USER GUIDE | DIGITIZATION | CLINICAL CURVES | PK/PD | RESEARCH

KurvMetric®

v2.0

Interactive digitization and statistical analysis of clinical and pharmacokinetic curves

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LEGAL NOTICE: This tool is a prototype for clinical decision support intended for research and educational purposes. It is NOT a validated medical device and does NOT substitute the clinical judgment of a licensed healthcare professional.

1. General Application Description

KurvMetric® is an interactive digitization and statistical analysis tool for clinical and pharmacokinetic curves from images. It allows you to load graphs published in scientific articles, clinical reports, or trials, calibrate the axes with precision, and digitize points manually on the image with the help of a floating 5x magnifying glass that amplifies the cursor area for maximum accuracy. It incorporates color-assisted curve auto-tracing (eyedropper + highlighter + auto-1click), image adjustment tools (brightness, contrast, binarization, rotation), basic pharmacokinetic parameter calculation (Cmax, Tmax, trapezoidal AUC), descriptive statistics, comparative clinical parameters (HR, ARR, NNT, RMST), and full dashboard export as a self-contained interactive HTML file. The entire working session can be saved as a JSON file and reloaded later to continue digitization from where it was left off. Designed for researchers, clinical pharmacists, and physicians who need to extract precise quantitative data from published graphs.

2. Use Cases and Applicability

KurvMetric can be used in the following clinical and pharmacological research scenarios:

- Extraction of numerical data from graphs published in scientific articles (graph digitizing): Kaplan-Meier survival curves, response curves, pharmacokinetic concentration-time curves, dose-response curves.
- Digitization of pharmacokinetic (concentration-time) curves for the calculation of PK parameters: Cmax, Tmax, AUC (linear trapezoidal method).
- Visual and statistical comparison of multiple curves digitized simultaneously on the same reference image.
- Reconstruction of Individual Patient Data (IPD) from Kaplan-Meier curves using the Guyot 2012 algorithm, if the number of patients at risk table is available.
- Calculation of comparative clinical parameters between an experimental arm and a control arm: Hazard Ratio, Absolute Risk Reduction (ARR), Number Needed to Treat (NNT), and Restricted Mean Survival Time (RMST).
- Generation of interactive dashboards with graphs, statistics, and tables comparatives exportable as self-contained HTML for presentations and publications.
- Saving and retrieving digitization sessions in JSON format to continue work in another session without losing already digitized points.

3. Interface Structure: The Three Tabs

KurvMetric is organized into three tabs accessible from the top navigation bar. The normal workflow is: Tab 1 (load image and digitize) -> Tab 2 (configure metadata) -> Tab 3 (view statistics and export dashboard):

Tab 1 — Digitizer: Graph Canvas & Tools

- Main area with the graph canvas: displays the loaded image with all digitized points overlayed on it.
- Zoom Bar: zoom controls (-/+) with percentage display. Allows expanding the canvas up to 300% to view pixels clearly.
- Floating Magnifying Glass (5x): automatically follows the cursor over the canvas, showing a 5x magnified view of the target pixel to guarantee maximum precision when clicking.

- Image Adjustments: sliders to rotate (degrees), adjust brightness (%), contrast (%), remove grid (background grid suppression filter), and binarize (convert to black & white). Useful to clean and isolate curves.

- Calibration Button: active assistant to guide the setting of points X1, X2, Y1, Y2. It turns green when calibration is active and valid.

Tab 2 — Metadata & Configuration

- Title and Axes: fields to define the title of the analysis and the labels of the X and Y axes shown in the final graph.

- Curve Management (Panel 2): table to add, select, name, color, and define interpolation type (KM Step function or Linear) for each curve.

- Patients at Risk (IPD): optional input section to record the number of patients at risk at specific time points (Guyot 2012 algorithm requirements).

- Experimental/Control selection: dropdowns to designate the active comparison curves for statistical analysis (experimental vs. control arms).

Tab 3 — Results & Analytics Dashboard

- Interactive Chart: rebuilt chart using Chart.js displaying all digitized curves on a clean coordinate axis.

- PK Parameters: table displaying Cmax (maximum concentration), Tmax (time of Cmax), and AUC (Area Under the Curve) for each PK curve.

- Clinical Parameters: table showing comparative indicators (Hazard Ratio, ARR, NNT, RMST) between experimental and control curves.

- Descriptive Stats: mean, median, standard deviation, and key percentile landmarks (e.g. 50% survival time) for each curve.

- Dashboard Export: green button to download the interactive, self-contained HTML report.

4. Input Data (Inputs)

All input data necessary for the correct operation of the application:

Field / Parameter	Detailed Description	Range / Valid Values
Graph Image	Image file containing the curves to digitize. Supported formats: PNG, JPG, JPEG. Drag-and-drop or select file.	*PNG / JPG / JPEG*
Calibration Point X1	Click on the origin of the X axis on the image and enter its real numerical value (e.g., 0).	*Numerical value*
Calibration Point X2	Click on the maximum end of the X axis on the image and enter its real numerical value (e.g., 120).	*Numerical value*
Calibration Point Y1	Click on the origin of the Y axis on the image and enter its real numerical value (e.g., 0 or 100).	*Numerical value*
Calibration Point Y2	Click on the maximum end of the Y axis on the image and enter its real numerical value (e.g., 100).	*Numerical value*
Curve Name	Descriptive name of the curve	*Text*

	(e.g., "Experimental Arm", "Control Arm"). Editable in the curve table.	
Curve Color	Color representing the curve on the canvas and final chart. Assigned randomly, user-customizable.	*Color picker*
Interpolation Type	KM Step (step function for Kaplan-Meier survival curves) or Linear (continuous straight lines connecting points).	*KM Step | Linear*
Landmarks / Risk Table	Times and patient counts at risk to feed the Guyot IPD reconstruction algorithm.	*Time: N at risk*
Image Adjustments (Optional)	Brightness (50-150%), contrast (50-150%), binarization (0-255, for low-quality charts) and rotation (-5 to +5 degrees) to correct tilted images.	*Continuous sliders*

5. Digitizer Tools in Detail

Tab 1 (Digitizer) concentrates all the tools for interaction with the image. They are described below with their specific controls:

Floating Magnifying Glass (5x): Automatically appears when moving the cursor over the canvas when an image is loaded. Displays a 5x magnified view of the cursor area in a 100px diameter circular window. It also shows pixel coordinates in real time. Essential for placing points with precision on dense curves or low-resolution images.

Canvas Zoom: The zoom bar allows enlarging the image between 10% and 500% to digitize high-density areas. The + and - buttons increase or decrease the zoom in 10% steps. The "100%" button restores original zoom. The "Fit" button fits the image width to the container.

Eyedropper: Color capturing mode: when active, the next click on the image captures the color of the selected pixel and adds it to the palette. The palette accumulates captured colors and displays them as color dots. Used to define the target color before auto-tracing.

Highlighter: Brush mode: allows marking image regions by painting with a semi-transparent brush using the active palette color. The brush has adjustable size (5-65 px) and color tolerance (10-130) sliders.

Auto-1Click: Automatic tracing mode: with a single click on a point of the curve, the application automatically traces the entire curve using the active palette color and configured tolerance. Works best on solid color, well-defined curves.

Guided Calibration: The "START CALIBRATION" button activates a step-by-step assistant: prompts the user in which order to set the four points (X1 -> X2 -> Y1 -> Y2). The assistant status is shown in real time. Alternative: set points manually with X1/X2/Y1/Y2 buttons.

Image Adjustment: Binarize: Binarization slider (0-255): converts the image to black and white using a luminosity threshold. Useful for low-quality charts or grayscale prints where curves are hard to distinguish by color.

Image Adjustment: Rotate: Rotation slider (-5 to +5 degrees): corrects slightly tilted images (scanned or photographed) to ensure axes are perfectly horizontal and vertical before calibrating.

Remove Grid: "Remove Grid" button: applies image processing that attempts to remove background grid lines from the original chart, leaving only the curves to facilitate digitization.

Right-click on Canvas: Right-click on a previously placed point on the canvas: deletes that specific point from the active curve. Alternative: use the trash button in the coordinates table of Panel 4.

Save Session: Button in the top bar: exports the entire current session (image, calibration, curves, points, and metadata) to a downloadable JSON file. The file can be loaded in another session to resume work.

Load Session: Button in the top bar: loads a previously saved session JSON file, restoring the image, calibration, curves, and all points exactly as they were.

6. Available Results and Exports (Outputs)

The application generates the following results and allows the following exports:

- COORDINATES TABLE: list of digitized points (X, Y) in the real units of the axes, downloadable in CSV format from the Tab 3 panel.
- INTERACTIVE CHART: visualization of all reconstructed curves on a Chart.js plot with legend, hover tooltips, native zoom, and comparison with the reported HR if entered.
- DESCRIPTIVE STATISTICS PER CURVE: number of points, minimum and maximum X values, minimum and maximum Y values, weighted mean, and median of Y.
- PK PARAMETERS (concentration-time curves): Cmax (maximum concentration), Tmax (time to Cmax), and AUC calculated by the linear trapezoidal method.
- COMPARATIVE CLINICAL PARAMETERS (KM curves): estimated Hazard Ratio, Absolute Risk Reduction (ARR), Number Needed to Treat (NNT), and Restricted Mean Survival Time (RMST) to the chosen time horizon.
- LANDMARKS TABLE: estimated survival rate of each curve at specific times defined by the user.
- IPD RECONSTRUCTION (with N at risk active): individual patient data reconstructed using the Guyot 2012 Algorithm, Cox model, and Log-rank test.
- EXPORTED HTML DASHBOARD: self-contained and interactive HTML file with all charts, statistics, and tables, ready to share or embed in presentations without needing KurvMetric.
- JSON SESSION: saveable session file with all current digitization information to retrieve it later or share it with another user.

7. Step-by-Step Workflow

Follow this complete workflow to obtain an analysis dashboard from a curve image:

Step 1. Access KurvMetric from your browser. Ensure you are on Tab 1 (Digitizer), which is active by default.

Step 2. LOAD THE IMAGE: drag the graph image file (PNG, JPG) directly onto the graph canvas area (dotted background area) or click the "Select File" button. The image will be shown centered. Use zoom controls to expand if necessary.

Step 3. ADJUST THE IMAGE (optional): if the image is tilted, use the "Rotate" slider to correct it. If contrast is low, adjust "Brightness" and "Contrast" sliders. If background grid is thick, click "Remove Grid" or use "Binarize" slider.

Step 4. CALIBRATE AXES (mandatory step): click the red "START CALIBRATION" button to start the guided wizard. The wizard will prompt you to set points in this order: X1 (X-axis origin), X2 (X-axis end), Y1 (Y-axis origin), and Y2 (Y-axis end). Click the exact pixel on the image and enter its real numerical value. The floating 5x magnifying glass helps you click precisely. Confirm all 4 points to complete calibration.

Step 5. CREATE THE FIRST CURVE: in Panel 2 "Manage Curves", click the "+ Add" button. The app creates a new curve with a default name (editable) and random color. Click on the curve row to select it (it will be highlighted in teal). Choose the interpolation type (KM Step for survival curves, Linear for continuous curves).

Step 6. DIGITIZE POINTS MANUALLY: with the curve selected, click on the curve points on the image. Each click places a circular marker on the image and adds it to the table in Panel 4 with its calculated real coordinates. Use zoom and the magnifying glass for precision. Right-click any point to delete it, or use the trash button in the table.

Step 7. CURVE AUTO-TRACING (optional, for solid color curves): activate the eyedropper in Panel 1, click on the curve to capture its color, adjust tolerance and brush size, and click "Auto-1Click". Click any point on the curve, and the app will automatically trace its path.

Step 8. DIGITIZE ADDITIONAL CURVES: for each additional curve, repeat steps 5 and 6: click "+ Add", select the new curve, assign a name and color, and digitize its points.

Step 9. CONFIGURE METADATA (Tab 2): go to Tab 2 and fill in the analysis title, axis labels, cohort sizes, and select experimental and control curves. If you have the patients at risk table, enable the toggle and enter the data for IPD Reconstruction.

Step 10. VIEW THE DASHBOARD (Tab 3): go to Tab 3 to view the interactive chart, descriptive stats, PK parameters, clinical comparison metrics, and landmarks. Use sliders to adjust the RMST time horizon.

Step 11. EXPORT THE DASHBOARD: click the green "Export Dashboard" button in the top bar to download the self-contained HTML file. This file can be opened offline in any browser to show the interactive dashboard.

Step 12. SAVE SESSION: click "Save Session" in the top bar to download the current session JSON file. Use it on your computer to resume work later by clicking "Load Session".

8. Advanced Tips for Precision

- Use images of at least 1000 x 800 pixels to maximize digitization accuracy. Low-resolution images limit calibration precision.
- The floating 5x magnifying glass is your best tool for placing points accurately. Set zoom to 150-200% and use the glass for curve ends and calibration points.
- Place calibration points at the far corners of the graph plotting area, not close to each other. Greater distance between X1 and X2 (and Y1 and Y2) dramatically increases calibration accuracy.

- For Kaplan-Meier curves, always select the "KM Step function" interpolation type. Linear interpolation does not correctly represent step survival functions.

- If auto-tracing fails to detect the curve, try increasing the color tolerance in Panel 1 or capturing different color hues with the eyedropper tool.

- For curves that are very close to each other or overlap, digitize manually point-by-point. Auto-tracing can get confused by similar adjacent colors.

- Save your session frequently ("Save Session" button) during long sessions to avoid losing work due to accidental browser closures.

- If the graph has background grids, use "Remove Grid" first, or combine with the binarization slider to isolate the curves from the background.

9. Notes and Known Limitations

KurvMetric® is a research tool. Digitization accuracy depends on the resolution/quality of the loaded image, and the accuracy of the user-set calibration points.

AUC calculation utilizes the standard linear trapezoidal method. For advanced pharmacokinetic compartment modeling, specialized software is recommended (NONMEM, Monolix, Phoenix WinNonlin).

IPD reconstruction using the Guyot 2012 algorithm provides an estimation of individual patient data, not an exact calculation. Cox model and Log-rank test results derived from reconstructed IPD should be interpreted with caution and compared with the original paper.

KurvMetric does not store any images or data on external servers. All processing is done locally in the user's browser. The JSON session is only saved locally on the user's device.

The exported HTML dashboard file is completely self-contained: it includes all data and Chart.js libraries required for offline visualization. It can be shared via email or embedded in presentations.

For curves with many points (> 200), canvas rendering performance might be slightly reduced on lower-end devices. Modern browsers (Chrome,

Edge, Firefox) are recommended.