An "R-Shiny" Interface Designed As a One-Stop Solution for All Kinds of Survival **Analysis According to NICE Technical Support Documents 14 and 21**

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CONCLUSION

- The "Survlytics" R-Shiny interface standardizes survival analysis, delivering a powerful, userfriendly solution for both conventional and advanced methodologies used in HTA submissions
- Interactive dashboards, automated Excel outputs, and dynamically generated Word reports provide comprehensive visualizations and documentation, empowering decision-makers to make data-driven decisions
- The tool is highly secure, easy to use, and runs on the cloud, which means it's accessible from anywhere while keeping patient data safe. It can handle both simple and advanced analyses, allowing experts to explore different survival patterns in patient groups
- Future enhancements with Generative AI will elevate its capabilities, offering deeper insights and making Survlytics an indispensable tool in health economic evaluations

PLAIN LANGUAGE SUMMARY

- Survivities is a newly developed, user-friendly software that helps statisticians to predict how treatments impact patient survival and quality of life, even beyond the clinical trial follow-up. It uses a combination of simple and advanced statistical models to provide more accurate and reliable survival estimates
- This web-based tool is securely hosted on the cloud and allows users to analyze both patientlevel data from clinical trials and data digitized from published sources. It offers a range of models to suit different analysis needs, while keeping patient information secure
- Survlytics provides interactive dashboards, automatically generated reports, and easy-tounderstand charts, helping healthcare organizations make better decisions. Future enhancements will include AI-powered features to provide quick answers and deeper insights into patient data

INTRODUCTION

Survival analysis is a robust statistical approach used to evaluate the time to the occurrence of specific events, such as mortality, disease progression, or treatment discontinuation. It is a

RESULTS

Figure 2 presents the home page of the R-shiny interface where on the left-hand side is the

critical tool for estimating survival probabilities and identifying factors that influence patient outcomes over a specified period

- In the context of health technology assessment (HTA) submissions, survival analysis is helpful for assessing the effectiveness of interventions on patient survival and health-related quality of life. It enables the extrapolation of survival data beyond the clinical trial follow-up, providing essential insights for evaluating the long-term benefits of treatments
- Although various open-source R packages (i.e., survival, flexsurv, etc.) are available for conducting survival analysis, there is currently no integrated solution that consolidates all necessary functionalities into a single platform. This is where Survlytics addresses a critical gap by offering decision-makers a comprehensive tool for standardized survival analysis, enabling efficient model fitting, visualization, and reporting within a unified interface.

OBJECTIVE

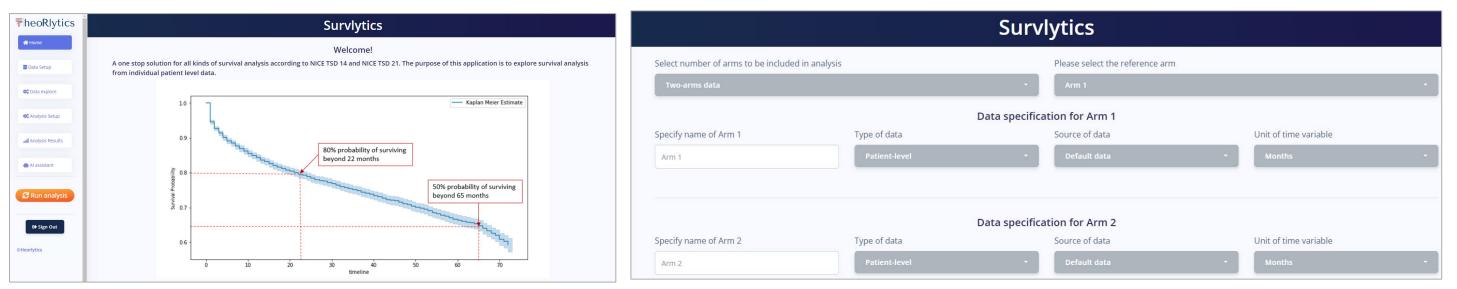
- The primary objective was to develop a unified R-Shiny platform leveraging open-source, validated R packages to streamline survival analysis required for HTA submissions or early economic models
- The aim was to provide users with a comprehensive tool that facilitates both conventional survival analyses and flexible survival modeling based on National Institute for Clinical Excellence (NICE) Technical Support Documents (TSD) 14 and 21. This platform is designed to enable users to seamlessly perform analyses, visualize the plots, and produce documentation, including estimates for Excel-based economic models, all within a single, integrated environment

METHODS

• The interface is built using R (v4.3.1), leveraging several open-source packages including shiny, dplyr, rmarkdown, highcharter, datatable, survival, flexsurvreg, and rhandsontable. It is deployed on an AWS server using Docker containers and integrates Auth0 for secure user authentication and management.

navigation pane with data setup, data explore, analysis setup, analysis results and AI assistant

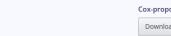
Figure 2: R-Shiny interface (Left: Home page; Right: Data setup page)



- The interface enables users to either upload individual patient-level data (IPD) directly or provide digitized data in a predefined format with a maximum of two-arms. If digitized data is uploaded, the platform automatically generates Pseudo-IPD using the Guyot algorithm, facilitating further analysis. The interface also enables users to upload life tables, allowing for the integration of background mortality into parametric estimates and supporting the use of cure fraction models.
- After uploading the data, the interface will facilitate users to see the survival behavior of the data which includes but is not limited to:
 - Median survival with confidence intervals and Restricted mean with standard errors, Kaplan-Meier plot, log-log plot, cumulative hazard plot, log-cumulative hazard plot, and various x-axis and y-axis transformations. Non-parametric statistical tests such as Mantel-Haenszel log-rank test and Gehan-Wilcoxon test for comparing two arms and checking if both arms differ significantly
 - Proportional hazard assumption tests (i.e. Global test, log-rank test, Grambsch-Therneau test with Schoenfeld residual plot and quantile-quantile (QQ) plot for checking Accelerated Failure Time (AFT) assumption

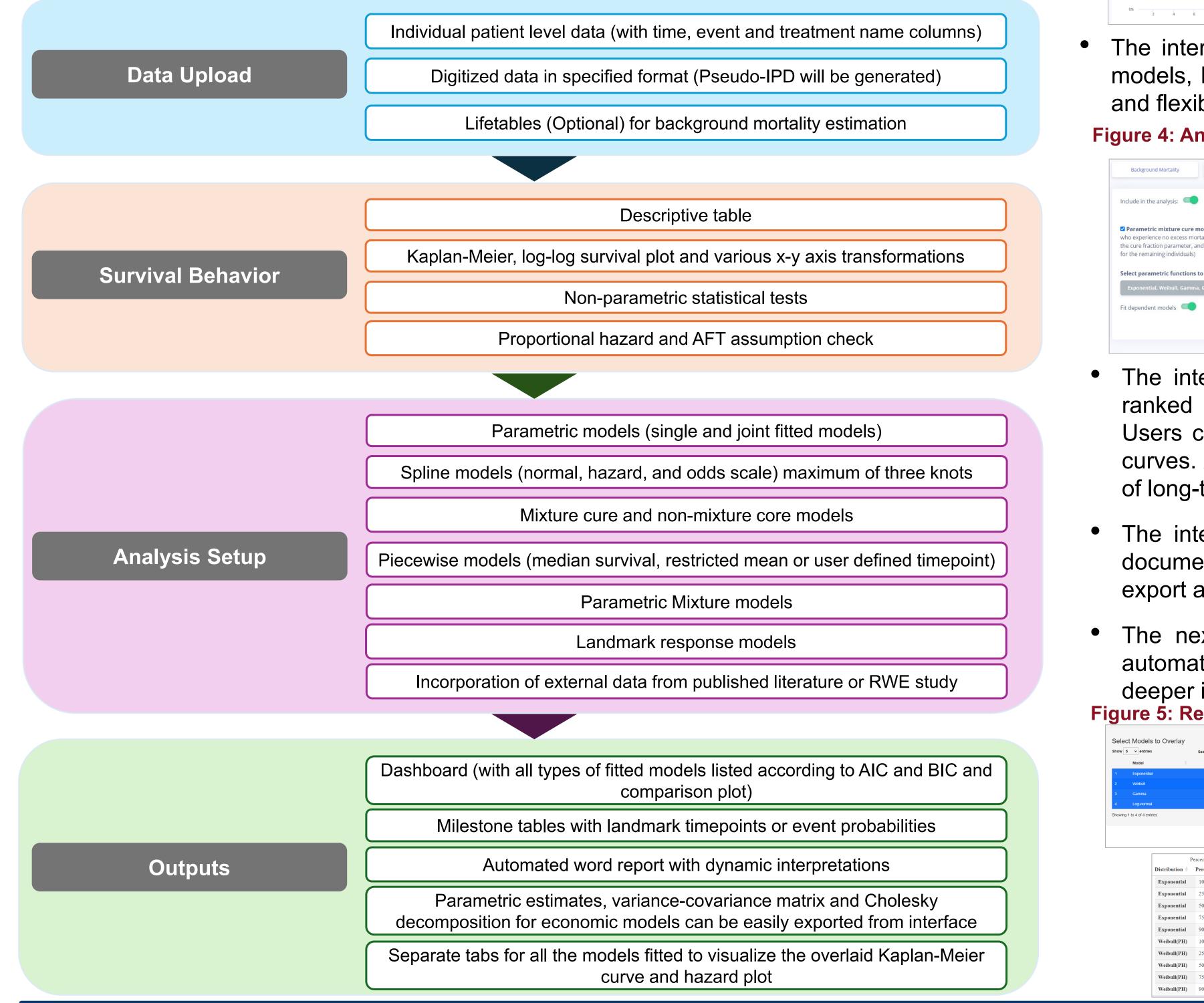
Figure 3: Data explore result tab (Left: Descriptives; Right: PH assumption test)

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The interface has been designed in a modularized architecture, enabling efficient scalability and adaptability. By organizing the platform into distinct, independent modules, it allows for seamless integration of new features and enhancements without disrupting existing functionalities.

Figure 1: Flowchart of the R-shiny web-based interface



Arm 🔶	No. of Patients	No. of Events	No. of Censored	Median Survival Time	Lower 95% Cl (Median)	(Median)	Restricted Mean Survival	Standard Error (Mean)	Test	square)	p-value	Interpretation	Description	Estimate
Arm 1	63	47	16	7.04	6.14	10.1	9.48	0.82	Grambsch- Therneau test	0.135043	0.71326	The Grambsch-Therneau test gives a p-value of 0.71326 (i.e. >0.05), indicating that the PH assumption holds.	Hazard ratio (vs Arm 1)	0.35
Arm 2	65	29	36	18.47	14.32		15.26	0.86				The log rank test gives a pivalue of 0 000012 (i.e. < 0.05) indicating that	Log of hazard ratio (logHR)	-1.046
									Log-rank test	19.121641	0.000012	the PH assumption does not holds.	Standard error (se logHR)	0.24
									Score (logrank) test	19.782144	0.000009	The Score (logrank) test gives a p-value of 0.000009 (i.e. <0.05), indicating	95% lower bound of HR	0.21
plan-Meier	rplot				Hazard plot X-axis transformatio		Y-axis transformation					that the PH assumption does not holds.	95% upper bound of HR	0.56
100% ●	- Arm 1	Arm 1 Censored	→ Arm 2 🔺 Arm	n 2 Censored	None		Log-cumulative hazar		Wald test	18.29	0.000019	The Wald test gives a p-value of 0.000019 (i.e. <0.05), indicating that the PH assumption does not holds.	Hazard ratio (vs Arm 2)	2.84
60%		· · · · ·	•] _{••}] _{•`•}	[↓] ▲ [↓]	→ 0 0 (C mmil ative hazard)	Jun		+++++++++++++++++++++++++++++++++++++++	-01 clicesiduals for treatment effect	· · · ·	· · ·	· · · · · · · · · · ·	<u> </u>	· <u>···</u> ···
0% —	2 4	6 8	10 12 1 me (in Months)	4 16 18 20	-4 0 2	4 6	8 10 12 14 Time (Months)	16 18 20		3.3 4.2		5 6.3 8.3 Time	12 14	18

The interface supports standard parametric models, spline models, piecewise models, cure models, landmark responder models, and parametric mixture models as type of conventional and flexible survival modeling approaches according to NICE TSD 14 and 21

Figure 4: Analysis Setup Tab (Left: Cure models; Right Top: Spline models; Right Bottom: Parametric Mixture Models)

Background Mortality	Parametric models	Spline Models	Piece-wise Models	Cure Models	Parametric mixture Models	Select spline models to be fitted on treatment a	rms in the data	Select maximum number of inter	mediate knots in spline models:	
						Log-cumulative hazards (hazards scale), Log-cu	nulative odds (odds scale), Probit of survival 👻	3 knots		•
who experience no excess mortal	dels (It assumes that that there exists a lity, with the proportion of such individ a parametric distribution representing	luals being given by			in existing parametric distribution such les the cure fraction parameter as time	Select All Log-cumulative hazards (hazards scale) Log-cumulative odds (odds scale) Probit of survival (normal scale) Select parametric functions for mixture 1	Deselect All	Select parametric functions for mixt	иге 2	
Select parametric functions to be fitted on all treatment arms in the data Exponential, Weibull, Gamma, Gompertz, Log-logistic, Log-normal, Generalized gamma			Select link function to be u	sed for estimation of the	e cure fraction	Exponential, Weibull, Gamma, Gompertz, Log-logis	tic, Log-normal, Generalized gamma 🔹	Exponential, Weibull, Gamma, Gompertz, Log-logistic, Log-normal, Generalized gamma		
			Logistic		•	Source of mixture weights				
Fit dependent models		Logistic Log-log			User specified weights					
					Minimum weight Maximum weight			Increment by		
			Probit			0.01	0.99		0.01	
			Identity			Licer defined weights for mixture 1 are: 0.01.0.02.0.0	3 0.04 0.05 0.06 0.07 0.08 0.00 0.1 0.11 0.1	2 0 13 0 14 0 15 0 16 0 17 0 18 0 10	, 0.2, 0.21, 0.22, 0.23, 0.24, 0.25, 0.26, 0.27, 0.28, 0.29,	03.0

- The interface generates a comprehensive dashboard that lists all fitted models in a table ranked by the Akaike Information Criterion (AIC) and Bayesian information criterion (BIC). Users can select multiple models to overlay on Kaplan-Meier plots to visualize extrapolated curves. Additionally, a milestone event probabilities table is included to facilitate quick analysis of long-term estimates
- The interface includes functionality to generate automated reports in MS Word format for documentation or HTML format for interactive visualizations. It also has the functionality to export all the parametric estimates, including variance-covariance matrix for economic models

The next steps involve integrating Generative AI capabilities into the platform to enable automatic extraction of data points from published Kaplan-Meier curves and provide users with deeper insights through an AI-powered Q&A chatbot. Figure 5: Results Tab (Left Top: Interactive graph; Left Bottom: Milestone tables; Right : Parametric Estimates)

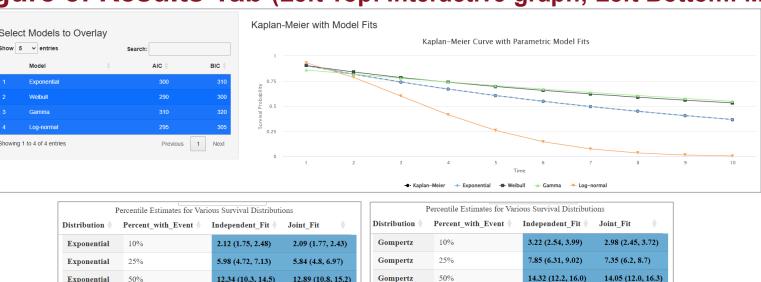
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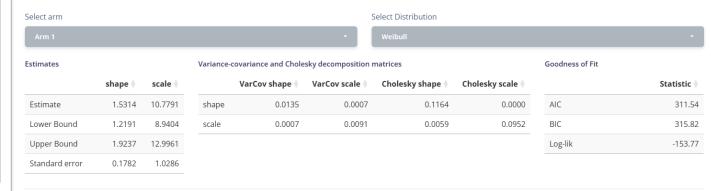
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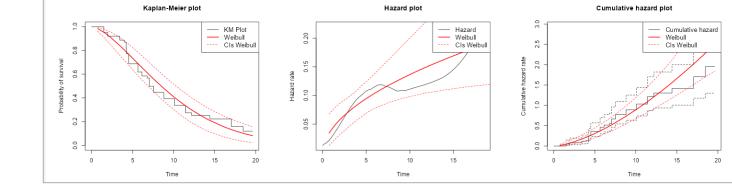
4.25 (3.6, 5.02

2 (3.5, 4.89)



Log-logistic





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Disclosures

The authors, SP, AS, SK, RK, BS, and KP, declare that they have no conflict of interest.

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