Data Analysis of Cobalt and Chromium Ion Levels in Arthroplasty Patients

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on behalf of accessUTS Pty Ltd

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TABLE OF CONTENTS

1. INTRODUCTION

This report provides a statistical analysis of relationships in the concentrations of cobalt and chromium ions in joint fluid, blood serum and cerebrospinal fluid of Anthroplasty patients who presented at the practice of Dr Lawrence Kohan. All data was collected by Dr Lawrence Kohan and provided to Access: UTS for analysis.

The specific relationships considered include:

1. Relationship between concentrations of cobalt and chromium ions in joint fluid
2. Relationship between concentrations of cobalt and chromium ions in blood serum
3. Relationship between concentrations of cobalt and chromium ions in cerebrospinal fluid
4. The effect of the concentration of cobalt ions in blood serum on concentration of cobalt ions in cerebrospinal fluid (CSF)
5. The effect of the concentration of chromium ions in blood serum on concentration of cobalt ions in cerebrospinal fluid (CSF)
6. The effect of the concentration of cobalt ions in joint fluid on concentration of cobalt ions in blood serum
7. The effect of the concentration of cobalt ions in joint fluid on concentration of cobalt ions in blood serum

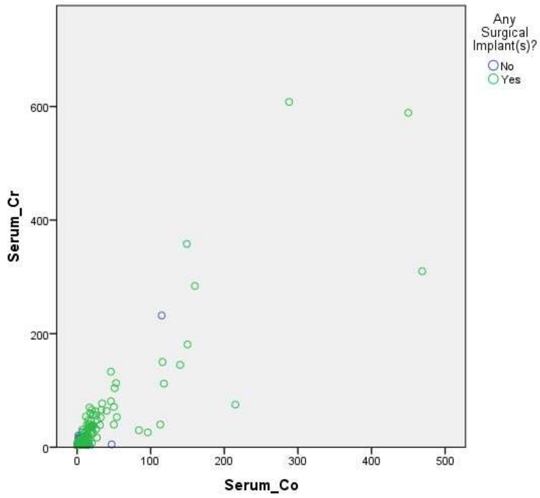
For each of these relationships, the first step involved exploratory analysis, in which the pairwise distributions of the concentrations of cobalt and chromium ions were examined. Based on this examination, a log transformation was applied to the variables, and the distributions were re-assessed. A linear regression models were then developed for each relationship, and the strength of each relationship was assessed. Finally, a power analysis was performed to determine whether the sample size was adequate to generalize the inferences. The results of these analyses are provided in section 2. With the exception of the power analyses, all analyses were performed using IBM SPSS version 20. The power analyses were performed using GPower version 3.1.

2. RELATIONSHIPS IN THE CONCENTRATIONS OF COBALT AND CHROMIUM IONS IN JOINT FLUID, BLOOD SERUM AND CEREBROSPINAL FLUID

2.1 Exploratory Analysis

The pairwise distributions of variables were examined visually for each pair of variables involved in the relationships enumerated in Section 1, above. This was achieved by generating scatter plots of the pairs of variables. A visual examination of each scatter plot showed that a large number of data points were concentrated towards the lower end of the scale, and a relatively small number of data points occurred toward the upper end of the scale. A scatter plot showing the relationship between concentration of cobalt ions and chromium ions in blood serum is displayed in Figure 1, below, as an example. The others are included in Appendix A.

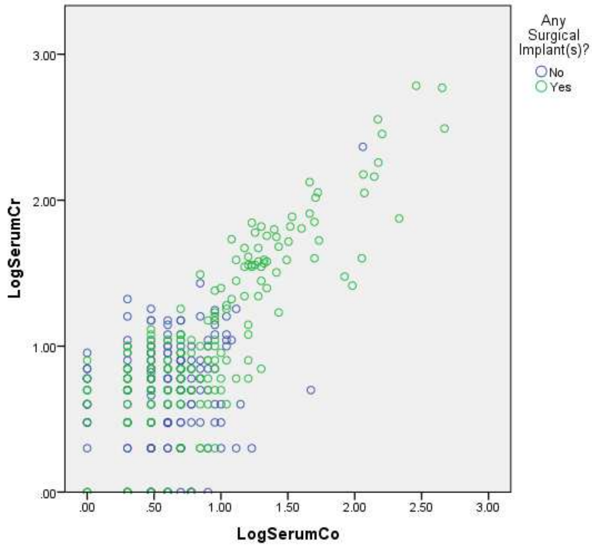
Figure 1: Scatter Plot showing the relationship between concentration of cobalt ions and chromium ions in blood serum



This kind of variability in distribution is typical of concentration data. The recommended technique to analyse the relationships between such data is to use a log transform. This involves taking the logarithm of each “concentration” variable. While the base of the logarithm is not relevant from a statistical perspective, the most commonly used logarithms are the natural logarithm (base *e*) or the common logarithm (base 10). This is due to the fact that these logarithms are built into most software packages and calculators. For all analysis performed in this report, the common logarithm (base 10) was used. The common logarithm was preferred to the natural logarithm because it facilitates interpretation of the results of the analysis from a more practical (non-mathematical) perspective.

After taking the common logarithm of each variable, the scatter plots of the newly created variables were re-examined. The spread of the log transformed variables was more even across the entire range, and in most cases, a visual inspection suggested that a linear relationship between the transformed variables was plausible. Once again, a scatter plot showing the relationship between the log transformed concentrations of cobalt ions and chromium ions in blood serum is displayed as an example (see Figure 2). The others are included in Appendix A.

Figure 2: Scatter Plot showing the relationship between the log of concentration of cobalt ions and the log of the concentration of chromium ions in blood serum



Following the transformations of the variables and examinations of the distributions of the log-transformed variables, linear regression models were developed for each relationship enumerated in Section 1, above. The results of these regression analyses are presented in the following sections.

2.2 Relationship between concentrations of cobalt and chromium ions in joint fluid

A linear regression model was developed to examine the relationship between $log(Fluid\_Cr)$ and $log(Fluid\_Co)$. There was no clear indication as to which of these needed to be the dependent variable, and which one needed to be the independent variable. Therefore, $log(Fluid\_Cr)$ was arbitrarily selected as the dependent variable and$log(Fluid_Co)$ was entered as the predictor.

The number of data points for this analysis was relatively small $(n = 12)$. In spite of this, the data showed a strong and highly significant linear relationship between the variables, with the correlation coefficient being $r = 0.921$ $(p < 0.001)$.

The regression equation is: $Log(Fluid\_Cr) = 0.801 * Log(Fluid\_Co) + 0.627$

The regression coefficient for the predictor $log(Fluid\_Co)$ was $\beta = 0.801$ $(p < 0.001)$. This can be interpreted to mean that a one unit increase in $log(Fluid\_Co)$ is associated with an increase of 0.801 units in $log(Fluid\_Cr)$. In terms of the original data, this translates to a 10-fold increase in concentration of cobalt ions in the joint fluid being associated with a 6.3-fold increase in concentration of chromium ions (in the joint fluid). For example, an increase in cobalt ion concentration from 1 nmol/l to 10 nmol/l is associated with a 6.3 fold increase in chromium ion concentration from 4.24 nmol/l to 26.79 nmol/l. Similarly, a 10-fold increase in cobalt ion concentration from 10 nmol/l to 100 nmol/l is associated with a 6.3 fold increase in chromium ion concentration from 26.79 nmol/l to 169.43 nmol/l.

Table 2.2 below, shows this relationship for various values of cobalt ion concentration in the joint fluid.

Fluid Co (nmol/l)	Predicted Value of Fluid Cr (nmol/l)
1	4.24
10	26.79
20	46.68
50	97.25
100	169.43
500	615.00
1000	1071.52
2000	1866.92
3000	2583.30

Table 2.2: Modelled relationship between concentration of cobalt ions and concentration of chromium ions in the joint fluid

The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The error distribution showed minor deviations from normality, which could be due to the small sample size. Overall, given the limitation of the sample size, the model is an adequate fit to the data.

The SPSS output related to this analysis is presented in Appendix A.

2.3 Relationship between concentrations of cobalt and chromium ions in blood serum

A linear regression model was developed to examine the relationship between $log(Serum\_Cr)$ and $log(Serum\_Co)$. There was no clear indication as to which of these needed to be the dependent variable, and which one needed to be the independent variable. Therefore, $log(Serum\_Cr)$ was arbitrarily selected as the dependent variable and$log(Serum_Co)$ was entered as the predictor.

The data showed a strong and highly significant linear relationship between the variables, with the correlation coefficient being $r = 0.709$ $(p < 0.001)$.

The regression equation is: $Log(Serum\_Cr) = 0.760 * Log(Serum\_Co) + 0.305$

The regression coefficient for the predictor $log(Serum\_Co)$ was $\beta = 0.760$ $(p < 0.001)$. This can be interpreted to mean that a one unit increase in $log(Serum\_Co)$ is associated with an increase of 0.760 units in $log(Serum\_Cr)$. In terms of the original data, this translates to a 10-fold increase in concentration of cobalt ions in the blood serum being associated with a 5.75-fold increase in concentration of chromium ions (in the blood serum). For example, an increase in cobalt ion concentration from 1 nmol/l to 10 nmol/l is associated with a 5.75-fold increase in chromium ion concentration from 2.02 nmol/l to 11.61 nmol/l. Similarly, a 10-fold increase in cobalt ion concentration from 10 nmol/l to 100 nmol/l is associated with a 5.75-fold increase in chromium ion concentration from 11.61 nmol/l to 66.83 nmol/l.

Table 2.3 below, shows this relationship for various values of cobalt ion concentration in the joint fluid.

Serum Co (nmol/l)	Predicted Value of Serum Cr (nmol/l)
1	2.02
10	11.61
20	19.67
50	39.47
100	66.83
500	227.10

Table 2.3: Modelled relationship between concentration of cobalt ions and concentration of chromium ions in the serum

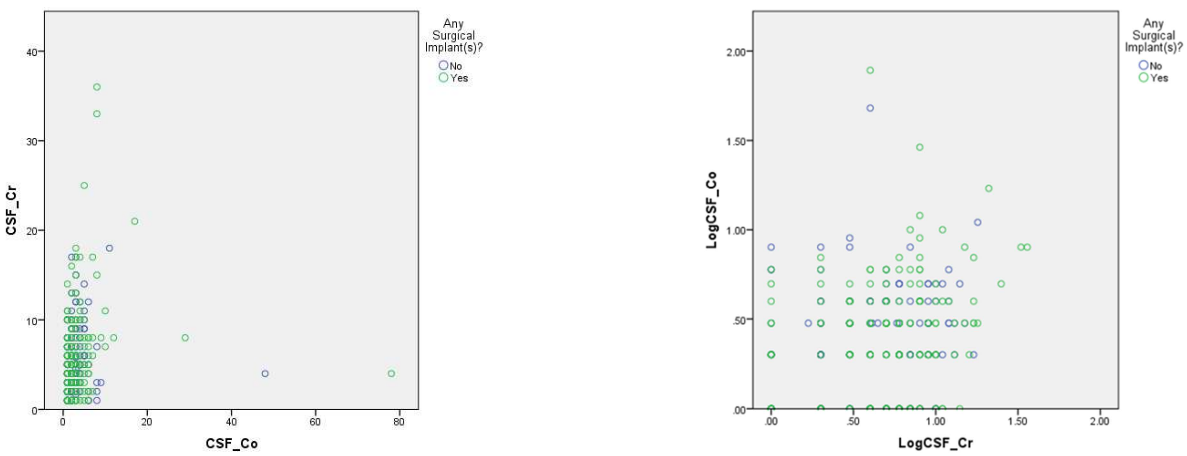
The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The regression diagnostics indicated that the model was a good fit to the data.

The SPSS output related to this analysis is presented in Appendix A.

2.4 Relationship between concentrations of cobalt and chromium ions in cerebrospinal fluid

In the cerebrospinal fluid, the scatter plots of both the raw data and the log-transformed data suggested that the relationship between the concentration of cobalt ions and the concentration of chromium ions was weak (see Figure 3 below). This was confirmed by determining the correlation coefficients of the relationships between the variables.

Figure 3: Scatter Plots showing the relationship between the concentration of cobalt ions and the concentration of chromium ions in cerebrospinal fluid



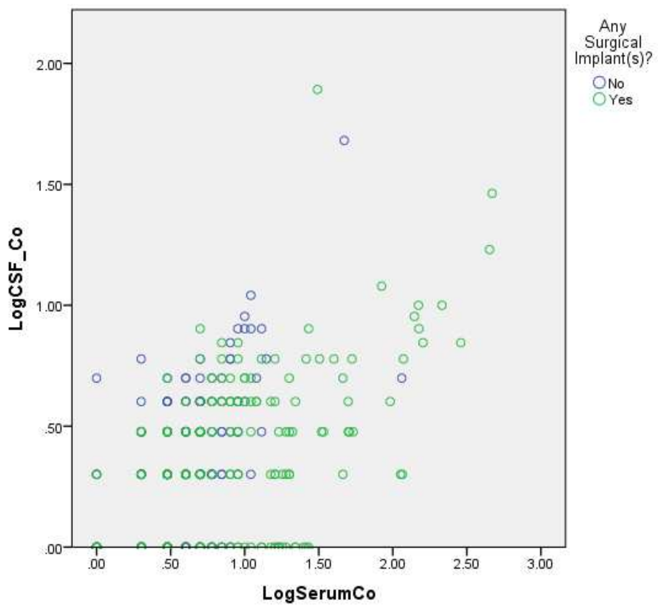
Both the Pearson's correlation coefficient, which is an indication of strength of a linear relationship, and the Spearman's (nonparametric) correlation coefficient, which is preferred when relationships are nonlinear, indicated weak relationships with coefficients ranging from 0.122 to 0.280. Although these relationships met the standard of statistical significance($p < 0.05$), this was primarily due to the large sample size ($n \sim 380$), and merely supports the conclusion that the correlation coefficient is higher than zero; it is not an indicator of the strength of the relationship. The complete table of correlation coefficients is presented in Appendix A.

Nevertheless, a linear regression model was developed to examine the relationship between $log(CSF\_Cr)$ and $log(CSF\_Co)$. As expected, the regression diagnostics showed a poor fit to the data with the distribution of errors being heterogeneous. The results of this regression analysis and its interpretation are included in Appendix A. These should, however, be interpreted with caution, and are therefore not included here.

2.5 Relationship between concentrations of cobalt ions in blood serum and cerebrospinal fluid

A scatter plot of $log(CSF\_Co)$ on $log(Serum\_Co)$ suggested the existence of a linear relationship, at least for values of $log(Serum\_Co) \geq 1.5$. The relationship was not as clear for values of $log(Serum\_Co) < 1.5$. This may have been due to the fact that there were a disproportionately large number of data points with $log(Serum\_Co) < 1.5$. The data suggested that a segmented regression approach may have been useful. However, the first step was to develop a linear regression model.

Figure 4: Scatter Plot showing the relationship between the log of concentration of cobalt ions in the blood serum and the log of the concentration of cobalt ions in CSF



A linear regression model was developed to examine the relationship between $log(Serum\_Co)$ and $log(CSF\_Co)$. Since minerals are believed to flow from the blood serum to the cerebrospinal fluid, $log(CSF\_Co)$ was entered as the dependent variable and$log(Serum_Co)$ was entered as the predictor.

The data showed a moderate but highly significant linear relationship between the variables, with the correlation coefficient being $r = 0.507$ $(p < 0.001)$.

The regression equation is: $Log(CSF\_Co) = 0.334 * Log(Serum\_Co) + 0.103$

The regression coefficient for the predictor $log(Serum\_Co)$ was $\beta = 0.334$ $(p < 0.001)$. This can be interpreted to mean that a one unit increase in $log(Serum\_Co)$ is associated with an increase of 0.334 units in $log(CSF\_Co)$. In terms of the original data, this translates to a 10-fold increase in concentration of cobalt ions in the blood serum being associated with an approximately 2-fold increase in concentration of cobalt ions in the cerebrospinal fluid. For example, an increase in cobalt ion concentration in the blood serum from 1 nmol/l to 10 nmol/l is associated with a 2.16 fold increase in cobalt ion concentration in the CSF from 1.27 nmol/l to 2.74 nmol/l. Similarly, a 10-fold increase in cobalt ion concentration in the blood serum from 10 nmol/l to 100 nmol/l is associated with a 2.16 fold increase in cobalt ion concentration in the CSF from 2.74 nmol/l to 5.90 nmol/l.

The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The regression diagnostics indicated that the model was a good fit to the data. Therefore, additional modelling was not pursued.

Table 2.5 below, shows this relationship for various values of cobalt ion concentration in the serum. The SPSS output related to this analysis is presented in Appendix A.

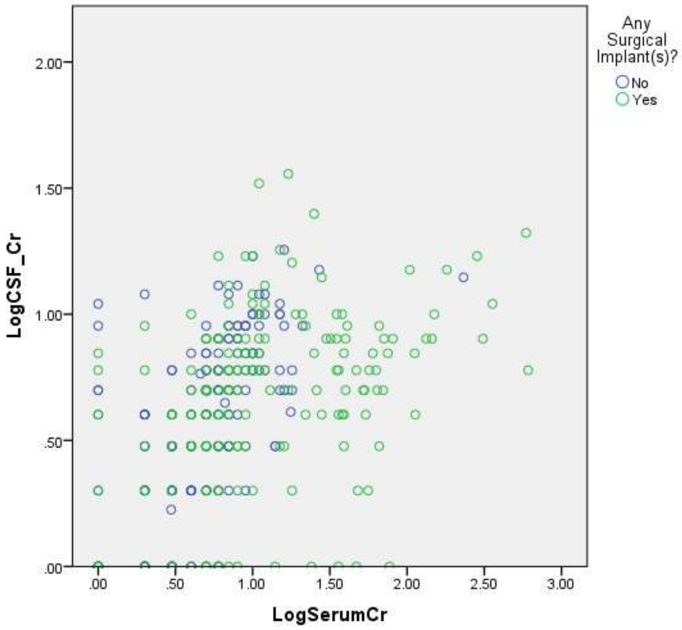
Serum Co (nmol/l)	Predicted CSF Co (nmol/l)
1	1.27
10	2.74
20	3.45
50	4.68
100	5.90
500	10.10

Table 2.5: Modelled relationship between concentration of cobalt ions in the serum and concentration of cobalt ions in the CSF

2.6 Relationship between concentrations of chromium ions in blood serum and cerebrospinal fluid

A scatter plot of $log(CSF\_Cr)$ on $log(Serum\_Cr)$ suggested the existence of a linear relationship, at least for values of $log(Serum\_Cr) \geq 1.5$. The relationship was not as clear for values of $log(Serum\_Cr) < 1.5$. This may have been due to the fact that there were a disproportionately large number of data points with $log(Serum\_Cr) < 1.5$. The data suggested that a segmented regression approach may have been useful. However, the first step was to develop a linear regression model.

Figure 5: Scatter Plot showing the relationship between the log of concentration of Cr ions in the blood serum and the log of the concentration of Cr ions in CSF



A linear regression model was developed to examine the relationship between $log(Serum\_Cr)$ and $log(CSF\_Cr)$. Since minerals are believed to flow from the blood serum to the cerebrospinal fluid, $log(CSF\_Cr)$ was entered as the dependent variable and $log(Serum\_Cr)$ was entered as the predictor.

The data showed a moderate but highly significant linear relationship between the variables, with the correlation coefficient being $r = 0.473$ $(p < 0.001)$.

The regression equation is: $Log(CSF\_Cr) = 0.321 * Log(Serum\_Cr) + 0.343$

The regression coefficient for the predictor $log(Serum\_Cr)$ was $\beta = 0.321$ $(p < 0.001)$. This can be interpreted to mean that a one unit increase in $log(Serum\_Cr)$ is associated with an increase of 0.321 units in $log(CSF\_Cr)$. In terms of the original data, this translates to a 10-fold increase in concentration of chromium ions in the blood serum being associated with an approximately 2-fold increase in concentration of chromium ions in the cerebrospinal fluid. For example, an increase in chromium ion concentration in the blood serum from 1 nmol/l to 10 nmol/l is associated with a 2.1 fold increase in chromium ion concentration in the CSF from 2.20 nmol/l to 4.61 nmol/l. Similarly, a 10-fold increase in chromium ion concentration in the blood serum from 10 nmol/l to 100 nmol/l is associated with a 2.1 fold increase in chromium ion concentration in the CSF from 4.61 nmol/l to 9.66 nmol/l.

The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The regression diagnostics indicated that the model was a good fit to the data. Therefore, additional modelling was not pursued.

Table 2.6 below, shows this relationship for various values of chromium ion concentration in the serum. The SPSS output related to this analysis is presented in Appendix A.

Serum Cr (nmol/l)	Predicted CSF Cr (nmol/l)
1	2.20
10	4.61
20	5.76
50	7.73
100	9.66
500	16.19

Table 2.6: Modelled relationship between concentration of chromium ions in the serum and concentration of chromium ions in the CSF

2.7 Relationship between concentrations of cobalt ions in joint fluid and blood serum

A linear regression model was developed to examine the relationship between $log(Fluid\_Co)$ and $log(Serum\_Co)$. Since minerals are believed to flow from the joint fluid to the blood serum, $log(Serum\_Co)$ was entered as the dependent variable and$log(Fluid_Co)$ was entered as the predictor.

The data was limited, with only 12 data points available for analysis. In spite of this, the data showed a significant linear relationship between the variables, with a moderate-high correlation coefficient of $r = 0.676$ $(p = 0.032)$.

The regression equation is: $Log(Serum\_Co) = 0.334 * Log(Fluid\_Co) + 0.643$

The regression coefficient for the predictor $log(Fluid\_Co)$ was $\beta = 0.334$ $(p = 0.032)$. This can be interpreted to mean that a one unit increase in $log(Fluid\_Co)$ is associated with an increase of 0.334 units in $log(Serum\_Co)$. In terms of the original data, this translates to a 10-fold increase in concentration of cobalt ions in the blood serum being associated with an approximately 2-fold increase in concentration of cobalt ions in the cerebrospinal fluid. For example, an increase in cobalt ion concentration in the joint fluid from 1 nmol/l to 10 nmol/l is associated with a 2.16 fold increase in cobalt ion concentration in the blood serum from 4.40 nmol/l to 9.48 nmol/l. Similarly, a 10-fold increase in cobalt ion concentration in the joint fluid from 10 nmol/l to 100 nmol/l is associated with a 2.16 fold increase in cobalt ion concentration in the blood serum from 9.48 nmol/l to 20.46 nmol/l.

The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The error distribution showed minor deviations from normality, as well as homogeneity of variance across the range. These could be due to the small sample size. Overall, given the limitation of the sample size, the model is an adequate fit to the data.

Table 2.7 below, shows this relationship for various values of cobalt ion concentration in the joint fluid. The SPSS output related to this analysis is presented in Appendix A.

Fluid Co (nmol/l)	Predicted Serum Co (nmol/l)
1	4.40
10	9.48

20	11.95
50	16.24
100	20.46
500	35.03
1000	44.16
2000	55.66
3000	63.73

Table 2.7: Modelled relationship between concentration of cobalt ions in the joint fluid and concentration of cobalt ions in the blood serum

2.8 Relationship between concentrations of chromium ions in joint fluid and blood serum

A linear regression model was developed to examine the relationship between $log(Fluid\_Cr)$ and $log(Serum\_Cr)$. Since minerals are believed to flow from the joint fluid to the blood serum, $log(Serum\_Cr)$ was entered as the dependent variable and$log(Fluid_Cr)$ was entered as the predictor.

The data was limited, with only 12 data points available for analysis. In spite of this, the data showed a significant linear relationship between the variables, with a high correlation coefficient of $r = 0.738$ $(p = 0.015)$.

The regression equation is: $Log(Fluid\_Cr) = 0.437 * Log(Serum\_Cr) + 0.402$

The regression coefficient for the predictor $log(Fluid\_Cr)$ was $\beta = 0.437$ $(p = 0.015)$. This can be interpreted to mean that a one unit increase in $log(Fluid\_Cr)$ is associated with an increase of 0.437 units in $log(Serum\_Cr)$. In terms of the original data, this translates to a 10-fold increase in concentration of chromium ions in the blood serum being associated with an approximately 2.73-fold increase in concentration of chromium ions in the cerebrospinal fluid. For example, an increase in chromium ion concentration in the joint fluid from 1 nmol/l to 10 nmol/l is associated with a 2.73 fold increase in chromium ion concentration in the blood serum from 2.52 nmol/l to 6.90 nmol/l. Similarly, a 10-fold increase in chromium ion concentration in the joint fluid from 10 nmol/l to 100 nmol/l is associated with a 2.73 fold increase in chromium ion concentration in the blood serum from 6.90 nmol/l to 18.88 nmol/l.

The model error (residual) distribution was examined to assess whether the linear model was a good fit to the data. The error distribution showed minor deviations from normality, as well as of homogeneity of variance across the range. These could be due to the small sample size. Overall, given the limitation of the sample size, the model is an adequate fit to the data.

Table 2.8 below, shows this relationship for various values of chromium ion concentration in the joint fluid. The SPSS output related to this analysis is presented in Appendix A.

Fluid Cr (nmol/l)	Predicted Serum Cr (nmol/l)
1	2.52
10	6.90
20	9.34

50	13.95
100	18.88
500	38.15
1000	51.64
2000	69.91
3000	83.46

Table 2.8: Modelled relationship between concentration of chromium ions in the joint fluid and concentration of chromium ions in the blood serum

2.9 Power Analysis

Post hoc power analysis performed on GPower 3.1 showed that all analyses had at least 80% power at a significance level of 0.05. This is the accepted standard for most medical research. It is also the standard expected by the NHMRC for most research proposals. The results are presented in Appendix B

2.10Limitations

The small sample size for all analyses that involved joint fluid data was small. This has been noted above, together with the minor violations of the assumptions of the related regression analyses. These were not considered to be serious issues though, and most models were considered to be good fits to the data; the one exception was the relationship between concentration of cobalt ions and chromium ions in the cerebrospinal fluid (which was not limited by low sample size).

In addition, thirteen patients provided samples of blood serum and CSF on more than one occasion. This was a relatively small proportion of the sample (3.5%), and an examination of these cases showed that the concentrations of cobalt and chromium ions in the blood serum and CSF were different on the different occasions they provided samples. One of these patients (8.3%) also provided two samples of joint fluid on separate occasions. This patient's cobalt and chromium ion concentrations in the joint fluid, blood and CSF were different on each occasion. In view of the fact that cobalt and chromium ion concentrations in these fluids can change over time, and related samples of joint fluid, blood and CSF were obtained on each occasion, these were treated as independent samples in the modelling. In this sense, the models developed for this report may be considered to be naïve models.

3. CONCLUSIONS

3.1 Relationship between Concentrations of Cobalt Ions and Concentrations of Chromium Ions in Joint Fluid, Blood Serum and Cerebrospinal Fluid

The data had a non-symmetric distribution across the range of values, with a large number of data points near the lower end of the scale. This was alleviated by taking the common log (base 10) of all concentrations.

The log-transformed data shows a strong relationship between concentration of cobalt and chromium ions in the joint fluid $r = 0.921$ $(p < 0.001)$ and in the blood serum $r = 0.709$ $(p < 0.001)$. In the cerebrospinal fluid, however, the relationship was weak, despite being statistically significant. This was demonstrated by the fact that the log transformed variables shared a Pearson's correlation coefficient value of $r = 0.256$ $(p < 0.001)$ and Spearman's nonparametric correlation coefficient having a value of $\rho = 0.240$ $(p < 0.001)$.

3.2 Relationship between Blood Serum and Cerebrospinal Fluid in Concentrations of Mineral Ions (Cobalt and Chromium)

The data had a non-symmetric distribution across the range of values, with a large number of data points near the lower end of the scale. This was alleviated by taking the common log (base 10) of all concentrations.

Based on the naïve models developed for this report, the amount of cobalt in the serum would have to increase by a factor of 10, in order for the cobalt in CSF to double. The same appears to be true for chromium: chromium in the serum would have to increase by a factor of 10, in order for the chromium in CSF to double. This suggests that there may be a "saturation effect" in the concentration of Chromium and Cobalt from serum to CSF: as the amount of chromium or cobalt in the CSF increases, there is a decrease in the effect of the concentration of these minerals in the serum. This saturation effect is demonstrated below in Figures 6 and 7.

Figure 6: Modelled saturation effect in the relationship between concentration of cobalt in the serum and the CSF

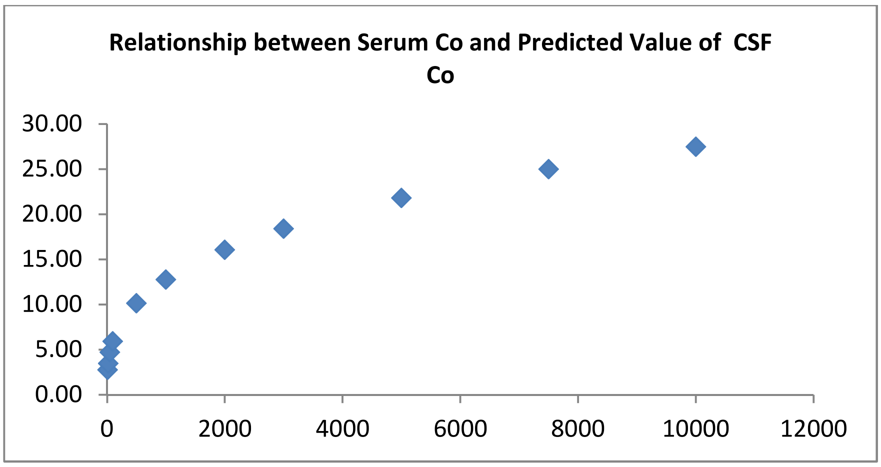
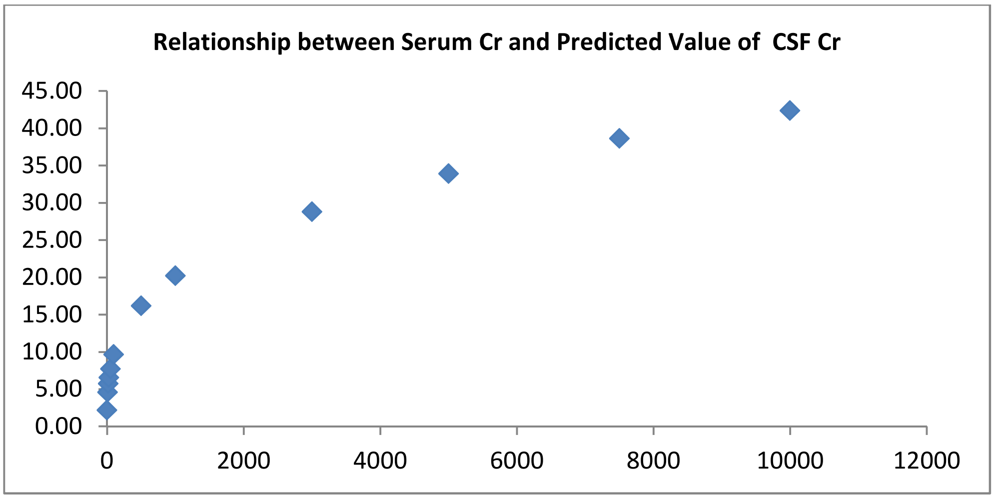


Figure 7: Modelled saturation effect in the relationship between concentration of chromium in the serum and the CSF



3.3 Relationship between the Joint Fluid and Blood Serum in Concentrations of Mineral Ions (Cobalt and Chromium)

The data had a non-symmetric distribution across the range of values, with a large number of data points near the lower end of the scale. This was alleviated by taking the common log (base 10) of all concentrations.

Based on the naïve models developed for this report, the amount of Cobalt in the Fluid would have to increase by a factor of 10, in order for the Cobalt in Serum to double, while Chromium in the Fluid would have to increase by a factor of 10, in order for the Chromium in Serum to increase by a factor of approximately 2.75. This suggests that there may be a “saturation effect” in the concentration of Chromium and Cobalt from joint fluid to the serum: as the amount of chromium or cobalt in the serum increases, there is a decrease in the effect of the concentration of these minerals in the joint fluid. This saturation effect is demonstrated below in Figures 8 and 9.

Figure 8: Modelled saturation effect in the relationship between concentration of Cobalt in the joint fluid and the serum

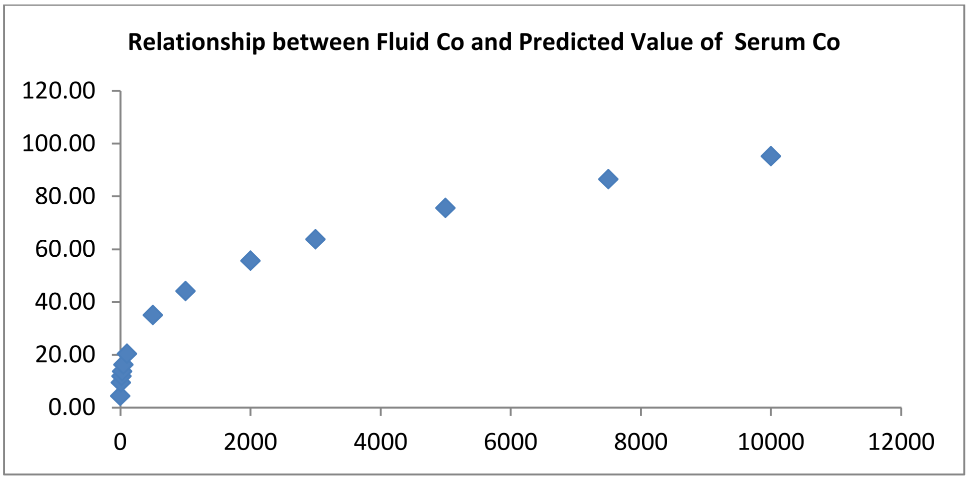
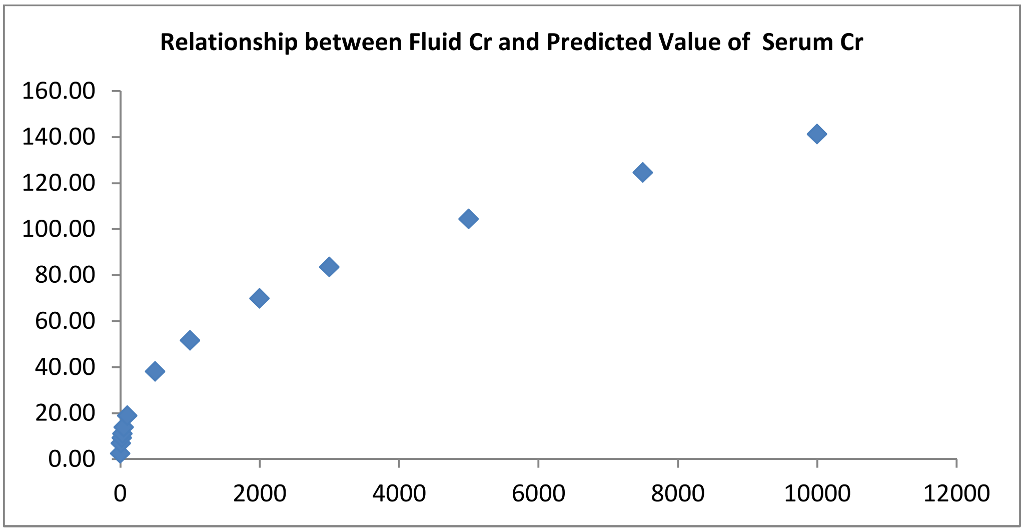


Figure 9: Modelled saturation effect in the relationship between concentration of Cobalt in the joint fluid and the serum



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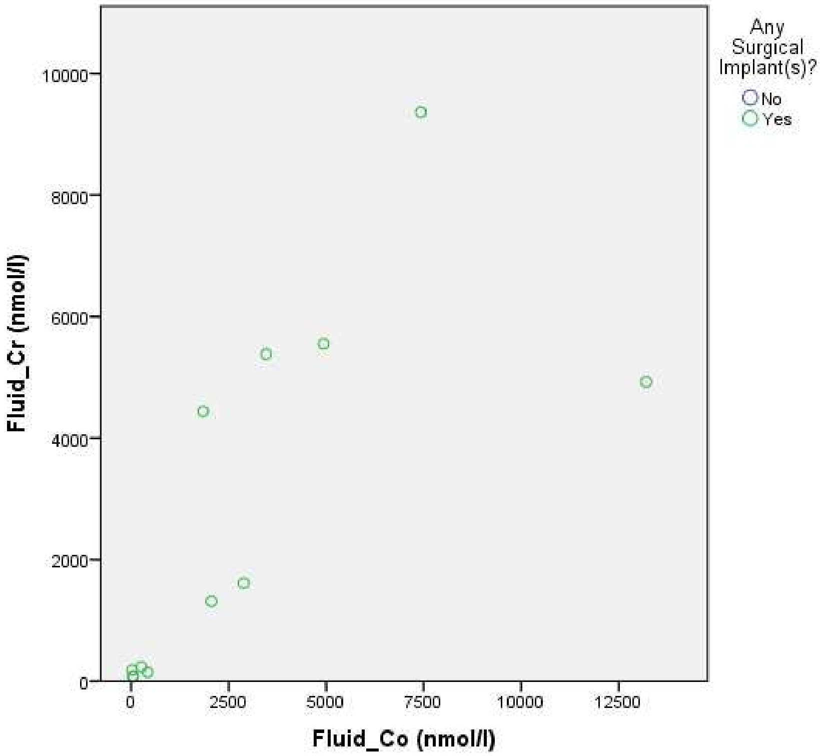
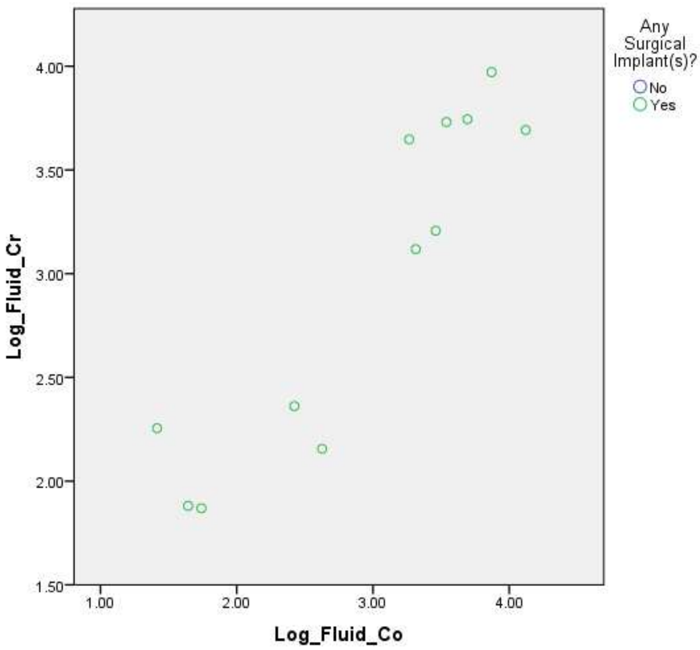
4. APPENDIX A – SPSS OUTPUT WITH COMMENTS

1. Relationship between Fluid Co and Fluid Cr





Regression of Log_Fluid_Cr on Log_Fluid_Co:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.921[a]	.849	.834	.32941

a. Predictors: (Constant), Log_Fluid_Co
b. Dependent Variable: Log_Fluid_Cr

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	6.098	1	6.098	56.196	.000[b]
	Residual	1.085	10	.109		
	Total	7.183	11			

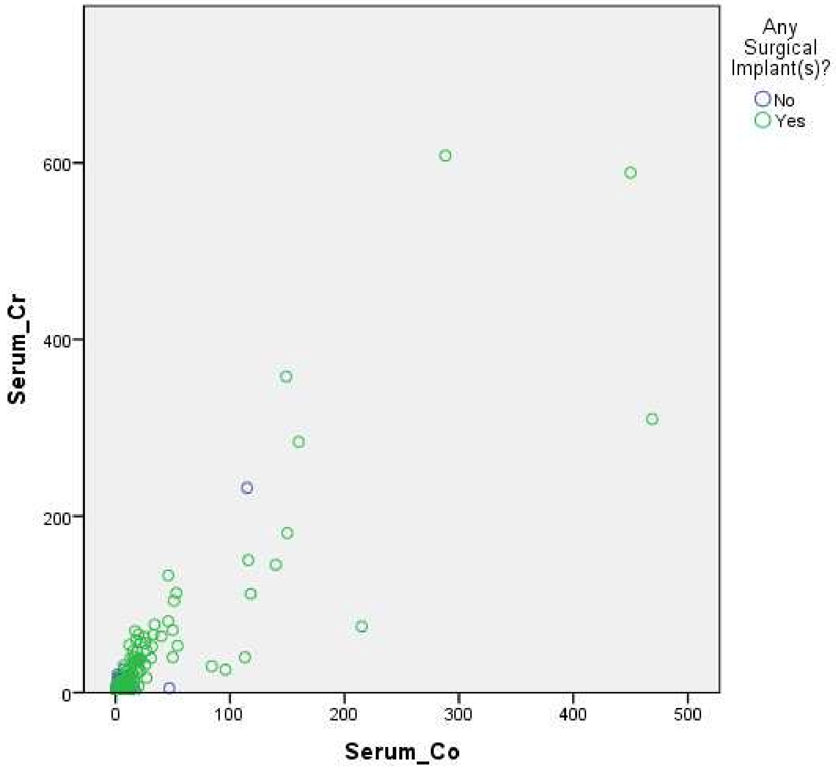
a. Dependent Variable: Log_Fluid_Cr
b. Predictors: (Constant), Log_Fluid_Co

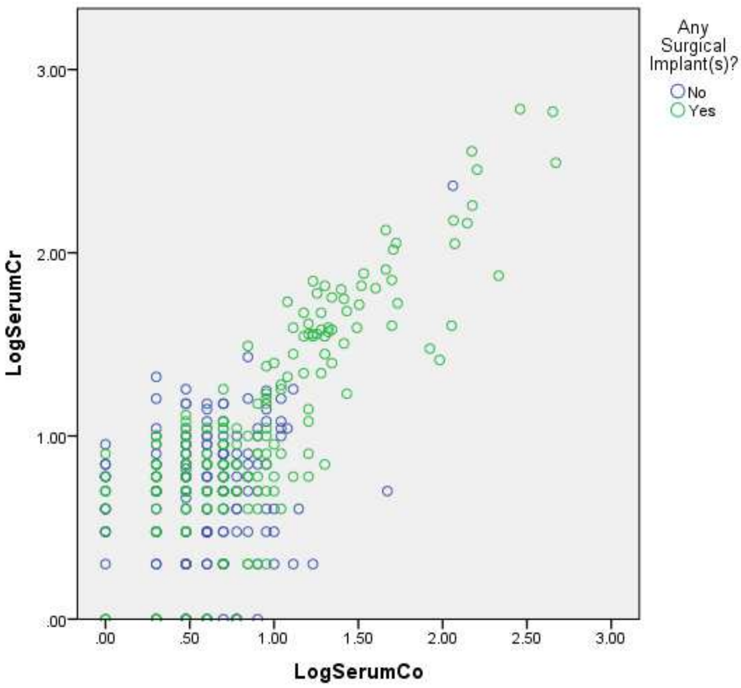
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.627	.327		1.919	.084
	Log_Fluid_Co	.801	.107	.921	7.496	.000

a. Dependent Variable: Log_Fluid_Cr

2. Relationship between Serum Co and Serum Cr





Regression of LogSerumCr on LogSerumCo:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.709[a]	.503	.502	.35014

a. Predictors: (Constant), LogSerumCo
b. Dependent Variable: LogSerumCr

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	47.703	1	47.703	389.095	.000[b]
	Residual	47.078	384	.123		
	Total	94.781	385			

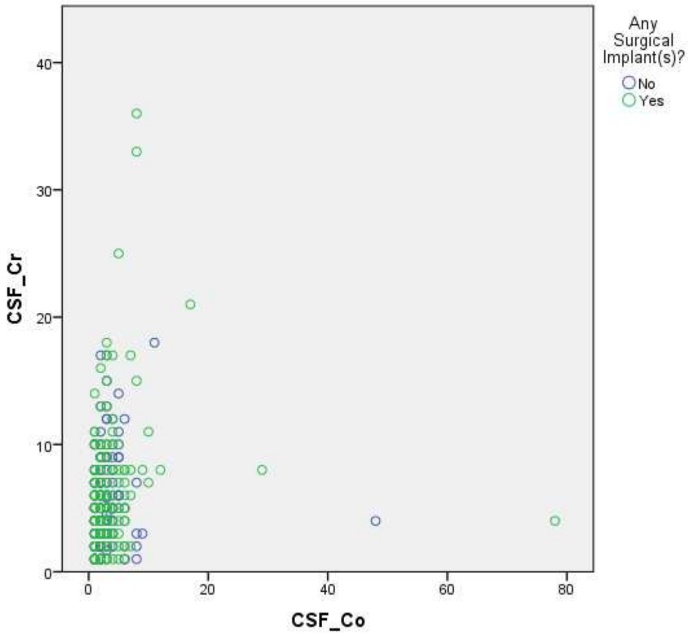
a. Dependent Variable: LogSerumCr
b. Predictors: (Constant), LogSerumCo

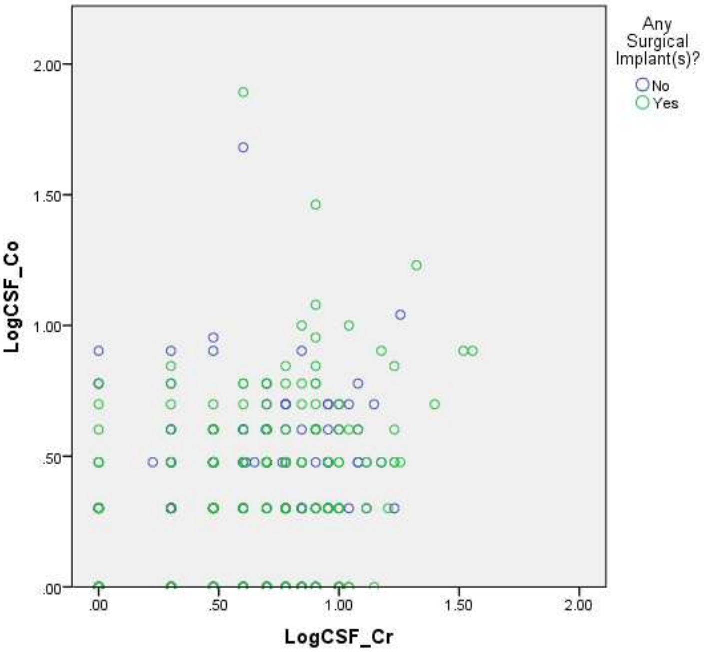
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.305	.034		9.052	.000
	LogSerumCo	.760	.039	.709	19.725	.000

a. Dependent Variable: LogSerumCr

3. Relationship between CSF Co and CSF Cr





<u>Regression of LogCSF_Cr on LogCSF_Co</u>:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.256[a]	.065	.063	.32810

a. Predictors: (Constant), LogCSF_Co
b. Dependent Variable: LogCSF_Cr

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	2.827	1	2.827	26.265	.000[b]
	Residual	40.477	376	.108		
	Total	43.304	377			

a. Dependent Variable: LogCSF_Cr
b. Predictors: (Constant), LogCSF_Co

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.523	.026		20.333	.000
	LogCSF_Co	.284	.055	.256	5.125	.000

a. Dependent Variable: LogCSF_Cr

Pearson's Correlation Coefficients for CSF_Co, CSF_Cr, LogCSF_Co and LogCSF_Cr:

Correlations

		CSF_Cr	CSF_Co	LogCSF_Cr	LogCSF_Co
CSF_Cr	Pearson Correlation	1	.122*	.868**	.280**
	Sig. (2-tailed)		.018	.000	.000
	N	378	378	378	378
CSF_Co	Pearson Correlation	.122*	1	.112*	.682**
	Sig. (2-tailed)	.018		.030	.000
	N	378	379	378	379
LogCSF_Cr	Pearson Correlation	.868**	.112*	1	.256**
	Sig. (2-tailed)	.000	.030		.000
	N	378	378	378	378
LogCSF_Co	Pearson Correlation	.280**	.682**	.256**	1
	Sig. (2-tailed)	.000	.000	.000	
	N	378	379	378	379

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

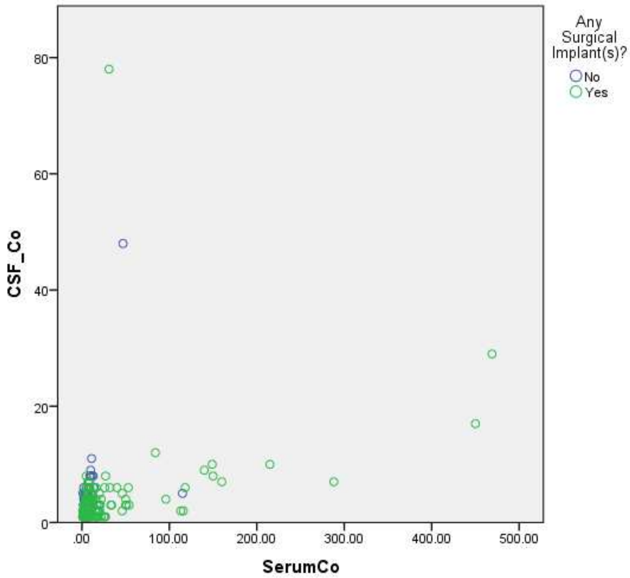
Spearman's Correlation Coefficients for CSF_Co, CSF_Cr, LogCSF_Co and LogCSF_Cr:

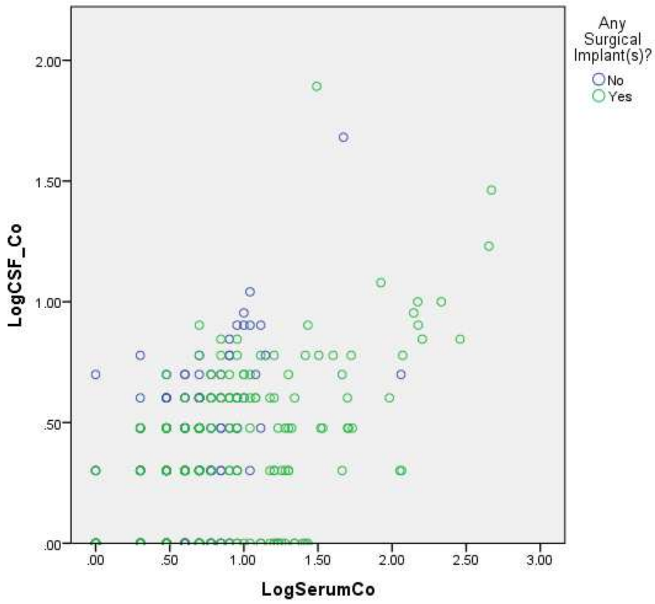
Correlations

			CSF_Cr	CSF_Co	LogCSF_Cr	LogCSF_Co
Spearman's rho	CSF_Cr	Correlation Coefficient	1.000	.240**	1.000**	.240**
		Sig. (2-tailed)	.	.000	.	.000
		N	378	378	378	378
	CSF_Co	Correlation Coefficient	.240**	1.000	.240**	1.000**
		Sig. (2-tailed)	.000	.	.000	.
		N	378	379	378	379
	LogCSF_Cr	Correlation Coefficient	1.000**	.240**	1.000	.240**
		Sig. (2-tailed)	.	.000	.	.000
		N	378	378	378	378
	LogCSF_Co	Correlation Coefficient	.240**	1.000**	.240**	1.000
		Sig. (2-tailed)	.000	.	.000	.
		N	378	379	378	379

**. Correlation is significant at the 0.01 level (2-tailed).

4. Relationship between Serum Co and CSF Co





Regression of LogCSF_Co on LogSerum_Co:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.507[a]	.257	.255	.26427

a. Predictors: (Constant), LogSerumCo
b. Dependent Variable: LogCSF_Co

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	9.091	1	9.091	130.171	.000[b]
	Residual	26.259	376	.070		
	Total	35.350	377			

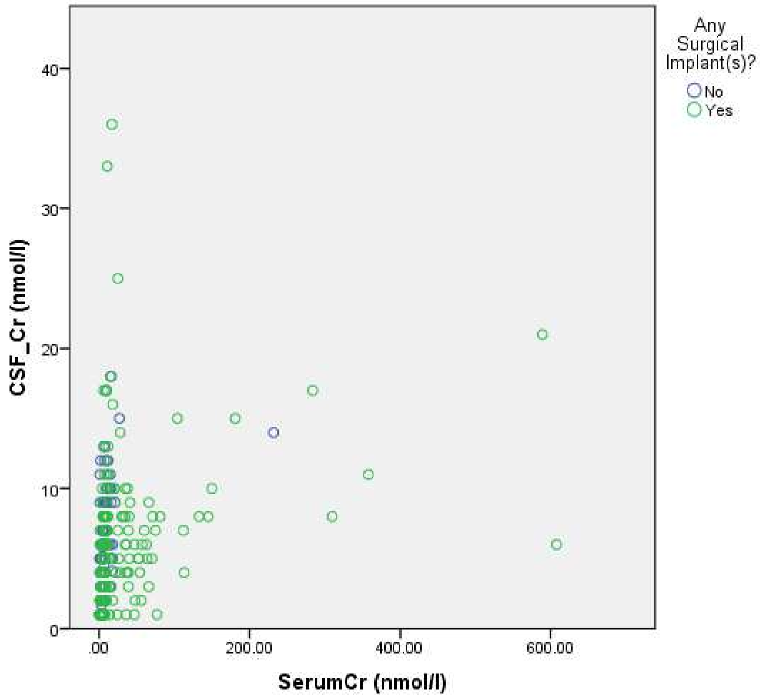
a. Dependent Variable: LogCSF_Co
b. Predictors: (Constant), LogSerumCo

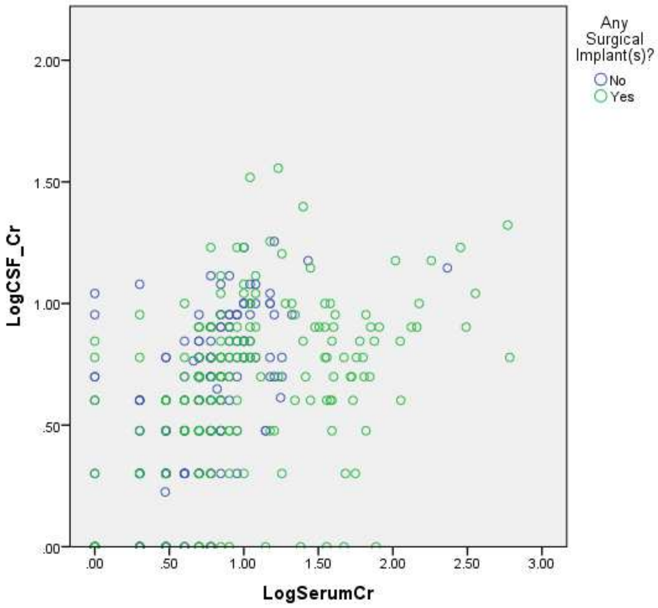
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.103	.026		3.995	.000
	LogSerumCo	.334	.029	.507	11.409	.000

a. Dependent Variable: LogCSF_Co

5. Relationship between Serum Cr and CSF Cr





Regression of LogCSF_Cr on LogSerumCr:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.473[a]	.223	.221	.29949

a. Predictors: (Constant), LogSerumCr
b. Dependent Variable: LogCSF_Cr

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	9.669	1	9.669	107.807	.000[b]
	Residual	33.635	375	.090		
	Total	43.304	376			

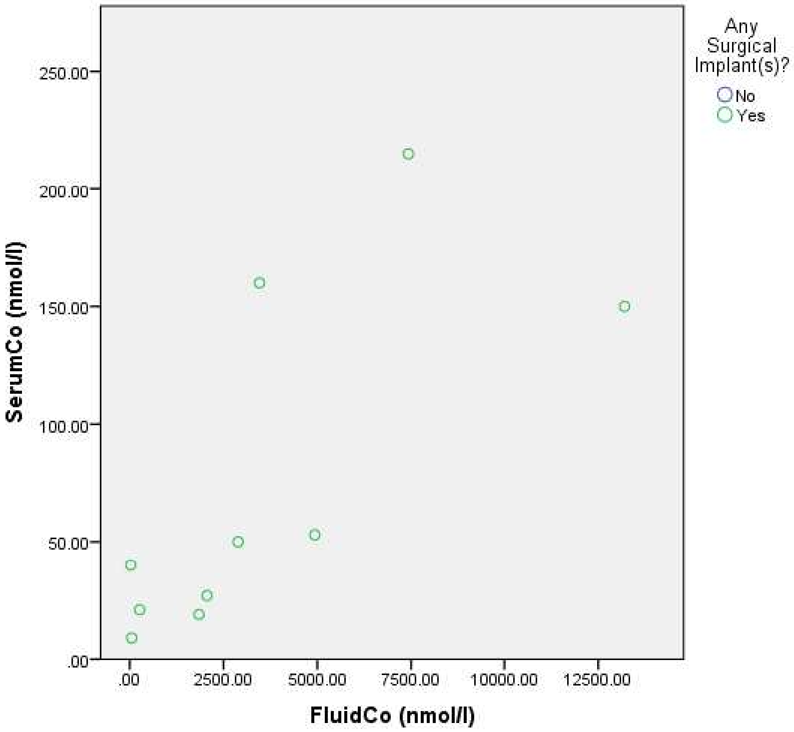
a. Dependent Variable: LogCSF_Cr
b. Predictors: (Constant), LogSerumCr

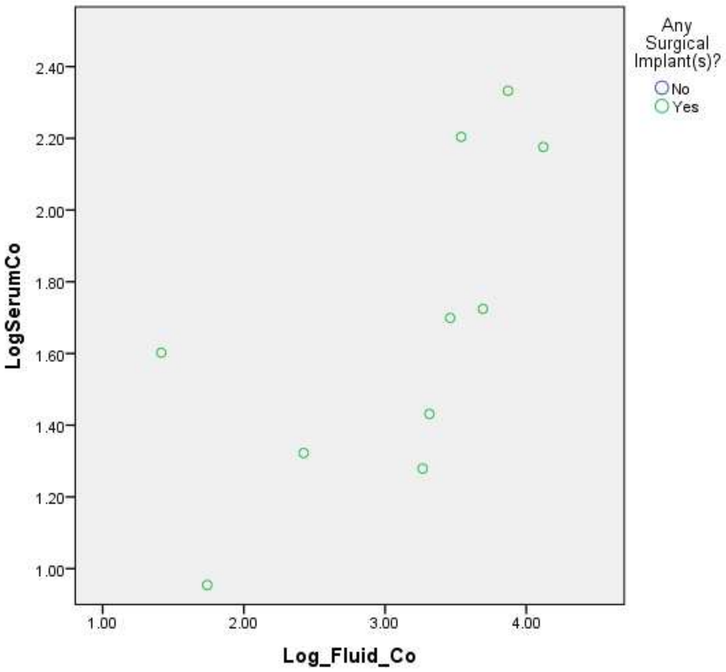
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.343	.031		11.067	.000
	LogSerumCr	.321	.031	.473	10.383	.000

a. Dependent Variable: LogCSF_Cr

6. Relationship between Fluid Co and Serum Co





Regression of Log_Fluid_Co on LogSerumCo:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.676[a]	.458	.390	.35245

a. Predictors: (Constant), Log_Fluid_Co
b. Dependent Variable: LogSerumCo

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.838	1	.838	6.747	.032[b]
	Residual	.994	8	.124		
	Total	1.832	9			

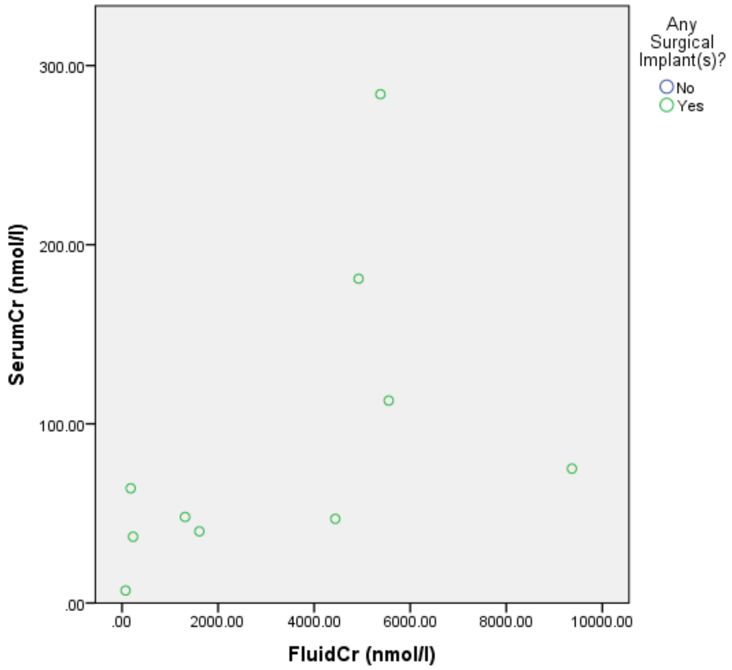
a. Dependent Variable: LogSerumCo
b. Predictors: (Constant), Log_Fluid_Co

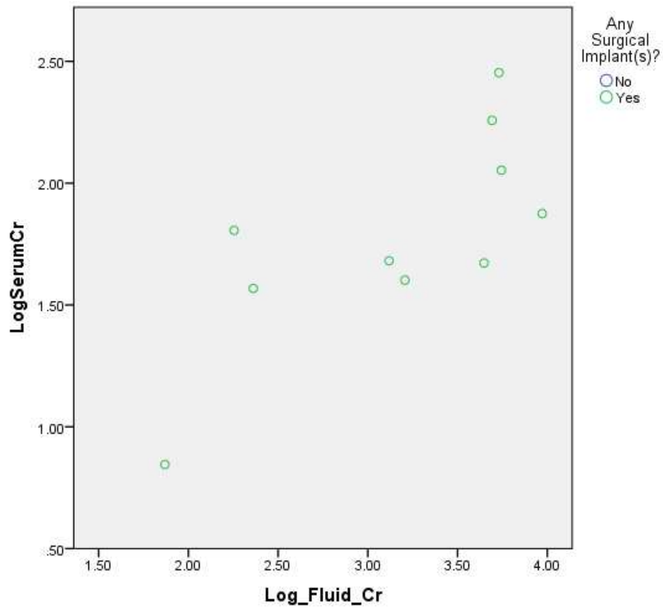
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.643	.412		1.563	.157
	Log_Fluid_Co	.334	.128	.676	2.597	.032

a. Dependent Variable: LogSerumCo

7. Relationship between Fluid Cr and Serum Cr





Regression of Log_Fluid_Cr on LogSerumCr:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.738[a]	.545	.488	.31429

a. Predictors: (Constant), Log_Fluid_Cr

b. Dependent Variable: LogSerumCr

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.948	1	.948	9.593	.015[b]
	Residual	.790	8	.099		
	Total	1.738	9			

a. Dependent Variable: LogSerumCr

b. Predictors: (Constant), Log_Fluid_Cr

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	.402	.456		.881	.404
	Log_Fluid_Cr	.437	.141	.738	3.097	.015

a. Dependent Variable: LogSerumCr

5. APPENDIX B - PROTOCOL OF POWER ANALYSIS PERFORMED ON GPOWER

This appendix contains a log of the protocol of all power analyses performed in relation to this project.
The protocol includes a priori, post hoc and sensitivity analyses.
All power analyses show at least 80% power at a significance level of 0.05.

[1] -- *Wednesday, September 04, 2013 -- 12:48:49* *Fluid Co -> Serum Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: A priori: Compute required sample size

Input:	Tail(s)	=	One
	Slope H1	=	0.3
	α err prob	=	0.05
	Power (1−β err prob)	=	0.8
	Slope H0	=	0
	Std dev σ_x	=	1
	Std dev σ_y	=	1
Output:	Noncentrality parameter δ	=	2.5158836
	Critical t	=	1.6698042
	Df	=	62
	Total sample size	=	64
	Actual power	=	0.8005036

[2] -- *Wednesday, September 04, 2013 -- 12:50:14* *Fluid Co -> Serum Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: A priori: Compute required sample size

Input:	Tail(s)	=	One
	Slope H1	=	0.3
	α err prob	=	0.05
	Power (1−β err prob)	=	0.8
	Slope H0	=	0
	Std dev σ_x	=	0.92
	Std dev σ_y	=	0.46
Output:	Noncentrality parameter δ	=	2.7041635
	Critical t	=	1.7958848
	Df	=	11
	Total sample size	=	13
	Actual power	=	0.8126118

[3] -- *Wednesday, September 04, 2013 -- 12:50:25 Fluid Co -> Serum Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: A priori: Compute required sample size

Input:	Tail(s)	=	One
	Slope H1	=	0.334
	α err prob	=	0.05
	Power (1–β err prob)	=	0.8
	Slope H0	=	0
	Std dev σ_x	=	0.92
	Std dev σ_y	=	0.46
Output:	Noncentrality parameter δ	=	2.8386340
	Critical t	=	1.8595480
	Df	=	8
	Total sample size	=	10
	Actual power	=	0.8270844

[4] -- *Wednesday, September 04, 2013 -- 12:51:35 Fluid Co -> Serum Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	One
	Slope H1	=	0.334
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.92
	Std dev σ_y	=	0.46
Output:	Noncentrality parameter δ	=	3.1095677
	Critical t	=	1.8124611
	Df	=	10
	Power (1–β err prob)	=	0.8933826

[5] -- *Wednesday, September 04, 2013 -- 12:52:03 Fluid Co -> Serum Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.334
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.92
	Std dev σ_y	=	0.46
Output:	Noncentrality parameter δ	=	3.1095677
	Critical t	=	2.2281389
	Df	=	10
	Power (1–β err prob)	=	0.7999000

[6] -- *Wednesday, September 04, 2013 -- 12:53:16 Fluid Cr -> Serum Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.437
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.808
	Std dev σ_y	=	0.496
Output:	Noncentrality parameter δ	=	3.5114204
	Critical t	=	2.2281389
	Df	=	10
	Power (1−β err prob)	=	0.8848118

[7] -- *Wednesday, September 04, 2013 -- 12:53:41 Fluid Cr -> Serum Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	One
	Slope H1	=	0.437
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.808
	Std dev σ_y	=	0.496
Output:	Noncentrality parameter δ	=	3.5114204
	Critical t	=	1.8124611
	Df	=	10
	Power (1−β err prob)	=	0.9469190

[8] -- *Wednesday, September 04, 2013 -- 12:54:04 Fluid Cr -> Serum Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Sensitivity: Compute required effect size

Input:	Tail(s)	=	One
	Effect direction	=	Slope > H0
	α err prob	=	0.05
	Power (1−β err prob)	=	0.8
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.808
	Std dev σ_y	=	0.496
Output:	Noncentrality parameter δ	=	2.6735847
	Critical t	=	1.8124611
	Df	=	10
	Slope H1	=	0.3750610

[9] -- Wednesday, September 04, 2013 -- 12:54:12 Fluid Cr -> Serum Cr

t tests – Linear bivariate regression: One group, size of slope

Analysis: Sensitivity: Compute required effect size

Input:	Tail(s)	=	Two
	Effect direction	=	Slope > H0
	α err prob	=	0.05
	Power (1–β err prob)	=	0.8
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.808
	Std dev σ_y	=	0.496
Output:	Noncentrality parameter δ	=	3.1099681
	Critical t	=	2.2281389
	Df	=	10
	Slope H1	=	0.4100886

[10] -- Wednesday, September 04, 2013 -- 12:54:46 Fluid Cr -> Serum Cr

t tests – Linear bivariate regression: One group, size of slope

Analysis: Sensitivity: Compute required effect size

Input:	Tail(s)	=	Two
	Effect direction	=	Slope > H0
	α err prob	=	0.05
	Power (1–β err prob)	=	0.8
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.93
	Std dev σ_y	=	0.46
Output:	Noncentrality parameter δ	=	3.1099681
	Critical t	=	2.2281389
	Df	=	10
	Slope H1	=	0.3304322

[11] -- Wednesday, September 04, 2013 -- 12:55:06 Fluid Cr -> Serum Cr

t tests – Linear bivariate regression: One group, size of slope

Analysis: Sensitivity: Compute required effect size

Input:	Tail(s)	=	Two
	Effect direction	=	Slope > H0
	α err prob	=	0.05
	Power (1–β err prob)	=	0.8
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.92993
	Std dev σ_y	=	0.46315
Output:	Noncentrality parameter δ	=	3.1099681
	Critical t	=	2.2281389
	Df	=	10
	Slope H1	=	0.3327199

[12] -- *Wednesday, September 04, 2013 -- 12:57:19* *Fluid Co -> Fluid Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Sensitivity: Compute required effect size

Input:	Tail(s)	=	Two
	Effect direction	=	Slope > H0
	α err prob	=	0.05
	Power (1−β err prob)	=	0.8
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.92993
	Std dev σ_y	=	0.80808
Output:	Noncentrality parameter δ	=	3.1099681
	Critical t	=	2.2281389
	Df	=	10
	Slope H1	=	0.5805124

[13] -- *Wednesday, September 04, 2013 -- 12:58:26* *Fluid Co -> Fluid Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.801
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.92993
	Std dev σ_y	=	0.80808
Output:	Noncentrality parameter δ	=	8.2359693
	Critical t	=	2.2281389
	Df	=	10
	Power (1−β err prob)	=	1.0000000

[14] -- *Wednesday, September 04, 2013 -- 13:00:07* *Serum Co -> CSF Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.334
	α err prob	=	0.05
	Total sample size	=	12
	Slope H0	=	0
	Std dev σ_x	=	0.46315
	Std dev σ_y	=	0.30582
Output:	Noncentrality parameter δ	=	2.0312618
	Critical t	=	2.2281389
	Df	=	10
	Power (1−β err prob)	=	0.4507149

[15] -- *Wednesday, September 04, 2013 -- 13:00:25 Serum Co -> CSF Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.334
	α err prob	=	0.05
	Total sample size	=	375
	Slope H0	=	0
	Std dev σ_x	=	0.46315
	Std dev σ_y	=	0.30582
Output:	Noncentrality parameter δ	=	11.3550989
	Critical t	=	1.9663443
	Df	=	373
	Power (1–β err prob)	=	1.0000000

[16] -- *Wednesday, September 04, 2013 -- 13:01:19 Serum Co -> Serum Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.760
	α err prob	=	0.05
	Total sample size	=	375
	Slope H0	=	0
	Std dev σ_x	=	0.46315
	Std dev σ_y	=	0.49617
Output:	Noncentrality parameter δ	=	19.4923630
	Critical t	=	1.9663443
	Df	=	373
	Power (1–β err prob)	=	1.0000000

[17] -- *Wednesday, September 04, 2013 -- 13:02:50 CSF Co -> CSF Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.284
	α err prob	=	0.05
	Total sample size	=	375
	Slope H0	=	0
	Std dev σ_x	=	0.30582
	Std dev σ_y	=	0.33892
Output:	Noncentrality parameter δ	=	5.1339633
	Critical t	=	1.9663443
	Df	=	373
	Power (1–β err prob)	=	0.9992132

[18] -- *Wednesday, September 04, 2013 -- 13:03:50* *Serum Co -> CSF Co*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.334
	α err prob	=	0.05
	Total sample size	=	375
	Slope H0	=	0
	Std dev σ_x	=	0.46315
	Std dev σ_y	=	0.30582
Output:	Noncentrality parameter δ	=	11.3550989
	Critical t	=	1.9663443
	Df	=	373
	Power (1–β err prob)	=	1.0000000

[19] -- *Wednesday, September 04, 2013 -- 13:04:40* *Serum Cr -> CSF Cr*

t tests – Linear bivariate regression: One group, size of slope

Analysis: Post hoc: Compute achieved power

Input:	Tail(s)	=	Two
	Slope H1	=	0.321
	α err prob	=	0.05
	Total sample size	=	375
	Slope H0	=	0
	Std dev σ_x	=	0.49617
	Std dev σ_y	=	0.33892
Output:	Noncentrality parameter δ	=	10.3095687
	Critical t	=	1.9663443
	Df	=	373
	Power (1–β err prob)	=	1.0000000