

Optimizing Time to Chemotherapy After Primary Debulking Surgery in Epithelial Ovarian Cancer: Health System-Level Implications

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Background

- Epithelial ovarian carcinoma (EOC) is a deadly gynecologic malignancy affecting active-duty Service Members, retirees, and military beneficiaries despite implementation of contemporary multimodal standards of care.
- Within the Military Health System (MHS), coordination of Gynecologic Oncology surgical and chemotherapy care across primary and tertiary CONUS and OCONUS Military Treatment Facilities (MTFs) influences survival outcomes, military readiness and healthcare system performance.
- Although early initiation of adjuvant chemotherapy following primary debulking surgery is often prioritized, prior studies report conflicting findings and guidelines do not define an optimal time to chemotherapy (TTC).

Objective and Hypothesis

- Study Objective:** To evaluate the relationship between TTC and overall survival (OS) in EOC and explore whether this relationship varies across subgroups.
- Hypothesis:** TTC following PDS would not be linearly associated with survival.

Why This Matters to the MHS

- Addresses a modifiable aspect of cancer care that can be targeted through quality improvement efforts.
- Provides military-relevant evidence on the relationship between treatment timing and survival outcomes.
- Supports evidence-based oncology practice optimization across primary and tertiary OCONUS and UCONUS MTFs.

Methods

- Study Design:** Retrospective National Cancer Database Cohort Study (2006-2020).
- Inclusion Criteria:** Identified 67,340 patients with epithelial ovarian, tubal, or primary peritoneal carcinoma who underwent surgery followed by adjuvant chemotherapy.
- Statistical Approach:**
 - TTC as weeks from PDS to chemotherapy initiation, and patients with TTC > 12 weeks were excluded.
 - Restricted cubic splines to model TTC nonlinearly, from which TTC was binned as <3 (early) vs 3-12 weeks (standard).
 - Kaplan-Meier curves and Cox proportional hazards models, including subgroup analyses by clinical factors.
 - Propensity score weighting balanced the cohort.

Results

(Effective Coordination Within Multimodal Gynecologic Oncology Services and Across MTFs is Critical for Optimizing Survival Outcomes, Readiness and Health System Performance)

TTC had a nonlinear relationship with risk of death (p<0.001). Highest risk in early (<3 weeks) vs. standard (3-12 weeks) TTC.

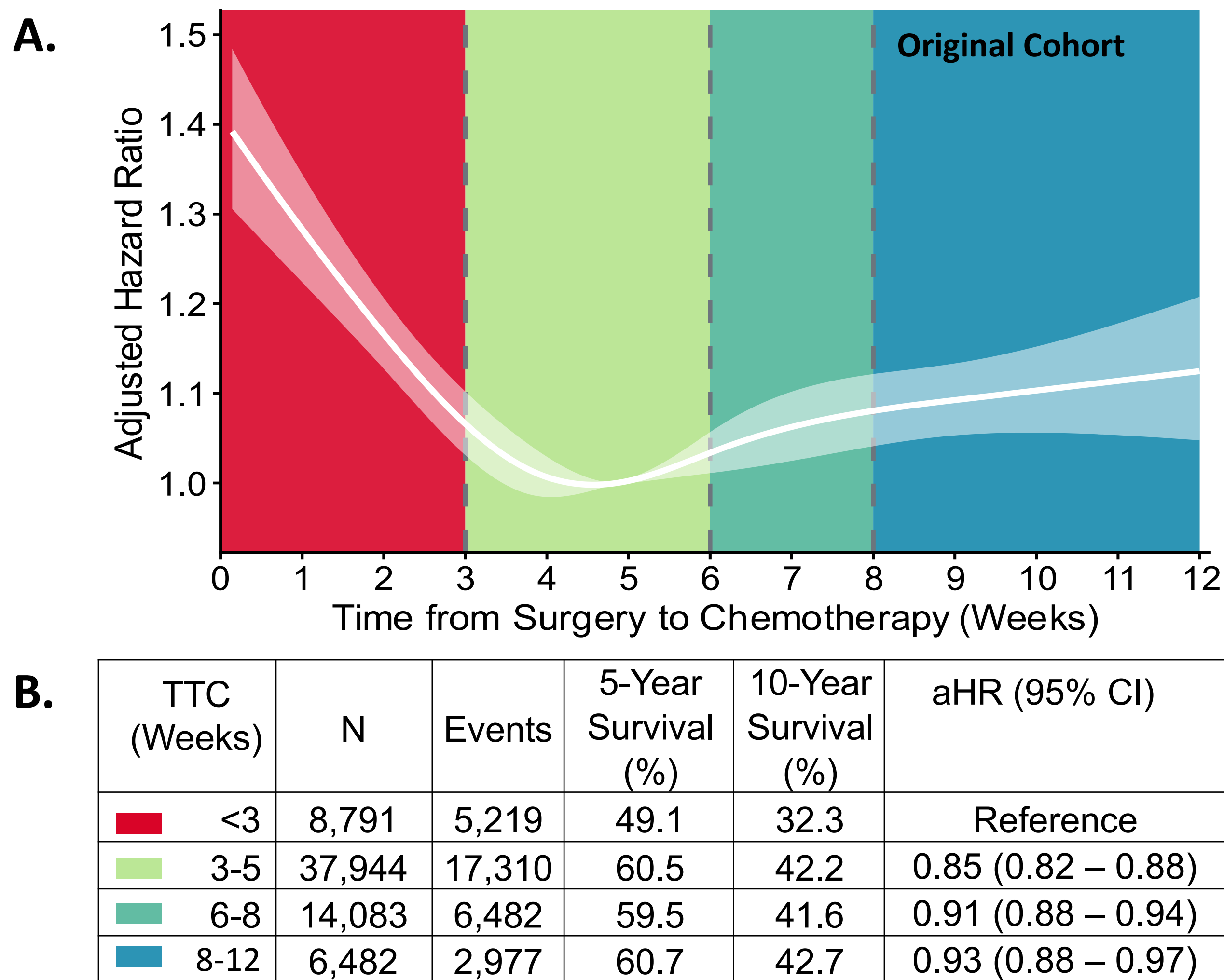


Figure 1. TTC and Risk of Death in Original Cohort. (A.) Adjusted hazard ratio (aHR) for death modeled using restricted cubic splines. (B.) Display of sample size, events, survival rates, and aHRs (95% CIs). Pairwise differences between ≥3-week groups supported dichotomization.

Patient with early TTC presented with more aggressive features (advanced stage, high grade and residual disease).

Table 1. Differences between EOC patients receiving early TTC (<3 weeks) vs. standard TTC (3-12 weeks).

Characteristic	Early TTC	Standard TTC	P-value
Stage			
Early stage	2047 (23.3)	21,108 (36.1)	<0.001
Advanced stage	6744 (76.7)	37,441 (63.9)	
*Tumor Grade			
G1	334 (3.8)	3676 (6.3)	<0.001
G2	974 (11.1)	6916 (11.8)	
G3	6277 (71.4)	39817 (68.0)	
*Residual Disease Status			
No Residual Tumor	3231 (36.8)	26448 (45.2)	<0.001
Residual Tumor	2995 (34.1)	13313 (22.7)	

* Not Reported groups are not shown.

Clinical Practice Pearls: (1) Recovery from extensive surgery should remain a priority. (2) Earlier chemotherapy is not necessarily better. (3) Disease biology and surgical outcome remain dominant determinants of survival.

After propensity score weighting to mitigate bias, early TTC still had worse survival than standard TTC.

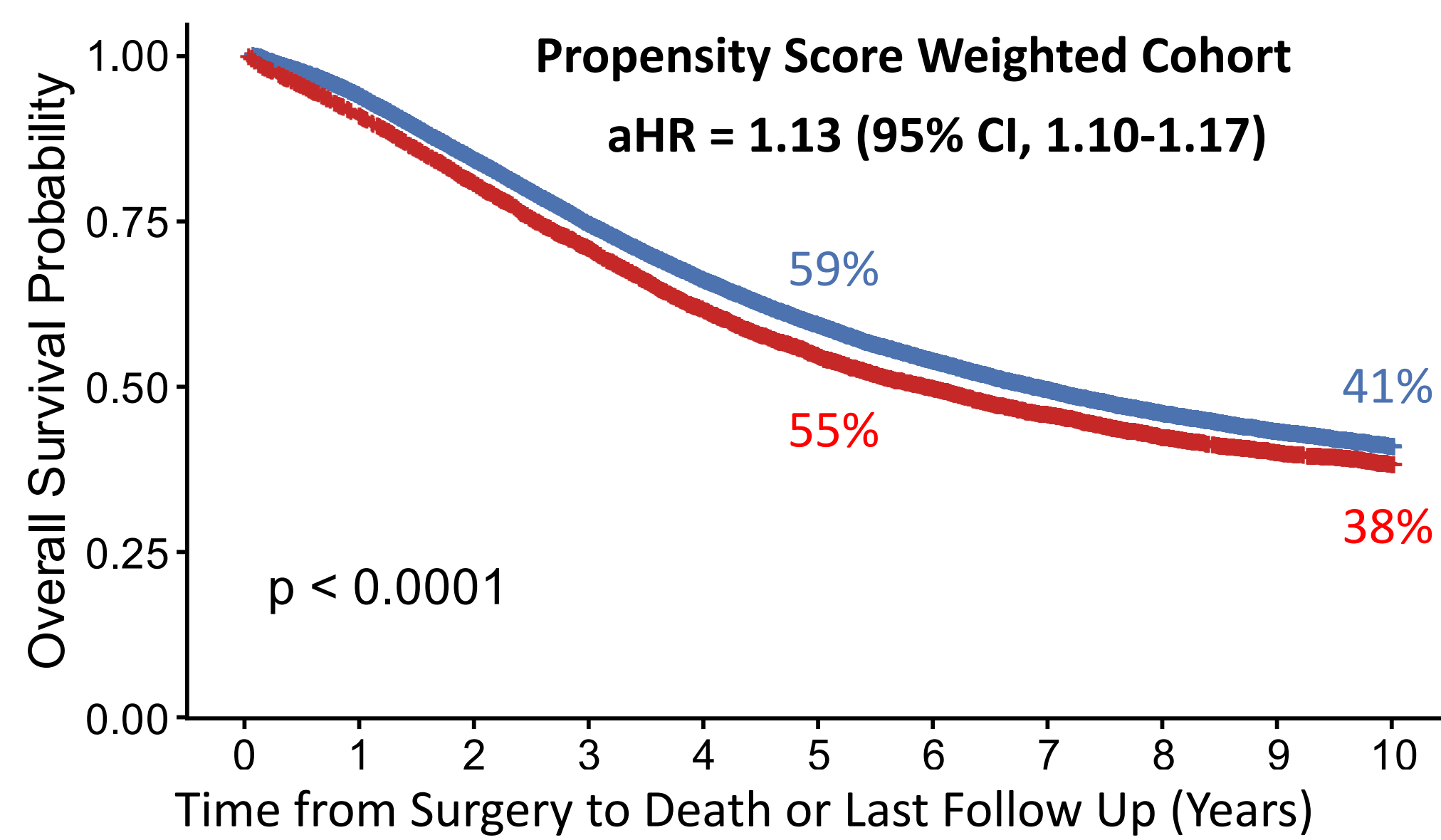


Figure 2. TTC and Risk of Death in Propensity Score Weighted Cohort. Weighted Kaplan-Meier curves for overall survival by early TTC (red) vs. standard TTC (blue, reference) with 5- and 10- survival rates and adjusted risk of death.

Increased risk of death for early TTC in age and racial groups, advanced stage, histologic subtypes, grade 2/3 disease, and both residual disease groups.

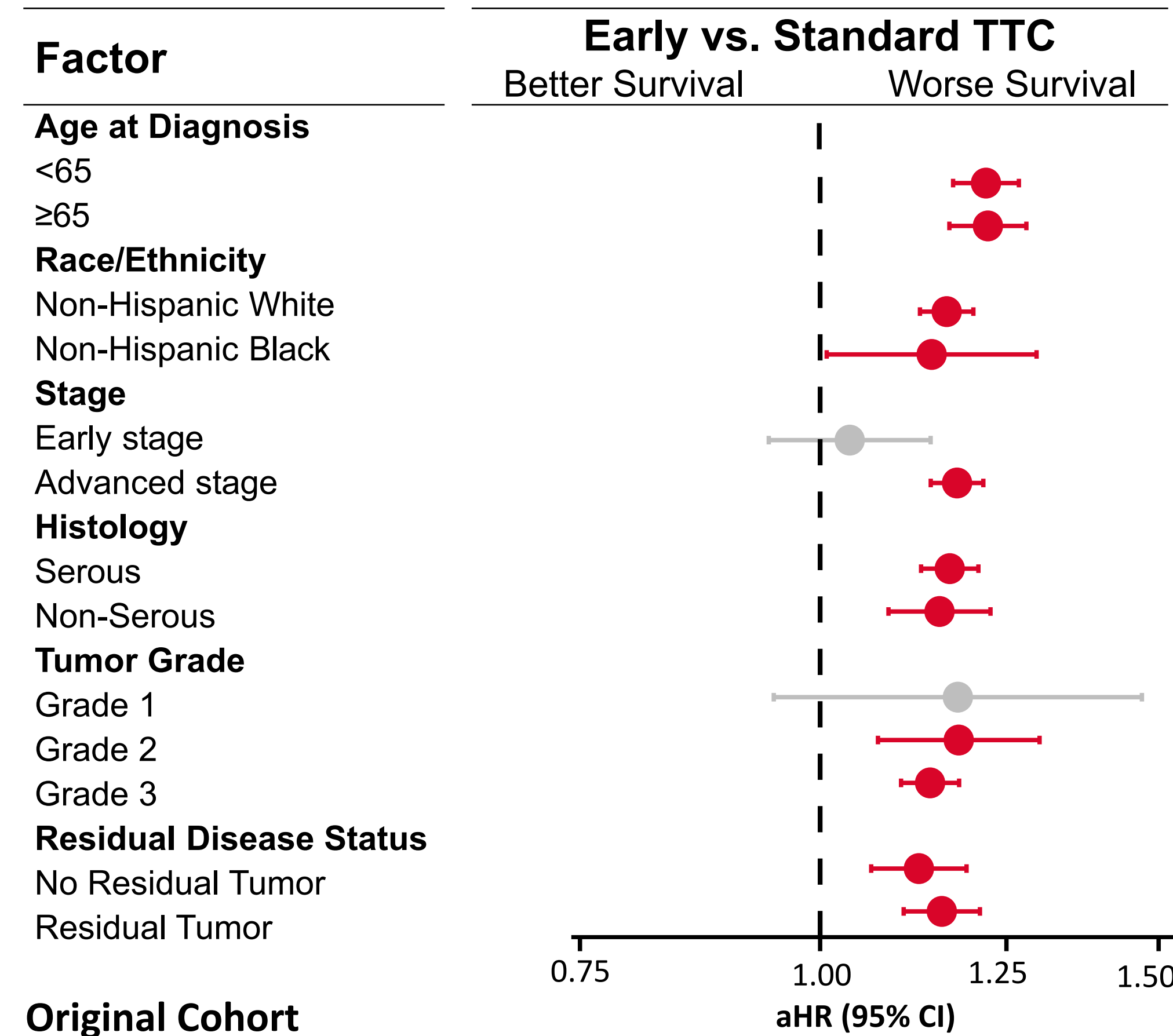


Figure 3. Subgroup-Specific aHRs and 95% CIs for early TTC (<3 weeks) vs. standard TTC (≥3 weeks). The TTC relationship with adjusted risk of death was not uniform across all subgroups.

Established prognostic factors have stronger relationships with overall survival than TTC in patients with EOC.

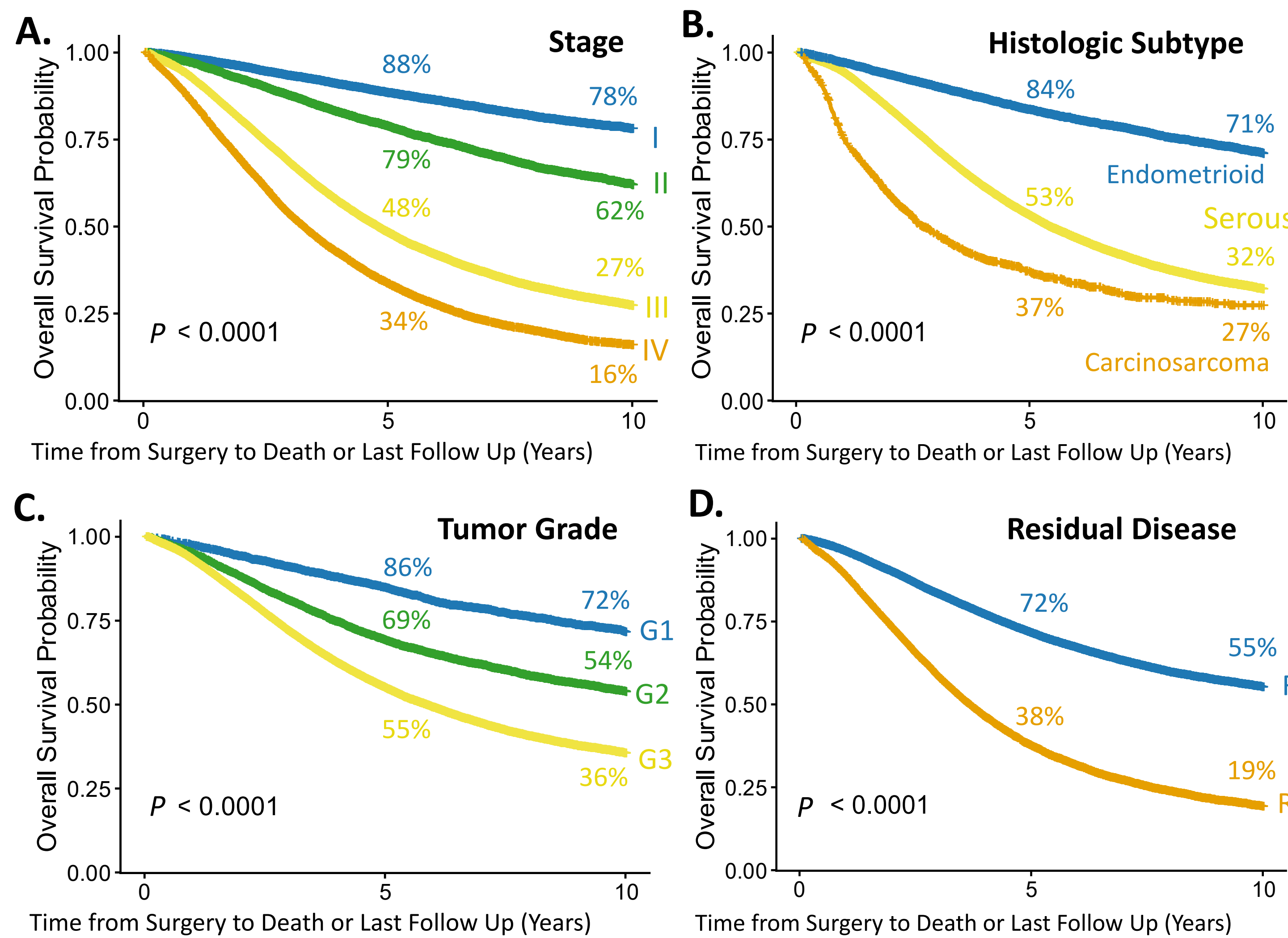


Figure 4. Survival Relationships for Key Prognostic Factors (A.) Stage, (B.) Histologic Subtype, (C.) Tumor Grade, and (D.) Residual Disease in the Original Cohort. Comparisons used log-rank test and 5- and 10-year survival rates. Stage, histologic subtype, tumor grade and residual disease remained dominant independent prognostic factors in patients with EOC undergoing primary debulking surgery.

Operational Implications for the Military Health System:

- Avoid unnecessary pressure to meet arbitrary TTC targets.**
- Emphasize readiness through optimization of postoperative recovery, disease severity assessments and treatment intolerance.**
- Inform MHS oncology quality metrics and optimization efforts.**

Conclusions

- Chemotherapy initiation within 3 weeks of primary debulking surgery was associated with modestly worse overall survival.
- This relationship likely reflects patient selection and disease severity rather than a detrimental effect of early treatment.
- Established prognostic factors, including stage, histology, grade, and residual disease exerted substantially greater influence on survival than TTC.
- Findings support individualized postoperative treatment planning rather than universal early-treatment benchmarks.