

A Graphical Approach to Examine the Completeness of Epidemiological Data: Patient Profile Plots (PPPs) and Centre Profile Plots (CPPs)

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ABSTRACT

Non-interventional or observational research is often based on existing secondary data, which has been collected over an extended period of time. When the nature of the research initiative requires the examination of a large number of variables, the increased volume of the data renders its exploration and understanding a more difficult task. More important, the quality of any analysis is dependent upon the availability of data over time. The aims of this paper are, to communicate the need for a graphical approach when evaluating the completeness of epidemiological data; to demonstrate how we arrived at a SAS/GRAPH® based solution to addressing this need (the PPPs and CPPs); to explain the programming principles behind the PPPs and CPPs; and to place PPPs and CPPs in the context of other graphical approaches and discuss their strengths and limitations. Patient Profile Plots (PPPs) and Center Profile Plots (CPPs) are novel graphical tools that allow the investigator to evaluate the quality and completeness of epidemiological data in a simple, easy to use graphical approach.

INTRODUCTION

Non-interventional or observational research is often based on existing secondary data, which has been collected over an extended period of time. When the nature of the research initiative requires the examination of a large number of variables, the increased volume of the data renders its exploration and understanding a more difficult task.

More important, the quality of any analysis is dependent upon the availability of data over time. Investigators performing epidemiologic studies wonder about the completeness of data available to them for statistical analysis. Here again, exploring the availability of a large number of variables, in relation to each other simultaneously, is a challenge.

THE NEED FOR A GRAPHICAL APPROACH WHEN EVALUATING THE COMPLETENESS OF EPIDEMIOLOGICAL DATA

Unlike data collected for randomised controlled trials, the completeness of data for epidemiologic studies can vary widely depending on the quality of the data capture process. **Figure 1** summarises the main characteristics of Interventional and Observational research and illustrates the problem of incomplete or unavailable data over time.

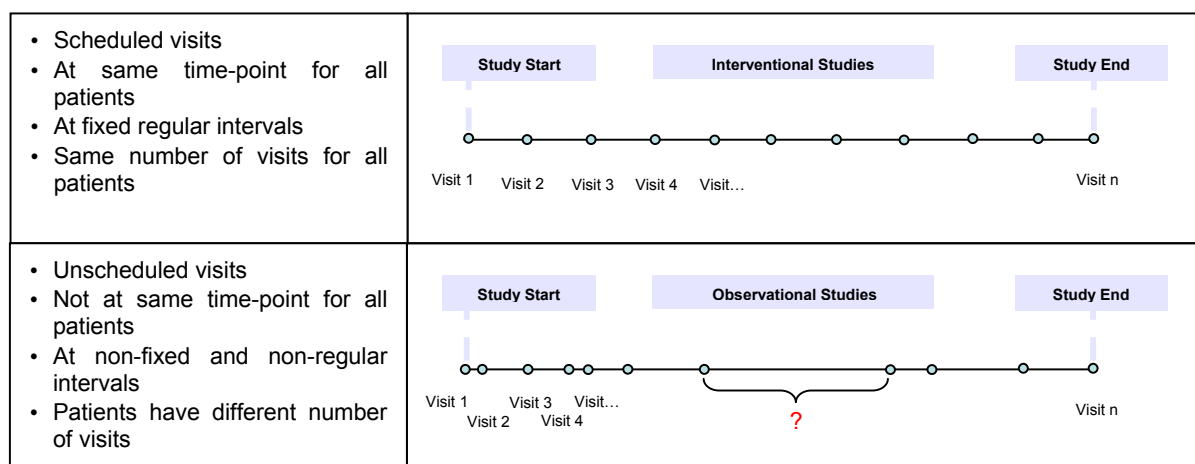


Figure 1: Characteristics of Interventional and Observational Research

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Trying to address this task by the means of tables will not be effective. It will result in to a very large number of tables, which will be hard to review and relate. This is quite a typical scenario. Investigators often use graphical output in response to such data problems that otherwise would be described by a large number of tables.

A graphical approach that appears immediately as a suitable candidate to address the problem at hand, is the traditional scatter plots¹. The investigator could plot for each patient, the values of each particular variable of interest, against the date/time that it was collected, and thus get a picture of the availability and completeness of each variable over time, but separately to each other (**Figure 2 and Figure 3**). They will then have to review a quite large number of graphical plots for a single patient, and the problem would escalate when they would try to relate the finding across different patients.

An improved attempt of using scatter plots would be to overlay on the same plot all lines representing the variables of interest (**Figure 4**). This method is not always possible as sometimes the range of values of the variables of interest may differ significantly. Even when this method is practically possible, it will only be effective when the number of variables of interest is small (**Figure 4**). When there are a large number of variables of interest the graphic is becoming blurry and difficult to comprehend (**Figure 5**).

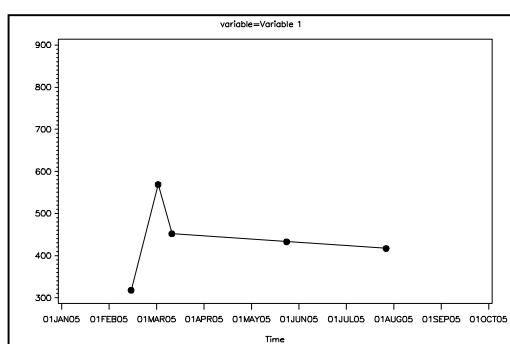


Figure 2: Line Plot for Variable 1

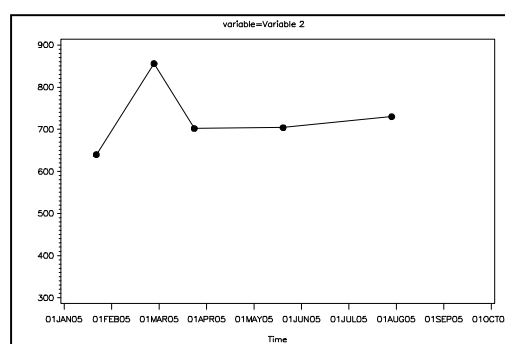


Figure 3: Line Plot for Variable 2

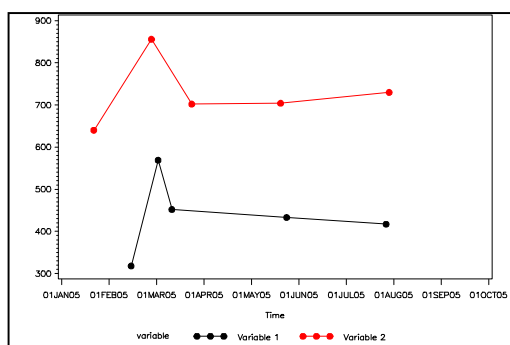


Figure 4: Line Plot for Variable 1 and Variable 2 Overlaid

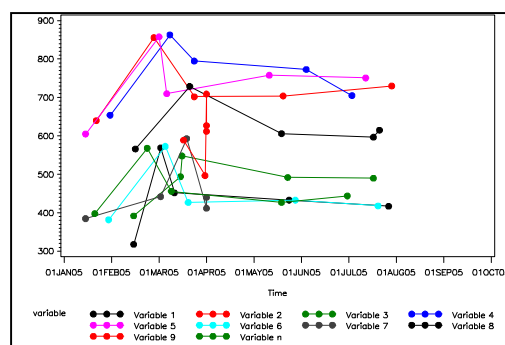


Figure 5: Line Plot for Ten Variables of Interest Overlaid

In fact, **Figure 5** contains the information that is needed to address the problem at hand, but this information is not presented appropriately. The content of the values (low/high/negative/positive etc.) of each variable of interest is irrelevant. What is of interest is the existence of a value or not. As we shall see, if we remove the depiction of the nature of the values of the variables of interest from the plot, it will become much more helpful.

Patient Profile Plots (PPPs) and Center Profile Plots (CPPs) are novel graphical tools that allow the investigator to evaluate the quality and completeness of epidemiological data in a simple, easy to use graphical approach.

The aims of this paper are to communicate the need for a graphical approach when evaluating the completeness of epidemiological data, to demonstrate how we arrived at a SAS GRAPH based solution to addressing this need (the PPPs and CPPs), to explain the programming principles behind the PPPs and CPPs, and to place them in the context of other graphical approaches and discuss their strengths and limitations.

¹ Or line plots when the plotted points are connected by a straight line

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A SAS GRAPH BASED SOLUTION: PATIENT PROFILE PLOTS AND CENTRE PROFILE PLOTS

The solution to the business need described in the previous section, arrived in the form of two types of graphical output. The Patient Profile Plots (PPPs) and the Centre Profile Plots (CPPs). In this section, we will use a simple case study to demonstrate the use and benefits of the solution we provided to the problem at hand. The same case study will be used in the next section to explain the programming principles behind it. Consider the following hypothetical scenario:

Investigate the relationship between laboratory measure A (Lab A) and the use of medication B (Med B), and the association of this relationship with events/outcomes.

This case study requires the analysis of Lab A and Med B data over time, and therefore the completeness of Lab A and Med B data over time would have a direct effect on the results of the analysis. The datasets containing Lab A and Med B data, which we will use in the following sections, are shown in **Table 1** and **Table 2**, respectively.

LABS		
patientid	date	measurement_value
X000001	13-Jan-05	300
X000001	16-Feb-05	500
X000001	28-Jun-05	400
X000002	28-Feb-05	400
X000002	05-May-05	400

Table 1: Lab A sample dataset sorted by patientid and date

MEDS			
patientid	prescription_start	prescription_end	dose
X000001	03-Jan-05	15-Jan-05	5000
X000001	20-Jan-05	04-Feb-05	6000
X000001	28-Sep-05		4500
X000002	26-Mar-05	04-Jul-05	6000
X000002	10-Jun-05	14-Jul-05	5000

Table 2: Med B sample dataset sorted by patientid, prescription_start, and prescription_end

The PPPs and CPPs can be viewed in relation to four data dimensions: “patient”, “time”, “variables of interest”, and “centre”. The “patient” dimension refers to the patient population. The “time” dimension refers to the time period that an investigation spans. The “variables of interest” dimension refers to the variables the data completeness we want to evaluate. Finally, the “centre” refers to the physical centers or facilities and clinics that the patients are associated with.

Patient Profile Plots

PPPs, as the name suggests, have patients as the central dimension. Each plot presents patient relating information. The “time” dimension is represented by the x-axis and the “variables of interest” by the y-axis (**Figure 6**).

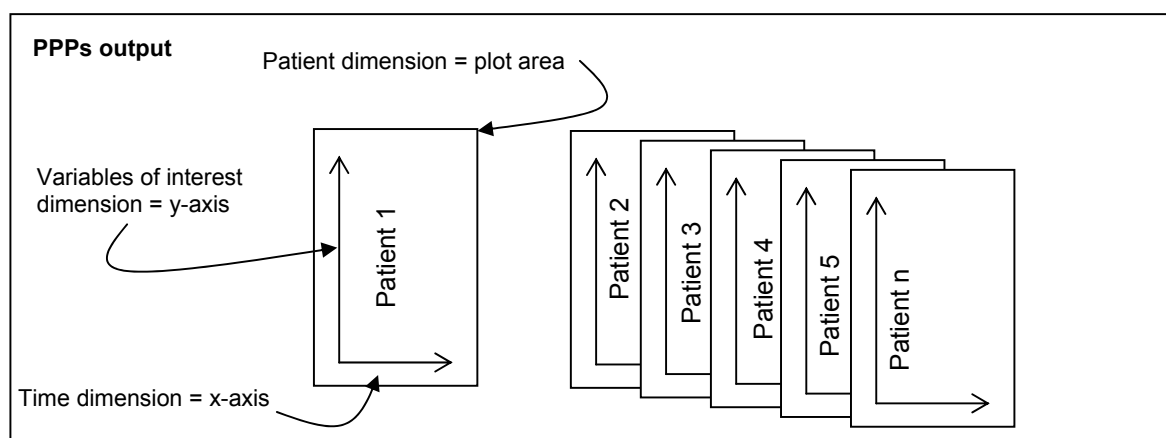


Figure 6: PPPs a Schematic View

A typical example of a PPP can be seen in **Figure 7**. Its various elements are described below:

1 Titles: At the top of the graphic, the titles feature the following:

- A descriptive title, in this example describing the subset of the total patient population that is plotted
- Frequency of the total population, as well as of the subset that is plotted and its proportion from the total population
- Patient identification number

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- 2 **x-axis:** The x-axis represents the “time” dimension. In our example it represents the duration of an epidemiological study. Each tick mark represents the first day of each month during the study period. i.e. The first tick mark represents the 01JAN2005, the second the 01FEB2005 and so on.
- 3 **y-axis:** The y-axis represents the “variables of interest” dimension. Each tick mark represents a specific variable of interest.
- 4 **Plot area:** The plot area consists of the following elements:
 - Two blue vertical lines indicating the beginning and the end of the follow-up period of each particular patient
 - Single floating red colored points indicating that there is a data value of the associated variable on the specific date
 - Red colored points connected with a red line, indicating that there are data values of the associated variable covering the period of time represented by the two dates
 - Red crosses are always associated with a y-axis variable. They are plotted either before the first or the last tick mark of the x-axis, and they indicate the existence of data prior to the start or after the end of the study period, for the associated y-axis variable.
- 5 **Legend:** The legend describes the various elements of the plot area.
- 6 **Annotation:** Finally, below the legend there is an annotation that displays key data for each patient (in our scenario, demographic and medical history data).

Figure 7 shows an example of a well populated data availability patient profile. Both Med B and Lab A data are available almost throughout the follow-up period. **Figure 8** on the other hand shows a poorly populated data availability patient profile. Here data completeness of Med B is very good, but Lab A data is not available during long periods of this patient's follow-up period. As we mentioned in the first section, in observational research data are not always collected for statistical analysis and the scenario presented in **Figure 8** is not as seldom as one may think. The absence of data during the follow-up period could have an effect on the results of the statistical analysis.

Centre Profile Plots

The central dimension of the CPPs is the “centre”. However, here each plot presents information relating to a single variable of interest. The “time” dimension is represented again by the x-axis. Now, the y-axis represents the “patient” dimension. The “centre” dimension is shaped through a combination of: subsetting the patient population based on the centre, and grouping together the individual plots of the variables of interest for each centre (**Figure 9**).

Figure 10 is a typical example of a CPP. The various elements of the CPPs are described below:

- 1 **Titles:** At the top of the graphic, the titles feature the same elements as in the PPPs, with the only difference being that instead of the patient identification number, the third title describes a specific variable of interest.
- 2 **x-axis:** The x-axis is exactly the same as in the case of the PPPs.
- 3 **y-axis:** Here the y-axis represents the “patient” dimension. Each tick mark represents a separate patient.
- 4 **Plot area:** The plot area consists of the following elements:
 - Single floating red colored points indicating that there is a data value of the associated variable on the specific date
 - Red colored points connected with a red line, indicating that there are data values of the associated variable covering the period of time represented by the two dates
 - Light blue stripes indicating the length of the follow-up period for each patient
 - Black crosses indicating the milestone indicating the death date when applicable
- 5 **Legend:** The legend describes the various elements of the plot area.

Figure 10 and **Figure 11** show a well populated data availability centre profile for both Lab A and Med B respectively. The availability of Lab A data in the particular centre is excellent. Furthermore, only few patients have no Med B data. Overall, this particular centre has good Med B data completeness. In **Figure 12** and **Figure 13** however, is shown a poorly populated data availability centre profile again for Lab A and Med B respectively. Here the availability of Lab A data is very limited, while several patients from the particular centre do not have any Med B data during their follow-up period. Moreover, a common seasonal pattern of absent Lab A data is observed in all patients. This could perhaps be an indication of some operating problem in the specific centre or perhaps of data extraction issues.

Subsetting the Patient Population

The nature of the subsetting conditions can vary and is dependent on the nature of the investigation. In general terms, the patient population can be subsetting based on either standard patient characteristics or on other more specific patient features, or on a combination of both types.

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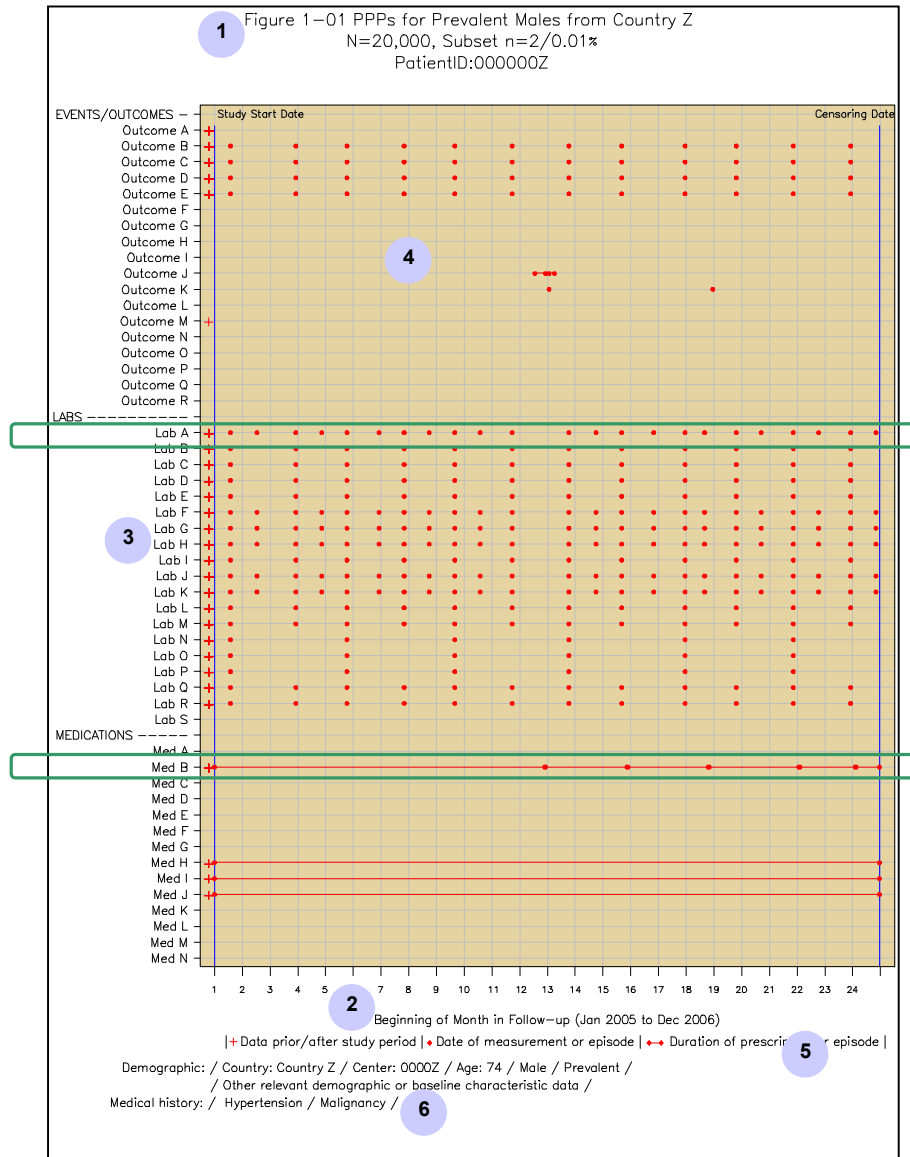


Figure 7: PPPs Example of a Well Populated Data Availability Patient Profile

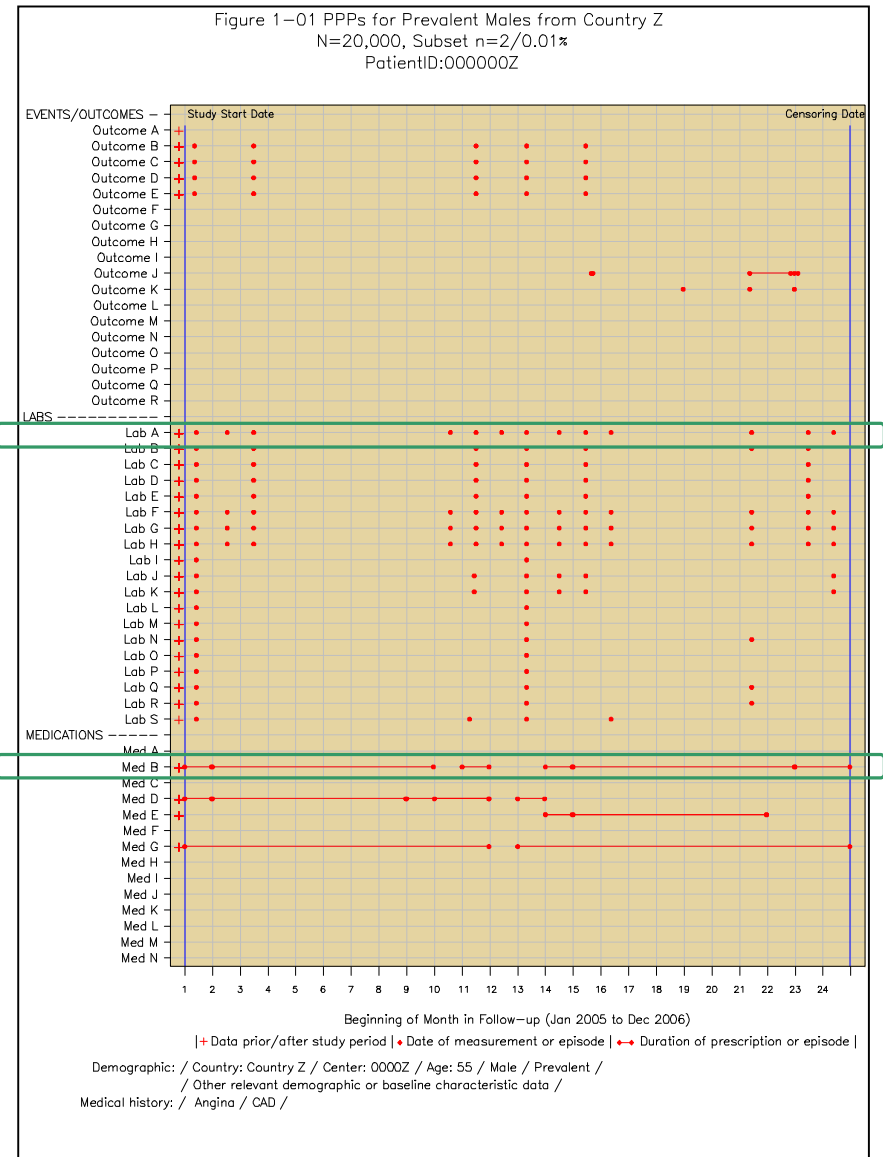


Figure 8: PPPs Example of a Poorly Populated Data Availability Patient Profile

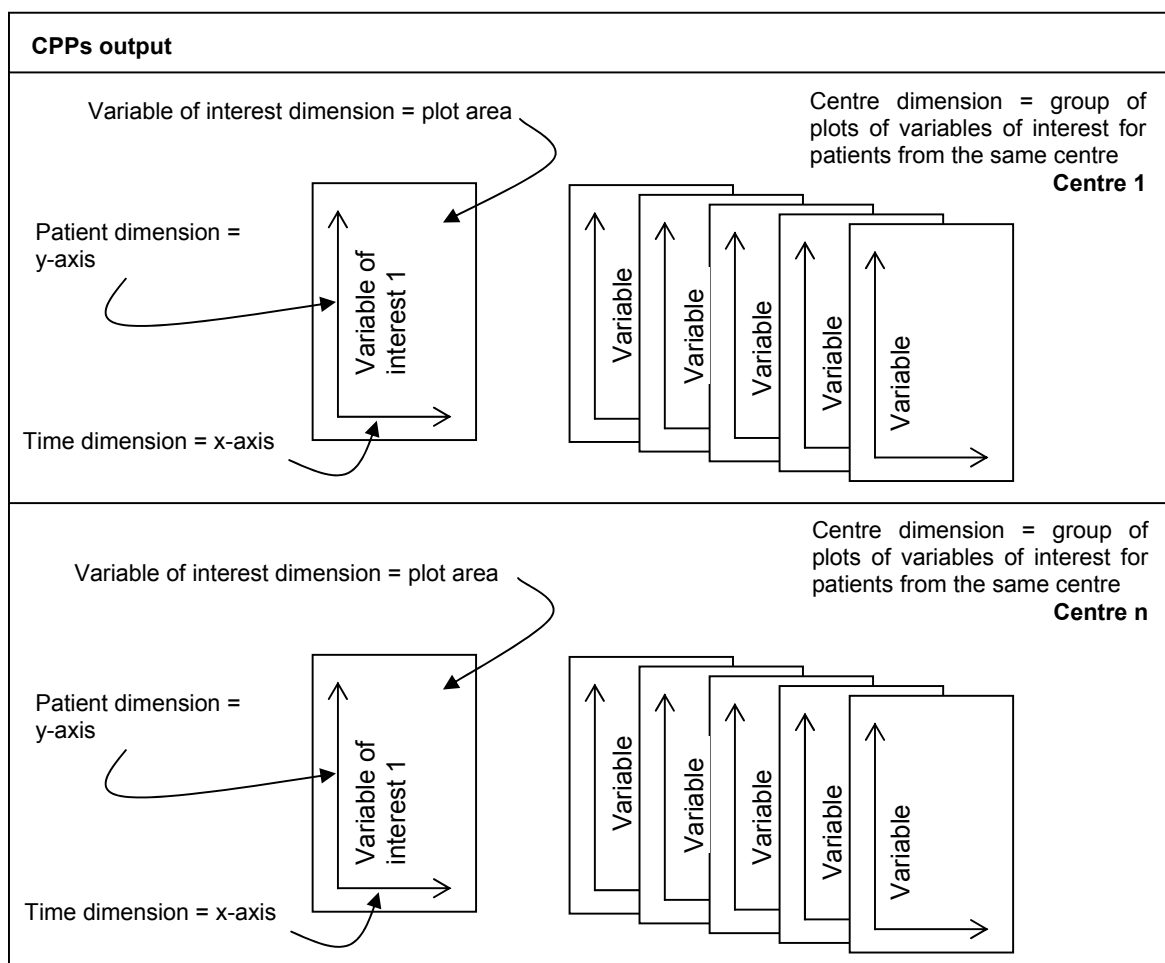


Figure 9: CPPs a Schematic View

As we have already mentioned, in the CPPs the “centre” dimension is shaped by: subsetting the patient population based on the centre, and grouping together the individual plots of the variables of interest for each subset (i.e centre). It was interesting for certain reasons inherent to our work, for all our CPP style plots to contain patients from the same centre. This explains the name of this type of output. Thus, here the function of subsetting is inextricably linked with the nature of the solution provided. Nevertheless, the use of subsetting has also practical meaning. Recall that the “patient” dimension is represented by the y-axis, plotting thousands of tick marks on a single plot would deem them unusable. The centre provided a convenient way to subset the patient population. Earlier in the PPPs section we saw two examples of the first type of subsetting. In **Figure 7** and **Figure 8**, for practical reasons the patient population is subsetting based on specific patient characteristics (vintage status, gender and country). The very large patient population would result in an equally large number of graphical plots. This would not be practical both in reviewing the output, but also because the resulting physical file would become extremely large.

An example of a combination of both types of subsetting would be: CPPs for all centres for which all patients, have no data of a particular variable of interest for at least three contiguous months (or perhaps for which all patients, have data of a particular variable of interest for at least six contiguous months).

Application of PPPs and CPPs in other settings

In this section we presented the two graphical tools that form the solution provided to the specific problem at hand (the investigation of the completeness of epidemiological data). We also demonstrated the benefits of using the PPPs and CPPs. In the next section we will be looking at the programming principles underpinning these two tools. Before we move to that, it is worth mentioning that since the first deployment of the two tools in production projects, the underpinning programming principles have been transferred to serve other applications too.

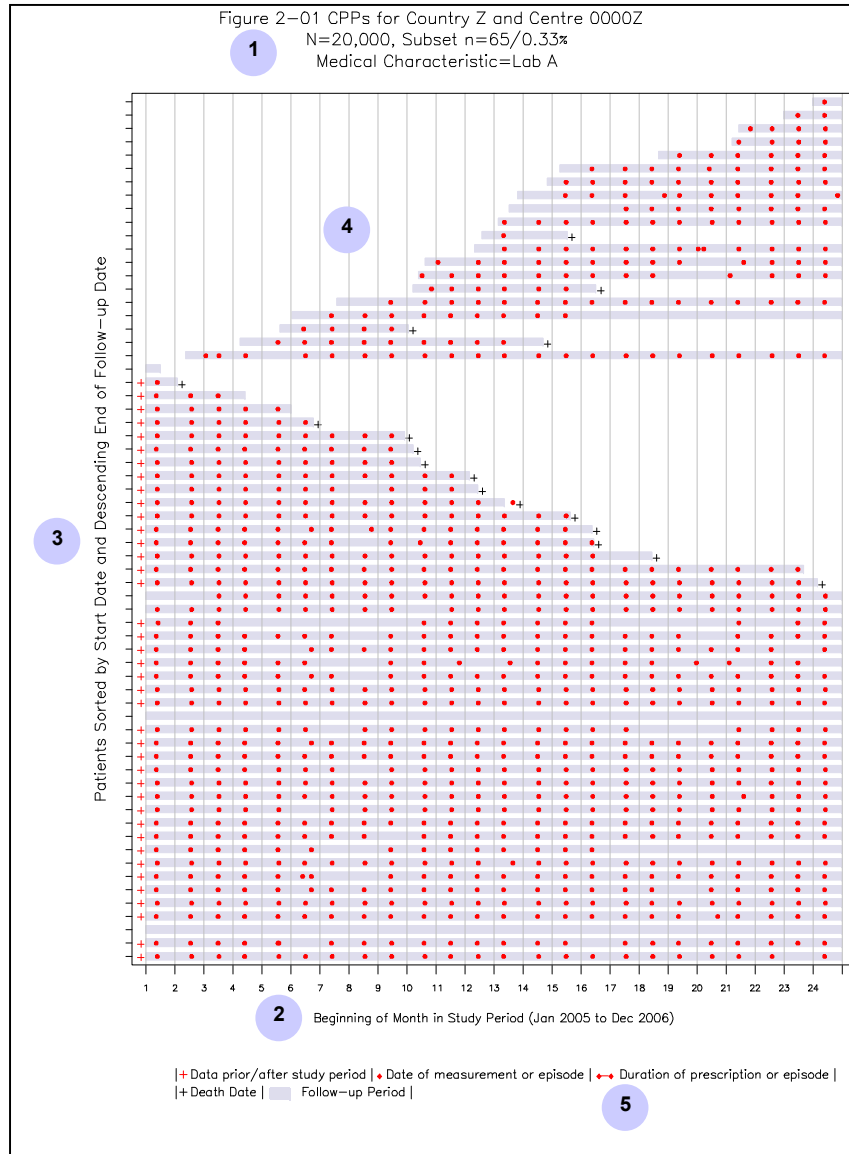


Figure 10: CPPs Example of a Well Populated Data Availability Center Profile

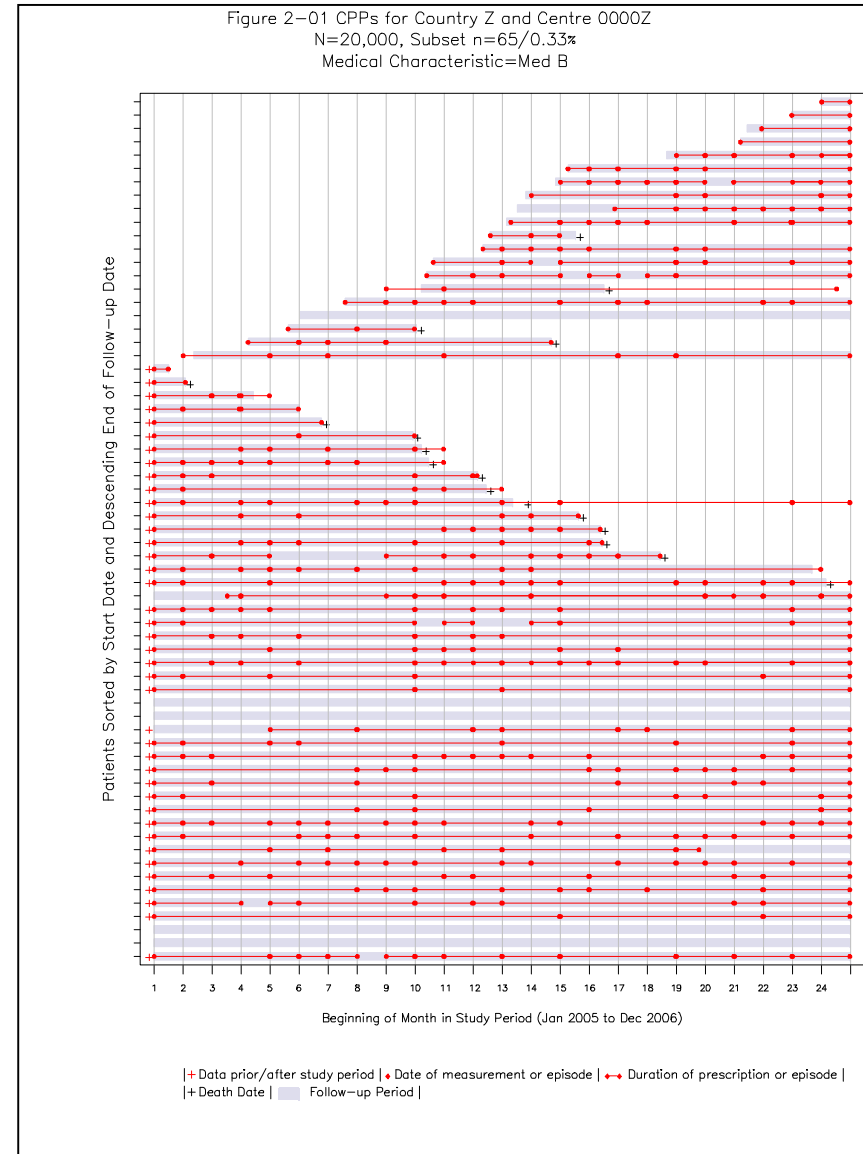


Figure 11: CPPs Example of a Well Populated Data Availability Centre Profile

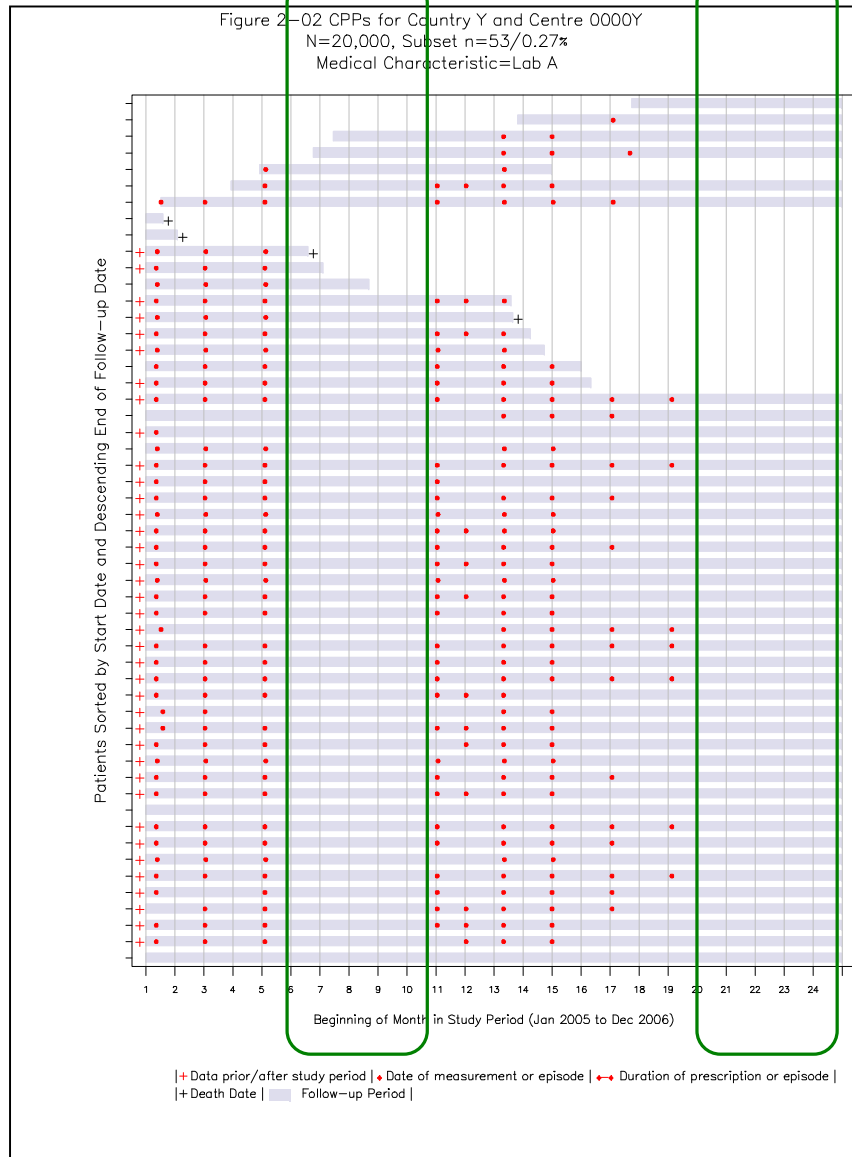


Figure 12: CPPs Example of a Poorly Populated Data Availability Centre Profile

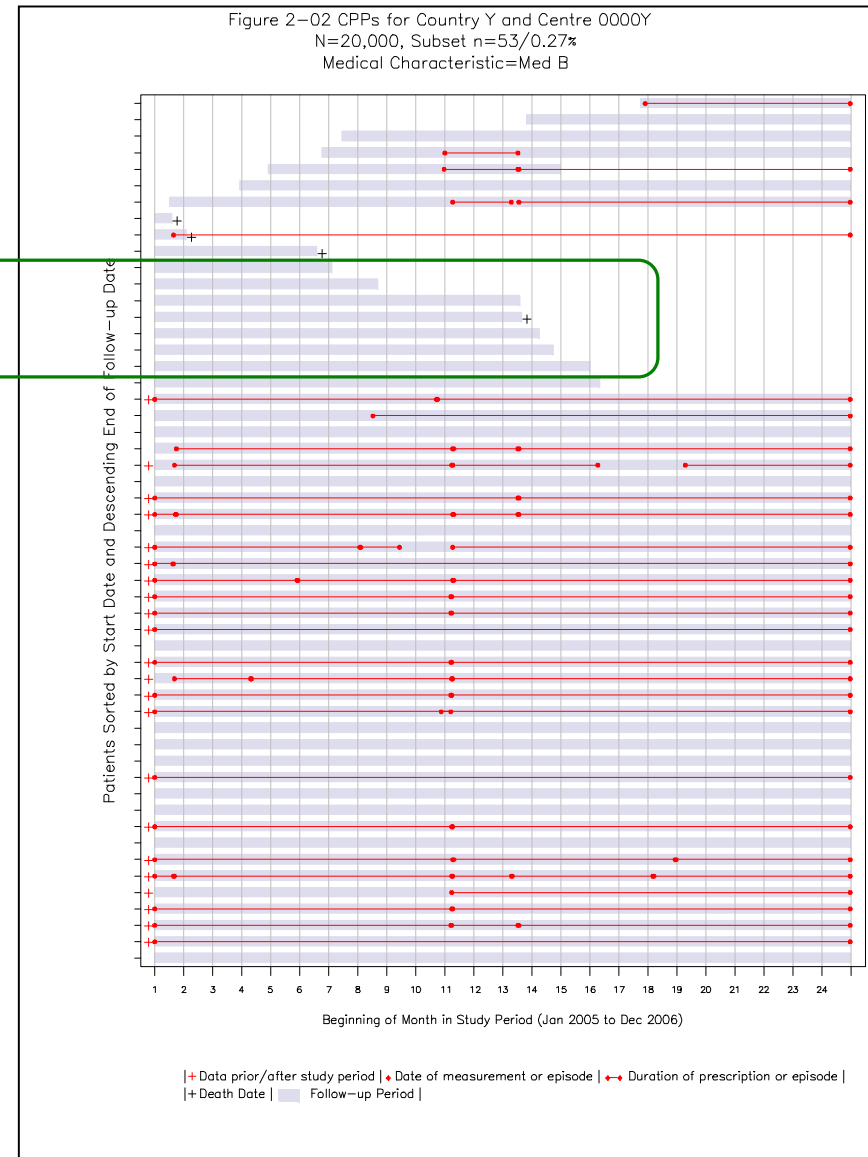


Figure 13: CPPs Example of a Poorly Populated Data Availability Centre Profile

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Consider the example of **Figure 14** where the Med B prescriptions have been plotted separately to each other, thus allowing the investigator to observe a patient's history of Med B use during the study period. Also, in **Figure 15** only Med B prescriptions of the same class are overlaid, thus allowing the investigator to observe the switching patterns between different Med B classes (i.e. brand names). Further more, the use of the PPPs and CPPs in interventional studies, is currently under evaluation. Finally, although PPPs and CPPs were developed in a pharmaceutical context, we believe that they could be equally useful in other settings too.

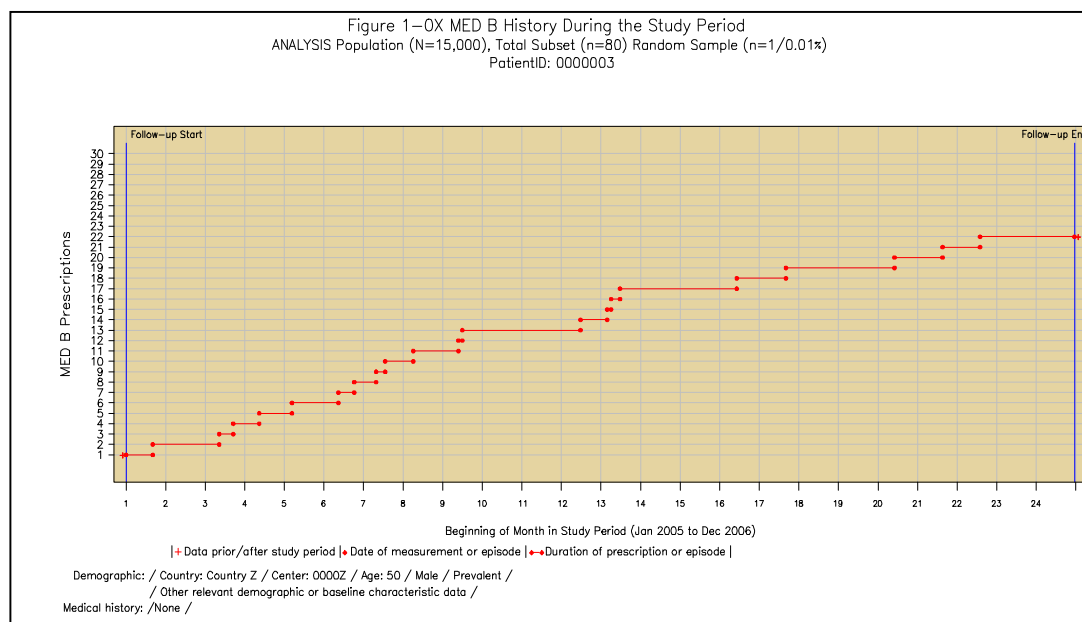


Figure14: PPPs Variation 1 - Med B History During the Study Period

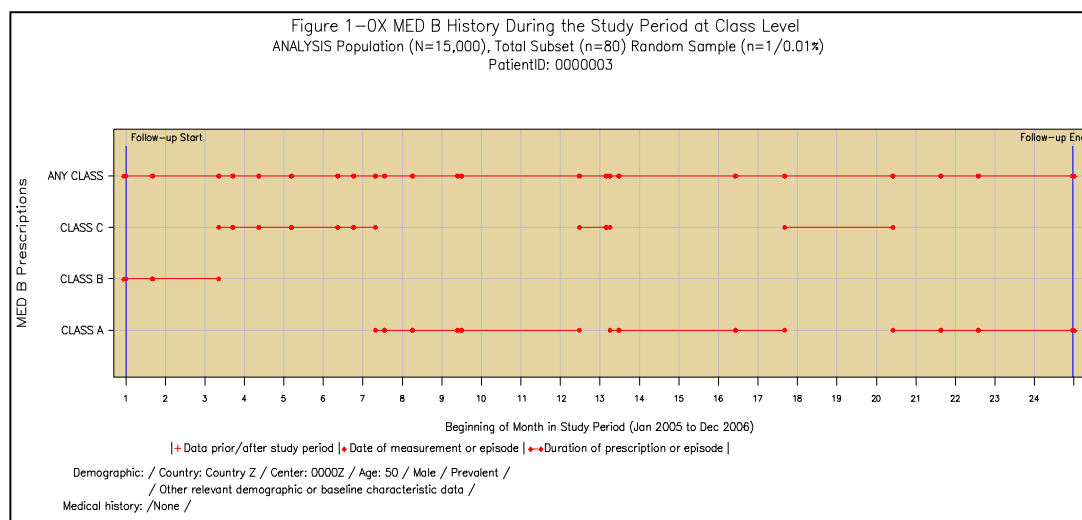


Figure15: PPPs Variation 2 - Med B History During the Study Period at Class Level

PROGRAMMING PRINCIPLES BEHIND PPPS AND CPPS

From a programming perspective the process of producing PPPs and CPPs can be split into two sub-processes: transforming the data to a desired structure, and producing the visual output. The data transformation will vary depending on the data structure you start with, while the process of producing the visual output remains independent of such factors. In this section we explain the programming principles behind both of these processes, using the same case study that was used in the previous section. **Table 1** and **Table 2** display sample Lab A and Med B datasets respectively. In relation to the dimensions discussed in the previous section Lab A and Med B are two variables of interest.

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The main aim of the data transformation process is to create two variables, one to represent either the variables of interest (in PPPs) or the patients (in CPPs), and one to represent the time points and time periods of the variable(s) of interest. The first variable will be plotted on the y-axis, and the second variable will be plotted on the x-axis.

Patient Profile Plots

First we create the numerical and ordinal variable TYPE_CODE that will be plotted on the y-axis and will define the order of the variables of interest in this axis (**Figure 16**). Next we need to create the variable that will be plotted on the x-axis. As it can be seen in **Table 2** a time period is described by two date variables. A transformation is required in such a way that the same information is captured in a single variable. **Figure 16** illustrates the creation of a new variable called DATE, by transposing the prescription start and end date variables. A key data structure requirement is the padding of each date value representing a time-point, or pair of date values representing a time period, with a missing value (**Figure 16**). Once this is done, the two resulting datasets LABS3 and MEDS4, are appended to produce the final dataset ALL (**Table 3**), which will be used in the plotting procedure.

Figure 17 illustrates how the PPPs can be plotted using SAS/GRAPH. The plot statement plots in the plot area, each data point that describes the data availability of a particular variable of interest over time. The INTERPOL=JOIN option of the symbol statement, connects data points with straight lines. If the data contain missing values, the observations are omitted, but the plot line is not broken. It is the use of the SKIPPMISS options that breaks the plot line, thereby creating the representation of the time period. Finally the BY statement ensures that each plot is specific to a single patient. **Figure 18** shows the PPP for patient X000001 from the results of submitting the SAS code we have described.

Centre Profile Plots

The data transformations that we described earlier aiming at the production of PPPs are also required in order to produce CPPs. Thus using the dataset ALL (**Table 3**) as the starting point, there is some additional data structure requirements. Remember that in the CPPs the y-axis represents the “patient” dimension. We need to create the variable that will be plotted on the y-axis. Similarly to the creation of variable TYPE_CODE in the case of the PPPs, here we create variable PATIENTID_CODE as is illustrated in **Table 4**. Notice that the data are now sorted by TYPE_CODE.

Figure 19 contains the SAS code that is used to produce CPPs for our case study data. Notice here, that it is the PATIENTID_CODE variable that is plotted on the y-axis while the TYPE_CODE variable is used in the BY statement, thus ensuring that each plot contains data for all patients of the population, and for a single variable of interest. **Figure 20** shows us the resulting CPP for both patients in our case study data. Due to the very small patient population of our case study data, it has not been possible to demonstrate the creation of the centre dimension. The centre dimension is shaped by subsetting the patient population, and in practice it would have been implemented via the use of the WHERE statement.

Enhancements and Delivery Method of PPPs and CPPs

We presented how you can plot your data using simple and straightforward programming techniques. The resulting output can be enhanced further, through the use of the annotate facility, to feature customised annotations. One such example is the duration of each patient’s follow-up period in the CPPs, which is represented by the light blue stripe (**Figure 10**).

Finally, in **Figure 17** and **Figure 19** we have demonstrated how PPPs and CPPs can be delivered in RTF format using the SAS Output Delivery System® (ODS). ODS allows the production of more output formats, such as HTML and PDF. The benefit of the RTF and PDF formats is that it delivers a big number of stand alone graphics in a single file. We have found that the same PPPs or CPPs when delivered in PDF format, occupy significantly less physical disc space. Furthermore, the bookmarks feature of the PDF format is particularly helpful to navigate through and review the PPPs and CPPs. The drawback of the PDF format is that the graphics are embedded in the PDF document, thus preserving their visual quality when copying and pasting them is a problem. On the other hand the graphics exist as individual objects within an RTF document, and thus they can be copied and pasted elsewhere (e.g. in presentation slides) while preserving their visual quality.

PPPS AND CPPS IN THE CONTEXT OF OTHER RELATED GRAPHICAL APPROACHES AND THEIR STRENGTHS AND LIMITATIONS.

We have presented a technical problem: the need for a mechanism to evaluate the completeness of epidemiologic data. We have then presented the solution we developed to address this need. We have demonstrated its use and the benefits that it provides. And finally we have explained the programming principles that underpin this solution. A question that remains unanswered is “how does this approach compare to other approaches?”. This question becomes even more relevant in light of the fact that there are commercial off-the-shelf (COTS) software applications that could be an alternative solution to the problem at hand.

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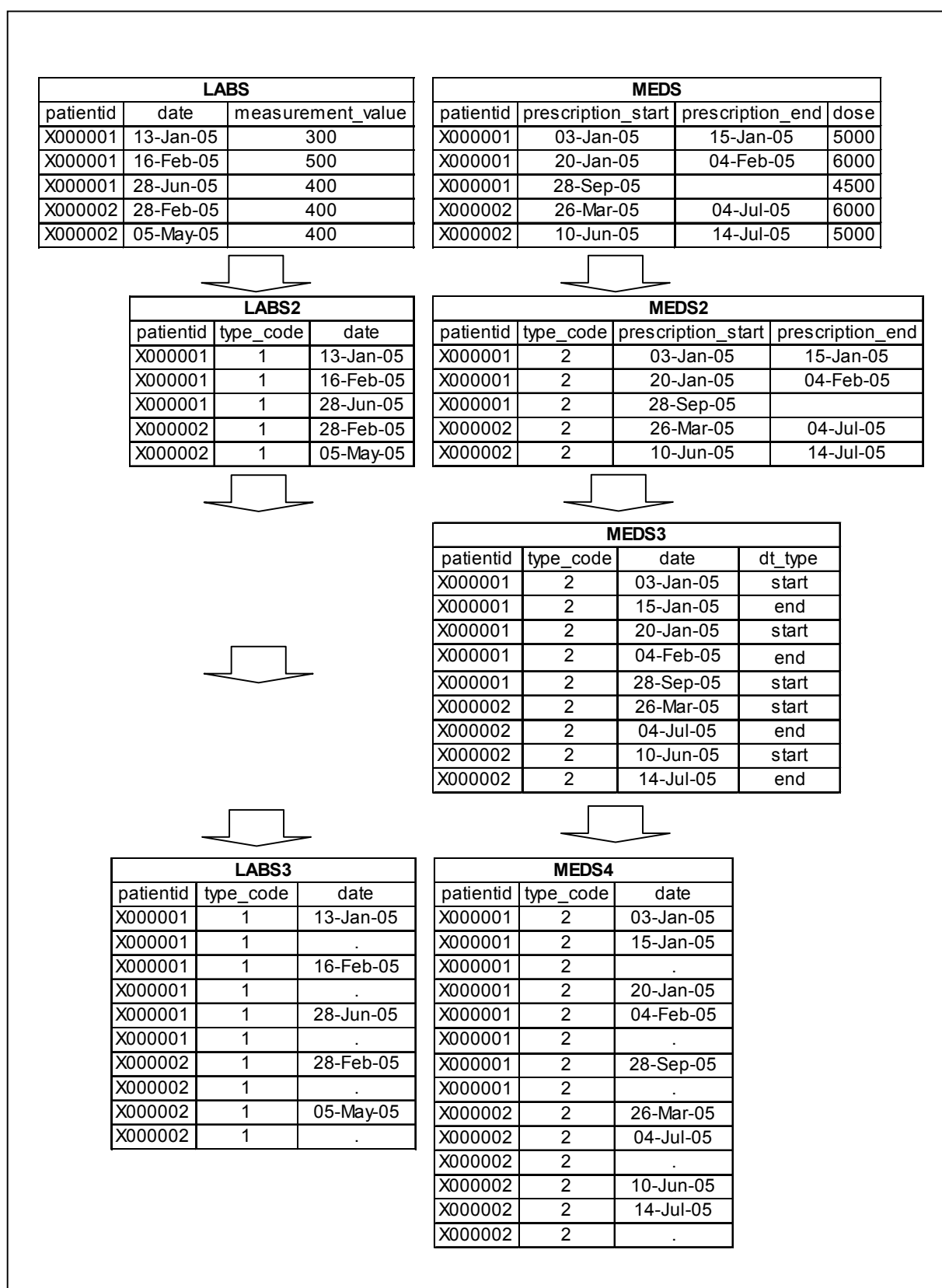


Figure 16: Data Transformation Process

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ALL			
patientid	type	type_code	date
X000001	LAB A	1	13-Jan-05
X000001	LAB A	1	.
X000001	LAB A	1	16-Feb-05
X000001	LAB A	1	.
X000001	LAB A	1	28-Jun-05
X000001	LAB A	1	.
X000001	MED B	2	03-Jan-05
X000001	MED B	2	15-Jan-05
X000001	MED B	2	.
X000001	MED B	2	20-Jan-05
X000001	MED B	2	04-Feb-05
X000001	MED B	2	.
X000001	MED B	2	28-Sep-05
X000001	MED B	2	.
X000002	LAB A	1	28-Feb-05
X000002	LAB A	1	.
X000002	LAB A	1	05-May-05
X000002	LAB A	1	.
X000002	MED B	2	26-Mar-05
X000002	MED B	2	04-Jul-05
X000002	MED B	2	.
X000002	MED B	2	10-Jun-05
X000002	MED B	2	14-Jul-05
X000002	MED B	2	.

Table 3: PPPs Data Transformed and Ready for Plotting

ALL2				
patientid	type	type_code	date	patientid_code
X000001	LAB A	1	13-Jan-05	1
X000001	LAB A	1	.	1
X000001	LAB A	1	16-Feb-05	1
X000001	LAB A	1	.	1
X000001	LAB A	1	28-Jun-05	1
X000001	LAB A	1	.	1
X000002	LAB A	1	28-Feb-05	2
X000002	LAB A	1	.	2
X000002	LAB A	1	05-May-05	2
X000002	LAB A	1	.	2
X000001	MED B	2	03-Jan-05	1
X000001	MED B	2	15-Jan-05	1
X000001	MED B	2	.	1
X000001	MED B	2	20-Jan-05	1
X000001	MED B	2	04-Feb-05	1
X000001	MED B	2	.	1
X000001	MED B	2	28-Sep-05	1
X000001	MED B	2	.	1
X000002	MED B	2	26-Mar-05	2
X000002	MED B	2	04-Jul-05	2
X000002	MED B	2	.	2
X000002	MED B	2	10-Jun-05	2
X000002	MED B	2	14-Jul-05	2
X000002	MED B	2	.	2

Table 4: CPPs Data Transformed and Ready for Plotting

```

proc format;
  value type 1='LAB A' 2='MED B';
run;

goptions reset=all ymax=11in xmax=8.5in hsize=7.0in vsize=4.5in
  rotate=portrait ftext=simplex htext=8 pt;

axis1 label=(h=0.8
  "Beginning of Month in Study Period (Jan 2005 to Dec 2006)")
  origin=(,5) minor=none offset=(0.3cm,0.3cm)
  order=('01JAN05'd to '01JAN07'd by month)
  value=(h=0.6 '1' '2' '3' '4' '5' '6' '7' '8' '9' '10' '11' '12'
    '13' '14' '15' '16' '17' '18' '19' '20' '21' '22' '23' '24' ' ');
axis2 label=( " ") value=(h=0.8) order=(1 to 10 by 1)
  minor=none offset=(,0.5cm);

symbol v=dot height=0.4 width=2 c=red interpol=join;

ods rtf file="example1.rtf" nogfootnote;
proc gplot data=all(keep=patientid type_code date);
  plot type_code*date / cframe=paoy frame skipmiss
    haxis=axis1 lhref=1 autohref cautohref=ligr
    vaxis=axis2 lvref=1 autovref cautohref=ligr;
  by patientid;
  format type_code type.;
run;quit;
ods rtf close;

```

Figure 17: PPPs Demo SAS Code

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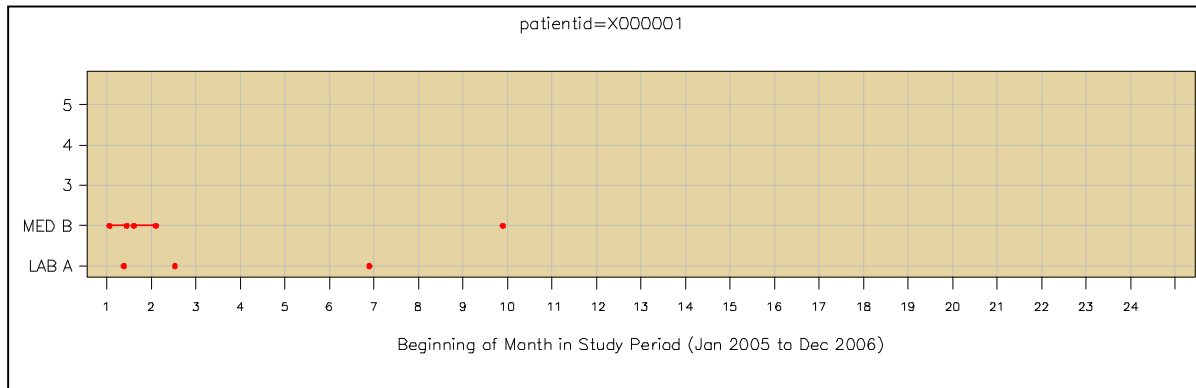


Figure 18: PPPs Demo Output

```
proc format;
  value type 1='LAB A'
            2='MED B';
run;

goptions reset=all ymax=11in xmax=8.5in hsize=7.0in vsize=4.5in
  rotate=portrait ftext=simplex htext=8 pt;

axis1 label=(h=0.8
  "Beginning of Month in Study Period (Jan 2005 to Dec 2006)")
  origin=(,5) minor=none offset=(0.3cm,0.3cm)
  order=('01JAN05'd to '01JAN07'd by month)
  value=(h=0.6 '1' '2' '3' '4' '5' '6' '7' '8' '9' '10' '11' '12'
    '13' '14' '15' '16' '17' '18' '19' '20' '21' '22' '23' '24' ' ');

axis2 label=(angle=90 "Patients Sorted by Study Start Date")
  value=(h=0.8) order=(1 to 10 by 1)
  minor=none offset=(,0.5cm) value=none;

symbol v=dot height=0.4 width=2 c=red interpol=join;

ods rtf file="example2.rtf" style = tempstyle nogfootnote;
proc gplot data=all2(keep=patientid code type_code date);
  plot patientid_code*date / frame skipmiss haxis=axis1 lhref=1
    autoref cautohref=ligr vaxis=axis2 ;
  by type_code;
  format type_code type.;
run;quit;
ods rtf close;
```

Figure 19: CPPs Demo SAS Code

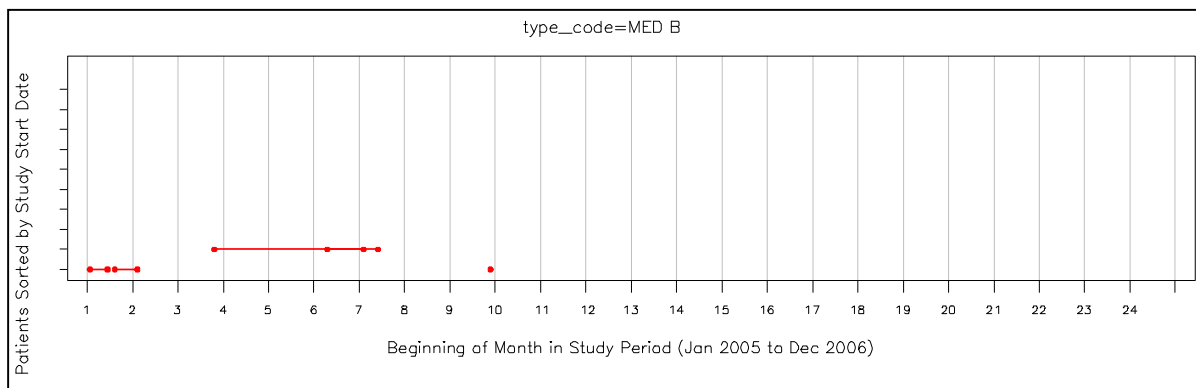


Figure 20: CPPs Demo Output

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Although a full scale evaluation based on theoretical models was not practically possible, we carried out a crude evaluation comparing the PPPs and CPPs solution, with two COTS software applications that were available at the time, which could form the bases for an alternative solution. The costing factor is probably the most striking distinction. In terms of license fees, in order to develop and deploy the PPPs and CPPs solution, only a license to use SAS/BASE® and SAS/GRAPH is required. Typically most biostatistics departments will have at least one license of these SAS software components. Basing a solution on a particular COTS application on the other hand, would incur an additional license fee of up to a few thousands of pounds. However, the PPPs and CPPs will require development time. Assuming though that a SAS programmer is already available, and considering that COTS applications are typically designed as all purpose graphical output production tools, it is arguable that the time taken to train a user on the multifaceted functions of a COTS application will equal the development time taken by a SAS programmer to develop the PPPs and CPPs. Finally, another significant advantage of the PPPs and CPPs solution is flexibility: in contrast to COTS applications that produce a specific visual output with limited customisation capabilities, the visual output of PPPs and CPPs can be modified and enhanced according to your needs and requirements.

CONCLUSION

Patient Profile Plots and Center Profile Plots are novel graphical tools that allow the investigator to evaluate the quality and completeness of epidemiological data in a simple, easy to use graphical approach.

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