

SURVIVAL ANALYSIS

Impact Of Chlorhexidine (0.12% VS 0.20%) In
Prevention Of Ventilator-Associated Pneumonia (VAP)

CAP STONE PROJECT

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DATA DESCRIPTION

Chlorhexidine Trial Dataset – Ventilator-Associated Pneumonia (VAP) Study

1. Overview of the Dataset

This dataset contains patient-level information from a randomized controlled trial that evaluated the effectiveness of **two concentrations of chlorhexidine mouthwash (0.12% vs 0.20%)** in preventing **Ventilator-Associated Pneumonia (VAP)** among mechanically ventilated adult ICU patients.

The dataset includes **140 patients** (70 per treatment arm), with daily clinical measurements, demographic information, severity scores, and final outcome labels.

VAP was diagnosed using the **Clinical Pulmonary Infection Score (CPIS)**; a score ≥ 6 indicates probable VAP — as defined in the original study.

Original Trial Enrollment

- Total participants: 140
- 70 received 0.12% chlorhexidine
- 70 received 0.20% chlorhexidine

Survival-Analysis Dataset

- 106 rows loaded into the analysis
- 103 valid participants included in the final survival model
- 59 cases of 0.12% chlorhexidine data available
- 44 cases of 0.20% chlorhexidine data available

Reasons for Reduction

- Several patients had missing CPIS measurements
- Participants with no valid CPIS follow-up could not contribute to time-to-event analysis
- Approximately 25% of the original sample lacked sufficient CPIS follow-up and were excluded

2. Event Counts (VAP Cases)

| Group | Original Article | Survival Dataset |
|-----------|------------------|------------------|
| 0.12% CHX | 7 VAP | 7 |
| 0.20% CHX | 2 VAP | ~1~2 |

- Cox model used 8 total valid VAP events.
- One VAP case lacked a valid CPIS day → excluded from time-to-event analysis.

2. Structure of the Dataset

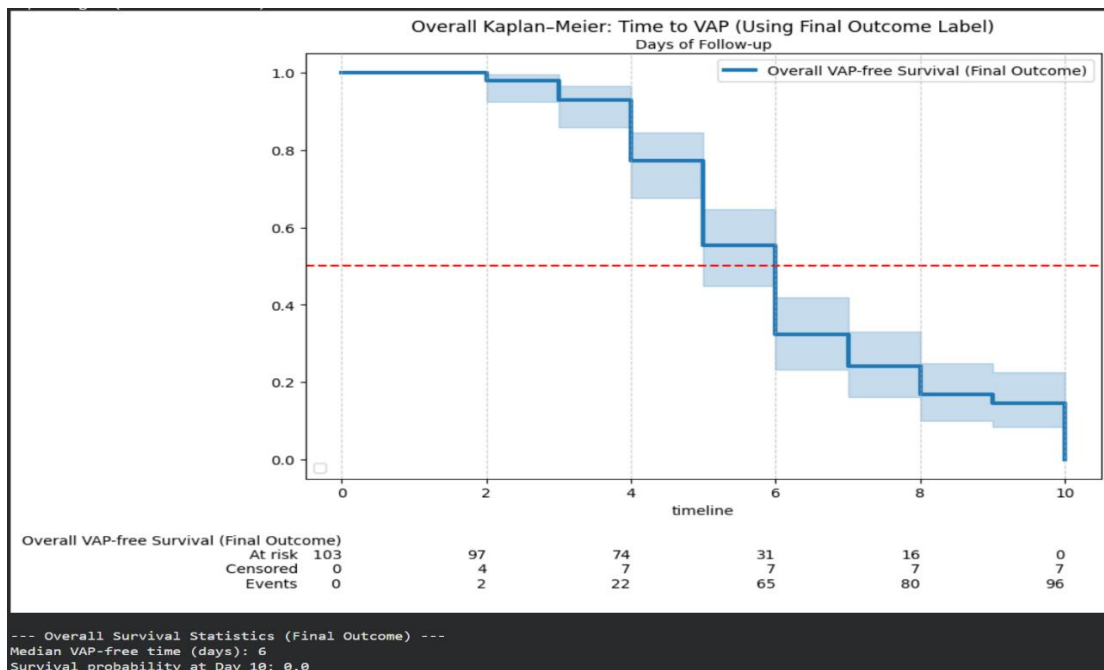
Each row corresponds to **one patient** enrolled in the trial.

Columns represent demographic variables, clinical characteristics like Trial Arm , Age, Gender, Outcome of the current episode , Outcome of current episode 2 , APACHE II Score , TLC Day 1-10, Band Form Day 1-10, Chest X ray Day 1-10 , CPIS Day 1-10 , ABG Day 1-10, Cluture Day 1-10, Ulcer Day 1-10.

| | | |
|--------------------------------|-------------|---|
| Trial Arm | Categorical | Indicates the assigned chlorhexidine concentration: 0.12% (Group 1) or 0.2% (Group 2). |
| Age | Continuous | Age of the patient in years at the time of ICU admission. |
| Gender | Categorical | Sex of the patient (Male / Female). Often recoded as Male=1, Female=0. |
| Outcome of the current episode | Binary | Final clinical outcome (e.g., VAP, No VAP, Improved). Used to derive final VAP event = 1/0. |
| Outcome of current episode 2 | categorical | Death, discharged, LAMA, Trachesotomy, CAP, HAP |
| APACHE II Score | Continuous | ICU severity score recorded at admission; higher score = more severe illness |
| TLC Day 1-10 | Continuous | Total leukocyte count (WBC count) for each day from Day 1 to Day 10. |
| Band Form Day1-10 | Numeric | Band neutrophils (immature neutrophils) count or percentage recorded daily (often zero in many ICU datasets) |
| Chest Xray 1-10 | Continuous | CPIS-related radiologic findings each day (e.g., infiltrates, densities). In Excel typically stored as a score (0,1,2). |
| CPIS Day 1-10 | Continuous | Daily Clinical Pulmonary Infection Score (0–12). Used to identify CPIS ≥ 6 events |
| ABG Day 1-10 | Continuous | Arterial blood gas oxygenation component of CPIS (PaO ₂ /FiO ₂ ratio). |
| Culture Day 1-10 | Categorical | Daily microbiology/culture results |
| O S microbial Day 1-10 | Continuous | Organism-specific microbial load or score |
| Ulcer Day 1-10 | Binary | Presence of stress ulcer |

Clinical Question: Does 0.20% chlorhexidine mouthwash improve VAP-free survival compared with 0.12% chlorhexidine in intubated ICU patients?

Primary Outcome: Time to VAP defined by CPIS ≥ 6 , consistent with the scoring system used in the original RCT
Time to VAP defined by CPIS ≥ 6 , consistent with the scoring system used in the original RCT. Methods Used: Kaplan–Meier Survival Curves (overall & by treatment group) Log-Rank comparison Cox Proportional Hazards Model Schoenfeld residual tests (PH assumption) Life table generation



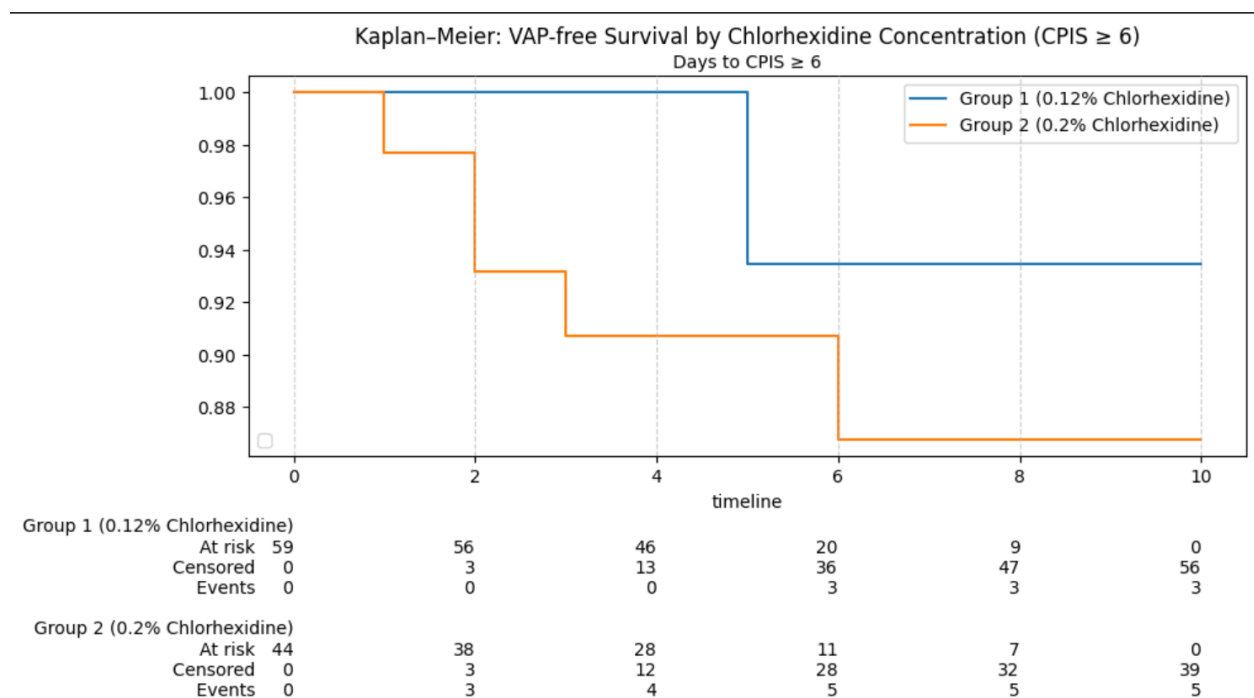
This KM curve estimates:

Time until the patient is eventually labeled as VAP in the final outcome field

It shows:

- The proportion of patients **not labeled VAP** in the final report **as follow-up time increases**.
- The plot shows that, based on the final outcome label, the cumulative proportion of patients labeled VAP increases steadily throughout the follow-up period, with about half of VAP-labeled patients identified by Day 6.
- No VAP at baseline.
- Some patients who were followed up to Day 3 were labeled as VAP.
- A group of patients whose **final recorded outcome was VAP**
- And whose **follow-up ended on that day**
- ✓ By Day 10, the curve approaches 0

Almost all VAP diagnoses (based on final outcome) occur by the time follow-up ends (Day 10).



Early VAP Risk

The **0.20% group** experiences VAP (CPIS ≥ 6) **earlier**, as shown by the early drops in survival.

Overall VAP-Free Survival

By Day 10:

- **0.12% group survival ≈ 0.945**
- **0.20% group survival ≈ 0.875**

This indicates that the **0.20% group had a higher cumulative hazard** of CPIS ≥ 6 during follow-up.

The KM curve reflects **timing**, not **total number** of events:

KM curve \neq final VAP incidence

It shows *when* CPIS ≥ 6 happened, **not** how many total VAP cases each group had.

```
Fitting Cox model with covariates: ['gender_bin', 'Age', 'APACHE II Score']
Observations: 103, Events: 8
Iteration 1: norm_delta = 3.77e-01, step_size = 0.9500, log_lik = -35.25960, newton_decrement = 5.42e-01, seconds_since_start = 0.0
Iteration 2: norm_delta = 5.95e-02, step_size = 0.9500, log_lik = -34.69268, newton_decrement = 1.09e-02, seconds_since_start = 0.0
Iteration 3: norm_delta = 3.99e-03, step_size = 0.9500, log_lik = -34.68173, newton_decrement = 4.74e-05, seconds_since_start = 0.0
Iteration 4: norm_delta = 4.53e-06, step_size = 1.0000, log_lik = -34.68169, newton_decrement = 6.13e-11, seconds_since_start = 0.0
Convergence success after 4 iterations.
```

```
--- Cox Proportional Hazards Model Summary (Hazard Ratios) ---
model          lifelines.CoxPHFitter
duration col    'duration'
event col       'event'
baseline estimation breslow
number of observations 103
number of events observed 8
partial log-likelihood -34.6817
time fit was run 2025-11-25 08:48:18 UTC
```

| | coef | exp(coef) | se(coef) | coef lower 95% | coef upper 95% | exp(coef) lower 95% | exp(coef) upper 95% | cmp to | z | p | -log2(p) |
|-----------------|---------|-----------|----------|----------------|----------------|---------------------|---------------------|--------|---------|--------|----------|
| gender_bin | 0.1249 | 1.1331 | 1.0726 | -1.9773 | 2.2271 | 0.1384 | 9.2730 | 0.0000 | 0.1165 | 0.9073 | 0.1404 |
| Age | 0.0067 | 1.0067 | 0.0209 | -0.0343 | 0.0477 | 0.9663 | 1.0489 | 0.0000 | 0.3207 | 0.7484 | 0.4181 |
| APACHE II Score | -0.0595 | 0.9422 | 0.0578 | -0.1727 | 0.0537 | 0.8414 | 1.0552 | 0.0000 | -1.0300 | 0.3030 | 1.7225 |

```
Concordance 0.6030
Partial AIC 75.3634
log-likelihood ratio test 1.1558 on 3 df
-log2(p) of ll-ratio test 0.3891
```

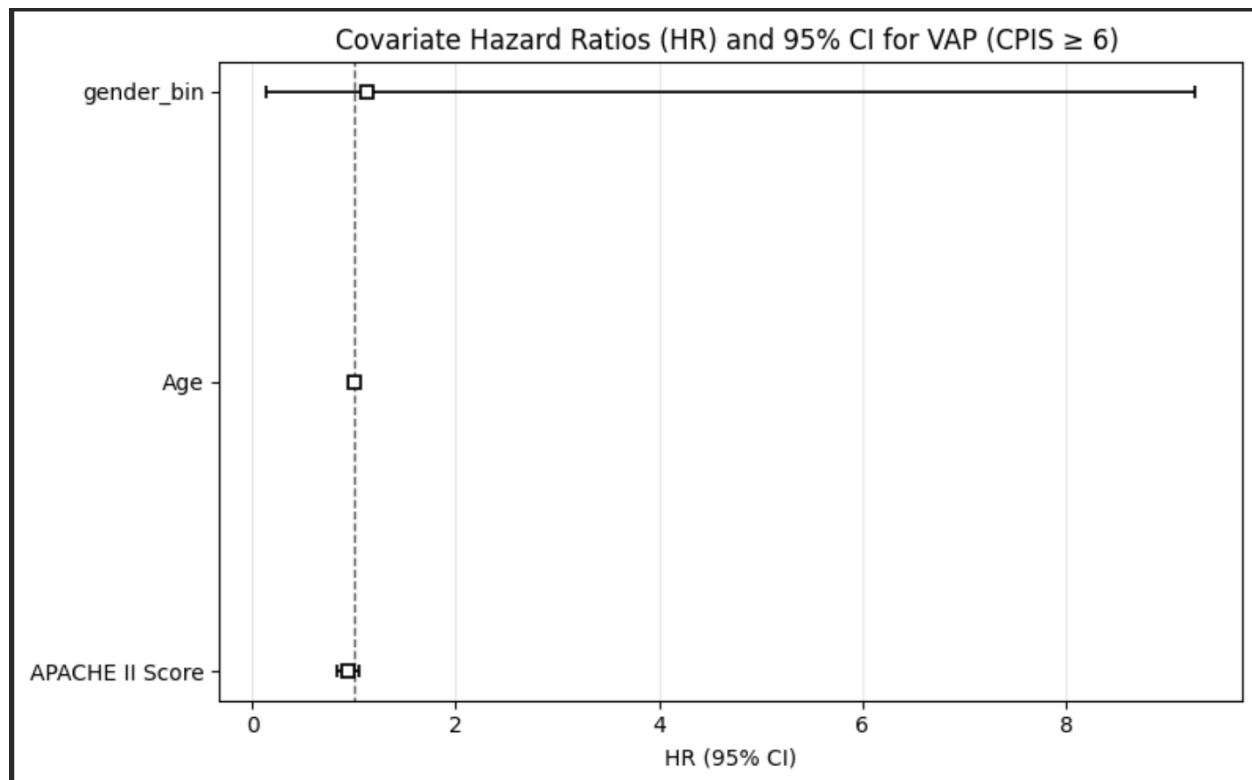
Overview of Model Performance

- **Number of observations:** 103
- **VAP events:** 8 (very low → unstable estimates)
- **Concordance:** 0.6030 → weak predictive ability
- **Partial AIC:** 75.36 → model fit not strong
- **Log-likelihood ratio test:** $\chi^2 \approx 1.1558$ on 3 df, **p = 0.748**
→ None of the variables collectively predict VAP.

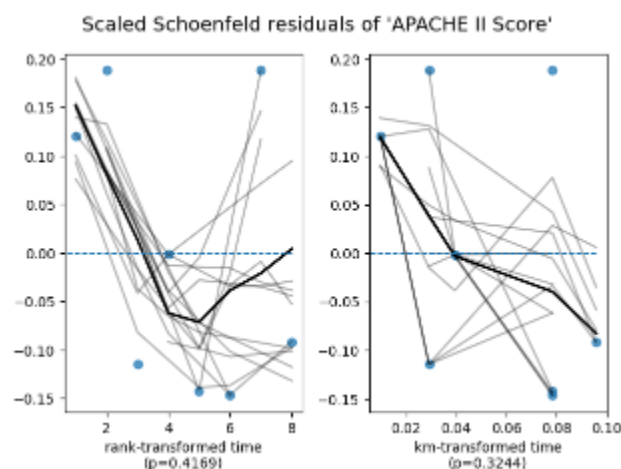
This shows:

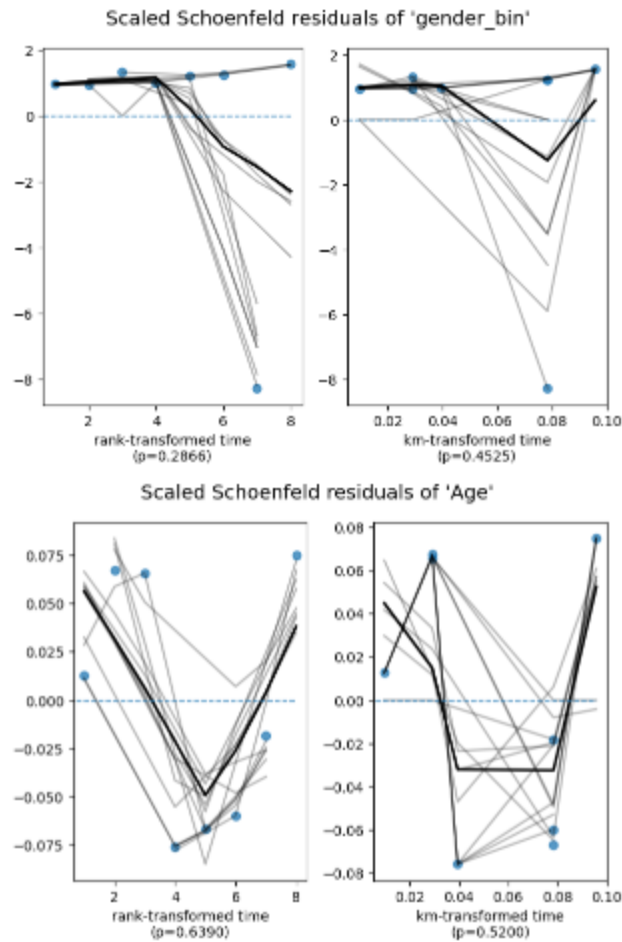
None of the three covariates—gender, age, or APACHE II score—were significantly associated with time to CPIS ≥ 6 .

Confidence intervals are wide and all cross 1.0, meaning the dataset provides **no evidence that these clinical or demographic variables influence the risk of VAP (as defined by CPIS ≥ 6).**



Adjusted survival estimates from the Cox model showed minimal differences in VAP-free survival across age groups (40–70 years). All four age-specific curves were nearly superimposed, with only a slight downward shift at higher ages. This visual pattern is consistent with the Cox regression results, where age was not a significant predictor of VAP (HR 1.0067; 95% CI 0.97–1.05; $p = 0.75$). Overall, age did not meaningfully influence the risk of developing CPIS ≥ 6 in this cohort.





Interpretation of Schoenfeld Residual Plots

Schoenfeld residuals vs. transformed time:

- Individual event-specific residuals (points)
- Smoothed trend line (black)
- Confidence band (gray)
- Horizontal dashed line at **0** (perfect PH assumption)
- Global p-value for each covariate

These diagnostics test whether the effect (hazard ratio) of each covariate **changes over time**.

If the PH assumption holds:

- The trend line should be roughly **horizontal**

- The residuals should scatter randomly around 0
- The **p-value should be > 0.05**

1. Gender (gender_bin):

The residuals do **not** show a systematic upward or downward pattern.

Conclusion:

Gender satisfies the proportional hazards assumption.

Its effect on VAP risk does **not** vary over time.

2. Age

The smoothed line shows a slight dip but stays close to zero.

No evidence of a time-dependent change in effect.

Conclusion:

Age meets the PH assumption.

Its (small) effect on VAP hazard is time-invariant.

3. APACHE II Score

The smoothed line trends slightly downward, but stays within noise.

The residuals scatter randomly, with no systematic pattern.

Conclusion:

APACHE II score also satisfies the PH assumption.

No evidence that its effect varies over time.

Overall PH Assumption Conclusion:

Schoenfeld residual analysis did not identify any violation of the proportional hazards (PH) assumption for gender ($p > 0.28$), age ($p > 0.52$), or APACHE II score ($p > 0.32$). The smoothed residual curves remained approximately horizontal, indicating that the covariate effects were constant over time. Therefore, the Cox proportional hazards model satisfied the PH assumption, and the lack of statistical significance in covariate effects is attributable to the low number of events rather than time-dependent bias.