroids for PI, steroid use was associated with increased mortality (9.68% vs 5.29%; HR 1.87, 95% CI 1.69–2.06; $p < 0.001$), ICU admission (4.83% vs 2.65%; RR 1.82, 95% CI 1.57–2.12; $p < 0.001$), and infection (7.50% vs 4.21%; RR 1.78, 95% CI 1.56–2.03; $p < 0.001$). In contrast, steroid use for PD or AI was not associated with increased mortality. PD was associated with higher ICU admission (3.35% vs 2.61%; RR 1.29, 95% CI 1.10–1.51; $p = 0.0027$) and infection (6.31% vs 4.23%; RR 1.49, 95% CI 1.31–1.70; $p < 0.001$), while AI was associated with increased ICU admission (3.63% vs 2.68%; RR 1.36, 95% CI 1.11–1.65; $p = 0.0039$) but not increased infection risk. These survival patterns persisted at longer follow-up, with higher mortality among patients with BM and PI at 6 months (BM HR 1.40, 95% CI 1.32–1.48; $p < 0.001$; PI HR 1.40, 95% CI 1.33–1.47; $p < 0.001$), 1 year (BM HR 1.40, 95% CI 1.33–1.47; $p < 0.001$; PI HR 1.36, 95% CI 1.31–1.42; $p < 0.001$), and 5 years (BM HR 1.30, 95% CI 1.24–1.35; $p < 0.001$; PI HR 1.32, 95% CI 1.27–1.37; $p < 0.001$), while no long-term survival decrement was observed for PD or AI. **Conclusions:** Baseline steroid use prior to ICI initiation is associated with increased early and long-term mortality in NSCLC in BM and PI but not PD and AI. Accounting for clinical indication is important to understand real-world ICI outcomes of patients using steroids. Research Sponsor: None.

Cardiovascular-related adverse events (CVD-AEs) and echocardiographic (Echo) changes with immunotherapy (IT): A real-world experience.

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Background: Immune-checkpoint inhibitors (ICI) are standard of care for many solid tumors but are linked to cardiovascular adverse events (CVD-AEs). Real-world comparative data on CVD-AE incidence between IT & non-IT therapies are limited & no prior studies have evaluated longitudinal Echo changes in IT vs. non-IT patients. **Methods:** We conducted a retrospective cohort of 5,556 adults with solid malignancies at Cleveland Clinic Ohio (2010–2022). IT patients were compared to non-IT systemic therapy. Cancers included bladder (II-III:476; IV:158), endometrial IV (157), gastric (II-III:797; IV:590), H&N IV (36), renal (III:88; IV:223), melanoma (45) & lung: NSCLC non-squamous (IIIB:206; IV:1609), NSCLC squamous (IIIB:182; IV:366) & SCLC IIIB-IV (623). Follow-up began at therapy start & continued until CVD-AE, last follow-up or death. Data were collected on demographics, CTCAE grade, management & outcomes. Incidence rates per 100 person-years (/100 Py) were estimated using Poisson regression, cumulative incidence (CIR) using Kaplan–Meier methods & adjusted hazard ratios (HRs) using time-dependent Cox models. Echo analyses (n = 418) compared baseline to follow-up studies using multinomial regression. **Results:** Of the cohort, 1,291 (23%) & 948 (17%) received 1st- & 2nd-line IT. Median age was 66; 38% were female, & 87% were White. ICI accounted for 99.9% of IT. During follow-up, 163 CVD-AEs occurred, including arrhythmias (n = 59), cardiac arrest (n = 35), myocarditis/heart failure (n = 21), pericarditis (n = 10) & acute coronary syndromes (NSTEMI n = 17, STEMI n = 15, unstable angina n = 5). Median follow-up was 14 months (CI 6–35). The CVD-AE CIRs were slightly higher in IT vs. non-IT groups (0.12 vs 0.11 /100 PY). The 4-year CIR was 5% in IT & 3.5% in non-IT (P = 0.4). In time-dependent Cox models, IT was not associated with a significant increase in composite CVD-AEs, though a borderline association with the composite of cardiac dysrhythmia & conduction disorders was observed (HR 1.43, P = 0.06). Echo analyses showed no association between IT & adverse changes in LV/RV systolic function (EF, GLS, TAPSE), pulmonary pressures or diastolic function (E/e'). In contrast, 1st-line IT was associated with increased odds of aortic root dilation (OR 2.95, p = 0.028), mitral valve sclerosis (OR 4.17, P = 0.02) & a trend toward mitral stenosis (OR 3.7, P = 0.05). Abnormal baseline Echo parameters remained the strongest predictors of future worsening. **Conclusions:** We found that IT was not associated with a significant rise in overall CVD-AEs or myocardial dysfunction, possibly reflecting less use of traditional cardiotoxic agents like anthracyclines. Novel associations with aortic root dilation & mitral valve sclerosis suggest vascular & structural remodeling effects. Findings highlight the need for long-term surveillance of structural heart changes beyond ejection fraction monitoring. Research Sponsor: None.

Socioeconomic and treatment-related determinants of long-term cancer survival: A population-based SEER outcomes analysis.

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Background: Cancer survival is shaped by tumor biology, treatment access, and socioeconomic context, yet population-level quantification of long-term survival disparities related to chemotherapy use and income is limited. We assessed five-year cancer-specific survival across demographic, treatment, and socioeconomic strata in a national registry. **Methods:** We performed a retrospective, population-based survival analysis using the Surveillance, Epidemiology, and End Results (SEER) database. Cancer-specific survival was evaluated at 12, 24, 36, 48, and 60 months after diagnosis. Outcomes were stratified by sex, race, chemotherapy receipt, and area-level median household income categories. Survival estimates were summarized descriptively and visualized using time-to-event curves. **Results:** Overall cancer-specific survival declined progressively over five years, from ~84% at 12 months to ~58% at 60 months. Sex differences were minimal, with similar five-year survival among males and females (~57–58%). Racial disparities were substantial: Asian/Pacific Islander patients demonstrated the highest survival across follow-up, while Black and American Indian/Alaska Native patients had lower early survival and persistent gaps at five years. Patients with recorded chemotherapy use had improved survival compared with those without or with unknown chemotherapy status; 12-month survival was ~88% versus ~80%, and five-year survival was ~65% versus ~57%, respectively. A pronounced socioeconomic gradient was observed: individuals in areas with median household income $\geq$ \$120,000 had higher five-year survival (~67%), whereas those in areas with income $<$ \$40,000 had markedly lower survival (~52%). **Conclusions:** In this national registry analysis, both chemotherapy utilization and higher socioeconomic status were strongly associated with improved long-term cancer survival, whereas persistent racial and income-related disparities remained evident. These findings highlight ongoing inequities in access to oncologic care and support the need for targeted policy interventions and equity-focused treatment delivery models. Interpretation should account for limitations inherent to observational registry data and potential residual confounding. Research Sponsor: None.

Impact of diabetes on respiratory infection risk and hospitalization following immune checkpoint inhibitor initiation in non-small cell lung cancer: A propensity-matched retrospective cohort analysis.

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Background: Immune checkpoint inhibitors (ICIs) are a cornerstone of treatment for non-small cell lung cancer (NSCLC); however, patients with diabetes mellitus may have altered immune responses and higher susceptibility to infections. Data comparing infectious respiratory outcomes, healthcare utilization, and mortality between diabetic and non-diabetic NSCLC patients treated with ICIs is limited. We aimed to evaluate these outcomes in NSCLC patients receiving ICIs, stratified by diabetes status. **Methods:** We conducted a retrospective cohort study using the TriNetX Global Collaborative Network. Adults (≥ 18 years) diagnosed with NSCLC who initiated immune checkpoint inhibitor therapy (PD-1/PD-L1 or CTLA-4 inhibitors) within one year of diagnosis were included. Two cohorts were defined: patients with type 2 diabetes mellitus (DM) and patients without diabetes (non-DM). Propensity score matching (1:1) was performed based on demographics, comorbidities, cancer stage surrogates, smoking history, chemotherapy exposure, radiation therapy, and concurrent medications. Outcomes were assessed from 30 days to 3 years after ICI initiation and included bacterial pneumonia, viral pneumonia, severe sepsis with or without shock, ER visit/hospitalization, critical care needs, and overall survival. Hazard ratios (HRs) with 95% confidence intervals (CIs) were reported. **Results:** After propensity score matching, 905 patients were included in each cohort. Baseline characteristics were well balanced between groups. Compared with the non-DM cohort, patients with diabetes had a significantly higher risk of severe infectious complications, including bacterial pneumonia (HR 1.44, 95% CI 1.01–2.08), severe sepsis (HR 1.79, 95% CI 1.29–2.49). Rates of viral pneumonia did not significantly differ between groups (HR 0.79, 95% CI 0.45–1.38). Diabetic patients also demonstrated higher incidence of hospitalization (HR 1.17, 95% CI 1.05–1.30) and critical care utilization (HR 1.27, 95% CI 1.02–1.57). However, no statistically significant difference in overall survival between cohorts was detected (HR 1.12, 95% CI 0.98–1.29). **Conclusions:** Among NSCLC patients treated with immune checkpoint inhibitors, diabetes mellitus is associated with higher risk of respiratory infections and severe sepsis. Hospital visits and critical care utilization were more frequent in the diabetic cohort, without a corresponding difference in overall survival. These findings highlight the importance of heightened infection surveillance and proactive supportive care in diabetic patients undergoing immunotherapy. Prospective studies are warranted to better define underlying mechanisms and to optimize risk mitigation strategies in this vulnerable population. Research Sponsor: None.

Association between selective serotonin reuptake inhibitor use and outcomes in metastatic melanoma treated with immune checkpoint inhibitors: A real-world cohort study.

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Background: Immune checkpoint inhibitors (ICIs) have transformed outcomes for metastatic melanoma, yet substantial variability in response remains. Evidence suggests that concomitant medications may modulate antitumor immunity and influence ICI effectiveness. For example, recent mechanistic and translational studies indicate that selective serotonin reuptake inhibitors (SSRIs) enhance T-cell-mediated antitumor immunity and may synergize with PD-1 blockade, with preliminary clinical signals of improved survival. However, real-world evidence in melanoma is limited. We conducted a real-world cohort study to assess the association between baseline SSRI use and outcomes among metastatic melanoma patients treated with ICIs. **Methods:** We performed a retrospective cohort study using a nationally representative real-world dataset from the Atropos Evidence Network integrating open claims and EHR data mapped to OMOP CDM v5.3. Adults with metastatic melanoma treated with first-line pembrolizumab, nivolumab, or ipilimumab were identified using ICD and RxNorm codes. The index date was ICI initiation. The SSRI cohort required ≥ 30 days of use prior to index; comparators had no prior SSRI exposure. Patients were matched 1:1 using high-dimensional propensity scores (hdPS) derived from ICD, CPT, and RxNorm features and fitted with LASSO-regularized logistic regression. Outcomes included 1-year overall survival (OS), time to ICI discontinuation, ICI duration, and post-index steroid use. **Results:** Among 3,597 metastatic melanoma patients initiating ICIs, 307 had baseline SSRI exposure and 3,290 had no prior SSRI use. After 1:1 hdPS matching, 304 well-balanced pairs were identified. Baseline SSRI use was associated with a numerically lower but not statistically significant risk of death at 1 year (HR 0.70; 95% CI 0.46–1.06; $p = 0.092$). No significant difference in ICI discontinuation was observed between cohorts (HR 1.07; 95% CI 0.87–1.31; $p = 0.53$). Mean duration of ICI was similar in the propensity-matched analysis (158.7 days in no-SSRI vs 142.4 days in SSRI; mean difference –16 days; 95% CI –40 to 7.3; $p = 0.175$). Post-index steroid use also did not differ between groups (IRR 1.02; 95% CI 0.60–1.73; $p = 0.94$). Across all endpoints, effect estimates were consistent with no clinically meaningful association between baseline SSRI exposure and immunotherapy outcomes. **Conclusions:** In this large real-world analysis, baseline SSRI use was not associated with improved OS, reduced discontinuation, or increased steroid use among metastatic melanoma patients treated with ICIs. Despite strong mechanistic rationale suggesting potential synergy, these findings highlight a disconnect between preclinical observations and real-world outcomes. Prospective studies are needed to identify subpopulations that may benefit. Research Sponsor: None.

Novel myeloma therapy utilization in digital health advocacy users: A large US cohort analysis of >1,500 patients.

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Background: Real-world data consistently demonstrates that access to novel myeloma therapies (CAR-T and Bispecific Antibodies [BsAb]) is restricted by "classic" disparities, including lower income, rural geography, and distance from academic medical centers. However, evidence suggests that strong institutional support and patient navigation can mitigate these factors. While direct-to-patient platforms remain underexplored, high digital engagement—driven by education and medical data ownership—are hypothesized to mitigate traditional barriers. To evaluate this, the HealthTree Registry was queried to determine if its engaged cohort exhibits the disparities observed in the general population. **Methods:** A total of 1,519 Multiple Myeloma patients, diagnosed after 2014, and who connected their Electronic Health Records (EHR) and provided survey data within the HealthTree, were originally extracted. Line of treatment data was extracted from clinical plan and progress notes. Eligibility for novel therapies was retrospectively determined based on FDA approval criteria (lines of therapy and dates). Utilization rates comparisons against demographic variables using Chi-square and ANOVA tests. **Results:** Among the cohort, 277 patients were eligible for CAR-T and 91 for BsAbs. Contrary to general population trends, digital engagement appeared to neutralize classic socioeconomic barriers. We found no significant difference in novel therapy utilization based on median zipcode income (Users: \$103k vs. Non-Users: \$95k, $p = 0.88$), distance to clinic ($p = 0.64$), or rural/urban status ($p = 0.808$). Utilization rates: 30% (84/277) of eligible patients received CAR-T compared to 54% (49/91) for BsAbs. Patients receiving novel therapies had a mean age of 65.9 years and initiated treatment 3.7 years after diagnosis. BsAbs were utilized later in the disease course (Mean Line of Therapy [LOTs]: 6.0) compared to CAR-T (Mean Line of Therapy: 4.8), due to FDA eligibility criteria restrictions. CAR-T utilization was high during early LOTs (2–4) at 48%. While economic and geographic barriers were mitigated, a significant gender disparity emerged in continuous therapy usage. For BsAbs, 66% (33/50) of eligible men received therapy, compared to only 39% (16/41) of eligible women ($p = 0.018$). No gender difference was observed for CAR-T ($p = 1.0$). **Conclusions:** In this cohort, although a greater proportion of patients met eligibility criteria for CAR-T than for BsAb, eligible patients were more likely to initiate BsAb treatment. However, digital engagement of patients facilitated early use of CAR-T therapy and reduced traditional barriers like distance and income, which may be less limiting than previously thought. In contrast, a pronounced gender disparity in BsAb therapy utilization suggests that continuous therapies may impose a disproportionate logistical burden on eligible female patients. Research Sponsor: HealthTree Foundation.

Trends and disparities in diabetes-associated cancer mortality in the United States, 1999–2020.

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Background: Diabetes mellitus (DM) is increasingly recognized as an important contributor to cancer mortality, yet long-term population-level trends and sociodemographic disparities in diabetes-associated cancer deaths in the United States remain insufficiently characterized.

Methods: We analyzed U.S. Multiple Cause of Death data from the CDC WONDER database for 1999–2020. Deaths with neoplasia as the underlying cause of death and diabetes mellitus listed as a contributing cause were included. Annual deaths and crude mortality rates were examined across year, Census region, state, 2013 urbanization level, 10-year age groups, sex, race, and Hispanic origin. Temporal trends were quantified using average annual percent change (AAPC) derived from log-linear regression models over the 1999–2020 period. **Results:** From 1999–2020, diabetes-related neoplasia deaths totaled 588,693 (mean 26,759/year), with annual deaths rising 77.9% (20,427 in 1999 to 36,343 in 2020) and crude mortality increasing 50.7% (7.3 to 11.0 per 100,000), corresponding to an overall AAPC +1.24%/year. By sex, trends increased faster in males (AAPC +1.75%) than females (AAPC +0.55%). By Census region, AAPC was highest in the West (+2.00%) and South (+1.98%), followed by the Midwest (+0.65%), while the Northeast declined (−0.30%). By 2013 urbanization, the steepest rises occurred in Noncore nonmetro (+2.43%) and Micropolitan nonmetro (+1.61%), exceeding Medium metro (+1.54%), Small metro (+1.22%), Large central metro (+0.97%), and Large fringe metro (+0.80%). By race, AAPC was highest for American Indian/Alaska Native (+2.38%) and Asian/Pacific Islander (+2.30%), followed by White (+1.45%) and Black (+0.30%). By Hispanic origin, AAPC was higher in Hispanic/Latino (+2.42%) than Not Hispanic/Latino (+1.33%) (Not stated: insufficient rate series for AAPC). By age, increases were greatest at 35–44 years (+1.45%) and 25–34 years (+1.18%), with smaller increases at 45–54 (+0.62%) and ≥85 (+0.62%), while older mid-life groups declined (65–74: −0.61%, 55–64: −0.27%, 75–84: −0.04%). State-level AAPC ranged from Kentucky (+6.55%), Arizona (+5.07%), Oklahoma (+4.81%), Colorado (+4.66%), and Arkansas (+4.61%) to District of Columbia (−3.44%), Connecticut (−2.91%), Massachusetts (−1.88%), Illinois (−1.38%), and Delaware (−1.24%).

Conclusions: Diabetes-associated cancer mortality increased substantially in the United States from 1999–2020, with widening disparities by geography, urbanization, race/ethnicity, sex, and age. The disproportionate rise in rural areas, younger adults, and select racial and ethnic groups underscores the need for integrated cancer–diabetes prevention strategies and targeted public health interventions to mitigate future mortality burden. Research Sponsor: None.

Time-dependent patterns of immune-related adverse events by obesity status following immune checkpoint inhibitor therapy: A real-world cohort analysis.

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Background: Immune checkpoint inhibitors (ICIs) substantially improve cancer outcomes but are frequently complicated by immune-related adverse events (irAEs). Obesity alters immune regulation and has been paradoxically associated with enhanced ICI efficacy; however, its influence on the timing and persistence of irAEs remains poorly defined. Prior studies have largely evaluated irAEs as binary outcomes, potentially obscuring time-dependent risk patterns. **Methods:** We conducted a retrospective cohort study using the TriNetX U.S. Collaborative Network. Adults with solid tumors initiating nivolumab, pembrolizumab, ipilimumab, or durvalumab were identified. Patients with pre-existing autoimmune disease, hematologic malignancy, organ transplantation, or prior irAEs were excluded. Patients were stratified by baseline body mass index (BMI ≥ 30 kg/m² vs 20–24.9 kg/m²). irAEs were identified using diagnosis-based groupings mapped to organ-specific toxicity categories. Survival analyses were performed using landmarked Cox proportional hazards models evaluating early (1–90 days), delayed (91–365 days), and late (366–1825 days) irAE risk. Adjusted hazard ratios (AHR) were calculated after adjustment for age, sex, cancer type, immunotherapy agent, smoking status, diabetes, chronic kidney disease, chronic pulmonary disease, liver disease, and cardiovascular comorbidity. **Results:** Among 29,564 eligible patients (obese: 13,958; normal BMI: 15,606), obesity was not associated with overall irAE risk across 5 years of follow-up (AHR 0.98, $p=0.19$). In landmark analyses, obesity was associated with lower early irAE risk (AHR 0.94, $p=0.003$), no significant difference during the delayed period, and a persistent increase in late irAE risk (AHR 1.11, $p=0.003$). Time-stratified associations were most pronounced for gastrointestinal, renal, endocrine, and dermatologic irAEs, while pulmonary and neurologic irAEs were not significantly increased after multivariable adjustment. **Conclusions:** Obesity demonstrated a time-dependent association with immune-related toxicity following ICI therapy, characterized by attenuated early risk and persistent late risk emerging beyond one year. These findings highlight the importance of time-stratified analytic approaches and suggest that absence of early irAEs may not confer long-term safety in obese patients receiving ICIs. Research Sponsor: None.

Outcome	Time Window	Adjusted HR (95% CI)	p value
Any incident irAE	1–90 d	0.94 (0.90–0.98)	0.003†
Any incident irAE	366–1825 d	1.11 (1.04–1.19)	0.003†
GI irAE	1–1825 d	0.82 (0.77–0.87)	<0.001†
GI irAE	1–90 d	0.76 (0.68–0.86)	<0.001†
GI irAE	91–365 d	0.82 (0.74–0.90)	<0.001†
GI irAE	366–1825 d	0.84 (0.75–0.93)	0.001†
Renal irAE	366–1825 d	1.14 (1.01–1.29)	0.031†
Endocrine irAE	91–365 d	1.04 (0.99–1.09)	0.089
Endocrine irAE	366–1825 d	1.05 (1.00–1.11)	0.069

† $p < 0.05$.

Patterns of upper endoscopy use prior to gastric cancer diagnosis among high-risk populations.

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Background: Gastric cancer is frequently diagnosed at advanced stages in the United States, contributing to poor survival. Although several populations carry elevated risk, real-world patterns of upper endoscopic evaluation before gastric cancer diagnosis remain poorly characterized. Understanding pre-diagnostic endoscopy utilization may identify gaps in care and inform future evaluation strategies. **Methods:** A retrospective cohort study using Epic Slicer-Dicer identified adults ≥ 18 years diagnosed with gastric adenocarcinoma at Tufts Medical Center between January 2021 and January 2026. Gastric cancer was identified by ICD-10 codes, excluding patients with prior disease. Upper endoscopy (EGD) performed 6–36 months before diagnosis was assessed overall and across high-risk subgroups. EGDs within 6 months were excluded to distinguish pre-diagnostic from index diagnostic procedures. High-risk features were defined by the 2025 AGA Clinical Practice Update and included Asian race, Hispanic ethnicity, interpreter requirement, and prior *Helicobacter pylori* infection, gastric intestinal metaplasia (GIM), or chronic atrophic gastritis (CAG). Rates of pre-diagnostic EGD utilization were described overall and by subgroup. **Results:** Among 258 patients diagnosed with gastric adenocarcinoma, 77 (29.8%) presented with metastatic disease. Overall, 118 patients (45.7%) underwent EGD 6–36 months before diagnosis, while approximately half had their first documented EGD at the time of cancer diagnosis. Rates were similar across racial groups: White (45.3%), Asian (46.3%), Black (43.8%), and Other (45.7%). Utilization was higher among Hispanic versus non-Hispanic patients (57.7% vs 46.2%) and among those requiring interpreter services (51.8% vs 47.0%). Patients with gastric precursor conditions (34.1%) had similar rates of pre-diagnostic EGD (52.3%), including prior *H. pylori* infection (40.0%), GIM (63.3%), and CAG (55.0%). Of 140 patients without pre-diagnostic EGD, 39 (27.9%) underwent colonoscopy alone, indicating access to endoscopic care without concurrent EGD. **Conclusions:** Most upper endoscopies occurred near the time of cancer diagnosis, suggesting predominantly diagnostic rather than preventive evaluation. Even among patients with recognized risk factors and gastric precursor conditions, only about half underwent prior upper endoscopic assessment. Colonoscopy without concurrent EGD highlights gaps in integrated, risk-based gastrointestinal cancer prevention and an opportunity to improve earlier recognition of gastric cancer in high-risk populations. Research Sponsor: None.

Upper endoscopy use before gastric cancer diagnosis.

High-Risk Feature	Total (N)	Total (%)	% w/ EGD (6–36 mo)
Overall population	258	—	45.7
Asian race	67	26.0	46.3
Hispanic ethnicity	26	10.1	57.7
Requires interpreter	56	21.7	51.8
<i>H. pylori</i> infection	35	13.6	40.0
GIM	60	23.3	63.3
CAG	20	7.8	55.0
Any <i>H. pylori</i> , GIM, or CAG	88	34.1	52.3

Distinct patient and product-specific phenotypes associated with toxicity and resource utilization after CAR T-cell therapy: A Nationwide Inpatient analysis.

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Background: Chimeric antigen receptor (CAR) T-cell therapy improves outcomes in relapsed or refractory hematologic malignancies but is associated with significant toxicity and inpatient resource utilization. Nationally representative real-world data remain limited. We evaluated the incidence, phenotype-specific predictors, and inpatient consequences of CAR T-cell-related toxicities in U.S. practice. **Methods:** We conducted a retrospective cohort study using the 2023 Nationwide Inpatient Sample, identifying adult elective hospitalizations involving CAR T-cell infusion using ICD-10-PCS New Technology Group 7 codes for FDA-approved CAR-T therapies. Interhospital transfers were excluded. Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and cytopenias were identified using ICD-10-CM codes during the index hospitalization; toxicity grade was unavailable. Functional status was assessed using APR-DRG loss of function severity. Primary outcomes were coded in-hospital CRS, ICANS, and cytopenias. Secondary outcomes included transfusion requirement, length of stay (LOS), and total inpatient cost, adjusted to 2023 U.S. dollars. Survey-weighted multivariable regression models evaluated predictors of toxicity and resource utilization. **Results:** The weighted cohort represented 3,405 CAR-T hospitalizations nationwide. Indications included multiple myeloma (42.6%), diffuse large B-cell lymphoma (32.0%), follicular lymphoma (9.0%), mantle cell lymphoma (8.6%), B-cell acute lymphoblastic leukemia (7.4%), and chronic lymphocytic leukemia (0.4%). Cytopenias were coded in 45.2% of hospitalizations, CRS in 62.6%, and ICANS in 30.1%. In adjusted analyses, cytopenias were associated with older age, B-cell acute lymphoblastic leukemia, moderate-to-severe functional impairment, and CAR-T product type. CRS risk varied by CAR-T product type and was higher among transplant recipients and patients with severe functional impairment. ICANS was associated with transplant history, selected comorbidities (including metastatic solid tumors), follicular lymphoma, older age, and CAR-T product type. Median LOS was 12 days (IQR, 9–16) and was longer among patients with neutropenia. Transfusion support was required in 6.6% of hospitalizations. Median total inpatient hospitalization cost exceeded \$1.3 million and was independently associated with diffuse large B-cell lymphoma, B-cell acute lymphoblastic leukemia, neutropenia, and autologous leukapheresis. **Conclusions:** CAR T-cell therapy is associated with substantial inpatient toxicities, prolonged hospitalization, and high cost, with risk varying by patient and product specific phenotypes. These findings support pre-infusion risk stratification and resource-aligned inpatient care models for CAR-T delivery. Research Sponsor: None.

Bridging the gap between clinical utility and coverage: Real-world impact of unreimbursed NGS testing.

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Background: Genomic testing is the cornerstone of precision oncology, revealing rare yet clinically actionable alterations that define diagnosis, risk stratification, and treatment choice. Despite its proven clinical utility, inconsistent coverage and inadequate reimbursement constrain routine use, reflecting a persistent misalignment between clinical value and payer policy. Evaluating real-world utilization and clinical impact of unreimbursed testing can highlight critical gaps in standard oncology care. **Methods:** Molecular profiles of 7,271 patients were analyzed by integrating Neogenomics sequencing data (09/2025 – 12/2025) with standardized clinical data (cancer diagnoses, ICD-10 codes, medication records, molecular testing results) extracted from comprehensive electronic medical records using the xCures platform. **Results:** Cohort of 7,271 patients insured by commercial (58%), managed (22%), or government (20%) plans had unreimbursed tests with orders originating primarily from hospitals (49%) and physician groups (42%). Testing predominantly targeted hematologic malignancies (> 90%), with solid tumors representing 8%. Among patients with available medical records (n = 3,409), hematologic panels remained most common (67%), led by the Neo Comprehensive Myeloid (n = 1,064), NeoTYPE MDS/CMML Profile (n = 485), Neo Comprehensive Heme (n = 385), NeoTYPE CLL Profile (n = 299) and NeoTYPE Lymphoid Disorders Profile (n = 211). Abnormal molecular findings were identified in 1,056 patients (%), including 470 patients with pathogenic or likely pathogenic variants (SNVs, deletions, insertions, fusions and substitutions), with 23% (104/470) of alterations (i.e. ABL1, ERBB3, KDR, MAP2K1, TOP1, TSC1, TSC2) not identified by previous methods. Of 66 patients receiving targeted therapy after testing, 4 (6%) were treated within 60 days for pathogenic alterations (, JAK2, KIT, BCR-ABL1) identified by Neogenomics. Eleven (17%), initially with unspecified diagnoses, received therapies (venetoclax, obinutuzumab, lenalidomide) for newly defined indications, and 2 (3%) were treated (venetoclax, lenalidomide) based on relevant biomarkers (NPM1, SF3B1) of sensitivity, all guided by test results within 60 days. Among 386 patients with initially unspecified conditions, EMR for 137 patients (36%) confirmed diagnoses within 60 days. **Conclusions:** Genomic testing delivers substantial clinical value by enabling rapid, definitive diagnoses and informing timely, targeted treatment decisions. Despite inconsistent payer coverage, these data show that NGS testing frequently identifies actionable alterations and biomarkers not previously identified by standard testing that directly impact patient management. Aligning reimbursement policies with anticipated clinical utility is critical to closing gaps in standard care and expanding equitable access to precision oncology. Research Sponsor: None.

Early mortality and hospitalization following cholangiocarcinoma diagnosis by statin exposure: A TriNetX real-world analysis.

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Background: Statins are widely prescribed among patients with cardiometabolic comorbidities and are frequently continued at the time of cancer diagnosis. While statins have been hypothesized to exert antitumor and immunomodulatory effects, real-world data evaluating early clinical outcomes associated with statin exposure in patients with cholangiocarcinoma are limited. We assessed short-term mortality and hospitalization outcomes following cholangiocarcinoma diagnosis using a large federated electronic health record network. **Methods:** We conducted a retrospective cohort study using the TriNetX US Collaborative Network, comprising 68 healthcare organizations. Adult patients (≥ 18 years) diagnosed with intrahepatic bile duct carcinoma (ICD-10 C22.1), extrahepatic bile duct carcinoma (C24.0), or ampullary carcinoma (C24.1) between January 1, 2010, and December 11, 2024 were included. Patients were classified based on exposure to statins (rosuvastatin, simvastatin, fluvastatin, pravastatin, lovastatin, atorvastatin, or pitavastatin) within a prespecified temporal window relative to cancer diagnosis, with the index event defined accordingly. Propensity score matching (1:1) was performed to balance demographics, comorbidities, and laboratory characteristics, mitigating confounding by indication and immortal time bias. Outcomes included all-cause mortality, hospitalization, and sepsis at 30 and 90 days following the index event. Risk estimates and Kaplan–Meier survival analyses were performed. **Results:** After propensity score matching, baseline characteristics were well balanced between statin-exposed and non-statin-exposed cohorts. At 30 days following diagnosis, statin exposure was not associated with a significant difference in all-cause mortality. In contrast, at 90 days, statin exposure was associated with higher all-cause mortality (risk ratio 1.23; hazard ratio 1.30; log-rank $P = .012$) and increased hospitalization (risk ratio 1.29; hazard ratio 1.37). No significant differences in sepsis risk or hazard were observed between cohorts at either time point. **Conclusions:** In this real-world, propensity score-matched analysis of patients with cholangiocarcinoma, statin exposure was not associated with improved 30-day survival and was associated with higher 90-day mortality and hospitalization. Although causality cannot be inferred, these findings highlight clinically meaningful early outcome differences during the peri-diagnostic period and suggest that commonly prescribed cardiovascular medications may identify patients with increased baseline vulnerability at the time of cancer diagnosis. Future work integrating medication exposure with comorbidity burden, treatment patterns, and early care trajectories may help refine risk stratification during initial cholangiocarcinoma management. Research Sponsor: None.

Osteoporosis and osteoporosis-related fractures among older male cancer patients: A nationwide study.

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Background: Osteoporosis is commonly viewed as a disease of postmenopausal women, leading to significant underdiagnosis in men. Older male patients with cancer experience accelerated bone loss due to androgen deprivation therapy, corticosteroid exposure, and malignancy-related skeletal remodeling. We examined the prevalence, tumor-specific risk factors, and outcomes of osteoporosis and related fractures in a national cohort of older male cancer patients. **Methods:** We analyzed Nationwide Readmissions Database hospitalizations from 2019–2022, identifying male patients aged ≥ 60 years with malignancy. Primary outcomes were osteoporosis (ICD-10-CM M80/M81) and major osteoporotic fractures (hip, spine, humerus, wrist); isolated hip fracture was a secondary outcome. Survey-weighted multivariable logistic regression models identified independent predictors, adjusting for age, cancer type, metastatic status, and clinical risk factors. **Results:** Among an estimated 5.17 million weighted cancer admissions, 2.79 million occurred in males. Osteoporosis was diagnosed in 1.29% of males versus 7.16% of females ($P < 0.001$); mean age at diagnosis was 76.5 vs 78.0 years. Men with osteoporosis had markedly higher fracture rates than those without, including hip fracture (5.11% vs 0.85%) and any major fracture (8.36% vs 1.60%) (all $P < 0.001$). In multivariable analysis, odds of osteoporosis diagnosis increased with age (OR 1.06 per year, $P < 0.001$). Diagnoses were most strongly associated with multiple myeloma (OR 1.63), prostate cancer (OR 1.33) (both $P < 0.001$), and leukemia (OR 1.16, $P = 0.008$). Hypogonadism (OR 4.77), hyperparathyroidism (OR 3.53), vitamin D deficiency (OR 2.51), and tobacco use (OR 1.08; $P = 0.009$) were independent clinical predictors. In fracture models, prior osteoporosis diagnosis was the strongest predictor of any major fracture (OR 4.11) and hip fracture (OR 2.41) (both $P < 0.001$). Modifiable risks, including tobacco use (OR 1.55–1.61) and vitamin D deficiency (OR 1.68–1.88) (both $P < 0.001$), consistently increased fracture risk. Prostate cancer increased odds of both major (OR 1.11) and hip fractures (OR 1.21) ($P < 0.001$), whereas multiple myeloma increased odds of major fracture (OR 1.19, $P = 0.004$) but was associated with lower odds of hip fracture (OR 0.80, $P = 0.03$). **Conclusions:** Older men with cancer face substantial, under-recognized risk for osteoporosis and fracture-related morbidity. Tumor-specific patterns and modifiable clinical factors identify clear opportunities for earlier risk assessment and integration of bone health strategies into routine oncologic care. Research Sponsor: None.

Sepsis severity and inpatient outcomes in metastatic cancer: A National Inpatient Sample study.

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Background: Sepsis is a major driver of acute decompensation and inpatient death in patients with cancer, with particularly poor outcomes reported among severe sepsis and septic shock. We evaluated national associations between sepsis severity and inpatient outcomes among metastatic cancer hospitalizations. **Methods:** We conducted a retrospective cross-sectional analysis of the National Inpatient Sample (2016–2020). Adult hospitalizations with metastatic cancer were identified using ICD-10-CM codes C77–C79. Sepsis severity was categorized as no sepsis, severe sepsis without shock, or septic shock using ICD-10 diagnosis codes. Survey-weighted multivariable logistic regression estimated adjusted odds ratios (aOR) for in-hospital mortality, mechanical ventilation, and ICU utilization. Survey-weighted linear regression estimated adjusted differences in length of stay (LOS) and total charges. Models adjusted for age group, sex, race/ethnicity, primary payer, hospital bed size, hospital region, and comorbidity burden using vwcheck (van Walraven score derived from Elixhauser comorbidities). **Results:** In the complete-case regression cohort (weighted N=1,011,365), severe sepsis was associated with higher in-hospital mortality versus no sepsis (aOR 1.49, 95% CI 1.44–1.54), and septic shock with markedly higher mortality (aOR 4.75, 95% CI 4.63–4.87). Sepsis severity strongly predicted escalation of care: mechanical ventilation (severe sepsis aOR 1.37, 95% CI 1.24–1.50; septic shock aOR 6.31, 95% CI 5.93–6.71) and ICU utilization (severe sepsis aOR 1.07, 95% CI 1.03–1.11; septic shock aOR 6.44, 95% CI 6.26–6.62). Relative to the Northeast, adjusted mortality odds were lower in the Midwest (aOR 0.72), South (aOR 0.77), and West (aOR 0.81). Septic shock was associated with higher resource use (+1.38 LOS days; +\$56,975 charges). **Conclusions:** In hospitalized patients with metastatic cancer, increasing sepsis severity was independently associated with stepwise increases in mortality, need for ICU-level care, and healthcare utilization. Patients with septic shock represented a particularly high-risk subgroup, with markedly elevated mortality and resource use even after adjustment for comorbidity burden. These findings emphasize that sepsis, rather than malignancy alone, is a major driver of inpatient outcomes in advanced cancer and highlight the importance of early recognition and timely escalation of supportive care for this vulnerable population. Research Sponsor: None.

Association of sepsis severity with inpatient outcomes among metastatic cancer hospitalizations (NIS 2016–2020).

Outcome	Severe sepsis (aOR or Δ, 95% CI)	Septic shock (aOR or Δ, 95% CI)
In-hospital mortality	1.49 (1.44–1.54)	4.75 (4.63–4.87)
Mechanical ventilation	1.37 (1.24–1.50)	6.31 (5.93–6.71)
ICU utilization	1.07 (1.03–1.11)	6.44 (6.26–6.62)
Length of stay, days	–0.42	+1.38
Total hospital charges, \$	–3,325	+56,975

Real-world utilization and outcomes of lenalidomide in MDS with low blasts and isolated deletion 5q (MDS w 5q).

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Background: Lenalidomide is the preferred first-line agent for lower risk MDS w 5q. It is associated with higher rates of transfusion independence and cytogenetic remission and has demonstrated survival benefit in selected clinical trial populations. Large nationwide studies are lacking in this subgroup. **Methods:** We identified adults aged > 18 years with MDS w 5q diagnosed between 2006 and 2021 using the National Cancer Database (NCDB), corresponding to Lenalidomide approval. Demographic, socioeconomic characteristics, insurance status, Charlson-Deyo comorbidity index (CCI), and treatment variables were extracted. The primary outcome was receipt of lenalidomide therapy. Secondary outcomes included overall survival (OS). Patients were categorized into pre-Affordable Care Act (ACA) and post ACA periods. Multivariable logistic regression and relative risk models were used. OS was estimated using Kaplan-Meier methods and differences between groups were compared with log-rank tests. Multivariable Cox proportional hazards model was used to assess factors associated with survival. $P < 0.05$ was considered significant. **Results:** We identified 3,328 individuals with MDS w 5q, median age of 77 years; 56.1% were women. The majority were non-Hispanic white 87%, followed by 6% non-Hispanic blacks and 4% Hispanic patients. Predominant insurance type was Medicare (78.3%). CCI score of 2 and higher was present in 15%. Overall, 21% of patients received Lenalidomide. Utilization increased significantly in the post-ACA, compared with pre-ACA (32% vs 12%, $p < 0.001$). On multivariable analysis, post -ACA period was independently associated with higher odds of Lenalidomide receipt (OR 3.01-4.34, $P < 0.001$), while Medicaid was associated with lower likelihood of treatment compared with Medicare (OR 0.26-0.96, $p = 0.04$). Other demographic and socioeconomic variables were not independently associated with treatment receipt. Median OS for the overall cohort was 15.7 months. In multivariable Cox analysis, worse OS was associated with age > 80 (HR 1.0; ref = 61-70), receipt of chemotherapy (HR 1.35) and increasing commodity burden [CDS: HR 1.27; CDS:2 HR 1.45, CDS 3: HR 1.95; all $p < 0.001$]. Female sex was associated with improved survival (HR 0.76; $p < 0.001$). Lenalidomide receipt was not independently associated with OS after adjustment (HR 1.05; $p = 0.27$). **Conclusions:** This is the largest study evaluating receipt of lenalidomide in MDS with 5q deletion. Lenalidomide utilization increased substantially following ACA implementation, leading to improved access to disease modifying therapy. However, Medicaid insurance was associated with lower treatment receipts. Survival outcomes were primarily driven by age, commodity burden and treatment intensity rather than Lenalidomide receipt, highlighting persistent disparities and limitations of registry-based analysis. Research Sponsor: None.

A phase II, single-arm, exploratory study of GEMOX combined with tislelizumab and donafenib in the perioperative treatment of potentially resectable intrahepatic cholangiocarcinoma with high recurrence risk.

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Background: Biliary tract cancer (BTC) is characterized by strong invasiveness and poor prognosis, with a metastasis and recurrence rate of up to 67% within 1 year after surgery and a 5-year overall survival rate of only 5%~15%. Among BTC subtypes, intrahepatic cholangiocarcinoma (ICC) accounts for a relatively high proportion, and its unique biological behaviors result in persistently high postoperative recurrence risk, which seriously endangers patients' life and health. Currently, major guidelines recommend that patients with potentially resectable ICC at high recurrence risk participate in clinical trials to explore optimal treatment strategies. For patients evaluated as "technically resectable but with high-risk recurrence" before surgery, clinical practice has shown that neoadjuvant therapy can effectively eliminate micrometastases and reduce the difficulty of R0 resection; postoperative adjuvant therapy can further prevent recurrence. Therefore, we innovatively propose a perioperative treatment model aimed at breaking through the existing therapeutic predicament. **Methods:** This study is a phase II, single-arm, exploratory study with a fixed sample size of 20 patients. The inclusion criteria are intrahepatic cholangiocarcinoma (ICC) (TNM stage T1-4, N0-1, M0) based on preoperative assessment, initial technical resectability per imaging, and at least one high-risk recurrence factor. High-risk recurrence factors include: tumor diameter >5 cm, regional lymph-node positivity, satellite/multifocal lesions, radiological suspicion of diaphragmatic adhesion, CA19-9 >200 U/ml, and an anticipated surgical margin <1 cm on pre-operative imaging. Treatment involves two 21-day cycles of GEMOX (gemcitabine 1000mg/m² on day 1 and 8, oxaliplatin 100mg/m² on day 1) with tislelizumab (200mg on day 1) and donafenib (0.2g orally twice daily). If investigators confirm patients meet surgical criteria (R0 resection expected), surgery follows 1-2 weeks post-treatment. Post-surgery, adjuvant therapy starts within 5 weeks. The regimen is capecitabine (1250mg/m² orally twice daily on days 1-14) or S-1 (40-60mg orally twice daily on days 1-14, weight-adjusted) plus tislelizumab (200mg on day 1) and donafenib (0.2g orally twice daily), repeated every 21 days for six cycles. Primary endpoint is event-free survival (EFS). Secondary endpoints are objective response rate (ORR) and disease control rate (DCR) per RECIST1.1, R0 resection rate, major pathological response rate (MPR, the proportion of patients who underwent radical surgery and had ≤10% residual viable tumor in the postoperative specimen), treatment completion rate, overall survival (OS), disease-free survival (DFS), and safety (treatment-related adverse events' incidence and severity). Clinical trial information: ChiCTR2500112067. Research Sponsor: Suzhou Zelgen Biopharmaceuticals Co., Ltd.; BeOne Medicines.

Design of an innovative clinical development program using randomized controlled phase 2 trial data and real-world evidence from an expanded access protocol to assess mifomelatide (TCMCB07) in GI cancer cachexia.

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Background: Cachexia is common in GI cancers, occurring in ~50% of patients with colorectal cancer (CRC) and up to 80% of patients with pancreatic ductal adenocarcinoma (PDAC). Resulting muscle mass and energy store depletion reduces chemotherapy tolerance, often leading to dose reductions, treatment delays/discontinuation, and poorer survival outcomes (Franko J, *Eur J Cancer*; 2022:174; Dunne RF, *J Cachexia Sarcopenia Muscle*. 2024;15:1628). Therefore, body weight preservation during chemotherapy may improve treatment effectiveness and outcomes for patients with GI cancer. The central melanocortin (MC) system, including MC3 and MC4 receptors, plays essential roles in regulating appetite, body mass, and energy homeostasis and is a logical therapeutic target to prevent and treat cachexia. Mifomelatide is a novel peptide MC3R/MC4R dual antagonist that is being studied for cancer and chemotherapy-associated weight loss. Our previously published work showed that mifomelatide was safe and effectively ameliorated cancer- and chemotherapy-associated cachexia in preclinical studies of mice, rats, and pet dogs. In a Phase 1 trial, healthy volunteers tolerated mifomelatide and did not experience vital sign or CV abnormalities or drug-related SAEs; they also experienced a modest increase in body weight and hunger compared with placebo. These findings warranted further clinical development of mifomelatide. **Methods:** The mifomelatide clinical development program is designed to generate a multidimensional body of evidence from clinical trial and real-world datasets that span GI cancer types and cachexia stages. First, a randomized, double-blind, placebo-controlled Phase 2 trial is evaluating mifomelatide's effects in 120 patients with newly diagnosed mCRC and pre-cachexia or early weight loss (NCT06937177). Additionally, an intermediate-size Expanded Access Protocol (EAP) was cleared by the US Food and Drug Administration in January, 2026 to make mifomelatide available to 100 eligible cachectic PDAC patients (NCT number pending). In addition to providing mifomelatide for compassionate use to patients with PDAC who have high unmet need and no approved treatment options for their cancer cachexia, the EAP will also facilitate the collection of real-world data that, when combined with findings from the Phase 2 trial, will deepen our understanding of mifomelatide's safety, tolerability, and potential to optimize body weight in patients with GI cancer. Collectively, our innovative hybrid approach to the mifomelatide clinical development program will generate robust insights into the benefit-risk profile of MC3R/MC4R dual antagonism with mifomelatide to treat cachexia across GI cancers and guide key design considerations for a subsequent pivotal trial. Clinical trial information: NCT06937177. Research Sponsor: Endevica Bio, Inc.

Economic burden of non-approved alternative therapies among patients with stage IV cancer: A prospective observational study.

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Background: Complementary and alternative therapies, including herbal supplements and over-the-counter medications, are used by 9 to 81% of cancer patients post-diagnosis to alleviate symptoms, side effects, anxiety, depression, or to gain a sense of control. Prior studies suggest higher use among younger, female patients with higher socioeconomic status. However, in our institutional practice, we did not observe any specific pattern on alternative medicine use. Additionally, the financial burden (financial toxicity) of these often-out-of-pocket expenses remains understudied in advanced cancer populations. This prospective observational study aims to assess the financial toxicity and describe patterns of use of non-approved alternative therapies among patients with stage IV cancer. **Methods:** This is a prospective, single-center, observational study conducted at Mercy Clinic Oncology, Fort Smith, AR. Eligible patients are aged ≥ 18 years, diagnosed with any stage IV cancer, and currently receiving systemic therapy. Key exclusions include the inability to read/understand English, incarcerated patients, and patients only on supportive care. A convenience sample of 150 patients will be enrolled for initial analysis with plans to expand the study to a multi-institutional format. Patients meeting eligibility criteria are identified via clinic schedule review and approached in person by a research nurse. Interested patients receive a study information sheet and complete a one-time, anonymous, paper-based survey (approximately 5 minutes) either in-clinic or at home (returned at next visit). The survey includes 6 demographic/cancer/treatment questions and 6 questions on use of specific non-approved alternative therapies and estimated average monthly costs (categorized as $< \$25$, $\$26-\$50$, $\$51-\$100$, $> \$100$). A specific question on marijuana addresses use for cancer cure (recreational/symptom control categorized as "no"); responses are anonymous with no PHI collected to minimize risk. Analysis will use descriptive statistics (frequencies/percentages) for cost patterns (primary outcome) and therapy types (secondary outcome), with chi-squared tests for subgroup comparisons by demographics. Enrollment started beginning of January 2026, and in two weeks, nine patients were identified and approached, with seven patients completing the survey. No preliminary data are available. Clinical trial information: Not applicable (IRB-approved observational protocol 24-062). Research Sponsor: None.

A pragmatic, hybrid observational study evaluating the effectiveness of trastuzumab deruxtecan (T-DXd) in patients with human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) 3+ solid tumors: DESTINY-PanTumor04.

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Background: Patients with advanced or metastatic HER2 IHC 3+ solid tumors have limited treatment options beyond first-line settings, with generally poor outcomes. T-DXd is a HER2-directed antibody-drug conjugate approved in multiple countries, including in the US for patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior treatment and have no satisfactory alternative therapies. Building on existing clinical trial data, DESTINY-PanTumor04 evaluates the real-world effectiveness of T-DXd in HER2-positive (IHC 3+) solid tumors, using a hybrid data collection approach that enhances efficiency for sites and physicians and facilitates study implementation. **Methods:** DESTINY-PanTumor04 (NCT07124000) is a multicenter, pragmatic observational, real-world study evaluating the effectiveness of T-DXd (5.4 mg/kg IV Q3W) in adult patients in the US with previously treated, locally advanced, unresectable, or metastatic HER2-positive (IHC 3+ by local testing) solid tumors. Data collection will use a hybrid approach, combining primary data collection of baseline tumor burden, comorbidities, ECOG status, treatment response, and survival, with secondary data collection from electronic health record (EHR) abstraction for all other data. Approximately 100 patients will be enrolled across US sites, including community oncology practices and academic medical centers within an existing US oncology network from Paradigm Health. Participating sites will use technological resources that support the identification of eligible patients and enable efficient EHR-to-electronic data capture and transfer, minimizing physician time while improving compliance in data completeness and accuracy. Eligible patients must have disease progression following ≥ 1 prior systemic treatment for metastatic or advanced disease, have no alternative treatment options, and have a clinical decision for T-DXd treatment in accordance with the FDA label. Patients with breast cancer, colorectal cancer, non-small cell lung cancer, gastric or gastroesophageal junction cancers, or hematologic malignancies will be excluded. Primary endpoints are real-world objective response rate, defined as the proportion of patients with a complete response (CR) or partial response (PR) as determined by clinician assessment per criteria used in routine clinical practice; and real-world duration of response, defined as the time from first objective response (CR or PR) to disease progression as determined by clinician assessment per criteria used in routine clinical practice, or death. Secondary endpoints include real-world time to treatment discontinuation and real-world time to next treatment. Enrollment began in September 2025 and is ongoing. Clinical trial information: NCT07124000. Research Sponsor: AstraZeneca.