# ON ASSOCIATION BETWEEN SURGICAL HYPOTHERMIA AND SURGICAL SITE INFECTIONS

*A Project Report submitted to the*

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*in partial fulfillment of the requirements*

*of the Degree of*

**Master of Science**

*in*

**Mathematics with Data Science**

*by*

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## Supervisor's Certificate

This is to certify that the work presented in this project entitled "**ON ASSOCIATION BETWEEN SURGICAL HYPOTHERMIA AND SURGICAL SITE INFECTIONS**" by **Srimanta Ghosh**, University Roll Number: **E1773U233013**, is a record of original research/ review work carried out by him under my supervision and guidance in partial fulfillment of the requirements of the M.Sc. in Mathematics with Data Science. Neither this project nor any part of it has been submitted for any degree or diploma to any institute or university in India or abroad.

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Atanu Kumar Ghosh
(Supervisor's signature)

Dedicated to
Dr. Atanu Kumar Ghosh

# Declaration

I, **Srimanta Ghosh**, University Roll Number **E1773U233013**, hereby declare that this project entitled "**ON ASSOCIATION BETWEEN SURGICAL HYPOTHERMIA AND SURGICAL SITE INFECTIONS**" represents my original/review work carried out as an M.Sc. in Mathematics with Data Science student of IMA, Bhubaneswar and to the best of my knowledge, it is not a complete copy of previously published or written by another person, nor any material presented for award of any other degree or diploma of IMA, Bhubaneswar or any other institution. Any contribution made to this research by others, with whom I have worked at IMA, Bhubaneswar or elsewhere, is explicitly acknowledged in the dissertation. Works of other authors cited in this dissertation have been duly acknowledged under the section References.

Date: 09/12/2024

Srimanta Ghosh

(Student's signature)

# Acknowledgment

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Date: __09/12/2024___
**IMA, Bhubaneswar**

**Srimanta Ghosh**
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# Abstract

This study investigates the association between inadvertent perioperative hypothermia (IPH) and the risk of surgical site infections (SSIs) in patients undergoing colorectal surgery. During general anesthesia, the body's natural ability to regulate temperature is often compromised, leading to a reduction in metabolism and heat production, which can cause a significant drop in body temperature. When the core body temperature falls below 36°C (96.8°F), this condition is termed surgical hypothermia or IPH. Previous research suggests that IPH may reduce drug effectiveness, increase surgical bleeding, delay postoperative recovery, and heighten the risk of SSIs.

To explore the potential link between IPH and SSIs, this study analyzed data from 7,908 patients who underwent colorectal surgery between 2005 and 2014. Only patients whose surgeries lasted more than one hour and required general anesthesia, with monitored esophageal core temperature, were included. The study utilized an Effect Size logistic regression model to assess the impact of intraoperative core temperature on the occurrence of serious infections within 30 days post-surgery. Additionally, survival analysis was performed to evaluate the influence of average core temperature on the duration of hospital stay. The findings contribute to a better understanding of the role of IPH in postoperative complications and highlight the importance of temperature management during surgery.

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# 1 Introduction

During general anesthesia at the time of any surgery, the body's automatic mechanisms for maintaining body temperature is often disrupted and the metabolism is also reduced. As a result, the patient's body uses less energy and produces less heat which can lead to a significant drop in their body temperatures. When the body temperature drops below 36°C (96.8°F), we call it "surgical hypothermia" or "inadvertent perioperative hypothermia" (IPH). Some research suggested that IPH could reduce the effectiveness of drugs, increase surgical bleeding, delay recovery from surgery and increase the risk of surgical site infections(SSIs). Hence a new study was conducted to explore whether there is an association between IPH and SSIs in patients who had colorectal surgery.
The data file contains information of 7,908 patients who had colorectal surgery between 2005 and 2014. IN this study, only those patients were whose surgery took more than one hour and required general anesthesia, and if their esophogeal core temperature was monitored and sufficient baseline and outcome data was collected.

# 2 Data Description

The dataset[5] used in this study includes records from 7,908 patients who underwent colorectal surgery. The variables encompass a wide range of patient demographics, clinical history, intraoperative parameters, and postoperative outcomes.

## 2.1 Variables under study:

```
 [1] "YEAR"                  "Age"                   "FEMALE"
 [4] "BMI"                   "CharlsonScore"         "SurgeryType"
 [7] "CHF"                   "VALVE"                 "DM"
[10] "RENLFAIL"              "LIVER"                 "METS"
[13] "TUMOR"                 "COAG"                  "OBESE"
[16] "WGHTLOSS"              "LYTES"                 "BLDLOSS"
[19] "ANEMDEF"               "DRUG"                  "SteroidHx"
[22] "ImmunosuppressantHx"   "SurgDuration"          "Open"
[25] "AbsessIntraAb"         "AbsessPelvic"          "Cdiff"
[28] "FascialDehiscence"     "DelayedHealing"        "Infection"
[31] "Sinus"                 "Pneumonia"             "Pneumonia.aspiration."
[34] "Sepsis"                "SSIDeep.fascia."       "SSIOrganSpace"
[37] "SSISuperficial.skin."  "WoundInfection"        "TWATemp"
[40] "LastReadingTemp"       "EndCaseTemp"           "AnyInfection"
[43] "SeriousInfection"      "SuperficialInfection"  "DurationHosp"
[46] "LOS"                   "DEAD"
```

**Demographics and Clinical History:**

- YEAR: Year of surgery.
- Age: Patient's age at the time of the surgery
- FEMALE: Patient's sex at birth (1=female,0=male)
- BMI: Patient's body mass index (BMI) at time of surgery
- CharlsonScore: Patient's Charlson Comorbidity Index score (higher numbers indicate more comorbidities that could lead to death)
- CHF: Does the patient have a history of congestive heart failure? (1=yes,0=no)

- VALVE: Does the patient have a history of peripheral vascular disease? (1=yes,0=no)
- DM: Does the patient have a history of diabetes without chronic complications? (1=yes,0=no)
- RENLFAIL: Does the patient have a history of renal failure? (1=yes,0=no)
- LIVER: Does the patient have a history of liver disease? (1=yes,0=no)
- METS: Does the patient have cancer that has metastasized? (1=yes,0=no)
- TUMOR: Does the patient have a solid tumor that has not metastasized? (1=yes,0=no)
- COAG: Does the patient have coagulopathy (a blood clotting disorder)? (1=yes,0=no)
- WGHTLOSS: Has the patient lost weight? (Time period and amount not specified;1=yes,0=no)
- LYTES: Does the patient have fluid or electrolyte disorders? (1=yes,0=no)
- BLDLOSS: Does the patient have chronic blood loss anemia? (1=yes,0=no)
- ANEMDEF: Does the patient have a deficiency anemia? (1=yes,0=no)
- DRUG: Does the patient abuse drugs? (1=yes,0=no)

**Surgical Details:**

- SurgeryType: This was meant to record the type of surgery (such as colostomy, ileostomy, or other procedures), but is missing for all patients
- SteroidHx: Did the patient use steroid drugs before surgery? (1=yes,0=no)
- ImmunosuppressantHx: Did the patient use immunosuppressive drugs before surgery? (1=yes,0=no)
- SurgDuration: Duration of the surgery, in minutes
- Open: Type of surgery. 1=open surgery,0=laparoscopic ("minimally invasive") surgery.

**Postoperative Records:**

- AbsessIntraAb: Did the patient have an intra-abdominal abscess (caused by infection) after the surgery? (1=yes,0=no)
- AbsessPelvic: Did the patient have a pelvic abscess (caused by infection) after the surgery? (1=yes,0=no)
- Cdiff: Did the patient have a Clostridium difficile infection after the surgery? (1=yes,0=no)
- FascialDehiscence: Did the patient suffer fascial dehiscence after surgery? This occurs when the fascia, which surround the organs in the abdomen and holds them in place, fails to heal after surgery and splits open. (1=yes,0=no)
- DelayedHealing: Was the patient's healing after surgery delayed? (1=yes,0=no)
- Infection: Did the patient have a post-surgical infection that doesn't fit into the other categories? (1=yes,0=no)
- Sinus: Did the patient develop an abdominal sinus after surgery? (1=yes,0=no)
- SSIDeep(fascia): Did the patient develop a surgical site infection deep in the fascia surrounding the organs? (1=yes,0=no)
- SSIOrganSpace: Did the patient develop a surgical site infection in the space surrounding the organs? (1=yes,0=no)

- SSISuperficial(skin): Did the patient develop a superficial surgical site infection in the skin around the incision? (1=yes,0=no)
- WoundInfection: Did the patient develop an infection in the wound created in surgery? (1=yes,0=no)
- TWATemp: Time weighted average of the patient's core temperature during surgery, °C
- LastReadingTemp: Last recorded core temperature prior to surgery, °C
- EndCaseTemp: Patient's core temperature at the end of surgery, °C
- AnyInfection: Did the patient develop any kind of infection, serious or superficial, within 30 days of surgery? (1=yes,0=no)
- SeriousInfection: Did the patient develop a serious infection within 30 days of surgery? This includes the infections in the SSIDeep(fascia), SSIOrganSpace, AbsessIntraAb, AbsessPelvic, Cdiff, Pneumonia, Pneumonia(aspiration), and Sepsis variables. (1=yes,0=no)
- SuperficialInfection: Did the patient develop a superficial infection within 30 days of surgery? This includes the infections in the SSISuperficial(skin), WoundInfection, and FascialDehiscence variables, as well as perineal wound problems. (1=yes,0=no)
- DurationHosp: Time the patient stayed in the hospital after surgery, in days
- LOS: Time the patient stayed in the hospital, including time before surgery, in days
- DEAD: Did the patient die in the hospital? (1=yes,0=no)

# 3 Plan of Analysis

This study is observational, as it does not involve any manipulation or intervention by the researchers. The data were collected from medical records and represent real-world clinical practices. Observational studies, while useful for identifying associations, have limitations in establishing causality due to potential biases.

**In this analysis I have tried to answer two questions.**

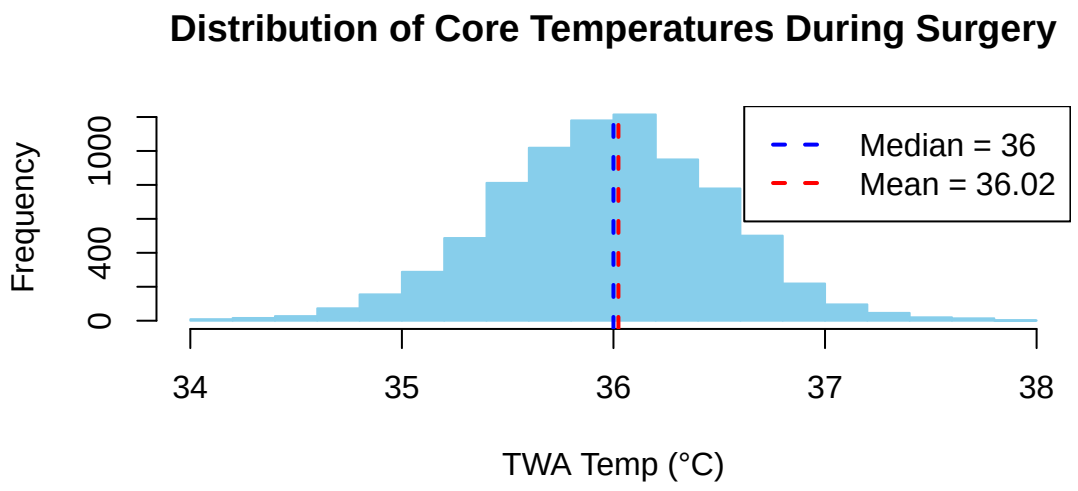
- What is the effect of Average core temperature of a patient during surgery on Serious Infection a patient has developed within 30 days of surgery?
- What is the hazard of a patient discharge alive from hospital after surgery and how it is affected by Average core temperature of the patient during surgery?

To answer the first question I have used Logistic Regression Analysis[1, 4] and for the second question I have used Survival Analysis[3, 2]. Before answering the questions let's start with some exploratory statistical analysis.

## 3.1 Exploratory Data Analysis

**Distribution of Core Temperatures (TWATemp):**

To understand the range and central tendency of core temperatures during surgery, I plotted the histogram of TWATemp along with the mean and the median core temperature.




**Results:**

From this plot we can see that The distribution of TWATemp is approximately normal, with a slight skew towards lower temperatures. The median TWATemp is 36°C.

**Group Comparisons**

- To investigate the impact of core temperature on Serious infection rate, I divided patients into two groups: those with TWATemp above the median and those below then compared proportion of Serious infections between these groups.

```
Above Median Below Median
  0.09031754   0.08042302
```

**Result:**

The Low Temperature Group (below median TWATemp) had a little lower proportion of serious infection compared to the High Temperature Group (above median TWATemp).

- Then, I have tested whether there is any significant difference in proportion of serious infection between two temperature group.

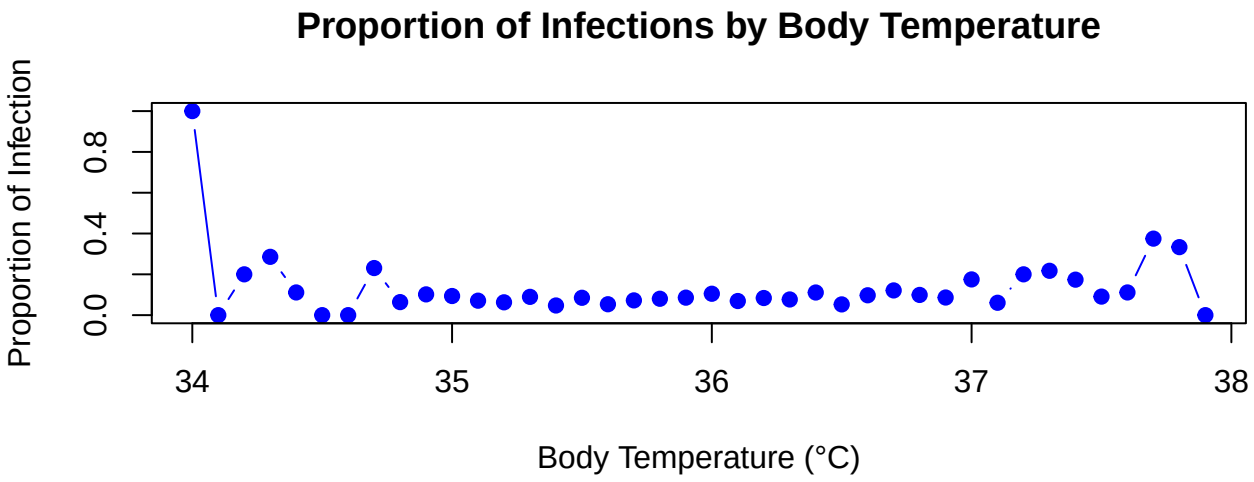
```
 Pearson's Chi-squared test with Yates' continuity correction

data:  table_infections
X-squared = 2.3552, df = 1, p-value = 0.1249
```

**Result:**

P-value = 0.1249 indicates there is no significant difference in proportion of serious infection when compared to this two different temperature groups.

**Plot**

Then, I have plotted proportion of serious infection for each temperature reading present in the dataset.




**Result:**

From this plot we can see that below 35°C and above 37°C there are some fluctuations in proportions of serious infections which indicate increased risk of getting serious infections for those temperature ranges.

**Now I address the first question, i.e.,**

- What is the effect of Average core temperature of a patient during surgery on Serious Infections a patient has developed within 30 days of surgery?

To answer this question I have built Effect Size Logistic Regression Models for different core temperature ranges and observed how Average core temperature affects Serious Infections for different temperature ranges. Before, going forward let's give a small idea about an Effect Size Regression Model.

The idea of an effect size model is, here, we see the effect of some exposure on some outcome.

$$Y = b_0 + b_1 X_1$$

Here, the coefficient $b_1$ captures the effect of exposure $X_1$ on the outcome $Y$. As, our study is observational is nature, we can write $b_1$ as,

$$b_1 = \beta_1 + \delta + \epsilon$$

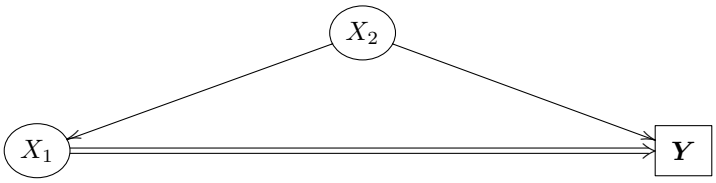
Here, $\beta_1$ is the true effect of $X_1$ on $Y$, $\delta$ is bias due to confounding, mediation, collinearity etc. and $\epsilon$ is the random error with $E(\epsilon) = 0$.

In observational studies while building an Effect Size model, we will inherently always have this bias $\delta$ due to confounding, mediation etc. So, we try to reduce it as much as possible.

Before moving forward let's give an brief idea about confounding and mediation.

**Confounding**

Confounding occurs when the Effect of our Variable of Interest ($X_1$) is mixed together with another variable ($X_2$).




***CONFOUNDING***

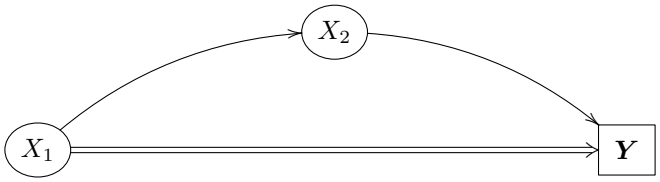
If $X_2$ is a potential confounder then it will satisfy the following criteria.

- $X_1$ is associated with $X_2$ but the direction of association is $X_2 \rightarrow X_1$, not the reverse.
- $X_2$ is associated with the outcome $Y$.
- $X_2$ is not in the pathway of $X_1 \rightarrow Y$.
- When we adjust for $X_2$, i.e., adding it or removing it from the model, $b_1$ changes a decent amount.

So, if $X_2$ is identifies as a confounder, we include it to the model to reduce the bias due to confounding.

**Mediation**

The idea of mediation is similar to confounding, only the difference is the nature of the association between $X_1$ and $X_2$. It occurs when some of the effect of our variable of interest $X_1$ goes through $X_2$.




***MEDIATION***

If $X_2$ is a potential mediator then it will satisfy the following criteria.

- $X_2$ is associated with $Y$.
- $X_1 \rightarrow X_2$ , There is an association between $X_1$ and $X_2$ with $X_2$ on the pathway $X_1 \rightarrow Y$.
- When $X_1$ is added to the model $b_1$ changes a decent amount.

So, if $X_2$ identifies as a mediator, we exclude it from the model as it absorbs some effects of $X_1$ (Variable of Interest) on $Y$ (Outcome).
Now, let's start with building Effecting Size Logistic Regression Models as here our outcome $Y$ is Binary.

### 3.2 Logistic Regression Analysis

Before Fitting I first dropped some columns containing Postoperative Records as they do not effect TWATemp (Variable under study) but can work as a mediator from the dataset and also so irrilavent columns like YEAR etc.

```
 [1] "Age"                 "FEMALE"              "BMI"
 [4] "CharlsonScore"       "CHF"                 "VALVE"
 [7] "DM"                  "RENLFAIL"            "LIVER"
[10] "METS"                "TUMOR"               "COAG"
[13] "OBESE"               "WGHTLOSS"            "LYTES"
[16] "BLDLOSS"             "ANEMDEF"             "DRUG"
[19] "SteroidHx"           "ImmunosuppressantHx" "SurgDuration"
[22] "Open"                "TWATemp"             "SeriousInfection"
[25] "SuperficialInfection" "DurationHosp"       "DEAD"
```

These are the columns I have used for the rest of my analysis. Now, Let's look at the summary these columns.

```
      Age          FEMALE        BMI         CharlsonScore    CHF      VALVE
 Min.   : 20.10   0:3906   Min.   : 0.60   Min.   : 0.000   0:7634   0:7462
 1st Qu.: 42.90   1:4002   1st Qu.:22.27   1st Qu.: 0.000   1: 274   1: 446
 Median : 56.20            Median :25.70   Median : 1.000
 Mean   : 55.74            Mean   :26.58   Mean   : 1.439
 3rd Qu.: 68.40            3rd Qu.:29.70   3rd Qu.: 2.000
 Max.   :105.40            Max.   :82.40   Max.   :13.000
 DM       RENLFAIL LIVER    METS     TUMOR    COAG     OBESE    WGHTLOSS
 0:7015   0:7565   0:7698   0:7379   0:6371   0:7331   0:6589   0:5813
 1: 893   1: 343   1: 210   1: 529   1:1537   1: 577   1:1319   1:2095




 LYTES    BLDLOSS  ANEMDEF  DRUG     SteroidHx ImmunosuppressantHx
 0:4705   0:7724   0:6083   0:7750   0:5173    0:7660
 1:3203   1: 184   1:1825   1: 158   1:2735    1: 248




  SurgDuration Open        TWATemp      SeriousInfection SuperficialInfection
 Min.   : 73   0:1404   Min.   :34.00   0:7234           0:7268
 1st Qu.:135   1:6504   1st Qu.:35.70   1: 674           1: 640
 Median :195            Median :36.00
 Mean   :214            Mean   :36.02
 3rd Qu.:269            3rd Qu.:36.40
 Max.   :850            Max.   :37.90
  DurationHosp     DEAD
 Min.   :  1.000   0:7874
 1st Qu.:  5.000   1:  34
 Median :  6.000
 Mean   :  8.145
 3rd Qu.:  9.000
 Max.   :144.000
```

This is the summary of the numerical and categorical variables I used for my analysis.

Now, I have fitted a Logistic regression model for SeriousInfection against TWATemp to see to rough estimated effect of core temperature on serious infections developed within 30 days of surgery.

$$\ln(\frac{p}{1-p}) = \beta_0 + \beta_1 * TWATemp$$

```
Call:
glm(formula = SeriousInfection ~ TWATemp, family = binomial,
    data = working_data)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -11.1532     2.7676  -4.030 5.58e-05 ***
TWATemp       0.2435     0.0767   3.175   0.0015 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 4608.2  on 7907  degrees of freedom
Residual deviance: 4598.0  on 7906  degrees of freedom
AIC: 4602

Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- The coefficient of the intercept $= -11.1532$ means, The log-odds of SeriousInfection when TWATemp equals to 0 is $-11.1532$.
- The coefficient of TWATemp $= 0.2435$ means, every 1°C increase in core temperature, the log-odds of SeriousInfection increases by 0.2435. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5 * 0.2435) \approx 1.13$ times the odds of those with temperature 0.5°C lower.

This means odds of serious infection increases with increase in core temperature. But, we have already seen that, proportion of serious infection increases also with decrease in serious temperature below 35°C. So, we broke the temperature into 4 categories and fit the model.

```
Call:
glm(formula = SeriousInfection ~ tempCAT, family = binomial,
    data = working_data)

Coefficients:
                  Estimate Std. Error z value Pr(>|z|)
(Intercept)        -2.1041     0.2368  -8.884   <2e-16 ***
tempCAT(35,36]     -0.4199     0.2461  -1.706   0.0879 .
tempCAT(36,36.9]   -0.2281     0.2430  -0.939   0.3479
tempCAT(36.9,37.9]  0.4085     0.2927   1.396   0.1628
---
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 4608.2  on 7907  degrees of freedom
Residual deviance: 4587.8  on 7904  degrees of freedom
AIC: 4595.8

Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- Here the reference category is $\leq 35°C$.
- For those patient whose core temperature during surgery was $(35°C, 36°C]$ have odds of getting serious infections $\exp(-0.4199) \approx 0.657$ times those whose core temperature during surgery was $\leq 35°C$.
- For those patient whose core temperature during surgery was $(36°C, 37°C]$ have odds of getting serious infections $\exp(-0.2281) \approx 0.796$ times those whose core temperature during surgery was $\leq 35°C$.
- For those patient whose core temperature during surgery was $(37°C, 38°C]$ have odds of getting serious infections $\exp(0.4085) \approx 1.5$ times those whose core temperature during surgery was $\leq 35°C$.

Then, we stratify the dataset into equal 4 parts according to quantiles of TWATemp,

```
 25%  50%  75%
35.7 36.0 36.4
```

and, fit models for each temperature ranges.
For, temperature $\leq 35.7°C$ the summary of the fit,

```
Call:
glm(formula = SeriousInfection ~ TWATemp, family = binomial,
    data = data1)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  16.1954     9.0116   1.797   0.0723 .
TWATemp      -0.5296     0.2548  -2.079   0.0377 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1218.6  on 2337  degrees of freedom
Residual deviance: 1214.5  on 2336  degrees of freedom
AIC: 1218.5

Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- The coefficient of TWATemp $= -0.5296$ means, every 1°C increase in core temperature, the log-odds of SeriousInfection decreases by -0.5296. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5 * (-0.5296)) \approx 0.767$ times the odds of those with temperature 0.5°C lower.

For, temperature $(35.7°C, 36°C]$ the summary of the fit,

```
Call:
glm(formula = SeriousInfection ~ TWATemp, family = binomial,
    data = data2)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  -56.641     36.932  -1.534    0.125
TWATemp        1.513      1.028   1.471    0.141

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1052.4  on 1727  degrees of freedom
Residual deviance: 1050.2  on 1726  degrees of freedom
AIC: 1054.2

Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- The coefficient of TWATemp $= 1.513$ means, every 1°C increase in core temperature, the log-odds of SeriousInfection increases by 1.513. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5 * (1.513)) \approx 2.13$ times the odds of those with temperature 0.5°C lower. But,

For, temperature $(36°C, 36.4°C]$ the summary of the fit,

```
Call:
glm(formula = SeriousInfection ~ TWATemp, family = binomial,
    data = data3)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -55.5050    25.5828  -2.170   0.0300 *
TWATemp       1.4654     0.7057   2.076   0.0379 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1244.8  on 2164  degrees of freedom
Residual deviance: 1240.5  on 2163  degrees of freedom
AIC: 1244.5
```

```
Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- The coefficient of TWATemp = 1.4654 means, every 1°C increase in core temperature, the log-odds of SeriousInfection increases by 1.4654. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5*(1.4654)) \approx 2.08$ times the odds of those with temperature 0.5°C lower.

For, temperature $\geq 36.4°C$ the summary of the fit,

```
Call:
glm(formula = SeriousInfection ~ TWATemp, family = binomial,
    data = data4)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -43.3871    10.4401  -4.156 3.24e-05 ***
TWATemp       1.1200     0.2837   3.948 7.89e-05 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1082.8  on 1676  degrees of freedom
Residual deviance: 1068.6  on 1675  degrees of freedom
AIC: 1072.6

Number of Fisher Scoring iterations: 5
```

**Interpretation:**

- The coefficient of TWATemp = 1.12 means, every 1°C increase in core temperature, the log-odds of SeriousInfection increases by 1.12. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5 * (1.12)) \approx 1.75$ times the odds of those with temperature 0.5°C lower.

As My study was for below 36°C, for further study, I chose the dataset for where core temperature $\leq 35.7°C$. I neglected the dataset where core temperature is $(35.7°C, 36°C]$, in that temperature range the effect of TWATemp is insignificant as the p-value was 0.141.

Now, For further analysis, to estimate the effect size of TWATemp on SeriousInfection, we used that following variables,

```
 [1] "Age"                 "FEMALE"              "BMI"
 [4] "CharlsonScore"       "CHF"                 "VALVE"
 [7] "DM"                  "RENLFAIL"            "LIVER"
[10] "METS"                "TUMOR"               "COAG"
[13] "OBESE"               "WGHTLOSS"            "LYTES"
[16] "BLDLOSS"             "ANEMDEF"             "DRUG"
[19] "SteroidHx"           "ImmunosuppressantHx" "SurgDuration"
[22] "Open"                "TWATemp"             "SeriousInfection"
```

fitted the full model with all covariates to see how it affects the effect of TWATemp on SeriousInfection,

$$\ln(\frac{p}{1-p}) = \beta_0 + \beta_1 * TWATemp + \sum_{j=2}^{m} \beta_j * Covariate_j$$

```
Call:
glm(formula = SeriousInfection ~ ., family = binomial, data = serious_data)

Coefficients:
                      Estimate Std. Error z value Pr(>|z|)
(Intercept)          12.7792801  9.4221901   1.356   0.1750
Age                  -0.0117949  0.0056841  -2.075   0.0380 *
FEMALE1              -0.0360489  0.1705755  -0.211   0.8326
BMI                  -0.0002321  0.0193224  -0.012   0.9904
CharlsonScore         0.0950233  0.1078551   0.881   0.3783
CHF1                  0.4918415  0.3896890   1.262   0.2069
VALVE1               -0.0985408  0.3456409  -0.285   0.7756
DM1                  -0.2195701  0.3031846  -0.724   0.4689
RENLFAIL1             0.4558901  0.3967962   1.149   0.2506
LIVER1                0.2848183  0.4574274   0.623   0.5335
METS1                -0.4591557  0.7215801  -0.636   0.5246
TUMOR1               -0.0470297  0.3096973  -0.152   0.8793
COAG1                 0.1056403  0.2684016   0.394   0.6939
OBESE1               -0.3008375  0.3243246  -0.928   0.3536
WGHTLOSS1             0.9871403  0.1897595   5.202 1.97e-07 ***
LYTES1                0.4117712  0.1914034   2.151   0.0315 *
BLDLOSS1              0.1533578  0.4119933   0.372   0.7097
ANEMDEF1             -0.0617651  0.1968311  -0.314   0.7537
DRUG1                 0.3275191  0.4810462   0.681   0.4960
SteroidHx1            0.0423382  0.1805780   0.234   0.8146
ImmunosuppressantHx1 -0.1879434  0.4653757  -0.404   0.6863
SurgDuration          0.0039229  0.0008315   4.718 2.38e-06 ***
Open1                -0.0299577  0.2392580  -0.125   0.9004
TWATemp              -0.4559901  0.2667094  -1.710   0.0873 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1218.6  on 2337  degrees of freedom
Residual deviance: 1111.2  on 2314  degrees of freedom
AIC: 1159.2

Number of Fisher Scoring iterations: 6
```

**Interpretation:**

- The coefficient of TWATemp $= -0.4559901$ means, every 1°C increase in core temperature, the log-odds of SeriousInfection decreases by -0.4559901 adjusting for the confounders. So, if we convert it to exponential scale, for every 0.5°C increase in core temperature the odds of serious infection is $\exp(0.5 * (-0.4559901)) \approx 0.796$ times the odds of those with temperature 0.5°C lower adjusting for the confounders.

So, We observe here, after adding all the potential confounders to the model, the odds increased from 0.767 to 0.796 times for each temperature decrease by 0.5°C. Now, let's see if the fitted model possess multicollinearity that might influence the effect of TWATemp on SeriousInfection. To see that, I calculated VIF (Variance Inflation Factor) of the full model. If, VIF score of any of the variable under study $> 5$, then we conclude that the variable causing multicollinearity.

```
               Age             FEMALE                BMI       CharlsonScore
          1.477056           1.073829           1.801997           10.012472
               CHF              VALVE                 DM            RENLFAIL
          1.509822           1.413105           1.463457            2.010445
             LIVER              METS              TUMOR                COAG
          1.274591           5.122722           2.506887            1.176844
             OBESE           WGHTLOSS              LYTES             BLDLOSS
          1.625029           1.331952           1.323788            1.045372
           ANEMDEF              DRUG          SteroidHx ImmunosuppressantHx
          1.150398           1.130679           1.068319            1.079970
      SurgDuration               Open            TWATemp
          1.065785           1.068543           1.042465
```

for CharlsonScore and METS column we see that the VIF score $> 5$. So, We modified the model by removing them. Summary of the modified model,

```
Call:
glm(formula = SeriousInfection ~ . - CharlsonScore - METS, family = binomial,
    data = serious_data)

Coefficients:
                     Estimate Std. Error z value Pr(>|z|)
(Intercept)          12.7084124  9.4015626   1.352   0.1765
Age                  -0.0109877  0.0055812  -1.969   0.0490 *
FEMALE1              -0.0369153  0.1704080  -0.217   0.8285
BMI                   0.0003303  0.0193058   0.017   0.9864
CHF1                  0.6391684  0.3529113   1.811   0.0701 .
VALVE1                0.0234690  0.3127766   0.075   0.9402
DM1                  -0.0992060  0.2710073  -0.366   0.7143
RENLFAIL1             0.6701809  0.3170414   2.114   0.0345 *
LIVER1                0.4310120  0.4214054   1.023   0.3064
TUMOR1                0.1318759  0.2126108   0.620   0.5351
COAG1                 0.1227925  0.2672244   0.460   0.6459
OBESE1               -0.2977131  0.3241143  -0.919   0.3583
WGHTLOSS1             0.9900322  0.1896189   5.221 1.78e-07 ***
LYTES1                0.4260122  0.1906416   2.235   0.0254 *
BLDLOSS1              0.1533613  0.4111747   0.373   0.7092
ANEMDEF1             -0.0452425  0.1955056  -0.231   0.8170
DRUG1                 0.4054220  0.4668307   0.868   0.3851
SteroidHx1            0.0477415  0.1802390   0.265   0.7911
ImmunosuppressantHx1 -0.1921225  0.4632491  -0.415   0.6783
SurgDuration          0.0039256  0.0008279   4.741 2.12e-06 ***
Open1                -0.0288587  0.2389971  -0.121   0.9039
TWATemp              -0.4552271  0.2661177  -1.711   0.0872 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1218.6  on 2337  degrees of freedom
Residual deviance: 1112.0  on 2316  degrees of freedom
AIC: 1156

Number of Fisher Scoring iterations: 6
```

here, we see that there is a negligible amount of chance in coefficient of TWATemp.
Then, we did subset selection to remove some insignificant features from the model.

```
library(MASS)
Reduced_model_serious <- stepAIC(model_modified, direction = 'both')
```

The summary of the reduced model after model selection,

```
Call:
glm(formula = SeriousInfection ~ Age + CHF + RENLFAIL + WGHTLOSS +
    LYTES + SurgDuration + TWATemp, family = binomial, data = serious_data)

Coefficients:
               Estimate Std. Error z value Pr(>|z|)
(Intercept)  12.9338461  9.2671561   1.396   0.1628
Age          -0.0109821  0.0050325  -2.182   0.0291 *
CHF1          0.6595997  0.3368270   1.958   0.0502 .
RENLFAIL1     0.6470588  0.2985708   2.167   0.0302 *
WGHTLOSS1     1.0199932  0.1803948   5.654 1.57e-08 ***
LYTES1        0.4349584  0.1846144   2.356   0.0185 *
SurgDuration  0.0039080  0.0008081   4.836 1.32e-06 ***
TWATemp      -0.4622484  0.2611208  -1.770   0.0767 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 1218.6  on 2337  degrees of freedom
Residual deviance: 1116.3  on 2330  degrees of freedom
AIC: 1132.3

Number of Fisher Scoring iterations: 6
```

**Interpretation:**

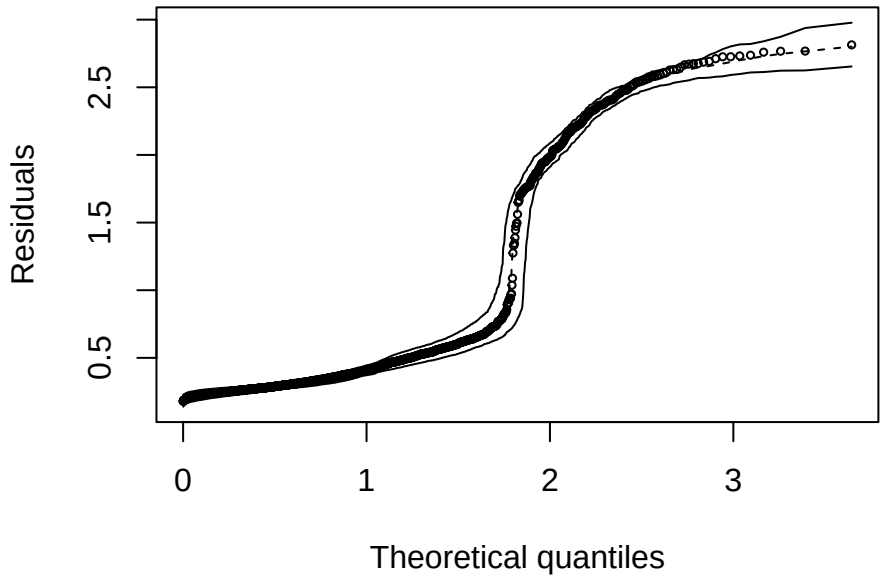
- Coefficient of The intercept term is 12.9338461, suggesting log-odds of SeriousInfection is 12.9338461 when all predictors are zero.
- The coefficient for Age is -0.0109821 with a p-value of 0.0291, indicating that for each additional year of age, the log-odds of a serious infection decrease by 0.0109821 adjusting for others variables.
- The coefficient CHF is 0.659597, indicating that a patient having CHF (history of congestive heart failure) have odds of getting SeriousInfection $\exp(0.659597) \approx 1.934013$ times the odds of Serious Infection for a patient who do not have CHF adjusting, for other factors.

- The coefficient of RENLFAIL is 0.6470588, indicating that a patient having RENLFAIL (history of renal failure) have odds of getting SeriousInfection exp(0.6470588) ≈ 1.91 times the odds of Serious Infection for a patient who do not have RENLFAIL, adjusting for other factors.
- With a coefficient of WGHTLOSS is 1.0199932, indicating that a patient having WGHTLOSS (history of weight loss) have odds of getting SeriousInfection exp(0.6470588) ≈ 1.91 times the odds of Serious Infection for a patient who do not have WGHTLOSS, adjusting for other factors.
- The coefficient of LYTES is 0.4349584, indicating that a patient having LYTES (fluid or electrolyte disorders) have odds of getting SeriousInfection exp(0.4349584) ≈ 1.545 times the odds of Serious Infection for a patient who do not have LYTES, adjusting for other factors.
- The coefficient of SurgDuration is 0.0039080, meaning that each additional minute of surgery increases the odds of a serious infection exp(0.0039080) ≈ 1.004 times the odds of 1 minute less surgery duration.
- The coefficient of TWATemp is -0.4622484, suggesting that 1°C of increase in core temperature decrease the odds of a serious infection exp(−0.4622484) ≈ 0.6298659 times the odds of getting Serious Infection for 1°C less core temperature during surgery.

**Half Normal Residual Plot:**

Half Normal Residual plot with an envelope is a diagnostic tool used to assess the goodness of fit for a generalized linear model (GLM). Points that lie within the envelope suggest that the model fits the data well for those observations. If most of the residuals fall within the envelope, it suggests that the model is appropriate.

```
Binomial model
```




In this plot, most of the points lie close to or within the envelope, suggesting the model fitted well.

**From this final model we can conclude that, IPH is a Potential Risk Factor of getting Serious Surgical Side Infections.**

**Now, We address the 2nd question, i.e.,**

- What is the hazard of a patient discharge alive from hospital after surgery and how it is affected by Average core temperature of the patient during surgery?

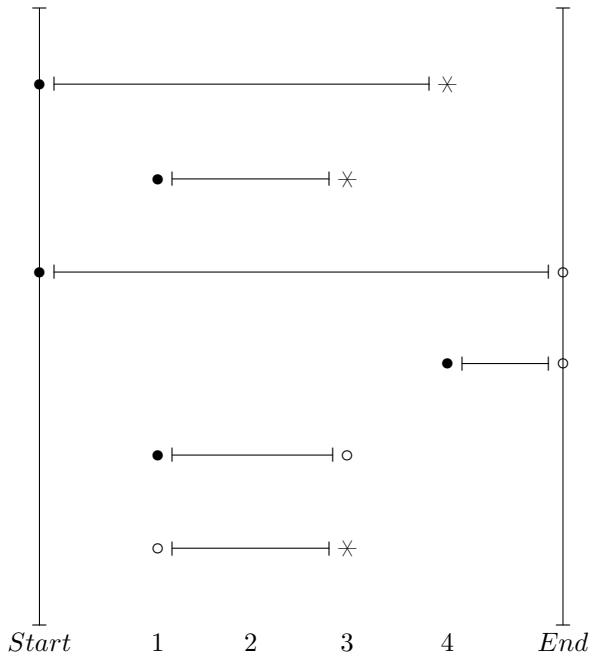
To attack this problem I have used Survival Analysis. Before moving forward to analysis let's give a brief introduction to survival analysis.

## 3.3 Survival Analysis

In Survival analysis, we consider a unique kind of outcome variable: the time until an event occurs.

For example, in my 144-day medical study, suppose I would like to fit a model to predict the time taken for a patient to be discharged from the hospital alive after surgery, using features such as baseline health measurements and postoperative details. At first pass, this may sound like a regression problem.

**So, why care?** Because, there is an important complication: hopefully some or many of the patients have stayed in the hospital until the end of the study. We know that it is at least 144 days, but we do not know its true value. Also some patients died in the hospital during this 144 days study, So we don't know if they wouldn't have died, what was the true value of their discharge. Such a patient's survival time is said to be censored: We do not want to discard this subset of surviving patients, as the fact that some survived at least 144 days and also some died amounts to valuable information.




**So, how to attack the problem?** For each individual, we suppose that there is a true survival time ( true time taken to be discharged from the hospital alive after surgery), T, as well as a true censoring time, C. The survival time represents the time at which the event of interest occurs: for instance, time taken to be discharged from the hospital alive after surgery. By contrast, the censoring time is the time at which censoring occurs: for

this study, the time at which the patient died or the study ends. We observe either the survival time T or else the censoring time C. Specifically, we observe the random variable

$$Y = min(T, C)$$

In other words, if the event occurs before censoring (i.e. $T < C$) then we observe the true survival time T; however, if censoring occurs before the event ($T > C$) then we observe the censoring time. We also observe a status indicator,

$$\delta = \begin{cases} 1 & if\ T \leq C \\ 0 & if\ T > C \end{cases}$$

Thus, $\delta = 1$ if we observe the true survival time, and $\delta = 0$ if we instead observe the censoring time.

So, We observe this $(Y, \delta)$ pairs, and model the data according to it.

Before, moving forward to the analysis, let's give a brief idea about the Things Of Interest, that I will be working with, throughout the study.

- Survival Function: Probability of survival beyond time $t$.

$$S(t) = P(T > t)$$

- Hazard (HAZ): Probability of occurrence of Event (left alive) in next few seconds given Event haven't occurred yet.

$$HAZ = P(T < t + \Delta | T > t)$$

- Hazard Ratio (HR): Relative HAZ,

$$\frac{HAZ_{,X=1}}{HAZ_{,X=0}}$$

  $HR = 2$, means at a given instance of time, someone who is exposed to $X$ has risk of occurrence of Event (leaving hospital alive) is 2 times with respect to someone who is not exposed to $X$.

Now, let's consider the task of estimating the survival curve. To estimate $S(t) = Pr(T > t)$, the probability that a patient stayed at hospital for at least t days, it is tempting to simply compute the proportion of patients who are known to have stayed past t days, i.e. the proportion of patients for whom $Y > t$.

However, this does not seem quite right, since $Y$ and $T$ represent different quantities. So, to estimate survival curve we use

**Kaplan-Meier Estimator,**

$$\widehat{S}(d_k) = \prod_{j=1}^{k} (\frac{r_j - q_j}{r_j})$$

- $d_1 < d_2 < .... < d_K$ are K unique leaving hospital alive time among the non censored patients,
- $q_k$ denote the number of patients who left alive at time $d_k$.
- For $k = 1, 2, ..., K$, $r_k$ denote the number of patients are in hospital and in the study just before $d_k$; these are the at risk patients.

For times $t$ between $d_k$ and $d_{k+1}$, we set $\widehat{S}(t) = \widehat{S}(d_k)$.

So, To estimate the Survival Function I fitted the K-M Survival Model on DurationHosp (the length of hospital stay) with the patients who died before hospital discharge were considered as never having the event(censored).

```
Call: survfit(formula = surv_object ~ 1, data = working_data, type = "kaplan-meier")

        n events median 0.95LCL 0.95UCL
[1,] 7908   7874      6       6       7
```

**Results:**

- Total no. of individuals is $n = 7908$.
- Total no. of Events (patients discharged alive) = 7874. Rest are censored(died in the hospital).
- Median Survival Time = 6, i.e., half the people stayed beyond 6 days after surgery.
- We are 95% confident that median survival is somewhere between 6 and 7.

Now, Let's look at the model summary

```
Call: survfit(formula = surv_object ~ 1, data = working_data, type = "kaplan-meier")

 time n.risk n.event survival  std.err lower 95% CI upper 95% CI
    1   7908      23 0.997092 0.000606     9.96e-01      0.99828
    2   7885     117 0.982296 0.001483     9.79e-01      0.98521
    3   7762     459 0.924209 0.002977     9.18e-01      0.93006
    4   7302    1166 0.776629 0.004686     7.67e-01      0.78587
    5   6133    1166 0.628977 0.005435     6.18e-01      0.63972
    6   4965    1043 0.496848 0.005626     4.86e-01      0.50800
    7   3920     840 0.390380 0.005491     3.80e-01      0.40129
    8   3077     706 0.300810 0.005163     2.91e-01      0.31110
    9   2370     492 0.238363 0.004798     2.29e-01      0.24795
   10   1878     337 0.195590 0.004467     1.87e-01      0.20454
   11   1540     265 0.161933 0.004149     1.54e-01      0.17027
   12   1274     217 0.134351 0.003842     1.27e-01      0.14210
   13   1056     157 0.114377 0.003586     1.08e-01      0.12163
   14    899     122 0.098855 0.003364     9.25e-02      0.10567
   15    776     115 0.084205 0.003130     7.83e-02      0.09057
   16    660     117 0.069278 0.002863     6.39e-02      0.07512
   17    541      82 0.058777 0.002654     5.38e-02      0.06422
   18    459      58 0.051350 0.002491     4.67e-02      0.05647
   19    401      45 0.045588 0.002355     4.12e-02      0.05045
   20    356      33 0.041362 0.002249     3.72e-02      0.04601
   21    323      35 0.036880 0.002129     3.29e-02      0.04130
   22    287      36 0.032254 0.001997     2.86e-02      0.03641
   23    251      39 0.027242 0.001841     2.39e-02      0.03110
   24    211      25 0.024015 0.001732     2.08e-02      0.02766
   25    186      21 0.021303 0.001634     1.83e-02      0.02476
   26    165      18 0.018979 0.001545     1.62e-02      0.02226
   27    146      15 0.017029 0.001466     1.44e-02      0.02016
   28    130      12 0.015457 0.001399     1.29e-02      0.01846
   29    118      10 0.014147 0.001341     1.17e-02      0.01703
   30    108      13 0.012444 0.001260     1.02e-02      0.01518
   31     93       7 0.011508 0.001214     9.36e-03      0.01415
   32     86       6 0.010705 0.001172     8.64e-03      0.01327
```

```
  33     80       4 0.010170 0.001144     8.16e-03      0.01268
  34     76       4 0.009634 0.001115     7.68e-03      0.01209
  35     72       7 0.008698 0.001061     6.85e-03      0.01105
  36     64       8 0.007611 0.000996     5.89e-03      0.00983
  37     56       5 0.006931 0.000952     5.30e-03      0.00907
  38     51       4 0.006387 0.000915     4.82e-03      0.00846
  39     47       4 0.005844 0.000877     4.36e-03      0.00784
  40     43       5 0.005164 0.000826     3.77e-03      0.00707
  41     38       4 0.004621 0.000782     3.32e-03      0.00644
  42     33       1 0.004481 0.000771     3.20e-03      0.00628
  43     32       5 0.003781 0.000711     2.61e-03      0.00547
  44     27       2 0.003501 0.000686     2.38e-03      0.00514
  45     25       1 0.003360 0.000672     2.27e-03      0.00497
  46     24       2 0.003080 0.000645     2.04e-03      0.00464
  47     22       1 0.002940 0.000631     1.93e-03      0.00448
  49     21       1 0.002800 0.000616     1.82e-03      0.00431
  50     20       2 0.002520 0.000585     1.60e-03      0.00397
  51     18       3 0.002100 0.000536     1.27e-03      0.00346
  54     15       1 0.001960 0.000518     1.17e-03      0.00329
  56     14       1 0.001820 0.000499     1.06e-03      0.00312
  57     13       1 0.001680 0.000480     9.60e-04      0.00294
  58     12       1 0.001540 0.000460     8.58e-04      0.00277
  59     10       1 0.001386 0.000439     7.45e-04      0.00258
  61      9       2 0.001078 0.000392     5.29e-04      0.00220
  65      7       1 0.000924 0.000365     4.26e-04      0.00200
  71      6       1 0.000770 0.000335     3.28e-04      0.00181
  85      5       1 0.000616 0.000301     2.36e-04      0.00161
  86      4       1 0.000462 0.000262     1.52e-04      0.00141
 104      3       1 0.000308 0.000215     7.82e-05      0.00121
 119      2       1 0.000154 0.000153     2.19e-05      0.00108
 144      1       1 0.000000      NaN           NA           NA
```

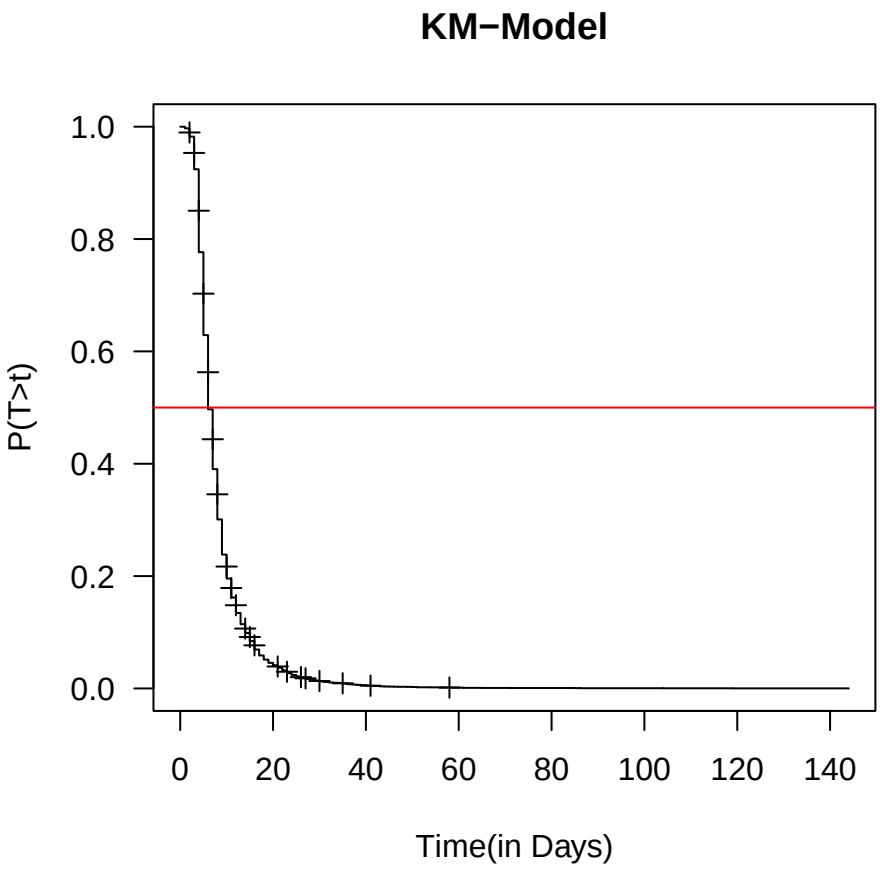
**Interpretation:**

If we just take any of the row, e.g., for row 3,

**at time 3,**

- No. of patient at risk (risk of discharge alive) = 7762
- No. of Events occurred (patients discharged alive) = 459
- Probability of staying in hospital beyond 3 days = 0.924209
- Standard error associated with survival = 0.002977
- We are 95% confident that there is somewhere between 91.8% to 93% chance of staying at hospital beyond 3 days.

Now, We look at the plot of the model,




This visualizes the Keplan-Meier Survival Curve, the red line indicates the median survival, and tick-mark indicates there is a censored observation.

We conducted a survival analysis to assess the impact of TWATemp on the length of hospital stay (DurationHosp). Patients were split into groups based on whether their TWATemp was above or below the median. The Kaplan-Meier method was used to estimate survival curves for each group.

Then, I have fitted a Kaplan-Meier model, relating TWATemp(core temperature during surgery) to Survival (DurationHosp) and see if there is a relation between hospital duration and TWATemp. Patients were split into groups based on whether their TWATemp was above or below the median.

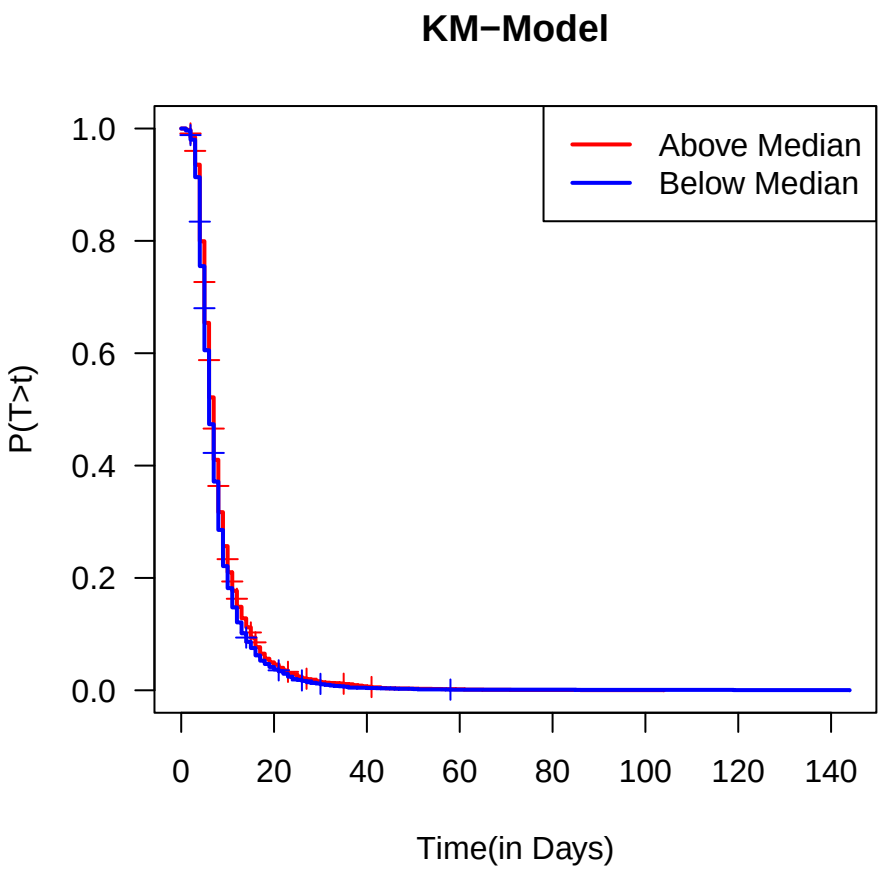
```
Call: survfit(formula = surv_object ~ TempGroup_surv, data = working_data)

                              n events median 0.95LCL 0.95UCL
TempGroup_surv=Above Median 3842   3823      7       7       7
TempGroup_surv=Below Median 4066   4051      6       6       6
```

**Results:**

- Total no. of individuals below median is 4066 & above median is 3842.
- Total no. of Events below median = 4052 & above median = 3823.
- Median Survival Time below median = 6, & above median = 7.

- We are 95% confident that median survival below median is 6 and above median is 7.

Now, we look at the plot of the model,




In the plot the red curve is the survival curve for above median core temperature group and the blue one is the survival curve of below median temperature group, and tick marks are for censored observations.

Now, to check whether the survival differs for these two groups, I did a

**Log Rank Test**

$$\begin{cases} H_0: & \textit{Survival in two groups are same} \\ H_a: & \textit{Survival in two groups are not same} \end{cases}$$

```
Call:
survdiff(formula = surv_object ~ TempGroup_surv, data = working_data)

                               N Observed Expected (O-E)^2/E (O-E)^2/V
TempGroup_surv=Above Median 3842     3823     4012      8.95      22.2
TempGroup_surv=Below Median 4066     4051     3862      9.30      22.2

 Chisq= 22.2  on 1 degrees of freedom, p= 3e-06
```

**Interpretation:**

Based on the P-value we reject $H_0$. We have evidence to believe Survival (Duration Hospital) is not the same for below median and above median temperature group.

Now, to check how survival if affected by Surgical Core Temperature, I fitted a

**Cox Proportional Hazards Model** This model estimates the hazard, or the instantaneous rate, of discharge from the hospital, with higher hazards indicating shorter stays.

$$HAZ = h_0(t) * e^{\sum_{i=1}^{p} bjXj}$$

- $h_0(t) \geq 0$ is an unspecified function, known as the baseline hazard. It is the hazard function for an individual with features $X_1 = \cdots = X_p = 0$.
- $e^{b_j}$ represents the hazard ratio.

Now, let's look at the summary of the fitted model

```
Call:
coxph(formula = surv_object ~ TWATemp, data = working_data)

  n= 7908, number of events= 7874

           coef exp(coef) se(coef)      z Pr(>|z|)
TWATemp -0.1084    0.8972   0.0205 -5.289 1.23e-07 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

        exp(coef) exp(-coef) lower .95 upper .95
TWATemp    0.8972      1.115    0.8619     0.934

Concordance= 0.522  (se = 0.004 )
Likelihood ratio test= 27.93  on 1 df,   p=1e-07
Wald test            = 27.98  on 1 df,   p=1e-07
Score (logrank) test = 27.98  on 1 df,   p=1e-07
```

**Interpretation:**

- $\exp(-coef)$, i.e., $\frac{1}{HR}$ for TWATemp is 1.115, means at a given instant of time, the probability of discharging alive for someone who had surgical core temperature 1°C lower is 10.8% higher than someone who had surgical core temperature 1°C higher.

Now, for further investigation, I splited the dataset into two parts with respect to median core temperature and fit the model for each temperature ranges. For, core temperature below median the summary of the fitted model,

```
Call:
coxph(formula = surv_object_below ~ TWATemp, data = data_below)

  n= 4066, number of events= 4051

           coef exp(coef) se(coef)     z Pr(>|z|)
TWATemp 0.07993   1.08321  0.04724 1.692   0.0907 .
```

```
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

        exp(coef) exp(-coef) lower .95 upper .95
TWATemp     1.083     0.9232    0.9874     1.188

Concordance= 0.516  (se = 0.006 )
Likelihood ratio test= 2.89  on 1 df,   p=0.09
Wald test            = 2.86  on 1 df,   p=0.09
Score (logrank) test = 2.86  on 1 df,   p=0.09
```

**Interpretation:**

- $\exp(coef)$, i.e., HR for TWATemp is 1.08321, means at a given instant of time, the probability of discharging alive for someone who had surgical core temperature 1°C higher is 8% higher than someone who had surgical core temperature 1°C lower.

For, core temperature above median the summary of the fitted model,

```
Call:
coxph(formula = surv_object_above ~ TWATemp, data = data_above)

  n= 3842, number of events= 3823

            coef exp(coef) se(coef)      z Pr(>|z|)
TWATemp -0.30112   0.73999  0.05216 -5.773  7.8e-09 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

        exp(coef) exp(-coef) lower .95 upper .95
TWATemp      0.74      1.351    0.6681    0.8196

Concordance= 0.531  (se = 0.006 )
Likelihood ratio test= 34.48  on 1 df,   p=4e-09
Wald test            = 33.33  on 1 df,   p=8e-09
Score (logrank) test = 33.35  on 1 df,   p=8e-09
```

**Interpretation:**

- $\exp(-coef)$, i.e., $\frac{1}{HR}$ for TWATemp is 1.351, means at a given instant of time, the probability of discharging alive for someone who had surgical core temperature 1°C lower is 35.1% higher than someone who had surgical core temperature 1°C higher.

Now, for further study I added the potential confounders to both the models to see if adding them makes any difference. so, for core temperature below median, the summary of the full model,

```
Call:
coxph(formula = surv_object_below ~ Age + FEMALE + BMI + CharlsonScore +
    CHF + VALVE + DM + RENLFAIL + LIVER + METS + TUMOR + COAG +
    OBESE + WGHTLOSS + LYTES + BLDLOSS + ANEMDEF + DRUG + SteroidHx +
    ImmunosuppressantHx + SurgDuration + Open + TWATemp, data = data_below)
```

```
  n= 4066, number of events= 4051

                           coef  exp(coef)   se(coef)       z Pr(>|z|)
Age                  -0.0037116  0.9962952  0.0010748  -3.453 0.000554 ***
FEMALE1               0.0590517  1.0608301  0.0320720   1.841 0.065589 .
BMI                  -0.0069610  0.9930631  0.0034790  -2.001 0.045406 *
CharlsonScore        -0.0443606  0.9566089  0.0221605  -2.002 0.045307 *
CHF1                 -0.1259380  0.8816695  0.0975231  -1.291 0.196577
VALVE1               -0.0286725  0.9717346  0.0748010  -0.383 0.701485
DM1                  -0.0277812  0.9726011  0.0592961  -0.469 0.639415
RENLFAIL1             0.1117446  1.1182272  0.0939857   1.189 0.234458
LIVER1                0.1508685  1.1628437  0.1097852   1.374 0.169375
METS1                 0.2277252  1.2557402  0.1459389   1.560 0.118662
TUMOR1                0.0278298  1.0282207  0.0598218   0.465 0.641780
COAG1                -0.2591456  0.7717107  0.0692634  -3.741 0.000183 ***
OBESE1                0.1198513  1.1273292  0.0569933   2.103 0.035474 *
WGHTLOSS1            -0.8320749  0.4351454  0.0441616 -18.842  < 2e-16 ***
LYTES1               -0.3141555  0.7304054  0.0368535  -8.524  < 2e-16 ***
BLDLOSS1             -0.1747566  0.8396613  0.1060014  -1.649 0.099224 .
ANEMDEF1              0.0336887  1.0342626  0.0396759   0.849 0.395826
DRUG1                -0.2036333  0.8157615  0.1204008  -1.691 0.090780 .
SteroidHx1            0.0801133  1.0834098  0.0354090   2.263 0.023666 *
ImmunosuppressantHx1 -0.1180424  0.8886584  0.0960367  -1.229 0.219020
SurgDuration         -0.0033921  0.9966137  0.0001981 -17.125  < 2e-16 ***
Open1                -0.1387046  0.8704851  0.0427865  -3.242 0.001188 **
TWATemp               0.0756647  1.0786009  0.0489610   1.545 0.122247
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

                     exp(coef) exp(-coef) lower .95 upper .95
Age                     0.9963     1.0037    0.9942    0.9984
FEMALE1                 1.0608     0.9427    0.9962    1.1297
BMI                     0.9931     1.0070    0.9863    0.9999
CharlsonScore           0.9566     1.0454    0.9159    0.9991
CHF1                    0.8817     1.1342    0.7283    1.0674
VALVE1                  0.9717     1.0291    0.8392    1.1252
DM1                     0.9726     1.0282    0.8659    1.0925
RENLFAIL1               1.1182     0.8943    0.9301    1.3444
LIVER1                  1.1628     0.8600    0.9377    1.4420
METS1                   1.2557     0.7963    0.9434    1.6716
TUMOR1                  1.0282     0.9726    0.9145    1.1561
COAG1                   0.7717     1.2958    0.6737    0.8839
OBESE1                  1.1273     0.8871    1.0082    1.2606
WGHTLOSS1               0.4351     2.2981    0.3991    0.4745
LYTES1                  0.7304     1.3691    0.6795    0.7851
BLDLOSS1                0.8397     1.1910    0.6821    1.0336
ANEMDEF1                1.0343     0.9669    0.9569    1.1179
DRUG1                   0.8158     1.2258    0.6443    1.0329
SteroidHx1              1.0834     0.9230    1.0108    1.1613
ImmunosuppressantHx1    0.8887     1.1253    0.7362    1.0727
SurgDuration            0.9966     1.0034    0.9962    0.9970
```

```
Open1                   0.8705     1.1488    0.8005    0.9466
TWATemp                 1.0786     0.9271    0.9799    1.1872

Concordance= 0.686  (se = 0.005 )
Likelihood ratio test= 1244  on 23 df,   p=<2e-16
Wald test            = 1101  on 23 df,   p=<2e-16
Score (logrank) test = 1139  on 23 df,   p=<2e-16
```

**Interpretation:**

- exp($coef$), i.e., HR for TWATemp is 1.0786, means at a given instant of time, the probability of discharging alive for someone who had surgical core temperature 1°C higher is 7.86% higher than someone who had surgical core temperature 1°C lower.

```
Call:
coxph(formula = surv_object_above ~ Age + FEMALE + BMI + CharlsonScore +
    CHF + VALVE + DM + RENLFAIL + LIVER + METS + TUMOR + COAG +
    OBESE + WGHTLOSS + LYTES + BLDLOSS + ANEMDEF + DRUG + SteroidHx +
    ImmunosuppressantHx + SurgDuration + Open + TWATemp, data = data_above)

  n= 3842, number of events= 3823

                          coef  exp(coef)   se(coef)       z Pr(>|z|)
Age                  -0.0053032  0.9947108  0.0011455  -4.629 3.67e-06 ***
FEMALE1              -0.0067720  0.9932509  0.0331622  -0.204  0.83819
BMI                  -0.0039264  0.9960813  0.0033268  -1.180  0.23792
CharlsonScore        -0.0134612  0.9866290  0.0255395  -0.527  0.59814
CHF1                 -0.2954045  0.7442305  0.1080206  -2.735  0.00624 **
VALVE1                0.0139170  1.0140143  0.0819887   0.170  0.86521
DM1                   0.0442911  1.0452866  0.0633726   0.699  0.48462
RENLFAIL1            -0.1037479  0.9014525  0.1080786  -0.960  0.33709
LIVER1                0.0457941  1.0468589  0.1054989   0.434  0.66424
METS1                -0.0106271  0.9894292  0.1638833  -0.065  0.94830
TUMOR1                0.0130396  1.0131250  0.0703079   0.185  0.85287
COAG1                -0.3938855  0.6744313  0.0655011  -6.013 1.82e-09 ***
OBESE1                0.0763878  1.0793811  0.0540496   1.413  0.15757
WGHTLOSS1            -0.8302335  0.4359475  0.0437676 -18.969  < 2e-16 ***
LYTES1               -0.3955999  0.6732760  0.0384325 -10.293  < 2e-16 ***
BLDLOSS1              0.0900772  1.0942588  0.1114221   0.808  0.41884
ANEMDEF1              0.0551503  1.0566994  0.0403755   1.366  0.17196
DRUG1                -0.2526891  0.7767094  0.1112806  -2.271  0.02316 *
SteroidHx1            0.0524126  1.0538104  0.0356176   1.472  0.14115
ImmunosuppressantHx1 -0.0644431  0.9375894  0.0914007  -0.705  0.48077
SurgDuration         -0.0028325  0.9971715  0.0001761 -16.085  < 2e-16 ***
Open1                -0.2499113  0.7788699  0.0424470  -5.888 3.92e-09 ***
TWATemp              -0.1570972  0.8546210  0.0524739  -2.994  0.00276 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

                     exp(coef) exp(-coef) lower .95 upper .95
```

```
Age                     0.9947     1.0053    0.9925    0.9969
FEMALE1                 0.9933     1.0068    0.9307    1.0600
BMI                     0.9961     1.0039    0.9896    1.0026
CharlsonScore           0.9866     1.0136    0.9385    1.0373
CHF1                    0.7442     1.3437    0.6022    0.9197
VALVE1                  1.0140     0.9862    0.8635    1.1908
DM1                     1.0453     0.9567    0.9232    1.1835
RENLFAIL1               0.9015     1.1093    0.7294    1.1141
LIVER1                  1.0469     0.9552    0.8513    1.2873
METS1                   0.9894     1.0107    0.7176    1.3642
TUMOR1                  1.0131     0.9870    0.8827    1.1628
COAG1                   0.6744     1.4827    0.5932    0.7668
OBESE1                  1.0794     0.9265    0.9709    1.2000
WGHTLOSS1               0.4359     2.2939    0.4001    0.4750
LYTES1                  0.6733     1.4853    0.6244    0.7260
BLDLOSS1                1.0943     0.9139    0.8796    1.3613
ANEMDEF1                1.0567     0.9463    0.9763    1.1437
DRUG1                   0.7767     1.2875    0.6245    0.9660
SteroidHx1              1.0538     0.9489    0.9828    1.1300
ImmunosuppressantHx1    0.9376     1.0666    0.7838    1.1215
SurgDuration            0.9972     1.0028    0.9968    0.9975
Open1                   0.7789     1.2839    0.7167    0.8464
TWATemp                 0.8546     1.1701    0.7711    0.9472

Concordance= 0.7  (se = 0.005 )
Likelihood ratio test= 1341  on 23 df,   p=<2e-16
Wald test            = 1170  on 23 df,   p=<2e-16
Score (logrank) test = 1211  on 23 df,   p=<2e-16
```

**Interpretation:**

- $\exp(-coef)$, i.e., $\frac{1}{HR}$ for TWATemp is 1.1701, means at a given instant of time, the probability of discharging alive for someone who had surgical core temperature 1°C lower is 17% higher than someone who had surgical core temperature 1°C higher.

# 4 Conclusion

This study highlights a multifaceted relationship between intraoperative core temperature and the development of serious surgical site infections (SSIs). The analysis reveals the following insights:

- The average core temperature (TWATemp) of the patients was approximately normally distributed with a median of 36°C.
- Patients were divided into two groups based on their core temperatures relative to the median. Initial group-level comparisons showed no statistically significant difference in the proportion of serious infections between those above and below the median (p-value = 0.1249). However, finer granularity showed fluctuating infection risks, particularly at temperature extremes.
- **Logistic Regression Findings:**
  - In an unadjusted model, the odds of serious infections increased with higher core temperatures. For instance, temperatures above 37°C were associated with a 1.5-fold higher risk of infections compared to temperatures below 35°C.

- Stratified regression analysis showed that patients with core temperatures between 35.7°C and 36.4°C exhibited the lowest odds of infection, while extreme low and high temperatures significantly increased the risk.
- Adjusted Models:
- When covariates such as age, comorbidities, surgical duration, and others were included in the regression, the effect size of TWATemp was moderated but remained significant.
  * Adjusted odds indicated that a 0.5°C increase in core temperature in the lower range (<35.7°C) decreased infection odds (OR ~ 0.77), but a similar increase in the higher range (>36.4°C) significantly elevated infection risks.
- **Conclusion:**
  * Maintaining core temperatures within a mid-range (~36°C) during surgery minimizes the risk of serious postoperative infections. Both hypothermia (≤35°C) and hyperthermia (≥37°C) are significant risk factors for SSIs. Effective intraoperative thermal management is critical in mitigating these risks.

• **Survival Analysis Findings:**

- Kaplan-Meier Analysis:
  * Patients with core temperatures above the median had a median hospital stay of 7 days, while those below the median had a stay of 6 days. This highlights longer recovery times associated with higher intraoperative temperatures.
  * The survival curves for these groups were significantly different (Log Rank Test, $p < 0.0001$), confirming that TWATemp affects discharge timing.
- Cox Proportional Hazards Model:
  * In the full cohort, a 1°C increase in core temperature was associated with a 10.8% reduction in the hazard (rate) of being discharged alive, suggesting prolonged hospital stays for patients with higher temperatures.
  * Stratified Cox models revealed a dichotomy:
    · For patients with temperatures below the median (≤36°C), higher temperatures increased the hazard of discharge (HR = 1.08, $p = 0.09$), although this was not statistically significant.
    · For patients with temperatures above the median (>36°C), higher temperatures significantly reduced the discharge hazard (HR = 0.74, $p < 0.001$), indicating prolonged stays.
  * Adjusted Analysis:
    · Incorporating confounders such as age, comorbidities, surgical duration, and postoperative complications refined the estimates. Even after adjustments, the relationship between extreme core temperatures and delayed discharge remained consistent.
    · The interaction of temperature with surgical complexity (duration) was significant, suggesting that prolonged surgeries exacerbate the impact of temperature extremes on recovery times.
- **Conclusion:**
  * While moderate increases in core temperature (up to 36°C) during surgery may aid quicker recovery, temperatures exceeding 36°C are linked to prolonged hospital stays. Conversely, hypothermia (<35°C) was also associated with suboptimal outcomes, albeit with a less pronounced effect. Proper thermal regulation is essential for optimizing recovery and minimizing hospital resource utilization.

# 5 R-Code used

```
data <- read.csv("D:/Internship_Presidency/core-temperature.csv")
names(data)

#EDA
median_temp <- median(data$TWATemp, na.rm = TRUE)
mean_temp <- mean(data$TWATemp, na.rm = TRUE)

hist(data$TWATemp, col="skyblue",border="skyblue",
     main="Distribution of Core Temperatures During Surgery",
     xlab="TWA Temp (°C)", ylab="Frequency")

abline(v=median_temp, col="blue", lty=2, lwd=2)
abline(v=mean_temp, col="red", lty=2, lwd=2)

legend("topright", legend=c(paste("Median =", round(median_temp, 2)),
                            paste("Mean =", round(mean_temp, 2))),
       col=c("blue", "red"), lty=2, lwd=2)


data$TempGroup <- ifelse(data$TWATemp > median_temp, "Above Median",
                         "Below Median")
proportion_seriousinfection <- tapply(data$SeriousInfection, data$TempGroup,
                                                    mean)
proportion_seriousinfection


table_infections <- table(data$TempGroup, data$SeriousInfection)
chi_test <- chisq.test(table_infections)
print(chi_test)

proportion_seriousinfection <- tapply(data$SeriousInfection, data$TWATemp,
                                                    mean)
proportion_seriousinfection
plot(as.numeric(names(proportion_seriousinfection)), proportion_seriousinfection,
     type = "b", pch = 19, col = "blue",
     xlab = "Body Temperature (°C)", ylab = "Proportion of Infection",
     main = "Proportion of Infections by Body Temperature")

#Effect Size Logistic Model
working_data <- subset(data, select = -c(YEAR, SurgeryType, AbsessIntraAb,
                                         AbsessPelvic, Cdiff, FascialDehiscence,
                                         DelayedHealing, Infection, Sinus,
                                         Pneumonia, Pneumonia.aspiration.,
                                         Sepsis, SSIDeep.fascia., SSIOrganSpace,
                                         SSISuperficial.skin., WoundInfection,
                                         LastReadingTemp, EndCaseTemp, AnyInfection,
                                         LOS, TempGroup))
```

```
names(working_data)
working_data$FEMALE = as.factor(working_data$FEMALE)
working_data$CHF = as.factor(working_data$CHF)
working_data$VALVE = as.factor(working_data$VALVE)
working_data$DM = as.factor(working_data$DM)
working_data$RENLFAIL = as.factor(working_data$RENLFAIL)
working_data$LIVER = as.factor(working_data$LIVER)
working_data$METS = as.factor(working_data$METS)
working_data$TUMOR = as.factor(working_data$TUMOR)
working_data$COAG = as.factor(working_data$COAG)
working_data$OBESE = as.factor(working_data$OBESE)
working_data$WGHTLOSS = as.factor(working_data$WGHTLOSS)
working_data$LYTES = as.factor(working_data$LYTES)
working_data$BLDLOSS = as.factor(working_data$BLDLOSS)
working_data$ANEMDEF = as.factor(working_data$ANEMDEF)
working_data$DRUG = as.factor(working_data$DRUG)
working_data$SteroidHx = as.factor(working_data$SteroidHx)
working_data$ImmunosuppressantHx = as.factor(working_data$ImmunosuppressantHx)
working_data$Open = as.factor(working_data$Open)
working_data$SeriousInfection = as.factor(working_data$SeriousInfection)
working_data$SuperficialInfection = as.factor(working_data$SuperficialInfection)
working_data$DEAD = as.factor(working_data$DEAD)

summary(working_data)

model_basic <- glm(SeriousInfection ~ TWATemp, data = working_data, family = binomial)
summary(model_basic)

working_data$tempCAT <- cut(working_data$TWATemp, breaks = 4)
model_cat <- glm(SeriousInfection ~ tempCAT, data = working_data, family = binomial)
summary(model_cat)

split_temps <- quantile(working_data$TWATemp, probs = c(0.25, 0.5, 0.75))
data1 <- subset(working_data, TWATemp <= split_temps[1])
data2 <- subset(working_data, TWATemp > split_temps[1] & TWATemp <= split_temps[2])
data3 <- subset(working_data, TWATemp > split_temps[2] & TWATemp <= split_temps[3])
data4 <- subset(working_data, TWATemp > split_temps[3])

model1 <- glm(SeriousInfection ~ TWATemp, data = data1, family = binomial)
model2 <- glm(SeriousInfection ~ TWATemp, data = data2, family = binomial)
model3 <- glm(SeriousInfection ~ TWATemp, data = data3, family = binomial)
model4 <- glm(SeriousInfection ~ TWATemp, data = data4, family = binomial)

summary(model1)
summary(model2)
summary(model3)
summary(model4)

serious_data <- subset(data1, select = -c(DEAD,DurationHosp,tempCAT,SuperficialInfection))
names(serious_data)
model_full_serious <- glm(SeriousInfection ~ ., data = serious_data, family = binomial)
```

```r
summary(model_full_serious)
library(car)
vif(model_full_serious)

model_modified <- glm(SeriousInfection ~ . - CharlsonScore - METS, data = serious_data,
                      family = binomial)
summary(model_modified)

library(MASS)
Reduced_model_serious = stepAIC(model_modified, direction = 'both')
summary(Reduced_model_serious)
library(hnp)
hnp(Reduced_model_serious)

superficial_data <- subset(data1, select = -c(DEAD,DurationHosp,tempCAT,SeriousInfection))
names(superficial_data)

model_full_superficial <- glm(SuperficialInfection ~ ., data = superficial_data, family = binomial)
summary(model_full_superficial)

vif(model_full_superficial)

model_modified_sup <- glm(SuperficialInfection ~ . - CharlsonScore - METS,
                          data = superficial_data, family = binomial)
summary(model_modified_sup)

Reduced_model_superficial = stepAIC(model_modified_sup, direction = 'both')
summary(Reduced_model_superficial)

#Suvival Analysis

library(survival)
library(survminer)


surv_object <- Surv(working_data$DurationHosp, working_data$DEAD == 0)
km.model <- survfit(surv_object ~ 1, data = working_data,
                    type = "kaplan-meier")
summary(km.model)
plot(km.model, conf.int=F, xlab = "Time(in Days)", ylab = "P(T>t)",
     main="KM-Model", las=1, mark.time = TRUE)
abline(h=0.5, col = "red")


median_TWATemp <- median(working_data$TWATemp, na.rm = TRUE)


working_data$TempGroup_surv <- ifelse(working_data$TWATemp > median_TWATemp,
                                      "Above Median", "Below Median")

#KM Model
```

```r
km.model_temp <- survfit(surv_object ~ TempGroup_surv, data = working_data)
km.model_temp
summary(km.model_temp)
plot(km.model_temp, conf.int=F, xlab = "Time(in Days)", ylab = "P(T>t)",
     main="KM-Model", col = c("red","blue"),las=1 ,lwd=2, mark.time = TRUE)

legend("topright", legend = c("Above Median", "Below Median"),lty = 1,
       lwd = 2, col = c("red","blue"))

#logrank Test
survdiff(surv_object ~ TempGroup_surv, data = working_data)

# Fit the Cox proportional hazards model
cox_model <- coxph(surv_object ~ TWATemp + SeriousInfection, data = working_data)
summary(cox_model)

data_below <- subset(working_data, TWATemp <= median_TWATemp)
data_above <- subset(working_data, TWATemp > median_TWATemp)

surv_object_below <- Surv(data_below$DurationHosp, data_below$DEAD == 0)

cox_model_below <- coxph(surv_object_below ~ TWATemp, data = data_below)
summary(cox_model_below)

surv_object_above <- Surv(data_above$DurationHosp, data_above$DEAD == 0)

cox_model_above <- coxph(surv_object_above ~ TWATemp, data = data_above)
summary(cox_model_above)

cox_model_below_full <- coxph(surv_object_below ~ Age + FEMALE + BMI +
                              CharlsonScore + CHF + VALVE + DM + RENLFAIL +
                              LIVER + METS + TUMOR + COAG + OBESE + WGHTLOSS +
                              LYTES + BLDLOSS + ANEMDEF + DRUG + SteroidHx +
                              ImmunosuppressantHx + SurgDuration + Open +
                              TWATemp + SeriousInfection + SuperficialInfection,
                              data = data_below)
summary(cox_model_below_full)
anova(cox_model_below, cox_model_below_full, test = "LRT")

cox_model_above_full <- coxph(surv_object_above ~ Age + FEMALE + BMI +
                              CharlsonScore + CHF + VALVE + DM + RENLFAIL +
                              LIVER + METS + TUMOR + COAG + OBESE + WGHTLOSS +
                              LYTES + BLDLOSS + ANEMDEF + DRUG + SteroidHx +
                              ImmunosuppressantHx + SurgDuration + Open +
                              TWATemp + SeriousInfection + SuperficialInfection,
                              data = data_above)
summary(cox_model_above_full)
```

# 6 References

## References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[5] Michael J Walters, Marianne Tanios, Onur Koyuncu, Guangmei Mao, Michael A Valente, and Daniel I Sessler. Intraoperative core temperature and infectious complications after colorectal surgery: A registry analysis. *Journal of clinical anesthesia*, 63:109758, 2020.