

## Post-surgical opioid pain medications usage evaluation using SAS® and Excel

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### ABSTRACT

Post-surgical pain management is often based on opioid administration. Opioids offer efficient pain control, but their use may, in some cases, lead to dependency. Opioid data for exploratory and clinical studies needs to be collected accurately and monitored periodically. To address potential dependence problem, this paper provides a systematic method, using Excel (with well-designed structure for data collection) and SAS® for periodical opioid usage (converted to morphine equivalents) evaluation. There are many ways to approach evaluation and the presented method is only a proposal for consideration. So far, it is not being used or implemented, up to the author's knowledge, anywhere. Reports are provided in the form of tables and boxplots. If higher than expected patient opioid usage is detected, medical staff may try to offer alternate, pain reduction, protocols [1].

### KEYWORDS

Opioids, morphine equivalent, Excel, Proc Import, Proc Transpose, Box Plot.

### INTRODUCTION

Post-surgical pain management is an inherent part of patient recovery. Opioid medications are used, in many cases, due to their efficient pain control. Unfortunately, the downside of their administration is potential future dependency. Usually, a compromise must be reached between efficient pain minimization and sparing opioids usage. To avoid unnecessary opioid exposure, periodical, accurate monitoring is needed. In case of high usage alternate protocols [1] may be offered. The presented method is a proposal only, in addition to other methods available. Up to author's knowledge, it is not used or implemented anywhere. The data used is a random selection of records with fictitious treatments A, B, C and is not representative of any study. The intention of the author was to present SAS tool (program) to handle Excel opioid data.

Surgical procedures are performed mainly in hospital or ambulatory settings. Various exploratory or clinical studies investigate procedures performed. For small or medium size studies (up to a few hundred subjects) patient data may be collected in Excel. This approach is inexpensive, easy to maintain by medical staff and does not require advanced databases. A periodic report, using SAS®, with tables and figures, containing summary information, will be a straightforward and easy way for the medical staff to review and make treatment decisions.

### EXCEL STRUCTURE

Well-designed Excel data organization structure is needed. One subject shall have one row allocated only. If for some subjects we have many entries of the same category (for instance medications), each cell should contain more than one record, separated by a separator of choice. The structure of each record must be the same. It is worthwhile to notice, that study data usually includes, among others, demographic, vital signs, surgery, medications, concomitant medications and questionnaires like pain scores, quality of life, length of stay and other. Study Excel may contain tens of columns.

We are interested in evaluation of opioid consumption. Essentially, subject id, treatment and medication details are of interest. An example of a few columns is presented below.

Table 1

ID	Age on Day of Surgery	Gender (M/F)	Laterality	Race	Insurance	Year of Surgery	ASA score	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )	Primary Diagnosis for Surgery	Deformity Assessment (4 point scale) Preop	Post-Op ROM 3 months	Comorbidities: (List All)	Previous Hip Surgery (Y/N) see next column	List Previous Hip Surgery	Joint Class Attended (Y/N)	H/O Smoking (Y/N)
1	68	Male	Right	Other	Medicare	2017	2	185.4	95.9	27.8	Primary localized osteoarthritis of right hip	4	5	NULL		NULL	Yes	Yes
2	58	Male	Left	Other	Medicare	2017	2	182.9	70.3	21.1	Primary localized osteoarthritis of right hip	4	5	NULL		NULL	Yes	No
<b>OPIOID MEDICATIONS COLUMN</b>																		
<b>HYDROcodone-acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 8:10AM~</b> <b>oxyCODONE (OxyCONTIN) 12 hr tablet 10 mg 10 Sep 21 2017 8:42PM~</b> <b>HYDROcodone-</b> <b>acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 5:15AM~</b> <b>HYDROcodone-</b> <b>acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 11:35AM~</b> <b>HYDROcodone-</b> <b>acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 21 2017 4:01PM</b>																		
<b>NULL</b>																		

Table 1. Structure of Study Data Excel.

The opioid columns presented above is updated each time a new opioid is administered. The new opioid is appended at the end after separator, Information from each medication is separated by a delimiter of choice like “~” and has the following format: medication name, dose, unit, dose form, dose frequency, date and time of administration. This structure must be maintained for each subject to assure correct data processing. Excel spreadsheet is usually populated by trained medical staff and opioid data are assumed to be complete. In case of missing entries, corresponding missing values will show up on the corresponding SAS® data set.

### EXCEL PRE-PROCESSING

We may create a work (=“ Opioids”) sheet on our Excel and copy their subject id, treatment, and opioid column. We shall separate the data in the opioid column over multiple columns using “Data” on the data ribbon and then “Text to Columns” with delimiter “~”. The number of columns generated will be driven by maximum number of opioids administered, over all subjects. The process is automatic, the resulting work Excel will be processed by SAS®. This process will generate a few columns. For example, if there is a subject with a maximum of 15 drug opioid administrations, 14 additional columns will be created.

### ANALYSIS SAS® DATA SET PREPARATION

After the working spreadsheet is created in Excel use Proc Import to create the initial SAS® data set.

```

PROC IMPORT OUT      = opioids(keep=id trt opioids)
  DATAFILE = "<Excel location>"
  DBMS      = EXCEL REPLACE ;
  GETNAMES  = NO;
  MIXED     = NO;
  SCANTEXT  = YES;
  USEDATE   = YES;
  SCANTIME  = YES;
  SHEET     = Opioids;

```

Run;

When Proc Import successfully creates opioids data set, we may employ Proc Transpose to create a vertical SAS® data set with all opioid administrations organized in one column.

```

proc transpose data = _opioids(rename=(F1=Id)
  out = tr_opioids(where=(col1>''));
  by trt id;
  var F:;
  where id >.;
run;

```

After proc transpose is executed, tr\_opioids data set has the following structure (\_NAME\_ \_LABEL\_ will be dropped):

Table 2

Trt	Id	_NAME_	_LABEL_	Col1
A	1	F2	F2	HYDROcodone-acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 8:10AM
A	1	F3	F3	oxyCODONE (OxyCONTIN) 12 hr tablet 10 mg 10 Sep 21 2017 8:42PM
A	1	F4	F4	HYDROcodone-acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 5:15AM
A	1	F5	F5	HYDROcodone-acetaminophen (NORCO 5) 5-325 mg per tablet 1 tablet 1 Sep 22 2017 11:35AM
...				

Table 2. Details of opioids administered.

The next step will be expanding drug information in Col1 into separate columns. The following data step demonstrates processing transposed data, which is based on specific Excel data format.

```

data all_opioids(keep=trt id med dose unit route tablet date time);
  retain id med dose unit route tablet date time;
  set tr_opioids;
  length unit $10. tablet $30.;

  /** (Adding delimiter '^' to split col1 data into columns. **)
  col1 = tranwrd(col1, ' ', '^');
  med  = scan(col1,1, '^');

  rest = scan(col1,2, '^');
  rest = tranwrd(rest, 'Jan', '^Jan');
  rest = tranwrd(rest, 'Feb', '^Feb');
  rest = tranwrd(rest, 'Mar', '^Mar');
  rest = tranwrd(rest, 'Apr', '^Apr');

```

```

rest    = tranwrđ(rest, 'May', '^May');
rest    = tranwrđ(rest, 'Jun', '^Jun');
rest    = tranwrđ(rest, 'Jul', '^Jul');
rest    = tranwrđ(rest, 'Aug', '^Aug');
rest    = tranwrđ(rest, 'Sep', '^Sep');
rest    = tranwrđ(rest, 'Oct', '^Oct');
rest    = tranwrđ(rest, 'Nov', '^Nov');
rest    = tranwrđ(rest, 'Dec', '^Dec');

date_time = scan(rest, 2, '^');
drginfo   = scan(rest, 1, '^');

date_time = tranwrđ(date_time, '10:', '^10:');
date_time = tranwrđ(date_time, '11:', '^11:');
date_time = tranwrđ(date_time, '12:', '^12:');
date_time = tranwrđ(date_time, ' 1:', '^1:');
date_time = tranwrđ(date_time, ' 2:', '^2:');
date_time = tranwrđ(date_time, ' 3:', '^3:');
date_time = tranwrđ(date_time, ' 4:', '^4:');
date_time = tranwrđ(date_time, ' 5:', '^5:');
date_time = tranwrđ(date_time, ' 6:', '^6:');
date_time = tranwrđ(date_time, ' 7:', '^7:');
date_time = tranwrđ(date_time, ' 8:', '^8:');
date_time = tranwrđ(date_time, ' 9:', '^9:');

date      = scan(date_time, 1, '^');
time      = scan(date_time, 2, '^');

    if index(drginfo, 'mg') > 0 then unit = 'mg';
else if index(drginfo, 'mcg') > 0 then unit = 'mcg';

_drgrinfo    = tranwrđ(drginfo, 'mg', '^mg');
_drgrinfo    = tranwrđ(drginfo, 'mcg', '^mcg');

dose         = scan(_drgrinfo, 1, '^');
    if index(dose, 'tablet') > 0 then do;
        dose = tranwrđ(dose, 'tablet', 'tablet^');
        dose = scan(dose, 3, '^');
    end;
_oth         = scan(drginfo, 2, '^');

drginfo      = tranwrđ(drginfo, 'tablet', '^tablet');
tablet1      = scan(drginfo, 2, '^');
tablet2      = scan(drginfo, 3, '^');
if tablet2 > '' then tablet = strip(tablet1)||' '||strip(tablet2);
else tablet  = tablet1;

/**/ Route calculation /**/

    if index(uppercase(coll), 'INJECTION') > 0 then Route='Injection';
else if index(coll, 'tab') > 0 then Route = 'Oral';
if med      = 'NULL' then do;
    unit     = '';
    route    = '';
end;

/**/ Dose calculation /**/

```

```

dose          = strip(tranwrd(dose, 'injection', ''));
tablet        = strip(tranwrd(tablet, 'tablet', ''));
if tablet > '' then dose = tablet;
if index(med, 'NORCO') > 0 then dose =
compress(scan(med, 3, ''), '');
if index(med, 'PERCOCET') > 0 then dose =
strip(put(5*input(scan(tablet, 1, ''), ??best.), ??best.));
if index(dose, 'mg') > 0 then dose = scan(dose, 1, 'mg');
if index(dose, '-') > 0 then dose = scan(dose, 1, '-');

```

run;

After application of the above step, we will have

Table 3

Id	Med	Dose	Unit	Route	Tablet	Date	Time Treatment
1	HYDROcodone-acetaminophen (NORCO 5)	5	mg	Oral	1 1	Sep 22 2017	8:10AM A
1	oxyCODONE (OxyCONTIN)	10	mg	Oral	10 mg 10	Sep 21 2017	8:42PM A
1	HYDROcodone-acetaminophen (NORCO 5)	5	mg	Oral	1 1	Sep 22 2017	5:15AM A
1	HYDROcodone-acetaminophen (NORCO 5)	5	mg	Oral	1 1	Sep 22 2017	11:35AM A
1	HYDROcodone-acetaminophen (NORCO 5)	5	mg	Oral	1 1	Sep 21 2017	4:01PM A

Table 3. Opioids administered.

## OPIOIDS CONVERSION TO MORPHINE EQUIVALENT

Standard conversion tables are available to provide conversion factors based on type of opioid medication. These factors allow conversion of opioid medications into morphine equivalents. Conversion depends on route of drug administration. In our example only orally administered meds are considered.

Table 4

Medication	Unit	Route	Factor
HYDROcodone-acetaminophen (NORCO 10)	mg	Oral	1
HYDROcodone-acetaminophen (NORCO 5)	mg	Oral	1
buprenorphine-naloxone (NALOXONE)	mg	Oral	0.2
Morphine (MSCONTIN)	mg	Oral	1
oxycodone (OxyCONTIN)	mg	Oral	1.5
oxycodone (ROXICODONE)	mg	Oral	1.5
oxyCODONE-acetaminophen (PERCOCET)	mg	Oral	1.5
Tapentadol (NUCYNTA)	mg	Oral	0.2
tramadol (ULTRAM)	mg	Oral	0.3

Table 4. Morphine Equivalent Dose (MED) / Morphine Milligram Equivalent (MME) Conversion Table.

Presenting the above table as Excel table, we can easily create corresponding SAS® data set (conv\_table), using Proc Import as before, and merge it with our opioids data set by medication name.

```

proc sort data=meds;
  by trt id;
run;

proc univariate data=meds noprint;

```

```

by trt id unit route;
var _dose;
output out=Tot_ops sum=sum;
run;

data Tot_ops;
set Tot_ops;
if sum = . then sum = 0;
run;

```

Table 5

trt	id	unit	route	sum
A	1	mg	Oral	35
A	2			0
A	3	mg	Oral	60
A	4	mg	Oral	157.5
A	5	mg	Oral	25
A	6	mg	Oral	40
A	7	mg	Oral	60
A	8	mg	Oral	65
A	9	mg	Oral	25
A	10	mg	Oral	45
A	11	mg	Oral	75
A	12	mg	Oral	45
.....				

Table 5. A snapshot of Tot\_ops data set records.

## REPORT

The main purpose of the report is a subject list presentation by treatment, whose opioid usage exceeds pre-specified morphine equivalent threshold. Additionally, a graphic presentation of treatment group opioid usage, in a form of a boxplot is available accompanied by summary stats.

### Output files

```

%let file1 = "\\<directory>\boxplot.rtf";
%let file2 = "\\<directory>\over&level.mg.xlsx";
%let file3 = "\\<directory>\stats.xlsx";

%macro report(level=);

data over&level.mg(keep=trt unit route id sum);
set Tot_ops;
if unit = 'mg' and sum > &level;
run;

/*** Outliers ***/

data test;

```

```

    set Tot_ops;
    _id = put(id, ??best.)||' ('||strip(put(sum, ??best.))||')';
run;

proc sort data=test;
  by trt sum;
run;

ods rtf file=&file1;
title1 j=center "Evaluation of opioid usage";
title2 j=center "All opioids dosage is presented as Morphine equivalent";
footnote1 j=left "Outlier annotations: Id (Total Dose)";

/**/ Boxplot figure /**/

axis2 order = (0 to 175 by 25);
proc boxplot data=test box =outliers;
  plot sum*trt / boxstyle = schematicid vaxis=axis2
    outbox = outliers;
  id _id;
  label trt = "Treatment"
    sum = "Total Dose (mg)";
run;

ods rtf close;
title;
ods listing;

ods excel file=&file2 options(embedded_titles="yes") ;
title1 j=center "Subjects with opioid usage over &level mg";
title2 j=center "All opioids dosage is presented as Morphine equivalent";

data over&level.mg;
  set over&level.mg;
  rename sum=tot_dose;
  subject = strip(put(id, ??best.));
run;

proc report data=over&level.mg;
  columns trt subject unit route tot_dose;
  define trt / "Treatment";
  define subject / "Subject Id";
  define unit / "Unit";
  define route / "Route";
  define tot_dose / "Total dose";
run;

ods excel close;
title;
ods listing;

/**/ Opioid usage /**/

data over&level.mg;
  set over&level.mg;
  rename sum=tot_dose;
  subject = strip(put(id, ??best.));

```

```

run;

proc report data=over&level.mg;
  columns trt subject unit route tot_dose;
  define trt          / "Treatment";
  define subject     / "Subject Id";
  define unit        / "Unit";
  define route       / "Route";
  define tot_dose    / "Total dose";
run;

ods excel close;
title;
ods listing;

ods excel file=&file3 options(embedded_titles="yes") ;
title1 j=center "Opioid stats";
title2 j=center "All opioids dosage is presented as Morphine equivalent";

data outliers;
  set outliers;
  select(_TYPE_);
  when ('N')          ord = 1;
  when ('MIN')        do; ord = 2;  _VALUE_ = round(_VALUE_, .1); end;
  when ('Q1')         do; ord = 3;  _VALUE_ = round(_VALUE_, .01); end;
  when ('MEAN')       do; ord = 4;  _VALUE_ = round(_VALUE_, .01); end;
  when ('MEDIAN')     do; ord = 5;  _VALUE_ = round(_VALUE_, .01); end;
  when ('Q3')         do; ord = 6;  _VALUE_ = round(_VALUE_, .01); end;
  when ('MAX')        do; ord = 7;  _VALUE_ = round(_VALUE_, .1); end;
  when ('STDDEV')     do; ord = 8;  _VALUE_ = round(_VALUE_, .001); end;
  when ('HIWHISKR')  do; ord = 9;  _VALUE_ = round(_VALUE_, .01); end;
  when ('HIGH')       do; ord = 10; _VALUE_ = round(_VALUE_, .01); end;
  when ('FARHIGH')   do; ord = 11; _VALUE_ = round(_VALUE_, .01); end;
  otherwise;
  end;
run;

proc sort data=outliers out=_outliers(keep=ord trt _TYPE_ _VALUE_);
  by ord;
run;

proc transpose data=_outliers out=tr_outliers(drop=_NAME_ _LABEL_)
  prefix=trt;
  var _VALUE_;
  by ord _TYPE_;
  id trt;
run;

proc report data=tr_outliers;
  columns _TYPE_ trtA trtb trtC;
  define _TYPE_      / "Stats";
  define trtA        / "Treatment A";
  define trtB        / "Treatment B";
  define trtC        / "Treatment C";
run;

```



```
ods excel close;
title;
ods listing;

%mend report;

%report(level=75);
```

All reports or only selected ones, like list of patients with opioid usage over 75 mg may be produced.

## EXAMPLE

As an example, for implementing the proposed method, sample study data was generated. Subjects were randomized into 3 treatments with 20 patients in each treatment group. Excel files with subject were created and processed as described in the paper. Proc Boxplot was used to present results. Proc Boxplot generates a corresponding data set with summary statistics. Results were presented in the attached Excel spreadsheet. If additional information is desired in the output report, regarding subjects consuming more opioids than expected, a threshold may be set to list subjects with dosage over the supplied threshold.

Table 6

Stats	Treatment A	Treatment B	Treatment C
N	20	20	20
MIN	0	5	0
Q1	37.5	15	10
MEAN	53.75	30.88	33.38
MEDIAN	52.5	21.25	23.75
Q3	68.75	46.25	52.5
MAX	157.5	75	92.5
STDDEV	32.932	23.06	28.588
HIWHISKR	80	.	.
HIGH	157.5	.	.

Table 6. Opioids stats with dosages as Morphine equivalent.

Table 7

Treatment	Subject Id	Unit	Route	Total dose
A	4	mg	Oral	157.5
A	16	mg	Oral	80
C	213	mg	Oral	90
C	220	mg	Oral	92.5

Table 7. Subjects with opioid usage over 75 mg with dosages as Morphine equivalents.

Figure 1

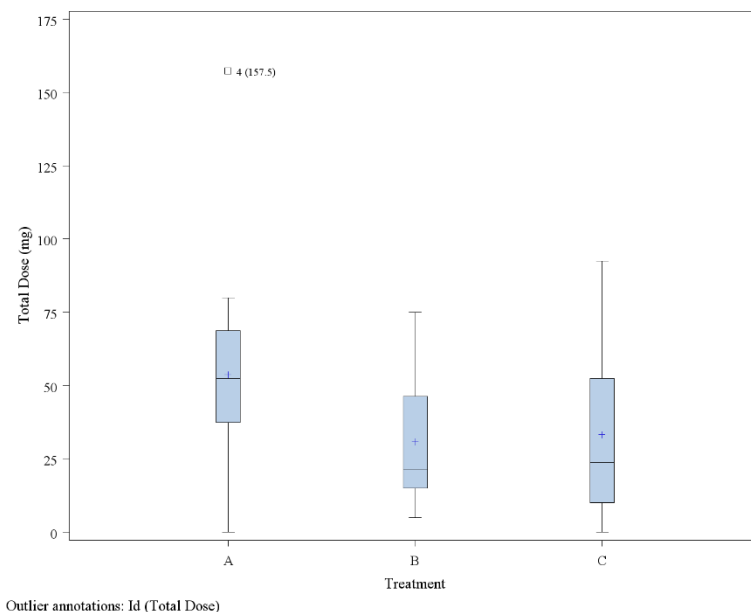


Figure 1. Opioid usage evaluation per treatment with dosages as Morphine equivalent.

After evaluation of the reports above it is apparent that there is one subject (Subject Id=4) with a high usage of opioids (total dose of 157.5 mg, over twice the amount of the threshold). The above subject has to be investigated and a potential reduction in opioid consumption considered. Alternate, non-opioid medication may suffice. However, if that option is not possible, the subject shall be followed up closely to prevent post-surgical opioid dependency.

It is also interesting to notice, that in case of treatments B and C average use of opioids is relatively similar (30.88 and 33.38) while Treatment A requires more opioids (average is 53.75). Please also note that all subjects in Treatment B received opioids below the set threshold. Essentially, boxplots allow seeing differences in average treatment between groups.

The developed SAS® data set with opioid usage can be used to perform more detailed statistical comparative analyses.

## REFERENCES

[1] Caleb A. Jones, MD, Thomas W. Throckmorton, MD, Jeff Murphy, BS, MS, Robert R. Eason, BS, MS, Myles Joyce, BS, David L. Bernholt, MD, Frederick M. Azar, MD, Tyler J. Brolin, MD; Opioid-Sparing Pain Management Protocol After Shoulder Arthroplasty Results in Less Opioid Consumption and Higher Satisfaction: A Prospective, Randomized Controlled Trial; Journal of Shoulder and Elbow Surgery, July 04, 2022.

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