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SAS® 9.3: Better graphs, Easier lives for SAS programmers, PK scientists and pharmacometricians

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ABSTRACT

Data visualization tools are widely used in PK analysis and PK/PD modeling and simulation. To date, even though the datasets are mostly in SAS data format, PK scientists and pharmacometricians usually choose to use other software for the production of graphs; however, this approach often requires changing data types and repeatedly transferring data between functional teams. With the new release of SAS 9.3 and the enhancement of SAS Graphs, it is now much easier for SAS programmers to make graphs to support analysis, modeling and simulation activities. This paper illustrates some commonly used graphs that are currently generated in other software applications, e.g. R/S-PLUS, that can now be generated in SAS. This change has the potential to significantly improve the process and productivity of model-support/based drug development.

INTRODUCTION

"A picture is worth a thousand words." This statement may sound a little exaggerated, but in the world of Pharmacokinetics/Pharmacodynamics (PK/PD), meaningful graphics do play a very important role.

In clinical research, tremendous volumes of data are produced in SAS format. Therefore, a more user-friendly tool for creating graphs in SAS would be desirable.

To create a graph in SAS before the release of version 9.1, an SAS programmer would typically need to perform an analytical procedure, save the numeric results in an output data set, manipulate the data with the Data step program, and finally display the data with a graphics procedure. These steps became unnecessary when ODS Graphics first became available in SAS 9.1. With the release of SAS 9.3, ODS Graphics moved to Base SAS, introducing more enhancements and eliminating the need for a SAS/GRAPH® software license. Many ODS Graphics functionalities also became default settings in SAS 9.3.

There are multiple ways to create graphs using ODS Graphics. The program automatically generates graphs for almost all analytical procedures that one can access and edit using ODS Graphics Editor. One can also create graphs using the SG (Statistical Graphics) procedures. Another option is the ODS Graphics Designer, a graphical user interface that uses point-and-click interaction to produce graphs. These three options require no, or minimal, graphic programming knowledge from users. This paper presents three examples to illustrate some commonly used graphs in PK/PD research; each example will use one of the available graphical methods.

A more advanced way to create graphs is to use GTL (Graph Template Language), which allows users to create their own complex customized graphs. GTL actually runs in the background of SG procedures and ODS Graphics Designer. When one uses ODS Graphics Designer to create graphs, it automatically generates GTL code, which is accessible from the programming code window. This feature serves as an effective starting point for one who is interested in learning this programming language.

These graphic methods can also be easily integrated into SAS macros or other automation tools. With ODS Graphics, making graphs in SAS becomes more intuitive and provides great opportunities for streamlined drug development processes.

CASE 1: EARLY DETECTION OF POTENTIAL DATA ERRORS

INDIVIDUAL CONCENTRATION-TIME PROFILE USING SG PROCEDURE

Data quality is critical in clinical research. In some situations, errors from a small portion of the data can redirect the conclusion of a study. Data errors can occur at any stage in clinical research, e.g. data collection, data transfer and mapping, data formatting, data derivation etc. Prior to PK analysis or modeling, data must be inspected. Early detection of potential data errors can provide benefits in many ways.

An individual PK concentration-time profile is a commonly used graph in PK studies. Currently, it takes complex processes and expertise in a number of areas before these graphs are available to PK scientists. In many cases, by

the time a PK scientist recognizes an error, it is too late for the data to be corrected. User-friendly graphical tools in SAS can provide opportunities to significantly improve this situation. Now, with the ODS Graphics SG procedure, this type of graph can be easily generated in SAS. Figure 1 is an example of a graph generated using the following SAS code:

```
title "Conc vs Time";
proc sgpanel data=mylib.pk_tm;
 panelby trt id;
 scatter  x=time y=conc / group=trt ;
 series  x=time y=conc / group=trt;
run;
```

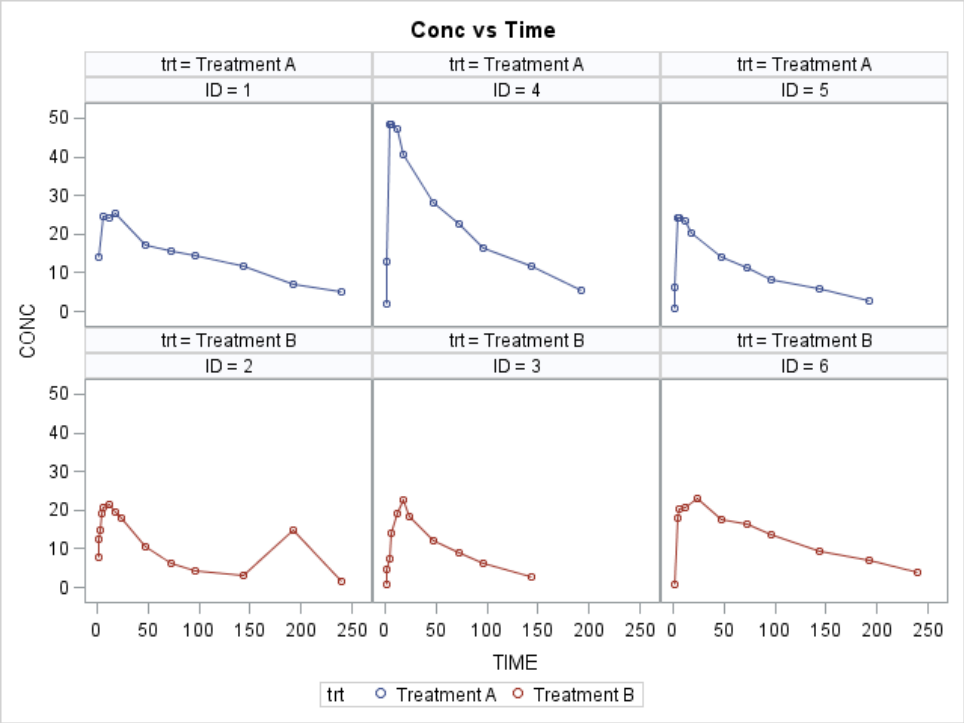

Figure 1: Individual Concentration-Time Profiles

These simple individual concentration-time profiles can make potential data issues visible. For example, the PK concentration value is questionable for ID 2 at Time 192; there are missing PK samples after Time 150 for ID 3; and the PK concentration values of ID 4 are systematically higher than other subjects. These visual clues can prompt follow-up investigation by the PK scientist to address potential causes of these findings.

With this tool, some data errors can be detected as early as the bioanalysis stage. A series of checks at each data collection and process milestone can be easily developed, enabling early data cleaning, data reconciliation and queries.

CASE 2: EXPLORING DATA FOR MODEL BUILDING

COVARIATE SCREENING USING ODS GRAPHICS DESIGNER

“All models are wrong, some are useful.” To build a model that best represents the real-life situation, pharmacometricians typically exam the observed data thoroughly prior to modeling. These activities are time consuming. It would be beneficial if this review process could be started as soon as raw data is available. User-friendly graphical tools provide timely visual access for data exploration. Since SAS is the major data type used in clinical research, early data exploration in SAS is desirable. ODS Graphics provides users great opportunities to evaluate the data as soon as they are accessible in SAS format. As a result, unnecessary data merging, reformatting and transferring could be eliminated.

ODS Graphics Designer is a graphical user interface that uses point-and-click interaction to produce graphs. The following example demonstrates step-by-step graph building to assist covariate searching in PK/PD modeling.

With SAS 9.3, one can start the ODS Graphic Designer from the Tools -> ODS Graphics Designer menu option (Figure 2). The designer can also be started by submitting the macro code "%sgdesign;" from the Program Editor window.

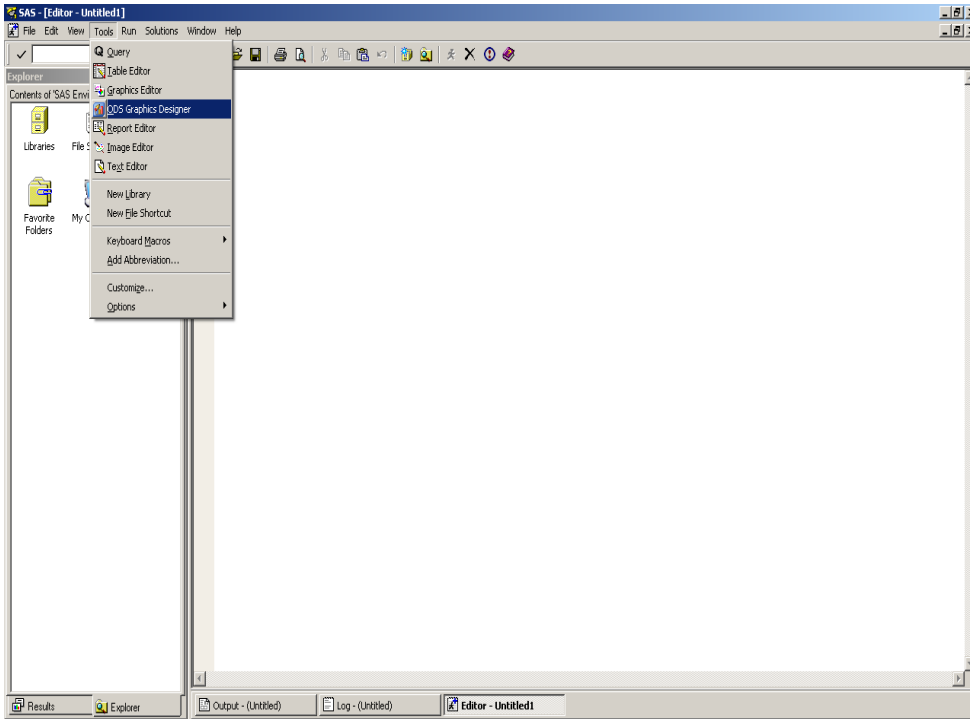

Figure 2: Start ODS Graphics Designer

When the ODS Graphic Designer is invoked, the application interface is on. A wide choice of pre-defined graphic templates are displayed. In Figure 3, the "Matrix+Histogram" option was selected under the Matrix tab of the Graph Gallery window.

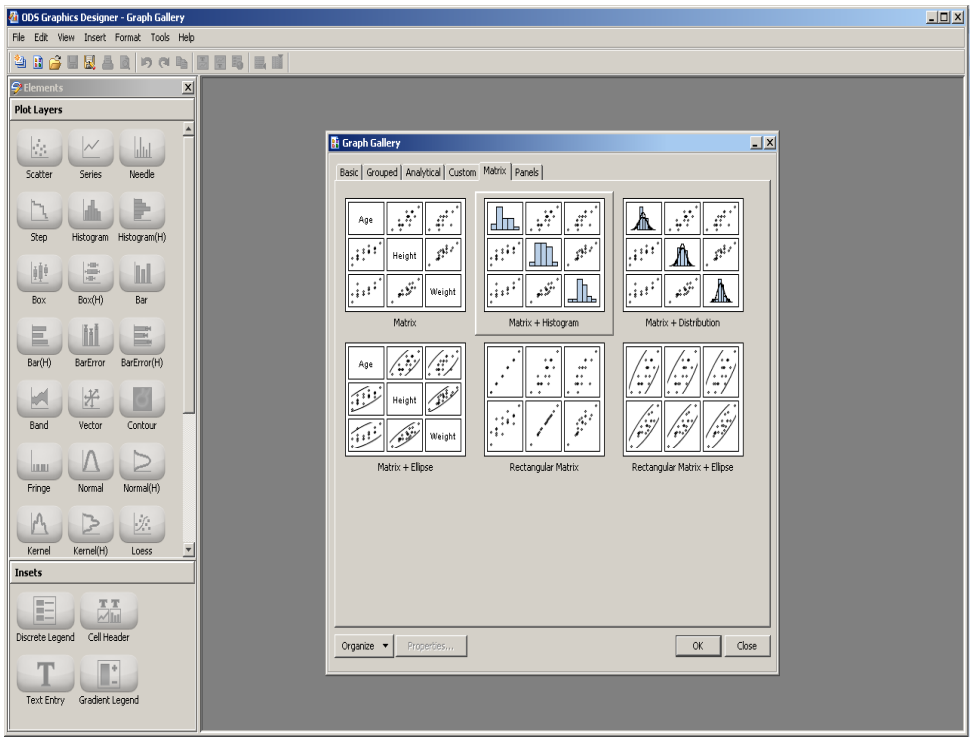

Figure 3: Graph Gallery Window

Then, choose the data to use and assign variables for the graph (Figure 4).

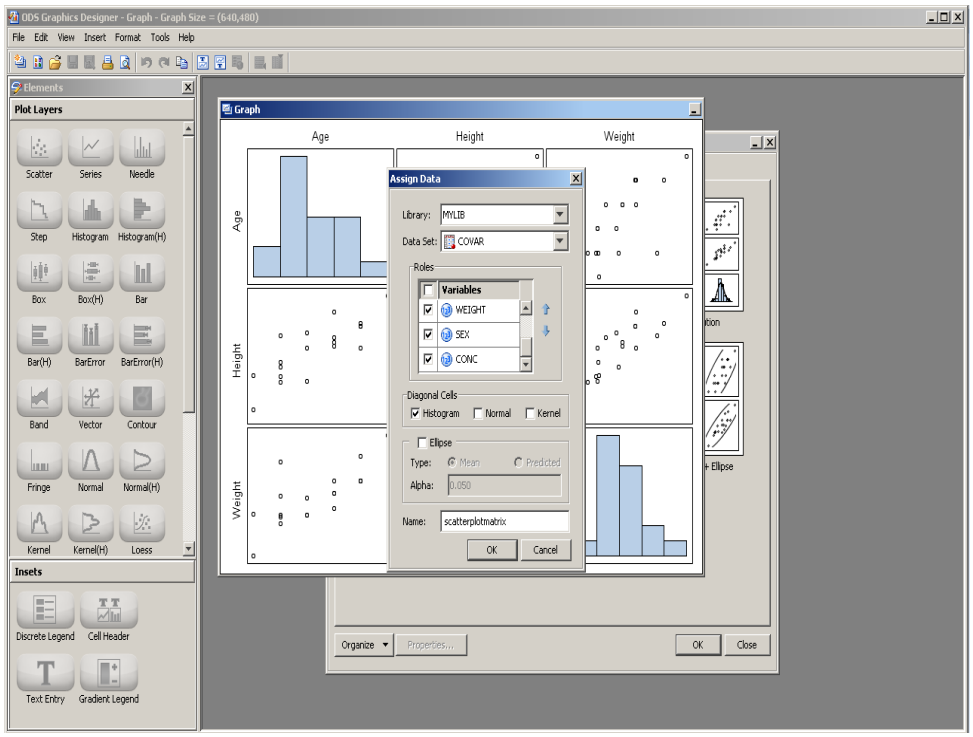

Figure 4: Assign Data

Click OK, and the graph is displayed (Figure 5).

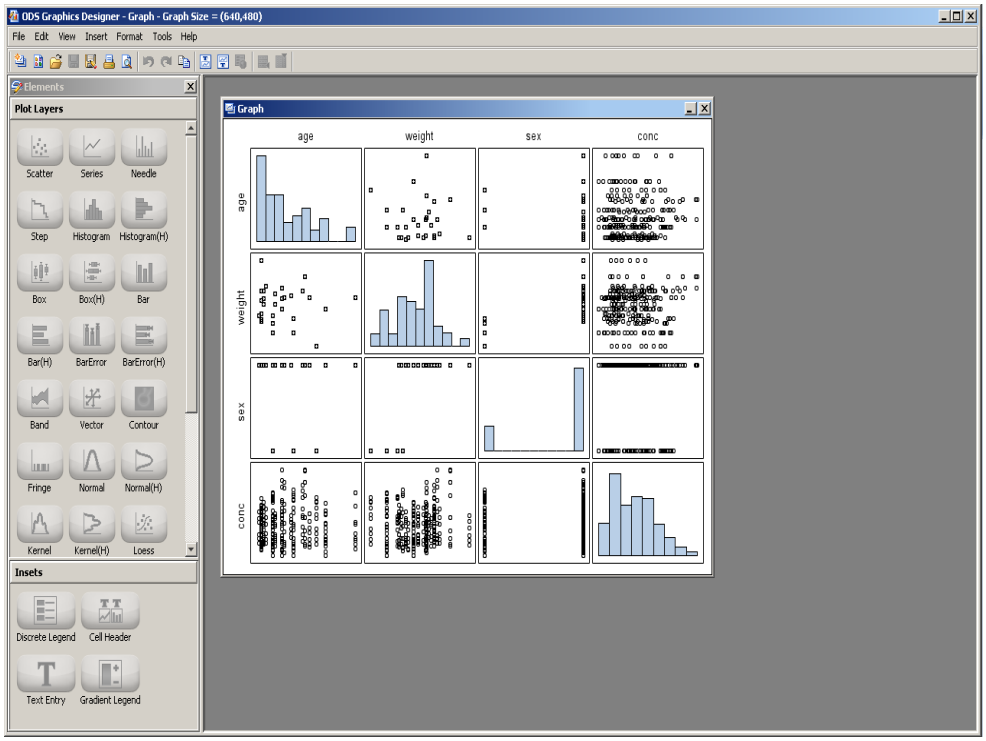

Figure 5: Generated Graph

GTL code is automatically generated and can be accessed from View -> code (Figure 6).

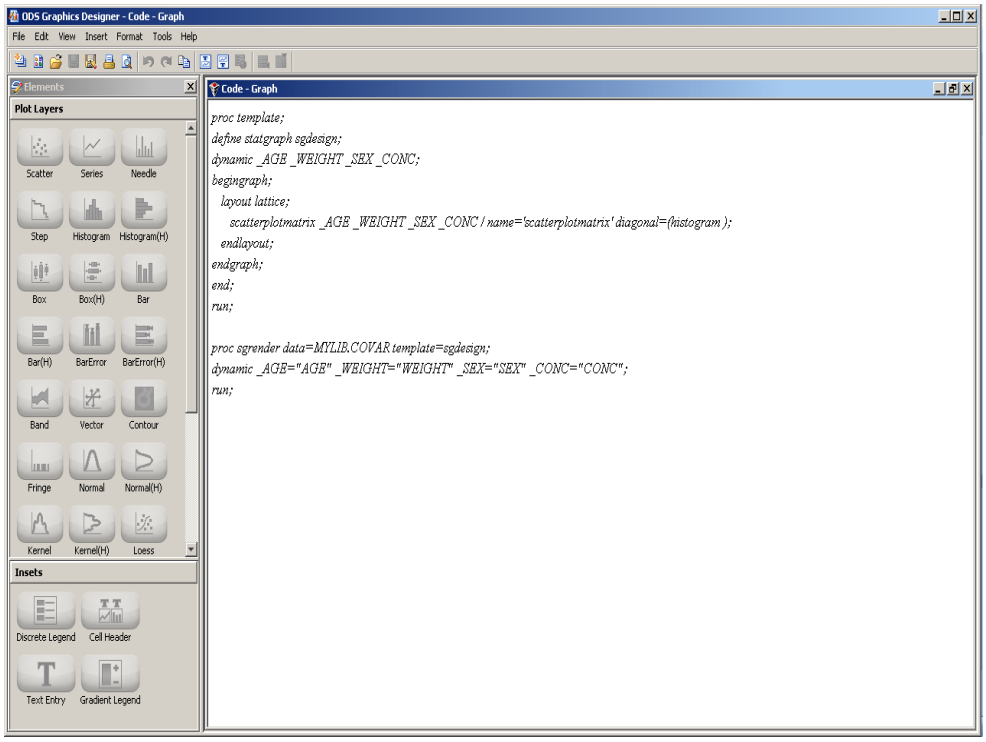

Figure 6: GTL Code

The whole process can be saved as an ".sgd" file by clicking File -> Save as. The file can then be reused, modified or integrated into an automation program.

CASE 3: REPORT YOUR FINDINGS

AUTOMATICALLY GENERATED GRAPHS FROM SAS STATISTICAL PROCEDURES

More than 70 SAS procedures can now automatically produce ODS Graphics outputs while producing tabular outputs. The graph output can also be sent to an editable .sge file by setting the SGE option in the LISTING destination. By double-clicking the .sge file in the Results window (Figure 7), the graph will open in the ODS Graphics Editor window for editing (Figure 8). The following simple example illustrates this functionality:

```
ods graphics on;
ods html style=journal;
ods listing sge=on;
 proc glm data=mylib.covar;
   ods select ParameterEstimates FitPlot;
   model cl=weight;
 quit;
ods listing close;
ods html close;
ods graphics off;
```

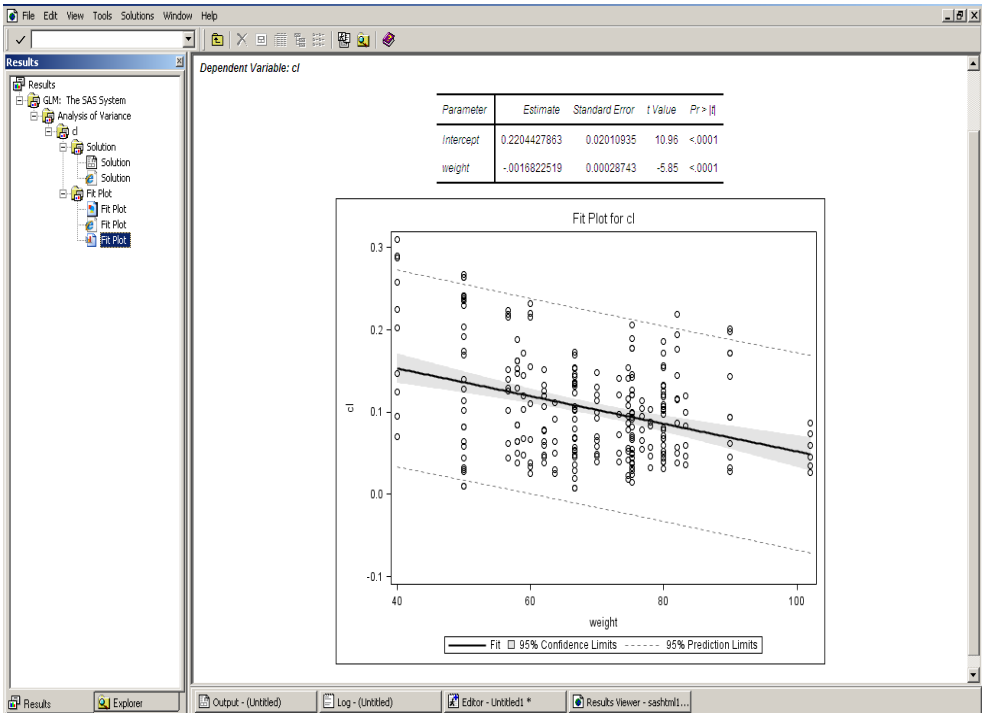

Figure 7: Results Viewer Window

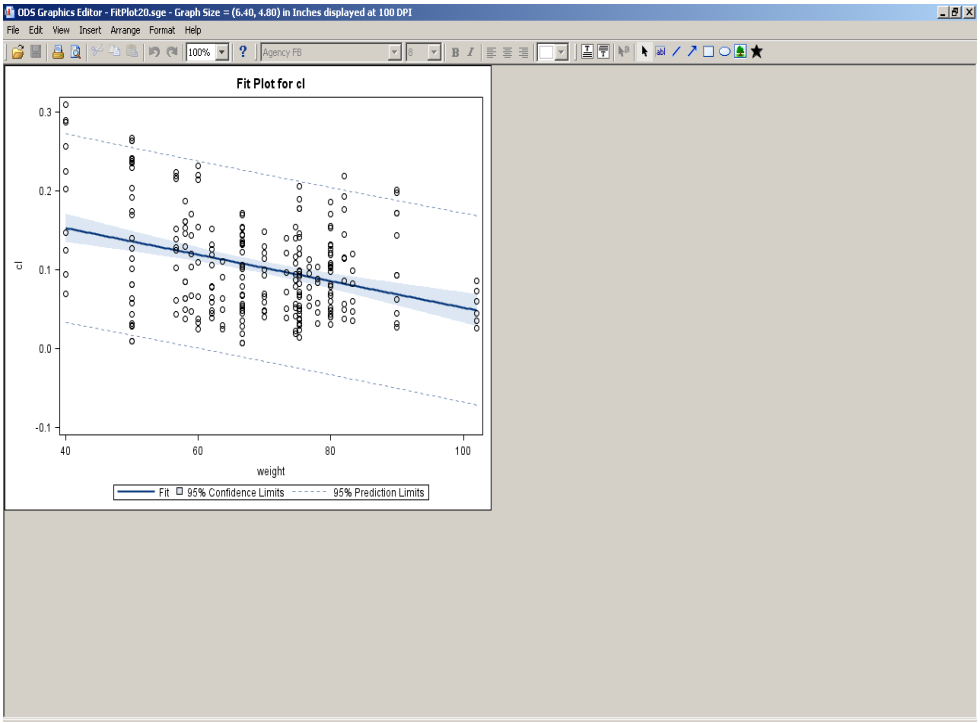

Figure 8: ODS Graphics Editor Window

Edited graphs can be easily placed into reports and presentations. The available styles can also easily coordinate with graphs generated from other software applications, providing a consistency in presentation format.

CONCLUSION

With ODS graphics in Base SAS 9.3, many commonly used graphs can be easily generated without the need to program or convert data for graph production using other software applications. As a result, clinical researchers, including PK scientists and phamacometricians, can focus on data exploration, analysis and interpretation, without struggling with programming languages. In practice, this user-friendly graphical tool offers benefits in a variety of areas, e.g. visual access to data as early in the process as possible; easily integrated in automation tools, etc., and provides great opportunities for a streamlined drug development process.

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