



Surveillance of Second Primary Lung Cancer among Long-Term Lung Cancer Survivors aged 60-74 using Target Trial Emulation in SEER-Medicare



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BACKGROUND & OBJECTIVE

- Lung cancer (LC) survivors are at **higher risk of developing second primary lung cancer (SPLC) and have worse survival.**
- Current guidance supports surveillance CTs every 6 months for 2-3 years post-therapy, then annual low-dose CT. **However, no evidence-based surveillance guidelines** exist for SPLC for long-term LC survivors (≥ 5 -year survival).
- The extent to which continued annual CT surveillance beyond five years improves lung cancer outcomes remains unclear.
- Objective:** Estimate the real-world effectiveness of continued annual CT surveillance beyond five-year survival on SPLC detection among long-term LC survivors (versus no / discontinued surveillance) and on 5-year lung-cancer-specific mortality.

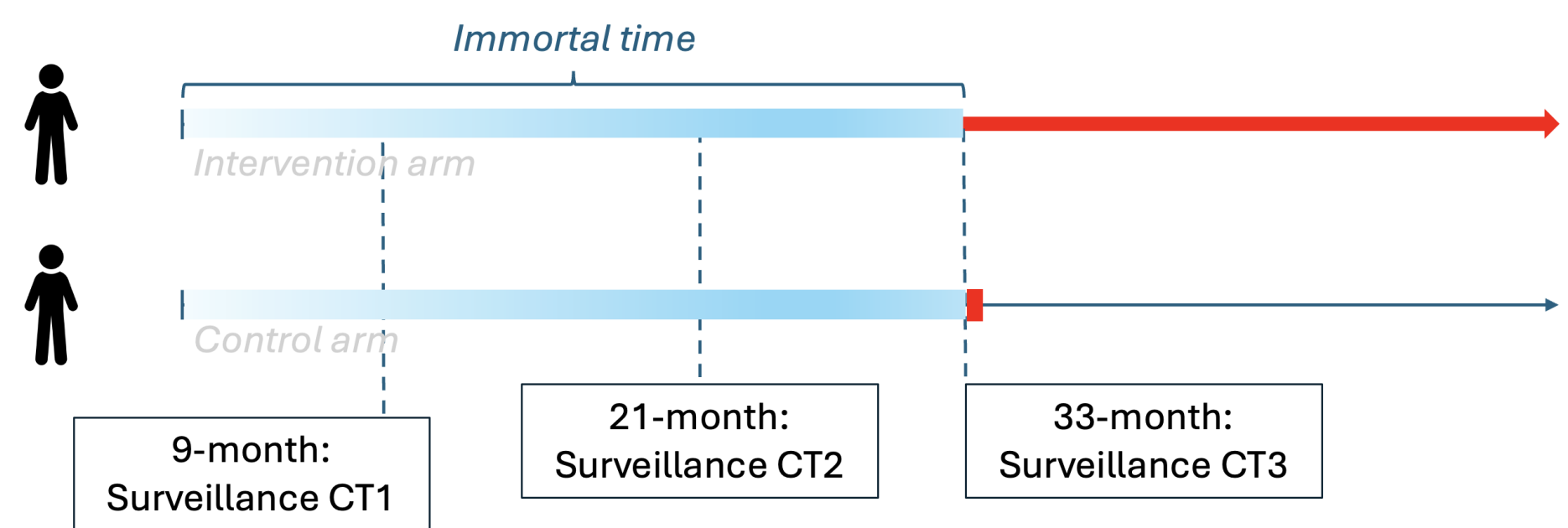
Hypothesis: Continued CT surveillance will benefit long-term (≥ 5 -year survival) LC survivors.

METHODS

- We implemented a **target trial emulation** design to emulate a randomized controlled trial (RCT) using US SEER-Medicare data from 1999-2020.

	Target trial	Emulated Trial (SEER-Medicare data)
Aim	To estimate the effect of CT surveillance for 3 years annually on SPLC detection and LC-specific mortality.	Same, in those <u>aged 65 and above.</u>
Eligibility	Inclusion: Long-term survivors (5 years since IPLC diagnosis) who received surgery for IPLC with no diagnosis of any cancer within 5 years of curative-intent therapy for IPLC.	Early-stage IPLC, surgically treated, ≥ 5 -year survival from IPLC diagnosis, age 60–74 at IPLC diagnosis, no other cancer/SPLC in 5-year window (N=9230 Patients)
Treatment Strategies	- Intervention: Continuous annual surveillance at 12-month intervals by low-dose CT exam for 3 years from 5-year IPLC survival - Control: No surveillance past 5 years from IPLC survival or stop annual surveillance	Intervention: Continuous annual chest CT surveillance for 3 rounds after baseline (grace period: 15 months for CT #1, +18 months for CT #2, +15 months for CT #3). Control: No surveillance, or surveillance that is not on schedule. - Time Zero: 5-year-survival from diagnosis
Outcome	(1) Detection of SPLC within 1 year of treatment assignment (2) 5-year LC-specific mortality	Same
Causal Contrast	Intention-to-treat & per-protocol effect s	Per-protocol effect only

Clone, Censor, Weight Strategy



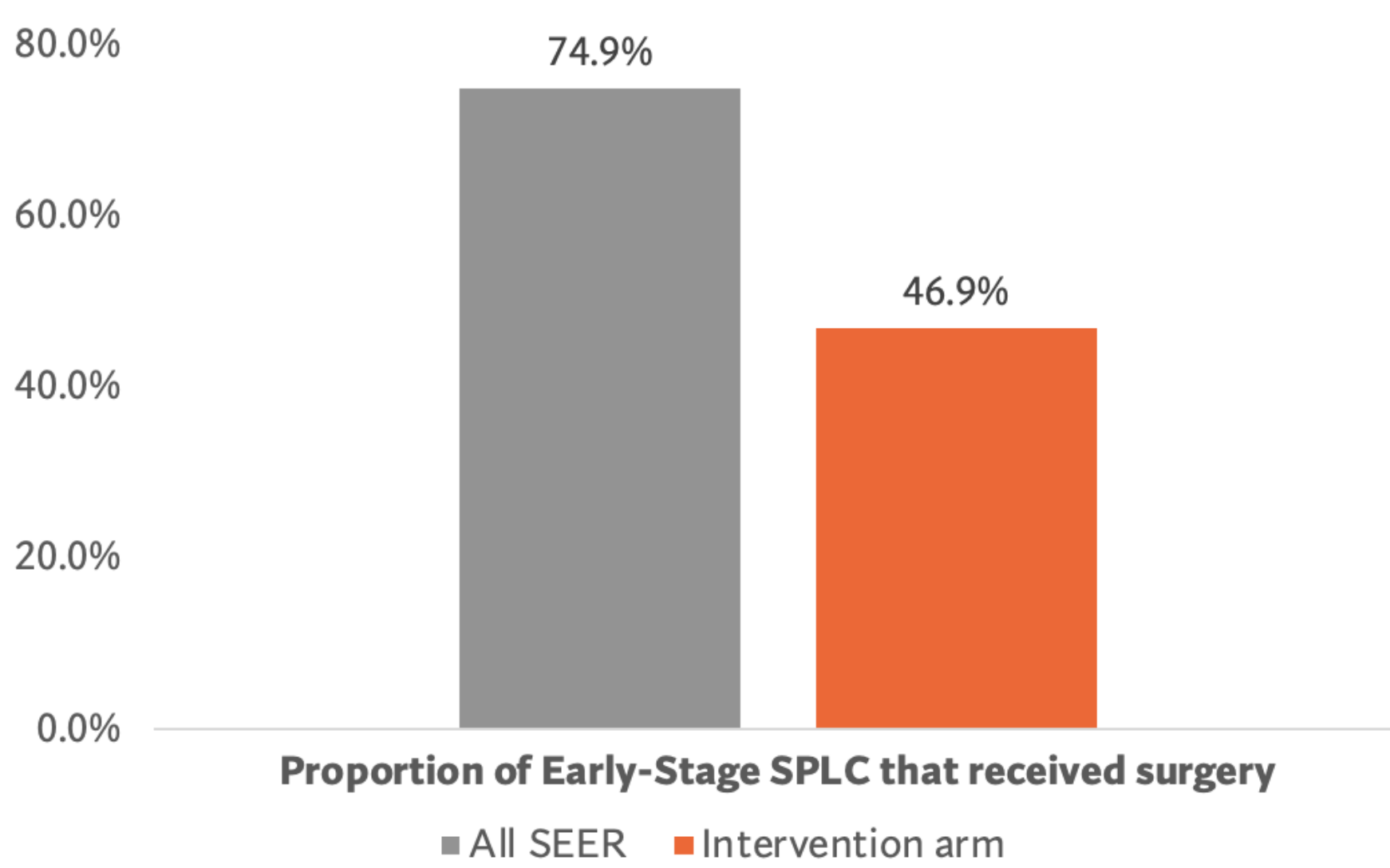
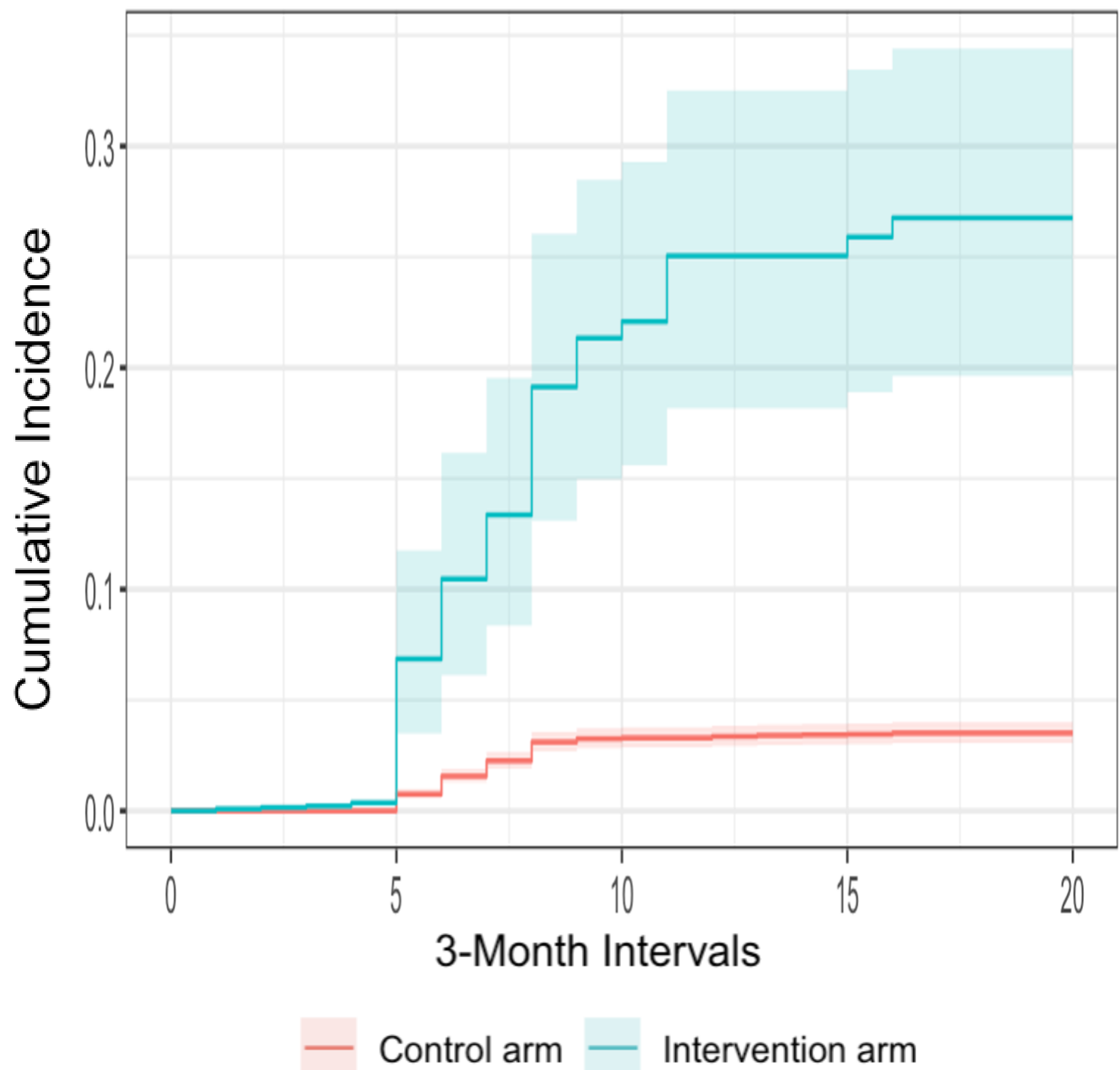
Inverse Probability Weighting (IPWs):

- IP(Treatment)W: Account for baseline confounding by treatment assignment
 - IP(Censoring)W: Account for potential selection bias from loss-to-follow-up and non-LC death
- Outcome Model:** “Continuous annual CT” vs. “no or stop continuous annual CT,” using:
- Cox regression for SPLC detection within 1 year of treatment assignment (primary endpoint)
 - Pooled logistic regression for 5-year LC specific mortality (secondary endpoint)

RESULTS

Result 1: Of the 9,230 patients, **N=167** remained in the **intervention arm** (receiving 3 surveillance CTs or died before the grace period) and **N=6487** (no surveillance CT or died before the grace period) **with the control arm**; 14.1% (n=1,305) received ≥ 1 surveillance CT beyond five-year survival, 5.0% (n=463) received a second, and 1.5% (n=140) received a third.

Result 2: Likelihood of **SPLC detection was significantly higher in the intervention vs. control arm (aHR: 6.57, CI: 4.56 – 9.47)**, with a **higher proportion of stage I - III SPLC** observed in the intervention vs. control arm (**74.2% vs. 59.2%, P=0.03**).



Result 3: Curative-intent surgery rates post-SPLC detection remained low → **Despite earlier detection, LC-specific mortality was not significantly reduced in the intervention arm** (aHR = 1.03, CI: 0.94-1.13). Curative-intent surgery rates post-SPLC detection remained low overall in this Medicare population with stage I - III SPLC, with 46.9% in the intervention arm and 36.0% in the control arm.

CONCLUSIONS

- Long-term LC survivors may benefit** from continued surveillance CTs beyond 5-year survival, demonstrating **significantly higher rates of SPLC detection.**
- The lack of an LC-specific survival benefit may be due to the **low rate of curative-intent surgery** despite early detection within this older study population.
- These estimates are derived from target trial emulation; residual confounding cannot be excluded

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