# AN EXPLORATORY ANALYSIS OF MORTALITY ASSOCIATED WITH DIABETIS

Exploring Mortality in Diabetic ICU Patients Using Cormobidity Indices

ELECTRONIC HEALTH RECORDS

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## Abstract

Managing the rising prevalence of chronic diseases is a major challenge for health-care systems around the world. Multimorbidity ("multiple comorbidities) is the co-occurrence of two or more chronic conditions and is associated with decreased quality of life, impaired functional status, and an increased burden on limited health care resources [1].

Diabetes is a serious health issue that can lead to a variety of long-term health problems, including renal, cardiovascular, and neuropathic complications[2]. Many of these issues can lead to higher health-care costs, as well as an increased lenght of ICU stay and mortality [2]. We intend to detect the most common comorbidities associated with type 2 diabetes, and its impact in their length of stay in the hospital and mortality rates.

Using the MIMIC-III database, statistics elements and the KaplanMeier estiamtor were applied to study mortality and length of stay in UCI. We did not find any correlation between diabetes and an increase in mortality. Additionally, this study demonstrated the need of selecting other variables and the application of machine learning models to predict the mortality risk.

## Introduction

Diabetes mellitus (DM) is a disease characterized by insufficient glucose control in the blood [3]. The two most common subtypes of diabetes are type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM), both of which are caused by defective insulin secretion (T1DM) and/or action (T2DM) . Type 1 is thought to be a genetic condition, whereas Type 2 is thought to be a result of poor lifestyle and dietary choices that cause chronic hyperglycemia [4]. Their pathogenesis is vastly different, resulting in distinct etiologies, presentations, and treatments[4,5].

Patients with type 2 diabetes mellitus (T2DM) frequently have and develop multiple co-occurring conditions, which has numerous implications for clinical care and patient quality of life. Numerous published resources and studies[6,7,8] suggest that there are three predominant cluster types in patients with T2DM-related multimorbidity, including cardiometabolic ,vascular, and neuropathological conditions. Furthermore, diabetic complications can have a direct impact on how patients are treated in the intensive care unit.

In addition, the effect of diabetes, for example, on a patient's risk of ICU mortality has been debated [9]. This is something we intend to look into. We want to see if having a diabetes diagnosis and cormobidities associated causes an increase in mortality rates.

The main focuse on this exploratory study is to know the profile of type 2 diabetic patients: what are the most common comorbidities that they present and the impact that diabetes with other conditions has on the lenght of stay in ICU and the mortality rates.

The inclusion criteria includes all the records of  patients diagnosed with diabetes included in the MIMICIII database.

Previous research has demonstrated the ability to predict risk of mortality in the ICU based on a variety of variables such as vital signs, lab results, surgical history, diagnoses, ventilator settings, and past medical history[10,11]. Furthermore, diabetic-specific machine learning has been used in a variety of contexts, including detecting hypoglycemia, predicting diagnosis and complications, and blood glucose classification[12]. Recently,this applications have been successful in predicting which diabetic patients are most at risk for specific complications (retinopathy, neuropathy, and nephropathy) [13,14]. Despite being useful in predicting complications, there are no current research that has examined at diabetic patients in the ICU.

As a result, the purpose of this study is to determine which of the established comorbidity indices best predicts mortality in diabetic patients in the ICU.

# Methods

SQL queries were used to extract data from a local MySQL database containing Medical Information Mart for Intensive Care III (MIMIC-III) data. The R programming language was used for pre-processing and analysis. After that, the data was transformed and other variables of interest were generated. We obtained the main conditions in diabetics by finding the presence of specific ICD-9-CM codes.

## Data and Variable Selection

For this study, we used the MIMIC-III database, which contains information on over 40,000 patients (16 and older) who were treated in the intensive care unit (ICU) between 2001 and 2012.This database contains detailed information on various aspects and procedures pertaining to patients. We chose data on admissions, ICU stays, ICD-9-CM diagnoses and demographics values for this study.

We considered sociodemographic variables: measurements obtained from each patient's medical history,such as: Sex, Insurance,Admission type,Date of birth(DOB), Date of Death(DOD) and Comorbidity information.

The main columns presented are:

- **Numerical columns:**

- LOS is the length of the ICU stay of a patient. The length of stay is measured in days.
- Number of diabetic patients.
- Mean of diabetic and non-diabetic people admitted.
- Dead: total number of patients with a distinct DEATHTIME

- **Categorical/ Binary columns:**

- Admission type columns: elective, emergency, newborn, urgent.
- Age: Divided in four groups.
- Status: 1 for diabetics and 0 for control group. Group 0: <50, Group 1: 50-60, Group 2: 60-70, Group 3: 70-80 and Group 4: >80.
- Insurance columns: government, Medicaid, Medicare, private, self-pay
- Ethnicity columns: there are 37 ethnicity columns. ASIAN, WHITE, BLACK/AFRICAN AMERICAN, HISPANIC OR LATINO, etc.
- Gender: M for males. F for females
- ICD9 code columns: Column names are 3-4 digit alphanumerics. 1 if a patient has a disease with the ICD9 code, 0 otherwise

## Subjects, procedure and Outcome

First we identified the study subjects to analyze the effect of diabetes mellitus on co-occurring pathologies. In order to proceed, we identify every subject with a diagnosis using the ICD9 code 25000: "Diabetes mellitus without mention of complication, type II or unspecified type, not stated as uncontrolled". In the data, this is the most common DM diagnosis relating to type II, which is significantly more common than type I. This is not an ideal selection procedure. We may lose some subjects who have received other DMII-related diagnoses but not the general 25000 code. Furthermore,the code also includes cases of unspecified type, so there may be subjects with type I diagnoses in other admissions.

We obtained 7370 patients with this ICD-9 code, which will serve as the subject sample for this study. We analyzed the presence of some categorical variables in diabeteic and non-diabetic patients.

Then we extracted the most common conditions in these diabetic patients and compared their prevalence to non-diabetic patients.Following that, we compared the length of stay for cormobidities in the study and control groups, in alive patients vs patients who died in the ICU.

Finally, we use the KaplanMeier estimator to evaluate the  mortality rates among the control and the study group.

### Data Processing

The comorbidity index scores were calculated for each study group. Demographic data were merged with the patient status into different data frames for analysis. Descriptive statistics for the sample were calculated.Admission type was used to determine which was the most frequent cause: “Elective” was defined as a previously planned hospital admission, while “emergent” or “urgent” were defined as unplanned medical care. Ethnicity was not fully considered due to the amount of categories althought white was the most common in diabetics and south american the least common.

### Statistical Analysis

We compared the characteristics of diabetic and non-diabetic patients with cormobidities in terms of mortality rates and length of stay.The mean is used to express quantitative variables, while absolute value and ratio are used to express qualitative variables.The prevalence of the various comorbidity variables is assessed using a 95% confidence interval.

We did not conduct any comparative analysis due to the nature of the data. All of the analyses are interpreted graphically and are considered significant at a p- value <0.05.

## Results

The study sample included 7370 people(**Table 1**) who were diagnosed with type 2 diabetes in 2001 based on the criteria outlined in the Methods.

| | ICD9_CODE | n |
|---|---|---|
| | <chr> | <int64> |
| 1 | 25000 | 7370 |
| 2 | 25060 | 887 |
| 3 | 25040 | 745 |
| 4 | 2536 | 473 |
| 5 | 25002 | 431 |

**Table 1.** Identification of the number of subjects with an ICD9 CODE of 25000

## Analysis of population

Men comprised 57% of the diabetic cohort and 56% of the control group. It seems that men might have higher rate of health complications than women. The average age at diabetes diagnosis was 65 years, with nearly 3/4 of those diagnosed being over 50 and only one-fourth being under 50. Moreover, 66% of the participants in the study had Medicare insurance (**Table 2**).Additionally, we discovered that diabetics had nearly twice as many hospital admissions as non-diabetics (2.43) (**Table 2**). The most frequent cause for admission was an emergency (in both the diabetic (80%) and control (81%).

A

A grouped_df: 4 × 4

| status | GENDER | n | ratio |
|---|---|---|---|
| <fct> | <fct> | <int> | <dbl> |
| 0 | F | 10924 | 0.4390852 |
| 0 | M | 13955 | 0.5609148 |
| 1 | F | 3010 | 0.4262249 |
| 1 | M | 4052 | 0.5737751 |

B

| status | age_group | n | ratio |
|---|---|---|---|
| <fct> | <fct> | <int> | <dbl> |
| 0 | 0 | 3939 | 0.15832630 |
| 0 | 1 | 4164 | 0.16737007 |
| 0 | 2 | 5205 | 0.20921259 |
| 0 | 3 | 5442 | 0.21873870 |
| 0 | 4 | 6129 | 0.24635235 |
| 1 | 0 | 452 | 0.06400453 |
| 1 | 1 | 1103 | 0.15618805 |
| 1 | 2 | 1866 | 0.26423110 |
| 1 | 3 | 2047 | 0.28986123 |
| 1 | 4 | 1594 | 0.22571509 |

C

| status | INSURANCE | n | ratio |
|---|---|---|---|
| <fct> | <chr> | <int> | <dbl> |
| 0 | Government | 592 | 0.023795169 |
| 0 | Medicaid | 1800 | 0.072350175 |
| 0 | Medicare | 14602 | 0.586920696 |
| 0 | Private | 7683 | 0.308814663 |
| 0 | Self Pay | 202 | 0.008119297 |
| 1 | Government | 121 | 0.017133956 |
| 1 | Medicaid | 460 | 0.065137355 |
| 1 | Medicare | 4686 | 0.663551402 |
| 1 | Private | 1761 | 0.249362787 |
| 1 | Self Pay | 34 | 0.004814500 |

D

| status | mean_adm |
|---|---|
| <fct> | <dbl> |
| 0 | 1.776640 |
| 1 | 2.439603 |

E

| status | ADMISSION_TYPE | n | ratio |
|---|---|---|---|
| <fct> | <chr> | <int> | <dbl> |
| 0 | ELECTIVE | 3933 | 0.15808513 |
| 0 | EMERGENCY | 20209 | 0.81229149 |
| 0 | NEWBORN | 33 | 0.00132642 |
| 0 | URGENT | 704 | 0.02829696 |
| 1 | ELECTIVE | 1158 | 0.16397621 |
| 1 | EMERGENCY | 5698 | 0.80685358 |
| 1 | URGENT | 206 | 0.02917021 |

**Table 2.** Summary statistics on the cohort of diabetic patients and control group. 0 is used to indentify control group and 1 the diabetic group.

The most common diseases in our diabetes cohort were those associated with the following codes: 4019, 41401, 4280, 42731, 2724, 5849, 51881, 2720, 5990, 2859. As can be seen, the majority are associated with vascular diseases such as hypertension and heart failure, among others (**Table 3**). We can also highlight the prevalence of these cormodibities in the study sample, with unspecified essential hypertension being the most common. From the 37 ethnicities decalred, these cormobidities in diabeteic patients were moslty found in white people.

As we can see in the table, we obtained the prevalence of these conditions in diabetics(**Table 3A**) and non diabetics(**Table 3B**). **Table 3C** shows both 3A and 3B combined in one. It is clear that the most common comorbidities in the diabetes population outnumber those in the general population, most by a factor of two.

A

| | ICD9_CODE | LONG_TITLE | n_subj | prevalence |
|---|---|---|---|---|
| | <chr> | <chr> | <int64> | <dbl> |
| 1 | 4019 | Unspecified essential hypertension | 4583 | 0.6218 |
| 2 | 41401 | Coronary atherosclerosis of native coronary artery | 3165 | 0.4294 |
| 3 | 4280 | Congestive heart failure, unspecified | 2748 | 0.3729 |
| 4 | 42731 | Atrial fibrillation | 2483 | 0.3369 |
| 5 | 2724 | Other and unspecified hyperlipidemia | 2198 | 0.2982 |
| 6 | 5849 | Acute kidney failure, unspecified | 1994 | 0.2706 |
| 7 | 51881 | Acute respiratory failure | 1506 | 0.2043 |
| 8 | 2720 | Pure hypercholesterolemia | 1473 | 0.1999 |
| 9 | 5990 | Urinary tract infection, site not specified | 1406 | 0.1908 |
| 10 | 2859 | Anemia, unspecified | 1215 | 0.1649 |

B

| | ICD9_CODE | n_subj | prevalence |
|---|---|---|---|
| | <chr> | <int64> | <dbl> |
| 1 | 4019 | 13030 | 0.3328 |
| 2 | 42731 | 7788 | 0.1989 |
| 3 | 41401 | 7610 | 0.1944 |
| 4 | 4280 | 7095 | 0.1812 |
| 5 | 5849 | 5693 | 0.1454 |
| 6 | 2724 | 5267 | 0.1345 |
| 7 | 51881 | 5213 | 0.1332 |
| 8 | 5990 | 4373 | 0.1117 |
| 9 | 2720 | 3862 | 0.0986 |
| 10 | 2859 | 3778 | 0.0965 |

C

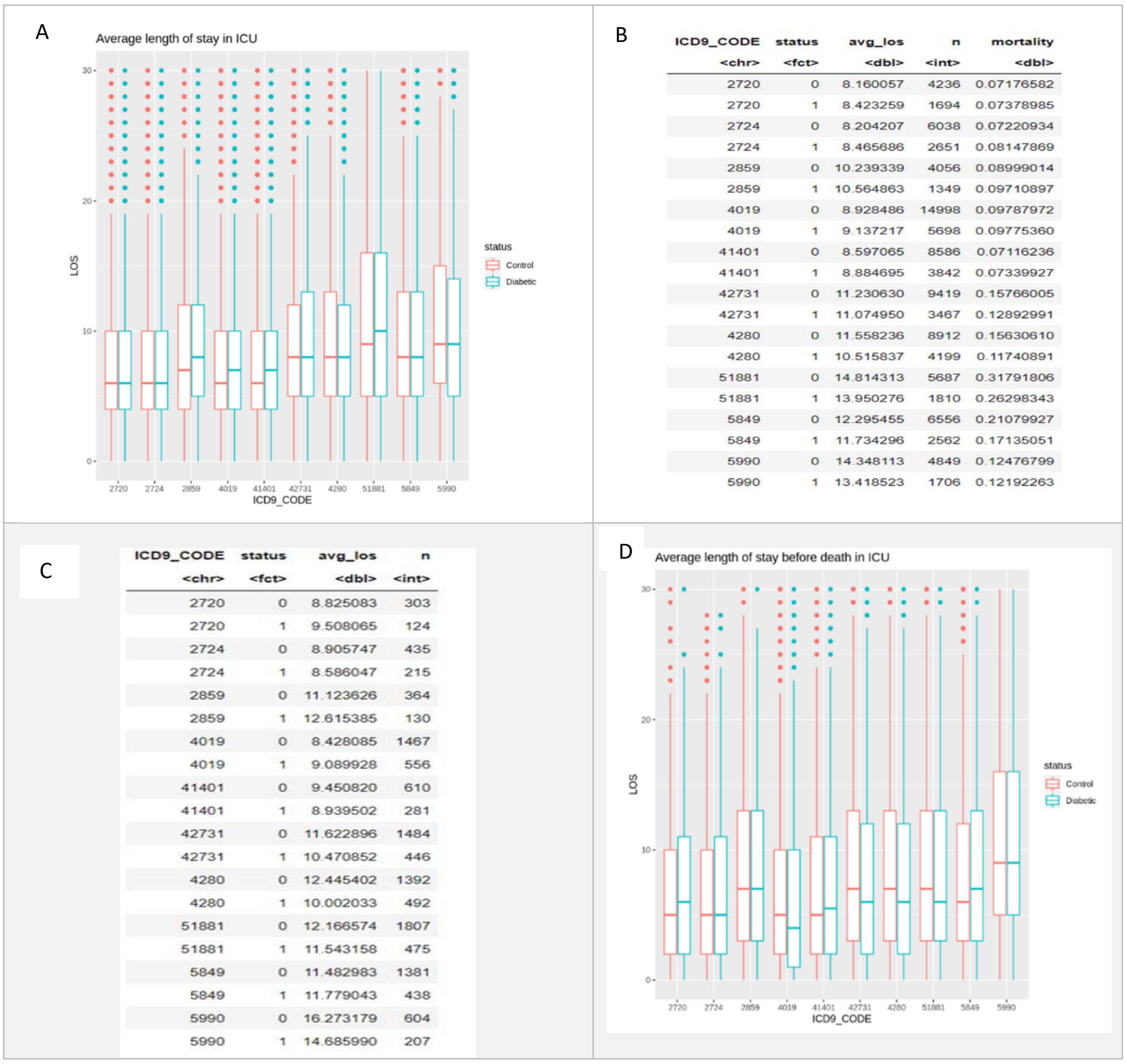
| | ICD9_CODE | LONG_TITLE | n_subj | prevalence | h_subj | h_prev |
|---|---|---|---|---|---|---|
| | <chr> | <chr> | <int64> | <dbl> | <int64> | <dbl> |
| 4 | 4019 | Unspecified essential hypertension | 4583 | 0.6218 | 13030 | 0.3328 |
| 5 | 41401 | Coronary atherosclerosis of native coronary artery | 3165 | 0.4294 | 7610 | 0.1944 |
| 7 | 4280 | Congestive heart failure, unspecified | 2748 | 0.3729 | 7095 | 0.1812 |
| 6 | 42731 | Atrial fibrillation | 2483 | 0.3369 | 7788 | 0.1989 |
| 2 | 2724 | Other and unspecified hyperlipidemia | 2198 | 0.2982 | 5267 | 0.1345 |
| 9 | 5849 | Acute kidney failure, unspecified | 1994 | 0.2706 | 5693 | 0.1454 |
| 8 | 51881 | Acute respiratory failure | 1506 | 0.2043 | 5213 | 0.1332 |
| 1 | 2720 | Pure hypercholesterolemia | 1473 | 0.1999 | 3862 | 0.0986 |
| 10 | 5990 | Urinary tract infection, site not specified | 1406 | 0.1908 | 4373 | 0.1117 |
| 3 | 2859 | Anemia, unspecified | 1215 | 0.1649 | 3778 | 0.0965 |

**Table 3**. Main common comorbidities of the diabetes population, and their prevalence in the study group and control group.

## Compare length of stay between comorbidities

We first want to see if there's a link between length of stay and diabetes + comorbidities. As illustrated in **Figure 1 A.** As the box plots show, there does not appear to be a significant difference in the distributions of length of stay between the diabetic and non-diabetic populations. This graphical representation is intended to demonstrate that whether or not you are diabetic while having these conditions is not a determinant factor in the length of stay in the ICU. **Figure 1B** shows the mortality rates for the same condition (ICD9 CODE) among diabetics and non-diabetics. There is no statistical significance between these groups, and the mortality rates differ by 1-7%.**Figure 1C** compares the average length of stay and number of deaths.

In terms of the average length of stay in ICU in patients before death**(Figure 1D)**, diabetics appear to die sooner, though there is no statistical significance. Differences between the patients with the outcome of death and those who were alive are shown.




| ICD9_CODE <chr> | status <fct> | avg_los <dbl> | n <int> | mortality <dbl> |
|---|---|---|---|---|
| 2720 | 0 | 8.160057 | 4236 | 0.07176582 |
| 2720 | 1 | 8.423259 | 1694 | 0.07378985 |
| 2724 | 0 | 8.204207 | 6038 | 0.07220934 |
| 2724 | 1 | 8.465686 | 2651 | 0.08147869 |
| 2859 | 0 | 10.239339 | 4056 | 0.08999014 |
| 2859 | 1 | 10.564863 | 1349 | 0.09710897 |
| 4019 | 0 | 8.928486 | 14998 | 0.09787972 |
| 4019 | 1 | 9.137217 | 5698 | 0.09775360 |
| 41401 | 0 | 8.597065 | 8586 | 0.07116236 |
| 41401 | 1 | 8.884695 | 3842 | 0.07339927 |
| 42731 | 0 | 11.230630 | 9419 | 0.15766005 |
| 42731 | 1 | 11.074950 | 3467 | 0.12892991 |
| 4280 | 0 | 11.558236 | 8912 | 0.15630610 |
| 4280 | 1 | 10.515837 | 4199 | 0.11740891 |
| 51881 | 0 | 14.814313 | 5687 | 0.31791806 |
| 51881 | 1 | 13.950276 | 1810 | 0.26298343 |
| 5849 | 0 | 12.295455 | 6556 | 0.21079927 |
| 5849 | 1 | 11.734296 | 2562 | 0.17135051 |
| 5990 | 0 | 14.348113 | 4849 | 0.12476799 |
| 5990 | 1 | 13.418523 | 1706 | 0.12192263 |

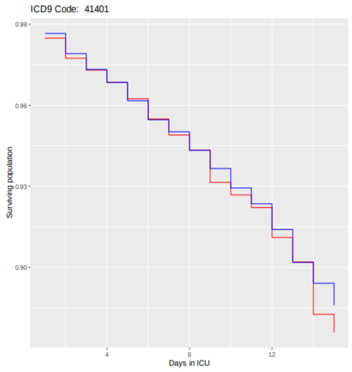
| ICD9_CODE <chr> | status <fct> | avg_los <dbl> | n <int> |
|---|---|---|---|
| 2720 | 0 | 8.825083 | 303 |
| 2720 | 1 | 9.508065 | 124 |
| 2724 | 0 | 8.905747 | 435 |
| 2724 | 1 | 8.586047 | 215 |
| 2859 | 0 | 11.123626 | 364 |
| 2859 | 1 | 12.615385 | 130 |
| 4019 | 0 | 8.428085 | 1467 |
| 4019 | 1 | 9.089928 | 556 |
| 41401 | 0 | 9.450820 | 610 |
| 41401 | 1 | 8.939502 | 281 |
| 42731 | 0 | 11.622896 | 1484 |
| 42731 | 1 | 10.470852 | 446 |
| 4280 | 0 | 12.445402 | 1392 |
| 4280 | 1 | 10.002033 | 492 |
| 51881 | 0 | 12.166574 | 1807 |
| 51881 | 1 | 11.543158 | 475 |
| 5849 | 0 | 11.482983 | 1381 |
| 5849 | 1 | 11.779043 | 438 |
| 5990 | 0 | 16.273179 | 604 |
| 5990 | 1 | 14.685990 | 207 |

**Figure 1**. Average length of stay in UCI graphs and mortality and number of death tables.

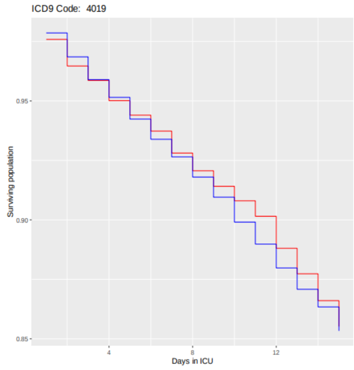
## KaplanMeier estimator for survival rates in cormobidities

Figure 2 shows that, despite the fact that the reviewed conditions are far more common in the diabetic population, there is no significant difference in their progression between the two populations. ICD9_CODEs 5849,4280,42731, and 51881 may appear to have some differences in terms of mortality, but they are not statistically significative(**Figure 1B**). The difference in mortality between both groups (diabetics and non-diabetics) differs only a 5%.

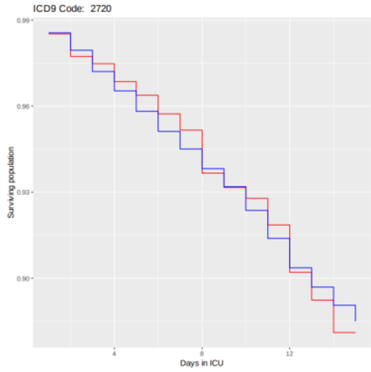
Coronary atherosclerosis of native coronary artery



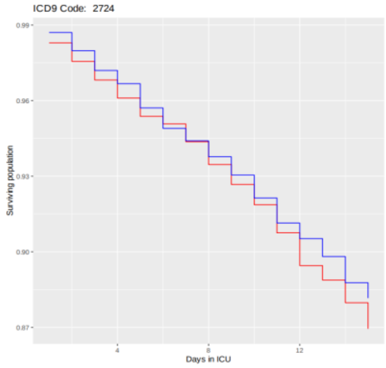

Unspecified essential hypertension



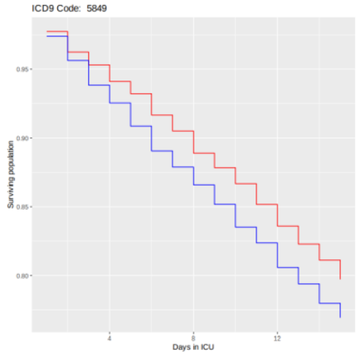

Pure hypercholesterolemia



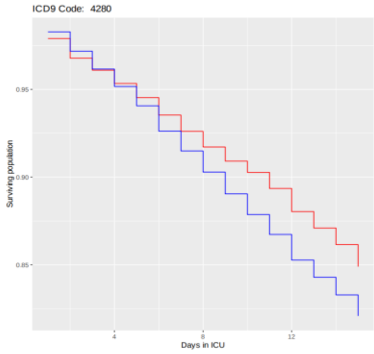

Other and unspecified hiperlipidemia



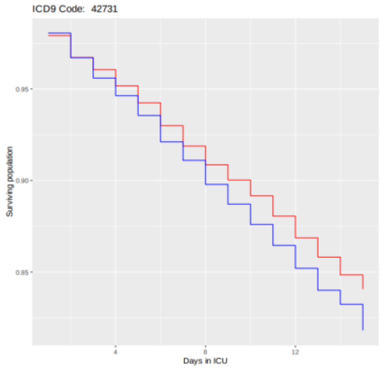

Acute kidney failure, unspecified



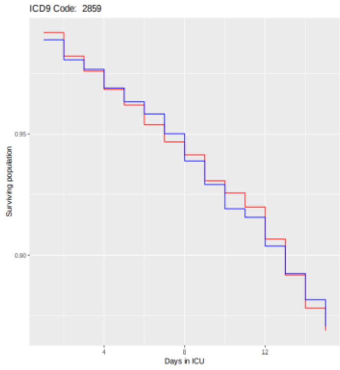

Congestive heart failure, unspecified



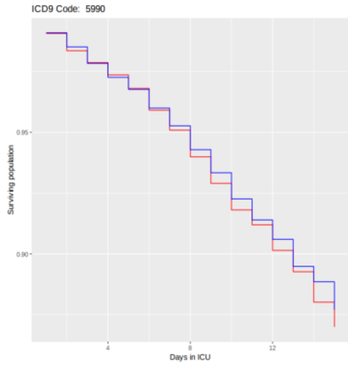

Atrial fibrillation




Anemia, unspecified




Urinary tract infection




Acute respiratory failure

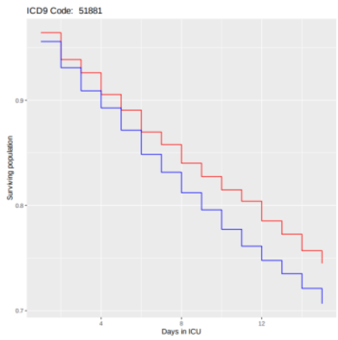



**Figure 2:**

KaplanMeier estimation plots of all the main ICD9_code cormobidities diabetes associated, comapring the surviving population and the days in the ICU. In red is represented the diabetic patients and in blue the control group

## Discussion

Despite the fact that diabetic patients are more likely to develop multiple conditions, we found no correlation in terms of mortality or length of stay. This increased risk of multicormobidity reflects the fundamental impact that prolonged exposure to high glucose and insulin resistance has on multiple organ systems, most notably on microvasculature, macrovasculature, and immune response[15,16]. These effects usually increase the risk of developing a myocardial infarction in people with type 2 diabetes mellitus (T2DM). This is consistent with our findings. The most common are vascular conditions, as we can see. However, the impact on multiple conditions is also due in part to declining mortalities, increased life expectancy, and varying trends in cause-specific mortality, resulting in a diversification of cause of death and complications.[17]

Although we did not explicity studied patient ethnicity, type of emergency and insurance,they did not seem to be significantly associated with mortality. Nonetheless, several studies have shown that patients with private insurance get better treatments that result in decreasing  mortality rates [18,19]

According to the data in Figure 1, no single existing comorbidity score or single variable has a significant influence on mortality rates. Based on the findings of the Kaplan-Meier mortality analysis, although having cormobidities associated in diabetic patients worse their outcome, it did not increase the risk of mortality in the ICU,owing to, we cannot conclude that diabetes is a factor influencing ICU survival rates. Nonetheless, we should keep in mind that ICU mortality is a multifactorial problem influenced by the severity of the admitting disease, the quality of care, and infections, among other things[20]. In terms of mortality and length of stay, the ICD-9-CM CODE appears to be the most representative variable.

Considering other studies, it is clear that we should have focused on other variables, such as,for example, mean glucose or mean HbA1c[21], since they are clinically used as a measure of diabetic health and could be a more explainatory elements on the progression of the patients .

We should also keep in mind that there is a lot of missing data and values that could affect our results.

### Conclusion

Diabetes patients are more likely to suffer from multicormobidities, which can have a negative impact on their lives. There was no significant difference in length of stay or mortality between the ICU population with type 2 diabetes and the control group. This, however, only addresses the progression of critical conditions and not the overall health impact of T2DM. Further research with different samples is needed to obtain conclusive and significant results that can characterize the model.

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