

A Comparison of Graph Digitization Software for the Reconstruction of Published Kaplan Meier Curves

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INTRODUCTION

- As healthcare budgets continue to increase, network meta-analysis and economic evaluations have become more important in assessing how healthcare resources are allocated
- However, the results reported in trials with survival outcomes do not always include the key summary statistics needed for a network meta-analysis or economic evaluation
- For evidence synthesis, an essential step is to use estimates of median survival or estimates of the hazard ratio
- Because of the poor, limited, and/or inconsistent reporting of results, it is possible to extract data from the published Kaplan Meier (KM) curves to obtain pseudo-individual patient data (IPD) and re-estimate key summary survival statistics
- The objective of this study was to compare the usability and the accuracy of free graph digitization software to reproduce published KM curves to enhance the quality of secondary data analysis

IMETHODS

- A Google search identified 13 different free graph digitization software tools. Of those available on Windows 10, the five most popular software tools were reviewed:
 - Engauge Digitizer (EG)¹
 - Graph Grabber (GG)²
 - GetData Graph Digitizer (GD)³
 - Plot Digitizer (PD)⁴
 - Web Plot Digitizer (WD)⁵
- The characteristics (versatility, user-friendliness, and accuracy) were evaluated after digitizing five different published KM curves
 - Versatility:** Platform/requirements for installing, import/export file format, and software size
 - User-friendliness:** Language support, user guide, axis settings, grid line, auto trace function, flexibility for tracing the graph, undo/redo function, zooming in/out, and visual validation
 - Accuracy:** Difference of median overall survival (OS) and hazard ratios (HR) between the originally published data and the reconstructed summary data after digitization
- KM curve digitization and reconstruction of KM curves
 - Extracted KM curves from a PDF article
 - Imported the figure of KM curves into the software
 - Defined X and Y axis
 - Traced the curve and/or selected points to read from the curve
 - Adjusted and deleted the points as needed (e.g. if there is an outlier)
 - Exported the digitized data (reconstructed coordinates)
 - Reconstructed the KM curves and survival summary statistics by R (version 4.0.1) using the published reconstruction algorithm (Guyot et al. 2012)⁶
 - Analyzed median OS and/or HR and compared to the available original reported statistics

RESULTS

Versatility (Table 1)

- GD and GG worked only with Windows
- Installation of PD required Java 1.6 or later
- GD accepted only JPG files whereas the other software recognized PNG and GIF files as well as JPG files
- GD exported the digitized data as XLS (MS Excel), text file, XML, DXF, or EPS file formats whereas the other software only exported as XLS (CSV)

Table 1. Versatility of the digitization software

	Engauge Digitizer (ED)	GetData Graph Digitizer (GD)	Graph Grabber (GG)	Plot Digitizer (PD)	Web Plot Digitizer (WD)
	Engauge Digitizer	GetData Graph Digitizer	Graph Grabber 2.0.2	Plot Digitizer	WebPlotDigitizer
Developer	Mark Mitchell	getdata-graph-digitizer	Quintessa Ltd.	Joseph A. Huwaldt and Scott Steinhorst	Ankit Rohatgi
The latest version (Released on)	Version 12.1 (29 Nov 2019)	Version 2.26 (19 Jun 2013)	Version 2.0.2 (3 Feb 2020)	Version 2.6.9 (10 Oct 2020)	Version 4.3 (7 Jul 2020)
Platform for installing	Windows, MacOS, Linux	Windows XP, 7, 8 and 10	Windows 10	Windows, MacOS, Linux	Web based Google Chrome, Firefox, Safari, Internet Explorer and Microsoft Edge
Requirement for installing	N/A	N/A	Provide e-mail address, name and purpose	Install Java 1.6 or later	N/A
Import file format					
JPG	✓	✓	✓	✓	✓
PNG	✓	X	✓	✓	✓
GIF	✓	X	✓	✓	✓
Export file format					
XLS	CSV	MS Excel	CSV	CSV	CSV
TXT	X	Text file	X	X	X
XML	X	✓	X	X	X
DXF	X	Auto CAD	X	X	X
EPS	X	PostScript	X	X	X
Software size	16.7 MB	1,086 KB	26.7 MB	1.2 MB	N/A

User-friendliness (Table 2)

- All software was available in English, PD also included French, and GD included 14 languages
- GD, GG, PD, and WD required four different points for X and Y axis settings, EG used the same value for X-min and Y-min, whereas PD had an option to use different values for X-min and Y-min or set X-min and Y-min to be the same
- GD and PD showed grid lines which helped to identify the points from the KM curve
- Technically all software had an auto-trace function (although PD required another software program for installation of auto-trace), however only WD worked well enough to read the whole line

Table 2. User-friendliness of the digitization software

	Engauge Digitizer (ED)	GetData Graph Digitizer (GD)	Graph Grabber (GG)	Plot Digitizer (PD)	Web Plot Digitizer (WD)
Language support					
Number of language	1	14	1	2	4
Language	English	Arabic, Bulgarian, Chinese, English, German, Greek, Indonesian, Italian, Japanese, Korean, Romanian, Russian, Spanish, Ukrainian	English	English and French	English, French, German and Chinese
User guide	Checklist guide is included the software main page	On website	Include software and YouTube on website	On website	PDF and YouTube on website
Axes setting	3 points (X/Y-min, X-max and Y-max)	4 points (X-min, X-max, Y-min and Y-max)	X and Y axes line	3 or 4 points (X and/or Y-min, X-max and Y-max)	4 points (X-min, X-max, Y-min and Y-max)
Grid lines	X	✓	X	✓	X
Auto trace	X	✓	✓	With another software	✓
Tracing	Between the identified points were recognized as a curved line	Unable for the colored line	Masking did not always work	The auto tracing software did not work	Able to select the interval of coordinates
Add point	✓	✓	✓	✓	✓
Adjust point	✓	X	✓	✓	✓
Delete point	X	✓	✓	X	✓
Undo/redo	Unlimited	Undo	X	Unlimited	X
Magnification	6.25% - 1600%	10% - 1500%	✓	60% - 700%	✓
Visual validation	Need a separate software	Need a separate software	Within the same software	Need a separate software	Need a separate software

RESULTS (cont.)

Accuracy (Figure 1 and Table 3)

- Figure 1 shows a comparison of the original KM curves with the ones reconstructed with each software. Overall they appeared to overlap, however there were some gaps between the original KM curves and reconstructed ones upon inspection under magnification. The gap between the original endpoints (i.e. median OS and/or HR) and the calculated endpoints was also obvious from the statistical analysis shown in Table 3
- Comparing the average total absolute difference of the KM curves from the 5 studies, GD had the smallest difference (1.87%) whereas ED had the largest difference (4.50%) when considering the percent difference between reconstructed median OS value (and HR for one study) and reported value from original study

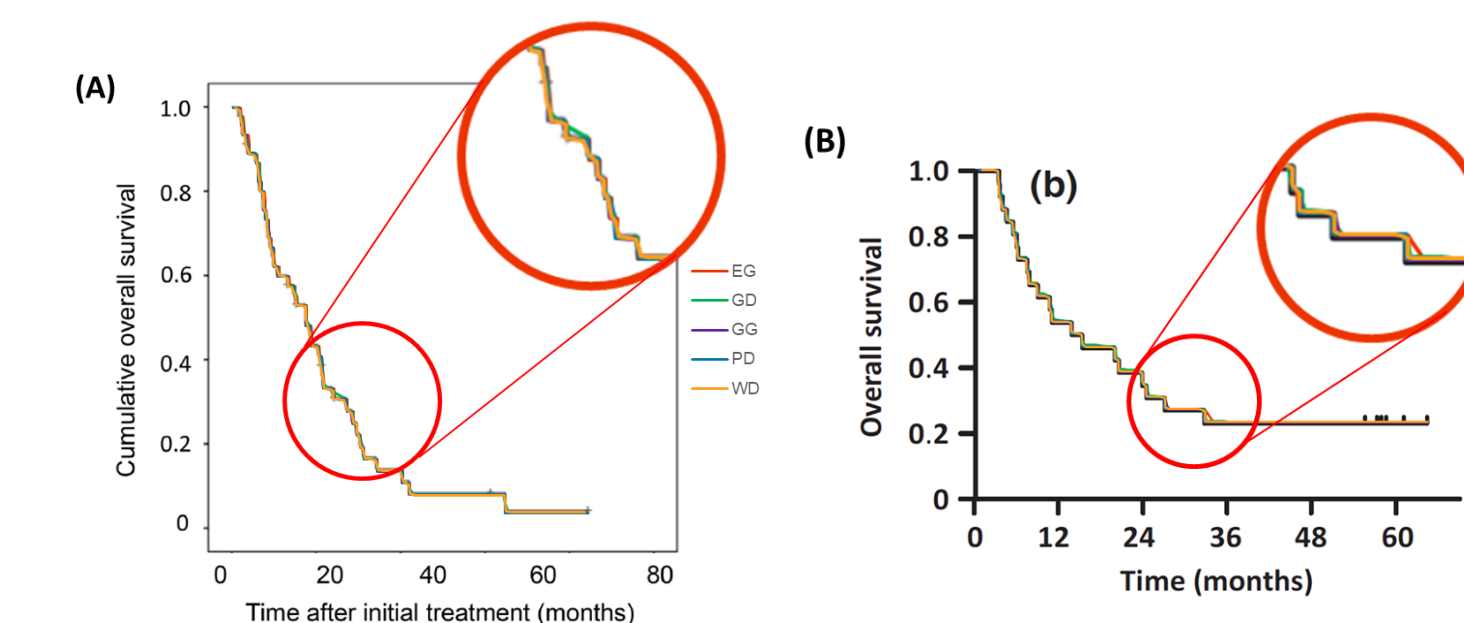


Figure 1. Visual example of the comparison between the original KM curves and the reconstructed KM curves after digitization by each software from Abe, et al (A) and Ishida, et al. (B)

Table 3. Accuracy of digitization

	ORIGINAL	Engauge Digitizer (ED)	GetData Graph Digitizer (GD)	Graph Grabber (GG)	Plot Digitizer (PD)	Web Plot Digitizer (WD)
Inoue (2018)						
Acute subgroup	0.31	0.33	0.31	0.32	0.31	0.31
Difference	-	8.52%	-0.31%	3.50%	1.35%	2.00%
Lymphoma subgroup	1.52	1.52	1.51	1.51	1.52	1.52
Difference	-	-0.59%	-2.54%	-1.57%	0.71%	1.37%
Average of absolute difference	-	4.56%	1.43%	2.54%	1.03%	1.69%
Choueiri (2018)						
Cabozantinib subgroup	8.60	8.70	8.92	8.60	8.67	8.68
Difference	-	1.16%	3.72%	0.00%	0.81%	0.93%
Sunitinib subgroup	5.30	5.52	5.27	5.39	5.41	5.39
Difference	-	4.15%	-0.57%	1.70%	2.08%	1.70%
HR	0.48	0.51	0.49	0.50	0.50	0.49
Difference	-	5.52%	2.10%	5.02%	4.58%	2.60%
Average of absolute difference	-	3.61%	2.13%	2.24%	2.49%	1.74%
Abe (2020)	15.00	14.17	14.78	13.98	14.05	14.32
Difference	-	-5.53%	-1.47%	-6.80%	-6.33%	-4.53%
Ishida (2017)	14.40	14.64	14.66	14.68	14.61	14.66
Difference	-	1.67%	1.81%	1.94%	1.46%	1.81%
Kakugawa (2016)	2.80	2.60	2.87	2.84	2.84	2.64
Difference	-	-7.14%	2.50%	1.43%	1.43%	-5.71%
Average of total absolute difference	-	4.50%	1.87%	2.99%	2.55%	3.10%

CONCLUSIONS

- Based on our analysis, ED and WD were shown to have more versatility, GD and GG were more user-friendly, and GD had slightly more accurate results than the others
- The key to reconstructing accurate KM curves was the quality of the initial axis setting because all coordinates are based on this first axis setting
- Most software required manual trace, thus there may be error unaccounted by each researcher who conducted the manual trace
- Selection of the most appropriate tool may be dependent on the specific desired tool attributes and digitization purpose

REFERENCES

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