© 2025 by the authors. This is an open access article distributed under the terms and conditions of the Creative Commons Attribution license. (CC BY) (https://creativecommons.org/licenses/by/4.0/).

Narrative review

Fundamentals and applications of survival analysis for health research

DOI: 10.5377/alerta.v8i3.20675

David Daniel Rivera Rosales[1]*, David A. Tejada[2]

1-2 Ministry of Health, National Institute of Health, San Salvador, El Salvador.

Correspondence
ddaniel.rivera@salud.gob.sv

1. 0000-0002-8744-9403
2. 0000-0003-2502-1433

Abstract
Survival analysis is a statistical method that focuses on the time it takes for an event of interest to occur. It combines time, which is a continuous variable, with the occurrence of the event, a dichotomous variable; in addition, its distinctive feature is the presence of censored data. The Kaplan-Meier method is a nonparametric test that estimates the probability of survival over time, which is calculated each time an event occurs. The *log-rank* test is used to compare survival patterns between independent groups. Cox proportional hazards regression is the most widely used multivariate model in survival analysis; it evaluates predictive factors and estimates the *Hazard Ratio* as a measure of association. The use of traditional models requires assumptions such as proportional hazards and non-informative censoring, and when this criteria is not met, researchers must choose appropriate techniques according to their objectives, population and resources. Options include Bayesian models, stratified, time-dependent covariates or artificial intelligence techniques; the latter offers an alternative for modeling complex scenarios, handling large volumes of data and overcoming the limitations of conventional methods.
Keywords
Survival Analysis, Investigative Techniques, Biostatistics, Kaplan-Meier Estimate, Cox Model.

Resumen
El análisis de supervivencia es un método estadístico que se centra en el tiempo que tarda en ocurrir un evento de interés. Esta combina el tiempo, que es una variable continua, con la ocurrencia del evento, una variable dicotómica; además, su característica distintiva es la presencia de datos censurados. Se realizó una búsqueda de publicaciones del 2019 al 2024, con el objetivo de describir los principales métodos para realizar análisis de supervivencia y las diferentes opciones cuando no es posible usar los modelos tradicionales. Se elaboró una revisión narrativa de las técnicas más utilizadas, limitaciones y sesgos encontrados con mayor frecuencia en las investigaciones publicadas. El método Kaplan-Meier estima la probabilidad de supervivencia a lo largo del tiempo, el test de *log-rank* compara patrones de supervivencia entre dos grupos independientes. La regresión de riesgos proporcionales de Cox es el modelo multivariado usado con mayor frecuencia y estima la influencia de las variables predictoras en la probabilidad de supervivencia en un tiempo determinado usando el *Hazard Ratio* como medida de asociación. Para la utilización de estas pruebas se requiere cumplir supuestos como proporcionalidad de riesgos y censura no informativa, cuando esto no es posible, los investigadores deben elegir técnicas adecuadas según sus objetivos, población y recursos. Las opciones incluyen modelos bayesianos, estratificados, covariables dependientes del tiempo o técnicas de inteligencia artificial; esta última ofrece una alternativa para modelar escenarios complejos, manejando grandes volúmenes de datos y superando las limitaciones de los métodos convencionales.

Palabras clave
Análisis de Supervivencia, Técnicas de Investigación, Bioestadística, Estimación de Kaplan-Meier, Modelo de Cox.

OPEN ACCESS

Fundamentos y aplicaciones del análisis de supervivencia para la investigación en salud

Suggested citation:
Rivera Rosales DD, Tejada DA. Fundamentals and applications of survival analysis for health research. Alerta. 2025;8(3):305-314. DOI: 10.5377/alerta.v8i3.20675

Editor:
Nadia Rodríguez.

Received:
November 27, 2024.

Accepted:
June 26, 2025.

Published:
July 31, 2025.

Author contribution:
DDRR[1], DAT[2]: study conception, manuscript design, literature search, data collection, data or software management, data analysis, writing, revising and editing.

Conflicts of interest:
The authors declared there are not conflicts of interest.

Introduction

Survival analysis is a statistical method in which the variable of interest is the time it takes for an event to occur.[i,ii] This variable comprises two components: time, which is continuous, and the occurrence or non-occurrence of the event, which is dichotomous.[iii,iv] The method was originally used to analyze the time until death of patients, hence its name.[v,vi] While this remains one of its most common applications, the event of interest does not have to be death; it can also refer to the occurrence of a complication, such as acute myocardial infarction, or a patient's recovery from illness.[i,vii]

A distinctive feature of survival analysis is the presence of incomplete information, or "censored data".[v] This occurs when the event of interest does not happen during the patient's follow-up period.[viii] The most frequent form of censoring in this type of study is right-censoring, which occurs when the outcome happens after the end of the observation period.[iii,v]

Two other, less common types of censoring are left-censoring, which occurs when the event happens before observation begins.[v] For instance, a study examining the prevalence of dementia in Germany between 2004 and 2012 revealed how incorporating left-censored data (cases diagnosed prior to 2004) could impact the outcome of the analysis.[ix] The second type is interval censoring, where only the time interval during which the event occurred is known, not the exact time.[iii,v] This is common in school-based oral health programmes that rely on fixed-interval assessments, such as annual or biannual examinations, where the exact moment when a tooth cavity develops is unknown.[x] Censoring can be classified as either informative or non-informative. Non-informative censoring, also known as independent censoring, is not related to the risk of experiencing the event of interest.[v] Since failure to meet this assumption could bias the results, survival analysis assumes non-informative censoring.[iii] The presence of censored data requires the use of statistical methods that go beyond simple linear regression.[v]

Additionally, survival curves are non-negative, meaning they always show positive progression. This is because the events studied are cumulative, with their incidence accumulating over a defined period of time. Typically, survival time distributions are skewed, which limits the applicability of parametric models that assume a normal distribution. This requires either non-parametric models or logarithmic transformations for proper analysis.[vii,viii,xi]

Nowadays, survival analysis is frequently employed in cohort studies and clinical trials. It has proven useful in fields such as epidemiology, oncology and cardiology for comparing the efficacy and safety of medical and surgical treatments, and for estimating recovery time, time to recurrence as well as disease-free and complication-free periods.[ii,vi] Given how useful and frequent survival analysis is in health research and publications, it is crucial for health professionals to familiarize themselves with the methods used in these analyses.[xii] However, certain elements and methods are often overlooked in existing reviews, such as non-proportional hazard models, Bayesian approaches, artificial intelligence applications, and the common limitations and biases found in these types of studies.

A search was conducted in the PubMed, Virtual Health Library, Google Scholar and Scielo databases for articles published between 2019 and 2024, using the following keywords: "Survival Analysis", "Kaplan Meier", "Cox proportional hazards", "Non proportional hazard", "Proportional hazards assumption", "Análisis de supervivencia", "Riesgos proporcionales de Cox" and "Modelos de riesgos no proporcionales". Figures were generated in RStudio version 9.4.19 1370 using simulated data. The objective of the narrative review was to describe the main methods used in survival analysis in health research and outline alternative options when traditional models are not applicable.

Discussion

General considerations

The methodology of survival analysis can be summarized in three key steps. The first step involves estimating the survival function, also known as the survival curve. The second step involves comparing survival curves. The third step involves estimating the effects of explanatory variables on survival time.[v]

The "survival function" refers to the probability that a patient will survive for a given period of time.[xiii,xiv] A related concept is the "hazard function", which represents the probability of an event occurring within a specific time period.[v] "Median survival" is defined as the time at which the event has occurred in 50 % of observed subjects.[ii] A key assumption relating to the hazard function is the "proportional hazards assumption" (PHA), which posits that the risk of experiencing an event remains constant throughout the follow-up period.[xv]

In survival studies, two timepoints must be clearly defined: the start and end of follow-up, based on the study objectives. The follow-up period must be long enough to allow for the observation of a reasonable number of events.[iii]

Each patient has a different starting date for follow-up, known as "calendar time" or "secular time".[xiv] These dates are standardized to a common reference point in time, known as "time zero".[i,xvi] A patient's follow-up period spans from time zero until the event occurs or they are censored.[i,xvi] Regardless of the variable under analysis, the time it takes for the event to occur is commonly referred to as "survival time".[vii] In clinical trials, time zero is usually the

moment of randomization, or when the patient begins the intervention.
In observational studies, however, it can vary, potentially corresponding to study entry, the start of exposure to a risk factor, or the occurrence of an index event.[xvii]

Sample size calculation in survival analysis

Unlike other types of study, the reliability and power of survival analysis depend not on the total number of individuals in the sample, but on the number of observed events.[xviii]

A practical rule for determining the appropriate sample size is to ensure there are at least ten events per covariate for reliable Cox regression analysis. For example, if five covariates are to be analyzed, then 50 events would be required.[iii,xix] However, this approach may not reflect the complexity of the relationships between predictors and outcomes.[xx]

There are, statistical methods available for determining the appropriate sample size in such studies, including the Freedman, Schoenfeld and Lakatos methods.[xviii] First, the number of events required for the analysis must be calculated, and then the number of patients needed to observe that number of events must be estimated. [xxi] Thorough analysis of the population characteristics and study objectives is essential to select the appropriate sampling method and avoid methodological errors.[xxii,xxiii]

The actuarial life table

The study duration is divided into fixed-length time intervals, during which each patient is observed.[i,vi,xii] The length of these intervals is determined by the frequency of the event.[vi] Follow-up time is expressed as the number of intervals until the event or censoring occurs, based on the assumption that censoring occurs at the midpoint of each interval.[i]

Kaplan Meier

This is the most widely used method of survival analysis in health science.[vii,xxiv] It is a non-parametric test which estimates the probability of survival over time by updating this probability each time an event occurs. Therefore, there will be as many estimates as there are events, unless multiple events occur simultaneously.[vii,viii] For the model to be valid, censoring must be non-informative.[vii] The model is typically represented in graphs, with the X-axis denoting time and the Y-axis representing survival probability. Marks (*e.g.* "+" signs) are added to indicate censored data[xi,xiii] (Figure 1).

The software used for these analyses usually provides confidence intervals (CIs) for each survival probability point. Many researchers then connect these points to illustrate the confidence band of the curve. While these CIs are valid for each point, additional statistical adjustments are needed to depict the full confidence bands appropriately.[xxv] Other options to Kaplan-Meier include the Breslow estimator or the Breslow-Aalen method.[iii]

Log-rank test

This is a non-parametric test based on the chi-squared distribution, which is the most commonly used method for comparing survival curves.[iii,viii,xiii] Rather than comparing final or median survival, it compares overall survival patterns.[viii] The null hypothesis is that there is no difference between the survival curves of two or more independent groups[ii,v] (Figure 2). The survival curves must not cross; if they do, the test may fail to detect differences.[v,vii,viii] In such cases, weighted log-rank tests,[v,vii] or the Lin and Wang modified log-rank test[v] are recommended. The test's power increases if the PHA is met.[iii,vii] Otherwise, alternatives include the Tarone-Ware, Peto-Peto-Prentice or Fleming-Harrington tests.[iii]

Cox proportional hazards regression model

Cox Proportional Hazards Regression Model (CPR) is the most widely utilised multivariable model in the field of survival analysis.[iii,xiii] It is used to analyze predictive factors (covariates) that influence survival.[ii] It yields a measure of association known as the Hazard Ratio (HR), which is defined as the hazard function of the exposed or treated group divided by the hazard function of the unexposed or control group.[xxvi] The HR is analogous to the Odds Ratio (OR) from logistic regression and is interpreted similarly. HR > 1 indicates increased risk, HR = 1 indicates no difference, and HR < 1 indicates reduced risk.[iv,xv]

As with any statistical model, the Cox model is predicated on several assumptions: proportional hazards, non-informative censoring and independence of survival between individuals. The latter indicates that the survival of one participant does not impact the survival of another.[xiv] In addition, the log-linear assumption is referenced, which stipulates that the relationship between the natural logarithm of the

instantaneous hazard rate of the covariates or predictor variables must be linear.[xxvii]

Testing the Proportional Hazards Assumption

Prior to the formulation of inferences from the model, it is essential to verify the PHA; otherwise, the analysis may be biased.[iii] A number of methodologies are at researchers' disposal for the purpose of testing this assumption.[v,xxvi] The most common of these is the Schoenfeld residuals test, which compares observed versus expected events. The null hypothesis posits that the residuals are independent of time. In the event of its rejection, it is assumed that risks vary over time and the assumption is broken[xxvi] (Figure 3).

Another useful method is the *log-minus-log* plot. The survival function is changed using a double logarithmic transformation for the covariates. If the PHA holds, the resulting lines will be parallel and non-crossing.[v,xxvi] It is recommended to

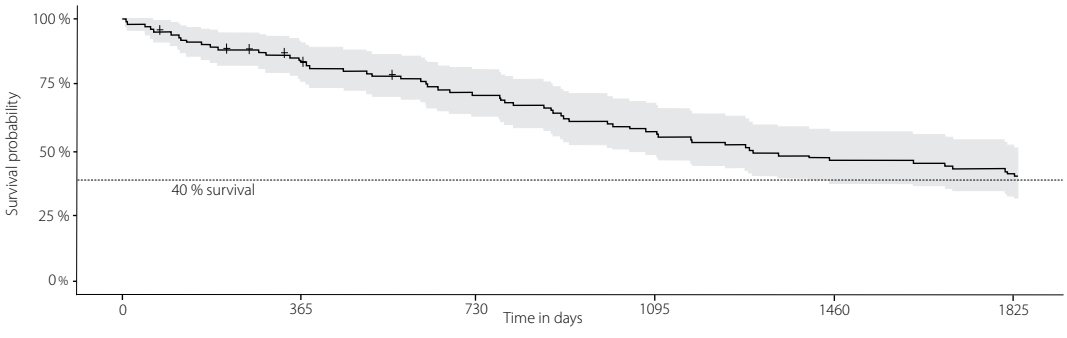

Figure 1. Kaplan-Meier Graph. Five-year survival of a group of patients with a given health condition. The curve starts at 100 % and decreases with each event. Crosses (+) represent censored data. In this example, the five-year survival rate is 40 %.

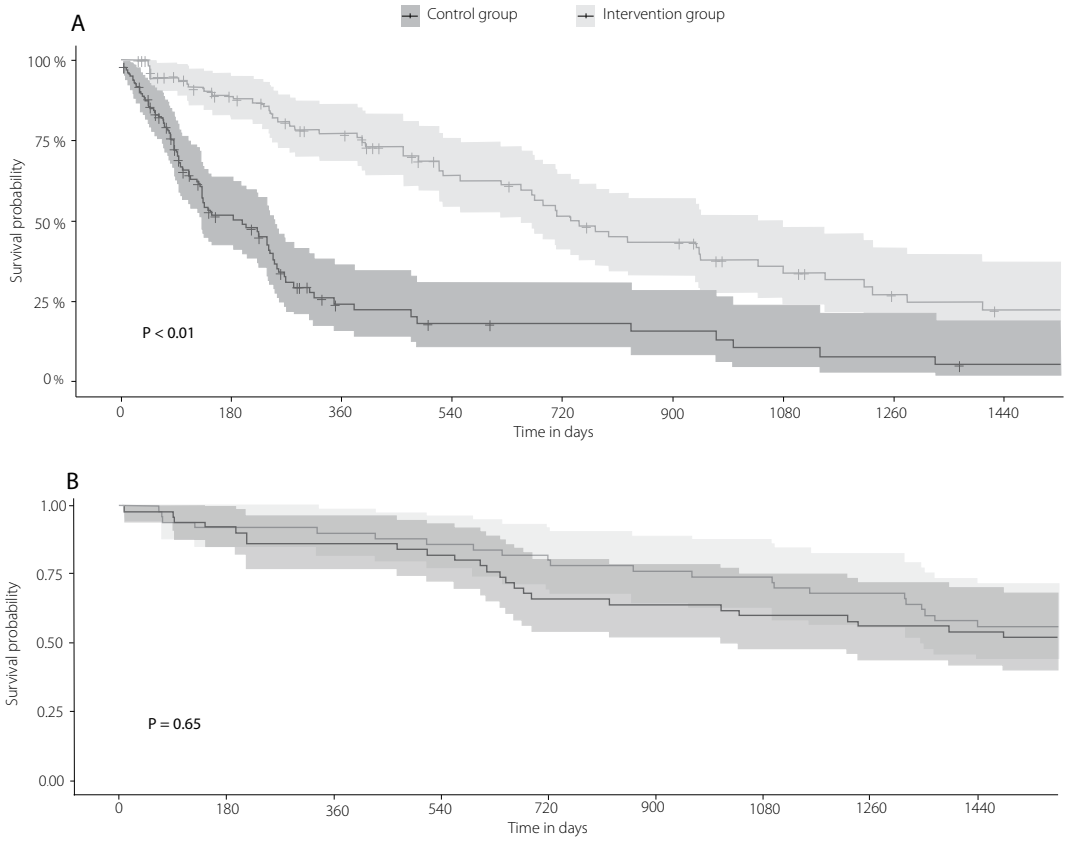

Figure 2. Log-Rank Test. This compares an intervention group with a control group. Figure 2A shows that $p < 0.01$, so the null hypothesis is rejected and a statistically significant difference between the groups is indicated. Figure 2B shows that $p = 0.65$, which means the null hypothesis is not rejected and suggests no significant difference between the groups.

use more than one method in order to verify this assumption.[xxvi]

Non-Proportional Hazard Models

A wide range of tests for analysing non-proportional hazards is available, and no clear consensus exists on the optimal approach.[xxviii] One preliminary strategy is to partition the follow-up period into intervals where the PHA holds and to construct separate models for each interval.[xxix] For instance, in a study that made a comparison between endovascular repair and open surgery for abdominal aortic aneurysms, since the PHA was not met, the analysis was divided into four time periods: six-month survival, four-year survival among those who survived the first period, eight-year survival, and survival beyond eight years.[xxx]

Further possibilities for exploration include the stratification of the model based on variables that contravene the PHA, and the extension of the model through the incorporation of time-dependent covariates.[xxix,xxxi] The latter approach is most frequently employed in the context of clinical trials.[xviii]

For example, a study analyzed the relationship between CA19-9 levels and survival in pancreatic cancer patients receiving chemotherapy. Following the discovery that the PHA had not been met, the researchers proceeded to implement a Cox model with time-dependent covariates. This entailed the introduction of periodic CA19-9 measurements into the model. The baseline HR was established at 1.56, with a maximum recorded of 2.0 HR attained two months following the commencement of chemotherapy treatment.[xxxii]

Additional techniques that may be employed include frailty or random effects models,[xxviii,xxxiii] parametric models such as piecewise exponential and accelerated failure time models, and machine learning (ML) approaches.[xxviii]

Bayesian Survival Models

Bayesian survival analysis is a flexible tool that allows for the modelling of the time to an event, such as death or recovery. This is achieved by integrating prior information through a priori distributions and enabling dynamic decision-making. In contrast to conventional methods, Bayesian approaches do not necessitate the PHA.Techniques such as the Integrated Nested Laplace Approximation have been proven to be especially useful due to their capacity to process large datasets with great expediency and accuracy. Bayesian models provide credibility intervals, which offer a more intuitive analysis in complex clinical and epidemiological settings by better reflecting uncertainty.[xxxiv]

They are also useful when the sample size or number of events is small in relation to the number of variables. For example, in a survival analysis of 299 heart failure patients, of whom 96 died, 11 variables were analyzed. According to traditional rules, at least 110 events would have been needed (ten per variable), so a Bayesian Cox regression provided a more reliable analysis in this context.[xxxv]

[i]

Use of Artificial Intelligence in Survival Analysis

Artificial intelligence (AI), along with its branches of ML and deep learning (DL), has become a valuable tool in survival analysis. These technologies facilitate the processing and analysis of large volumes of data, enabling the identification of complex patterns and relationships that are difficult to discern using traditional statistical methods.[xxxvi]

ML and DL methods have transformed survival analysis by overcoming the limitations of traditional models. Prominent ML models include multitask logistic regression networks, DeepSurv and survival random forests. These methods can handle complex and non-linear relationships, identify patterns in high-dimensional data and provide more accurate predictions. Their flexibility allows the integration of clinical, biomarker, and genomic data, thereby enhancing treatment personalization and informed decision-making.[xxxvii]

DL models are particularly effective at analyzing high-dimensional datasets where the number of features exceeds the number of observations, which is a challenge for traditional methods.[xxxviii] Deep neural networks can model complex nonlinear relationships between variables and outcomes, such as disease progression or death, thereby improving prediction accuracy. Their capacity to learn from large datasets enables them to identify significant patterns that traditional methods may overlook.[xxxviii,xxxix]

One example of the utility of machine learning (ML) in survival analysis is a study that analyzed 100 544 pathological images from 78 patients, successfully predicting one-year progression-free survival following immunotherapy in patients with small-cell lung cancer.[xl]

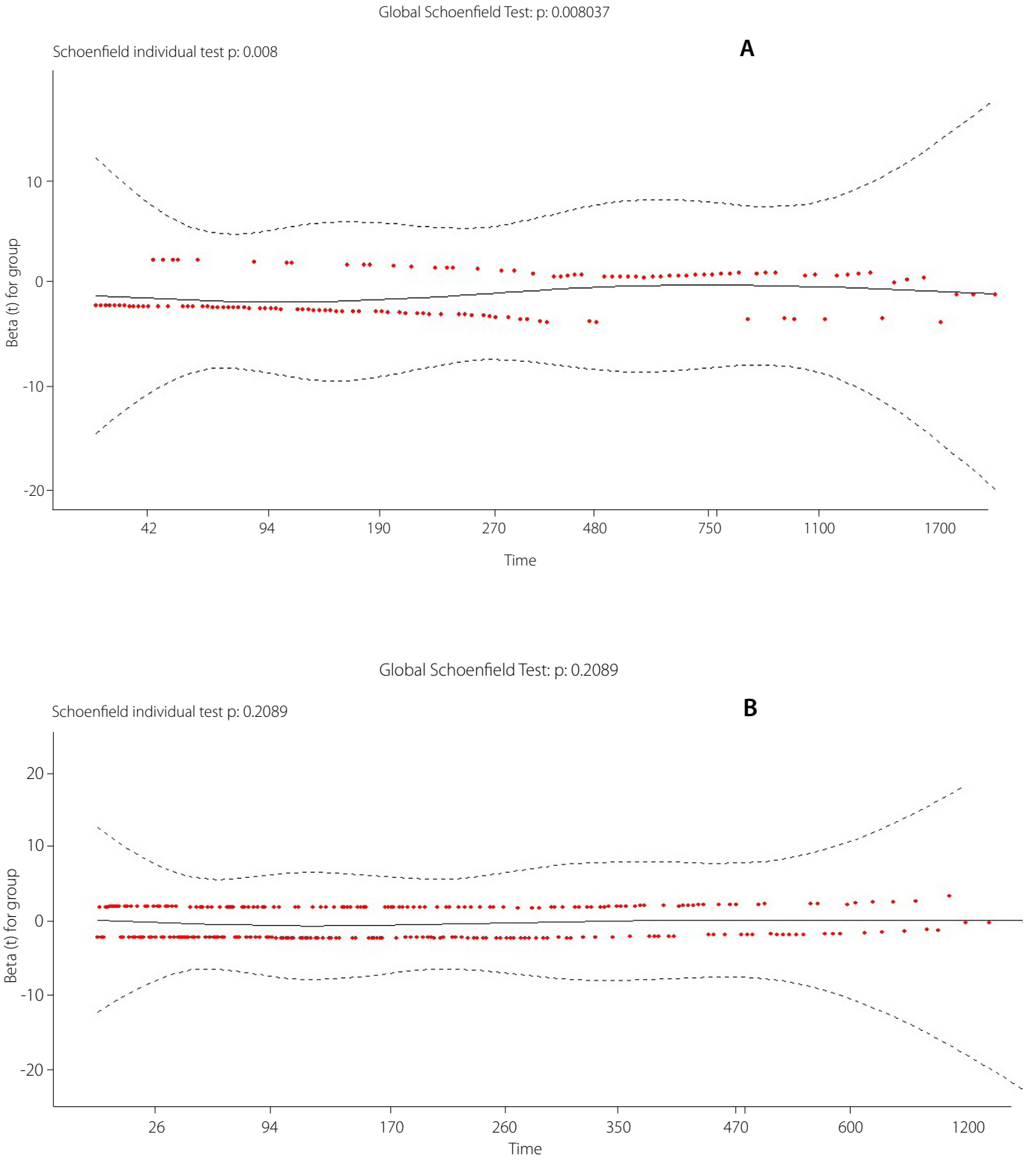

Figure 3. Schoenfield test. The objective of this study is to ascertain the factors that influence the probability of complications in patients undergoing surgical treatment one year after the intervention. It is necessary to determine whether the Cox proportional hazards model is adequate for the analysis. To this end, a Schoenfeld test will be performed to ascertain whether the variables included meet the assumption of proportionality of risks. Figure 3A rejects the null hypothesis ($p < 0.05$), thus indicating that the proportional hazards are not met. This implies that the risk of complications is not constant throughout the follow-up period, necessitating the use of an alternative model for the comparison of treatments. As depicted in Figure 3B, the null hypothesis is not rejected, thereby validating the proportionality of risks and affirming the efficacy of the Cox regression model.

Limitations of Survival Analysis

If the probability of the event of interest is low, a large sample size is required to ensure a sufficient number of events for reliable analysis. When the event takes a long time to occur, extended follow-up periods are necessary, which can lead to an increased number of censored cases due to patients dropping out of the study.[xli] Furthermore, the risk of the event occurring may vary over long timeframes, which breaks the PHA.[xxix]

Models recommended for long-term survival analysis, such as in cancer studies, include milestone survival analysis, restricted mean survival time analysis, area under the survival curve model, nomograms, and the previously mentioned accelerated failure time models and ML techniques.[xxix,xlii]

Biases in Survival Analysis

Informative censoring is regarded as a form of selection bias, arising when censored subjects exhibit a higher or lower risk of the event in comparison to those who remain in the study.[ii,v]

An illustration of this phenomenon can be found in the context of a clinical trial, in which a patient was excluded from further participation due to the emergence of an adverse effect related to the study medication or the necessity to modify the therapeutic regimen.[v]

In instances where the occurrence of informative censoring is suspected, researchers may decide to exclude these patients from the analysis or utilize adjusted models such as stratified models, standard regression adjustments, joint modelling, or inverse probability of censoring weighting estimation.[v,vii]

Lead-time bias occurs when a disease is detected at an early stage, prior to the onset of symptoms, through screening,[v] which may lead to an overestimation of survival time and intervention effectiveness.[xliii,xliv] To exemplify this, consider the scenario in which two patients develop cancer at the age of 15 and both succumb at the age of 60. In this case, it can be deduced that the actual survival time for both patients is equivalent. However, if an individual is diagnosed at the age of 40 and another at 50, it may give the erroneous impression that the latter has a longer survival time. To circumvent this issue, it is imperative to initiate follow-up evaluations at the commencement of the intervention or exposure under scrutiny.[xlv]

The phenomenon of stage migration bias occurs when patients with cancer who are at the threshold between stages are more likely to be assigned to the more advanced stage. This approach has been shown to enhance survival outcomes in both stages of the disease. In the initial stage, it functions by excluding more aggressive cancers, while in the subsequent stage, it encompasses a relatively lower proportion of cases that are less severe. This phenomenon is referred to as the Will Rogers effect.[v]

A competing risk is defined as an event that either prevents or modifies the occurrence of the event of interest.[xlvi] To cite an example, in a study where the outcome is kidney failure, if a patient dies before developing this condition, death becomes a competing risk. In a similar vein, if the outcome is cardiovascular death and a patient dies from another cause, that other cause is also considered a competing risk.[xlvii]

The employment of classical methods, such as the Kaplan-Meier or Cox regression, in the context of competing risks may result in the introduction of bias and an overestimation of the effect of the treatment or exposure under investigation.[xlvi,xlvii] The most common methods for conducting these analyses are cause-specific hazard models and the Fine and Gray model.[xlvii]

It is imperative to exercise caution when conducting a comparative analysis of surgical interventions and conservative management strategies. Surgical complications are more likely to occur in the perioperative period, violating the PHA. Furthermore, the benefits of surgery often manifest over an extended timeframe, which may not be captured if the follow-up period is too brief.[xlviii] In such cases, it is advised that the efficacy and safety of the treatments be evaluated independently. In order to evaluate the effectiveness of preventive surgeries, it is advised that the follow-up process commence in the postoperative period.[xlviii]

Limitations of the Review and Recommendations

A broad spectrum of survival analysis methods and adjusted models exists for a variety of applications, rendering it impractical to describe all variations and statistical foundations in this review. Nevertheless, the objective of this study was to highlight the most commonly used methods, with a view to assisting researchers in selecting the most appropriate techniques for their research objectives and identifying common biases in such studies.

It is recommended that the event(s) of interest and the start and end points of follow-up be clearly defined; that potential biases be assessed before data collection; and that an appropriate sample size calculation method tailored to survival analysis be

applied. Following the selection of the statistical model in accordance with the study's objectives, it is imperative to undertake a thorough verification of the underlying assumptions and ensure their validity.

Conclusion

The most frequently employed methods for survival analysis are the Kaplan-Meier method and the CPR model. However, it is imperative to verify that the necessary assumptions for the application of these statistical techniques, such as PHA and non-informative censoring, are met prior to their implementation.

In instances where the implementation of conventional methodologies is unfeasible, researchers are required to select appropriate analytical techniques in accordance with their research objectives, the characteristics of their population, and the availability of resources.

The advent of technological advancements has enabled the integration of AI into survival analysis, thereby facilitating the modelling of complex scenarios, the management of voluminous data, and the identification of intricate patterns. This development has served to overcome the limitations of conventional approaches, consequently generating novel prospects in the domain of medical research.

Funding

No external funds were received for this work.

References

i. Barakat A, Mittal A, Ricketts D, Rogers BA. Understanding survival analysis: actuarial life tables and the Kaplan-Meier plot. Br. J. Hosp. Med. Lond. Engl. 2005. 2019;80(11):642-646. DOI: 10.12968/hmed.2019.80.11.642

ii. Lira RPC, Antunes-Foschini R, Rocha EM. Survival analysis (Kaplan-Meier curves): a method to predict the future. Arq. Bras. Oftalmol. 2020;83:V-VII. DOI: 10.5935/0004-2749.20200036

iii. Perera M, Dwivedi AK. Statistical issues and methods in designing and analyzing survival studies. Cancer Rep. 2019;3(4):e1176. DOI: 10.1002/cnr2.1176

iv. Andrade C. Survival Analysis, Kaplan-Meier Curves, and Cox Regression: Basic Concepts. Indian J. Psychol. Med. 2023;45(4):434-435. DOI: 10.1177/02537176231176986

v. Dey T, Mukherjee A, Chakraborty S. A Practical Overview and Reporting Strategies for Statistical Analysis of Survival Studies. CHEST. 2020;158(1):S39-S48. DOI: 10.1016/j.chest.2020.03.015

vi. Martínez Pérez JA, Pérez Martínez PS. Análisis de supervivencia. Med. Fam. SEMERGEN. 2023;49(5):101986. DOI: 10.1016/j.semerg.2023.101986

vii. Su P-F, Lin C-CK, Hung J-Y, Lee J-S. The Proper Use and Reporting of Survival Analysis and Cox Regression. World Neurosurg. 2022;161:303-309. DOI: 10.1016/j.wneu.2021.06.132

viii. Indrayan A, Tripathi CB. Survival Analysis: Where, Why, What and How? Indian Pediatr. 2022;59(1):74-79. DOI: 10.1007/s13312-022-2425-5

ix. Weißbach R, Kim Y, Dörre A, Fink A, Doblhammer G. Left-censored dementia incidences in estimating cohort effects. Lifetime Data Anal. 2021;27(1):38-63. DOI: 10.1007/s10985-020-09505-1

x. Ruff RR. Caries Incidence in School-Based Prevention Programs in the Presence of Interval Censoring. Children. 2024;11(11):1350. DOI: 10.3390/children11111350

xi. Vibha D, Prasad K. Introduction to Survival Analysis. Neurol. India. 2020;68(5):1172. DOI: 10.4103/0028-3886.299141

xii. Shreffler J, Huecker MR. Survival Analysis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560604/

xiii. Hess AS, Hess JR. Kaplan-Meier survival curves. Transfusion (Paris). 2020;60(4):670-672. DOI: 10.1111/trf.15725

xiv. Deo SV, Deo V, Sundaram V. Survival analysis—part 1. Indian J. Thorac. Cardiovasc. Surg. 2020;36(6):668-672. DOI: 10.1007/s12055-020-01049-1

xv. Deo SV, Deo V, Sundaram V. Survival analysis-part 2: Cox proportional hazards model. Indian J. Thorac. Cardiovasc. Surg. 2021;37(2):229-233. DOI: 10.1007/s12055-020-01108-7

xvi. Rebasa P. Conceptos básicos del análisis de supervivencia. Cir. Esp. 2005;78(4):222-230. DOI: 10.1016/S0009-739X(05)70923-4

xvii. Rossello X, González-Del_Hoyo M. Survival analyses in cardiovascular research, part I: the essentials. Rev. Esp. Cardiol. Engl. Ed. 2022;75(1):67-76. DOI: 10.1016/j.rec.2021.06.003

xviii. Lu K. Sample size calculation for logrank test and prediction of number of events over time. Pharm. Stat. 2021;20(2):229-244. DOI: 10.1002/pst.2069

xix. Austin PC, Allignol A, Fine JP. The number of primary events per variable affects estimation of the subdistribution hazard competing risks model. J. Clin.

Epidemiol. 2017;83:75-84. DOI: 10.1016/j.jclinepi.2016.11.017

xx. Zapf A, Wiessner C, König IR. Regression Analyses and Their Particularities in Observational Studies: Part 32 of a Series on Evaluation of Scientific Publications. Dtsch. Ärztebl. Int. 2024;121(4):128. DOI: 10.3238/arztebl.m2023.0278

xxi. Kieser M. Methods and Applications of Sample Size Calculation and Recalculation in Clinical Trials. Cham; 2020.

xxii. Caille A, Tavernier E, Taljaard M, Desmée S. Methodological review showed that time-to-event outcomes are often inadequately handled in cluster randomized trials. J. Clin. Epidemiol. 2021;134:125-137. DOI: 10.1016/j.jclinepi.2021.02.004

xxiii. Akbar MH, Ali S, Shah I, Alqifari HN. Sample size determination for time-to-event endpoints in randomized selection trials with generalized exponential distribution. Heliyon. 2024;10(5):e27013. DOI: 10.1016/j.heliyon.2024.e27013

xxiv. Martín-Conejero A. Sobrevivamos al análisis de supervivencia (primera parte). Angiología. 2022;74(4):157-161. DOI: 10.20960/angiologia.00393

xxv. Sachs MC, Brand A, Gabriel EE. Confidence bands in survival analysis. Br. J. Cancer. 2022;127(9):1636-1641. DOI: 10.1038/s41416-022-01920-5

xxvi. In J, Lee DK. Survival analysis: part II - applied clinical data analysis. Korean J. Anesthesiol. 2019;72(5):441-457. DOI: 10.4097/kja.19183

xxvii. Ortega Páez E, Ochoa Sangrador C, Molina Arias M. Estudios de supervivencia. Modelo de riesgos proporcionales. Regresión de Cox. Evid. En Pediatría. 2023;19(4). Available at: https://evidenciasenpediatria.es/articulo/8249/estudios-de-supervivencia-modelo-de-riesgos-proporcionales-regresion-de-cox

xxviii. Bardo M, Huber C, Benda N, Brugger J, Fellinger T, Galaune V, Heinz J, Heinzl H, Hooker AC, Klinglmüller F, *et al.* Methods for non-proportional hazards in clinical trials: A systematic review. Stat. Methods Med. Res. 2024;33(6):1069. DOI: 10.1177/09622802241242325

xxix. Meuli L, Kuemmerli C. The Hazard of Non-proportional Hazards in Time to Event Analysis. Eur. J. Vasc. Endovasc. Surg. 2021;62(3):495-498. DOI: 10.1016/j.ejvs.2021.05.036

xxx. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. The Lancet. 2016;388(10058):2366-2374. DOI: 10.1016/S0140-6736(16)31135-7

xxxi. Ananthakrishnan R, Green S, Previtali A, Liu R, Li D, LaValley M. Critical review of oncology clinical trial design under non-proportional hazards. Crit. Rev. Oncol. Hematol. 2021;162:103350. DOI: 10.1016/j.critrevonc.2021.103350

xxxii. Chen Y, Shao Z, Chen W, Xie H, Wu Z, Qin G, Zhao N. A varying-coefficient cox model for the effect of CA19-9 kinetics on overall survival in patients with advanced pancreatic cancer. Oncotarget. 2017;8(18):29925-29934. DOI: 10.18632/oncotarget.15557

xxxiii. Balan TA, Putter H. A tutorial on frailty models. Stat. Methods Med. Res. 2020;29(11):3424. DOI: 10.1177/0962280220921889

xxxiv. Alvares D, van Niekerk J, Krainski ET, Rue H, Rustand D. Bayesian survival analysis with INLA. Stat. Med. 2024;43(20):3975-4010. DOI: 10.1002/sim.10160

xxxv. Taheri Soodejani M, Tabatabaei SM, Mahmoudimanesh M. Bayesian statistics versus classical statistics in survival analysis: an applicable example. Am. J. Cardiovasc. Dis. 2021;11(4):484-488. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC8449193/

xxxvi. Chen Y, Xue J, Yan X, Fang D, Li F, Tian X, Yan P, Feng Z. Identification of crucial genes related to heart failure based on GEO database. BMC Cardiovasc. Disord. 2023;23(1):376. DOI: 10.1186/s12872-023-03400-x

xxxvii. Li X, Bao H, Shi Y, Zhu W, Peng Z, Yan L, Chen J, Shu X. Machine learning methods for accurately predicting survival and guiding treatment in stage I and II hepatocellular carcinoma. Medicine (Baltimore). 2023;102(45):e35892. DOI: 10.1097/MD.0000000000035892

xxxviii. Salerno S, Li Y. High-Dimensional Survival Analysis: Methods and Applications. Annu. Rev. Stat. Its Appl. 2023;10(Volume 10, 2023):25-49. DOI: 10.1146/annurev-statistics-032921-022127

xxxix. Moon I, LoPiccolo J, Baca SC, Sholl LM, Kehl KL, Hassett MJ, Liu D, Schrag D, Gusev A. Machine learning for genetics-based classification and treatment response prediction in cancer of unknown primary. Nat. Med. 2023;29(8):2057-2067. DOI: 10.1038/s41591-023-02482-6

xl. Shibaki R, Fujimoto D, Nozawa T, Sano A, Kitamura Y, Fukuoka J, Sato Y, Kijima T, Matsumoto H, Yokoyama T, *et al.* Machine learning analysis of pathological images to predict 1-year progression-free survival of immunotherapy in patients with small-cell lung cancer. J. Immunother. Cancer. 2024;12(2):e007987. DOI: 0.1136/jitc-2023-007987

xli. Emmerson J, Brown JM. Understanding Survival Analysis in Clinical Trials. Clin. Oncol. 2021;33(1):12-14. DOI: 10.1016/j.clon.2020.07.014
xlii. Bekiroglu GN, Avci E, Ozgur EG. What is the best method for long-term survival analysis? Indian J. Cancer. 2022;59(4):457. DOI: 10.4103/ijc.IJC_22_21
xliii. Syriopoulou E, Gasparini A, Humphreys K, Andersson TM-L. Assessing lead time bias due to mammography screening on estimates of loss in life expectancy. Breast Cancer Res. BCR. 2022;24:15. DOI: 0.1186/s13058-022-01505-3
xliv. Yang Z, Wong IO, Deng W, Chen R, Zhou J, Wei W. Lead-time bias in esophageal cancer screening in high-risk areas in China. Chin. J. Cancer Res. 2020;32(4):467. DOI: 10.21147/j.issn.1000-9604.2020.04.04
xlv. Gabr A, Kallini JR, Desai K, Hickey R, Thornburg B, Kulik L, Lewandowski RJ, Salem R. Types of Research Bias Encountered in IR. J. Vasc. Interv. Radiol. 2016;27(4):546-550. DOI: 10.1016/j.jvir.2016.01.013
xlvi. Li L, Yang W, Astor BC, Greene T. Competing Risk Modeling: Time to Put it in Our Standard Analytical Toolbox. J. Am. Soc. Nephrol. JASN. 2019;30(12):2284. DOI: 10.1681/ASN.2019101011
xlvii. Hageman SHJ, Dorresteijn JAN, Pennells L, van Smeden M, Bots ML, Di Angelantonio E, Visseren FLJ, on behalf of the UCC-SMART Study Group. The relevance of competing risk adjustment in cardiovascular risk prediction models for clinical practice. Eur. J. Prev. Cardiol. 2023;30(16):1741-1747. DOI: 10.1093/eurjpc/zwad202
xlviii. Darsaut TE, Rheaume AR, Chagnon M, Raymond J. The use and abuse of survival analysis and Kaplan-Meier curves in surgical trials. Neurochirurgie. 2024;70(4):101567. DOI: 10.1016/j.neuchi.2024.101567