**pkexamine — Calculate pharmacokinetic measures**

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**Description**

`pkexamine` calculates pharmacokinetic measures from concentration-and-time subject-level data. `pkexamine` computes and displays the maximum measured concentration, the time at the maximum measured concentration, the time of the last measurement, the elimination time, the half-life, and the area under the concentration–time curve ($AUC_{0,t_{max}}$). Three estimates of the AUC from 0 to infinity ($AUC_{0,\infty}$) are also calculated.

`pkexamine` is one of the pk commands. Please read [R] pk before reading this entry.

**Quick start**

Pharmacokinetic measures for concentrations `y` at times `tvar` where `idvar = 4`

```
   pkexamine tvar y if idvar==4
```

As above, but use trapezoidal rule to calculate $AUC_{0,t_{max}}$

```
   pkexamine tvar y if idvar==4, trapezoid
```

Plot concentration–time curve where `idvar = 2`

```
   pkexamine tvar y if idvar==2, graph
```

As above, and save graph as `mygraph`

```
   pkexamine tvar y if idvar==2, graph saving(mygraph)
```

**Menu**

Statistics > Epidemiology and related > Other > Pharmacokinetic measures
Syntax

```
pkexamine time concentration [if] [in] [ , options ]
```

```
options                     Description
Main
fit(#)                       use # points to estimate AUC<sub>0,∞</sub>; default is fit(3)
trapezoid                   use trapezoidal rule; default is cubic splines
graph                       graph the AUC
line                        graph the linear extension
log                         graph the log extension
exp(#)                      plot the exponential fit for the AUC<sub>0,∞</sub>
AUC plot
cline_options              affect rendition of plotted points connected by lines
marker_options             change look of markers (color, size, etc.)
marker_label_options       add marker labels; change look or position
Add plots
addplot(plot)              add other plots to the generated graph
Y axis, X axis, Titles, Legend, Overall
twoway_options            any options other than by() documented in [G-3] twoway_options
```

by and collect are allowed; see [U] 11.1.10 Prefix commands.

### Options

- **Main**

  - `fit(#)`: Specifies the number of points, counting back from the last measurement, to use in fitting the extension to estimate the $AUC_{0,\infty}$. The default is `fit(3)`, or the last three points. This value should be viewed as a minimum; the appropriate number of points will depend on your data.

  - `trapezoid`: Specifies that the trapezoidal rule be used to calculate the $AUC_{0,t_{max}}$. The default is cubic splines, which give better results for most functions. When the curve is irregular, `trapezoid` may give better results.

  - `graph`: Tells `pkexamine` to graph the concentration–time curve.

  - `line` and `log`: Specify the estimates of the $AUC_{0,\infty}$ to display when graphing the $AUC_{0,\infty}$. If the `graph` option is not also specified, then these options are ignored.

  - `exp(#)`: Specifies that the exponential fit for the $AUC_{0,\infty}$ be plotted. You must specify the maximum time value to which you want to plot the curve, and this time value must be greater than the maximum time measurement in the data. If you specify 0, the curve will be plotted to the point at which the linear extension would cross the $x$ axis. If the `graph` option is not also specified, then this option is ignored. This option is not valid with the `line` or `log` option.

- **AUC plot**

  - `cline_options`: Affect the rendition of the plotted points connected by lines; see [G-3] `cline_options`.

  - `marker_options`: Specify the look of markers. This look includes the marker symbol, size, color, and outline; see [G-3] `marker_options`.
*marker_label_options* specify if and how the markers are to be labeled; see [G-3] *marker_label_options*.

`addplot(plot)` provides a way to add other plots to the generated graph; see [G-3] *addplot_option*.

`twoway_options` are any of the options documented in [G-3] *twoway_options*, excluding by(). These include options for titling the graph (see [G-3] *title_options*) and for saving the graph to disk (see [G-3] *saving_option*).

### Remarks and examples

`pkexamine` computes summary statistics for a given patient in a pharmacokinetic trial. If *by idvar:* is specified, statistics will be displayed for each subject in the data.

#### Example 1

*Chow and Liu (2009, 13)* present data on a study examining primidone concentrations versus time over a 32-hour period after dosing a subject.

```
. use https://www.stata-press.com/data/r17/auc
(Primidone concentrations)
. list, abbrev(14)
```

<table>
<thead>
<tr>
<th>id</th>
<th>time</th>
<th>concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>.5</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>2.8</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>4.4</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>4.4</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>4.7</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>3.6</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>2.5</td>
</tr>
<tr>
<td>12</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>32</td>
<td>1.6</td>
</tr>
</tbody>
</table>

```
We use `pkexamine` to produce the summary statistics:

```
. pkexamine time concentration, graph
```

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum concentration</td>
<td>4.7</td>
</tr>
<tr>
<td>Time of maximum conc.</td>
<td>3</td>
</tr>
<tr>
<td>Time of last obs. (Tmax)</td>
<td>32</td>
</tr>
<tr>
<td>Elimination rate</td>
<td>0.0279</td>
</tr>
<tr>
<td>Half life</td>
<td>24.8503</td>
</tr>
</tbody>
</table>

Area under the curve

<table>
<thead>
<tr>
<th>AUC [0, Tmax]</th>
<th>AUC [0, inf.) Linear of log conc.</th>
<th>AUC [0, inf.) Linear fit</th>
<th>AUC [0, inf.) Exponential fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>85.24</td>
<td>142.603</td>
<td>107.759</td>
<td>142.603</td>
</tr>
</tbody>
</table>

Fit based on last 3 points.

The maximum concentration of 4.7 occurs at time 3, and the time of the last observation (Tmax) is 32. In addition to AUC\(_{0,T_max}\), which is calculated from 0 to the maximum value of time, `pkexamine` also reports AUC\(_{0,\infty}\), the AUC computed by extending the curve with each of three methods: a linear fit to the log of the concentration, a linear regression line, and a decreasing exponential regression line. See Methods and formulas for details on these three methods.

By default, all extensions to the AUC are based on the last three points. In looking at the graph for these data, it seems more appropriate to use the last seven points to estimate the AUC\(_{0,\infty}\):

```
. pkexamine time concentration, fit(7)
```

<p>| | |</p>
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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<td>Time of last obs. (Tmax)</td>
<td>32</td>
</tr>
<tr>
<td>Elimination rate</td>
<td>0.0349</td>
</tr>
<tr>
<td>Half life</td>
<td>19.8354</td>
</tr>
</tbody>
</table>

Area under the curve

<table>
<thead>
<tr>
<th>AUC [0, Tmax]</th>
<th>AUC [0, inf.) Linear of log conc.</th>
<th>AUC [0, inf.) Linear fit</th>
<th>AUC [0, inf.) Exponential fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>85.24</td>
<td>131.027</td>
<td>96.805</td>
<td>129.181</td>
</tr>
</tbody>
</table>

Fit based on last 7 points.
This approach decreased the estimate of the AUC$_{0,\infty}$ for all extensions. To see a graph of the AUC$_{0,\infty}$ using a linear extension, specify the graph and line options.

```
pkexamine time concentration, fit(7) graph line
```

```
Maximum concentration = 4.7
Time of maximum concentration = 3
Time of last observation (Tmax) = 32
Elimination rate = 0.0349
Half life = 19.8354
```

```
AUC [0, Tmax] AUC [0, inf.) Linear of log conc. AUC [0, inf.) Linear fit AUC [0, inf.) Exponential fit
85.24 131.027 96.805 129.181
```

Fit based on last 7 points.

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Stored results

`pkexamine` stores the following in `r()`:

Scalars

- `r(auc)`: AUC
- `r(half)`: half-life of the drug
- `r(ke)`: elimination rate
- `r(tmax)`: time at last concentration measurement
- `r(cmax)`: maximum concentration
- `r(tomc)`: time of maximum concentration
- `r(auc_line)`: AUC$_{0,\infty}$ estimated with a linear fit
- `r(auc_exp)`: AUC$_{0,\infty}$ estimated with an exponential fit
- `r(auc_ln)`: AUC$_{0,\infty}$ estimated with a linear fit of the natural log
Methods and formulas

Let $i$ index the observations sorted by time, let $k$ be the number of observations, and let $f$ be the number of points specified in the \texttt{fit(#)} option.

The $AUC_{0,t_{\text{max}}}$ is defined as

$$AUC_{0,t_{\text{max}}} = \int_0^{t_{\text{max}}} C_t dt$$

where $C_t$ is the concentration at time $t$. By default, the integral is calculated numerically using cubic splines. However, if the trapezoidal rule is used, the $AUC_{0,t_{\text{max}}}$ is given as

$$AUC_{0,t_{\text{max}}} = \sum_{i=2}^{k} \frac{C_{i-1} + C_i}{2} (t_i - t_{i-1})$$

The $AUC_{0,\infty}$ is the $AUC_{0,t_{\text{max}}} + AUC_{t_{\text{max}},\infty}$, or

$$AUC_{0,\infty} = \int_0^{t_{\text{max}}} C_t dt + \int_{t_{\text{max}}}^{\infty} C_t dt$$

When using the linear extension to the $AUC_{0,t_{\text{max}}}$, the integration is cut off when the line crosses the $x$ axis. The log extension is a linear extension on the log concentration scale. The area for the exponential extension is

$$AUC_{t_{\text{max}},\infty} = \int_{t_{\text{max}}}^{\infty} e^{\beta_0 + t \beta_1} dt = \frac{e^{\beta_0 + t_{\text{max}} \beta_1}}{-\beta_1}$$

where $\beta_0 > 0$ and $\beta_1 < 0$ are the intercept and slope, respectively, of an exponential accelerated failure-time regression of concentration on time.

The elimination rate $K_{eq}$ is the negative of the slope from a linear regression of log concentration on time fit to the number of points specified in the \texttt{fit(#)} option:

$$K_{eq} = -\frac{\sum_{i=k-f+1}^{k} (t_i - \bar{t}) \left( \ln C_i - \ln \bar{C} \right)}{\sum_{i=k-f+1}^{k} \left( t_i - \bar{t} \right)^2}$$

The half-life is

$$t_{\text{half}} = \frac{\ln 2}{K_{eq}}$$

Reference

Also see

[R] pk — Pharmacokinetic (biopharmaceutical) data