# Variation in 30-day mortality in Dutch hospitals after PCI-treatment for STEMI

***Master Thesis Health Economics, Policy and Law***
***Research report***


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***Word count:***
*9769*

***Rotterdam, 23-06-2021***

# Abstract

## Introduction

Coronary heart disease (CHD) is one of the main causes of mortality, especially myocardial infarction. Over the past five years the annual mortality after CHD has remained around 3 deaths per 10.000 inhabitants, after a decline in preceding years. A percutaneous coronary intervention (PCI) is the recommended treatment for an ST-elevated myocardial infarction (STEMI). Efficiency is one of the key pillars of health care in the Netherlands, which can be improved by increased effectiveness or decreased cost. The primary aim of this thesis is to improve the efficiency of PCI as treatment for STEMI through an increase in the effectiveness of PCI-treatments.

## Methods

A literature study was performed to identify the variables that are part of the process revolving around the treatment of a STEMI with a PCI. These variables are combined into a Directed Acyclic Graph (DAG) to check for confounding bias. Data of the hospital related variables was collected from the Inspectie Gezondheid en Jeugd (Inspection Health and Youth), IGJ, and patient related variables from the Centraal Bureau van de Statistiek (Central Bureau of Statistics), CBS, and Rijksinstituut Volksgezondheid en Milieu (Institute of Public Health and Environment), RIVM. Subsequently, two separate analyses were performed. The first investigated the variation in 30-day mortality rate between the hospitals by determining the deviation of the overall hospital mortality from the overall mean mortality. In the second analysis multiple univariate regression analyses are conducted in order to identify associations of the variables with the 30-day mortality after PCI as treatment for STEMI.

## Results

Of the 27 hospitals in this study, 4 hospitals had a significant deviation from the mean. AMC and Canisius-Wilhelmina Ziekenhuis had a significantly lower 30-day mortality, -1.10 (95% CI: -1.44, -0.77) and -1.04 (95% CI: -1.64, -0.43) percentage-point respectively. Catharina Ziekenhuis and Treant Zorggroep had a significantly higher 30-day mortality, 0.73 (95% CI: 0.23, 1.19) and 1.43 (95% CI: 0.52, 2.33) percentage-point respectively. The number of interventional cardiologists and the number of patients per interventional cardiologists are associated with a significant decrease in 30-day mortality. Male sex, age 80+, number of patients and longer door-to-PCI time are associated with a significantly higher 30-day mortality.

## Discussion

The results of this research suggest that there exists variation between hospitals in 30-day mortality after PCI as treatment for a STEMI. In order to improve their 30-day mortality rate, hospitals in the Netherlands, especially the two hospitals with a significantly higher 30-day mortality than average, should hire more interventional cardiologists, shorten the door-to-PCI time and make sure that the interventional cardiologists perform enough PCIs per year to maintain and improve their skills. Due to limited availability of data, only a part of the situation around PCIs as treatment for a STEMI is investigated and confounding bias has occurred. In future research the missing variables should be included, in order to prevent the confounding bias, and the financial consequences of suggested interventions need to be investigated.

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# Introduction

## Problem analysis

Coronary heart disease is one of the main causes of mortality, with myocardial infarction as most important factor (1) and is responsible for the largest number of DALY's in the Netherlands (2), indicating the high burden of this disease and the medical and societal relevance of additional research. Over the past 25 years the mortality caused by myocardial infarction in The Netherlands declined dramatically from 9,6 deaths per 10.000 inhabitants in 1996 to 3,1 deaths per 10.000 inhabitants in 2014 (3). However, over the past five years the annual mortality has hardly declined any further and remains around 3 deaths per 10.000 inhabitants.

During a myocardial infarction a thrombotic occlusion of one or multiple coronary arteries causes myocardial ischemia and ultimately necrosis of the affected cardiac tissue. When the coronary artery is completely occluded, transmural ischemia occurs, which is visible through ST-segment elevations at the ECG. This is called an ST-Elevated Myocardial Infarction (STEMI) (4).

There are three possible treatments for a myocardial infarction: i) coronary artery bypass graft (CABG), ii) percutaneous coronary intervention (PCI) and iii) thrombolytic treatment. However, a CABG takes more time to perform than a PCI or thrombolytic treatment. Therefore, this method is used in non-acute settings. The other two treatments are suitable for a myocardial infarction in the acute setting. During PCI a stent or balloon is used to compress the thrombus into the arterial wall. Thrombolytic treatment, also known as fibrinolysis, stimulates the immune system of the patient to dissolve the thrombus (5). The best treatment for a myocardial infarction in the acute setting is a PCI, because this results in a better survival rate (6). This is in accordance with the guidelines of the European

Cardiological Society, which advises to perform the PCI within two hours from STEMI diagnosis and within 12 hours from STEMI onset. Above this threshold fibrinolysis is recommended due to limited effect of PCI and possible complications of the intervention (7). A longer time between the onset of the myocardial infarction and the start of the PCI treatment is associated with worse outcomes and a higher mortality rate (8).

The overall health care costs in the Netherlands are rising, both in total as in percentage of Gross Domestic Product (GDP) (9). Medical expenses for coronary heart disease make up for 2,6% of the total healthcare costs in the Netherlands. The yearly costs incurred by Dutch hospitals in treating patients with coronary heart disease are 1,3 billion euros (10). For this reason, efficiency is one of the core pillars of our current healthcare system (11). Efficiency in healthcare stimulates achieving the largest possible health gain with the least required resources. This is achieved by treating the right patients and treating the patients right, providing patients with the care that best suits their pathology. Therefore, this thesis is aimed at improving the effectiveness of the treatment of STEMIs with PCIs, in order to achieve the maximum health gain possible.

The scientific relevance of additional research follows from the existence of a serious medical and societal problem that requires solving, most notably the fact that the decline of the myocardial infarction mortality has flattened, remaining around 3 death per 10.000 inhabitants (1). Finding a solution for this problem consists of two parts. The first part is to identify the hospitals in which mortality is significantly higher or lower compared to their peers. The second part is to identify which factors contribute to this higher or lower mortality in the respective hospitals. Therefore, in order to solve the problem, two questions need to be answered. The primary research question is “Which hospitals in the Netherlands have a higher mortality rate post-PCI-treatment for STEMI compared to the other Dutch hospitals that perform these treatments?” and the secondary research question is “Which factors are associated with a higher mortality rate post-PCI treatment for STEMI in Dutch hospitals, and what explains the low mortality rates of others?”

## Study aim

The primary aim of this research is to compare the 30-day mortality after a PCI as treatment for a STEMI, in all Dutch hospitals that perform PCI-treatments in the period between 2013 and 2019, in order to identify which hospitals have a higher mortality rate trend. The secondary aim is to explain the variability in mortality rates, with demographics, patient characteristics and hospital characteristics, such as sex, age and door-to-needle time. This information about the problems and success factors in hospitals regarding PCI-treatment for STEMI-patients can help hospitals to improve the effectiveness of the care they provide.

The layout of this thesis follows a number of logical steps to answer the research questions. The coming chapter, the theoretical framework, describes the background knowledge of percutaneous coronary interventions as treatment for a ST-elevated myocardial infarction. In the chapter Research methods, the data collection process is treated together with the empirical strategy of the statistical analyses. The results of these analyses are presented in the Result chapter. The Discussion contains the main findings of the statistical analyses, the validity and reliability of the results and recommendations for the Inspectie Gezondheidszorg en Jeugd, or IGJ (Inspection Healthcare and Youth), the hospitals that perform PCI-treatments and future research.

# Theory

Variation in treatment outcomes between hospitals exists. A part of this variation can be explained by patient characteristics and preferences. Being male, having a higher age and having comorbidities worsen the outcome in the case of a STEMI (12). The patient characteristics that are relevant for a STEMI are therefore age, sex and comorbidities. The majority of the literature agrees however, that this does not explain all variation (13-15). Therefore, variables describing the treatments and hospital processes regarding PCI-treatments for STEMIs must partially determine the outcome as well.

There are two treatments for myocardial infarction in the acute setting: percutaneous coronary intervention (PCI) or fibrinolysis. The best treatment for patients with a STEMI is a PCI within 90 minutes after onset of the myocardial infarction, because this treatment has a better survival rate than fibrinolysis (6). The most recent recommendation of the European Cardiological Society is that the PCI is performed within two hours after diagnosis of the STEMI and within 12 hours from STEMI onset. Above this threshold fibrinolysis is recommended due to limited effectiveness and possible complications of a PCI (7). In a PCI a stent or balloon is brought into the arterial circulation through the radial (wrist), brachial (arm) or femoral (leg) artery. The stent or balloon is used to press the thrombus into the arterial wall. The radial artery is the preferred entrance point since it gives the lowest risk of a bleeding at the puncture site (16). Fibrinolysis is performed when there is no technical expertise in the hospital to perform a PCI. This treatment activates molecules that break down the thrombus (5). There are two types of stents that can be used during a PCI: drug-eluting stents (DES) and bare metal stents (BMS). Of the drug-eluting stents there are early generation and new-generation stents. Early generation stents had similar results compared to bare metal stents regarding mortality and recidivism myocardial infarction, but had a slightly higher risk of stent thrombosis (17). New-generation drug-eluting stents have better outcomes in terms of mortality, stent thrombosis and revascularization than bare metal stents (18). Nonetheless, bare metal stents are still used in 20% of the PCI-treatments in the world (19). The transition of early generation to new-generation drug-eluting stents occurred during the study period. Hence, it is important to know which type of stent is used by the different hospitals, since there is a significant difference in mortality outcome between a PCI with new-generation drug-eluting stent and a PCI with a bare metal stent (18).

The choice of treatment after acute myocardial infarction not only depends on the patient’s preferences, but also on the preferences of the physician. Patients need to give consent for the treatment, as long as they are in a condition in which they are able to. The preference of the physician regarding the aggressiveness of the treatment, and the responsiveness to the eligibility of the patient to undergo the treatment also has an impact on the outcome (20). These preferences and convictions of physicians are not always evidence based (21). Besides the preferences and beliefs of physicians that determine the outcome after suffering a STEMI, the quality of the provided care also plays a relevant role. The next paragraphs will go through the process of treating a STEMI patient with PCI and highlight the factors that may have an association with the outcome.

The beginning of the process is the onset of the myocardial infarction. The first step is the transportation to the hospital and diagnosis of the STEMI. The time between onset of the infarction and the PCI is relevant, consisting of the onset-to-hospital and door-to-needle or door-to-balloon time, since it can have negative health outcomes for the patients when the time frame increases (8). The longer the time between the obstruction of the coronary artery and the removal of this obstruction, the more necrosis of myocardial tissue will have occurred due to the long-lasting ischemia, and the worse the outcome will be (4).

To clarify, the door-to-needle time is the time between the arrival in the hospital and the start of the PCI. The door-to-balloon time is the time between arrival in the hospital and the moment in the PCI-treatment that the balloon brought up through the arteries compresses the thrombus that causes the obstruction of the coronary artery.

The next step is treating the STEMI with PCI. The experience and skills of the physician, in this case an interventional cardiologist, is one of the key factors that determines the quality of care. Research indicates that there is a positive correlation between the number of PCIs, allowing physicians to gain more experience, and lower mortality rates (22). An interventional cardiologist who has a high caseload in PCI-treatments per year, performs better in terms of mortality rates and adverse events after PCI compared to an interventional cardiologist with a low caseload (23). Moon et al. found that mortality rates decline during the first two decades of a surgeon's professional life. In the third decade they stabilize and in the fourth decade the mortality rates increase (24). Furthermore, better survival rates are usually achieved in centers that perform a high volume of PCI-treatments (25).

The final step in the treatment is referral for cardiac rehabilitation (CR). CR consists of multiple parts and different specialists are involved. CR-programs are a combination of physical and mental exercises. Patients are encouraged to start working out more and education about risk factors and information how to change these factors is provided. The therapy aims for a positive change in the patient's behavior. Psychological help is offered where necessary. Physical training provides direct physiological effects through which benefits of CR-work and benefits are caused by change in behavior and risk factor moderation as well (26). Exercise-based cardiac rehabilitation significantly reduces the risk of cardiovascular mortality compared with no-exercise control group by 22% (27).

There is a model that accurately predicts the 30-day mortality after acute myocardial infarction (12). Despite the fact that this model used data from the period 1994 to 1996 and there have been significant developments in the treatment of acute myocardial infarctions in the past 25 years, it can still serve as a basis for identifying variables to be included in the analysis, especially patient related variables as sex and age. Furthermore, it underlines the effect of the presence of earlier diseases on mortality after suffering a myocardial infarction. Having suffered from a stroke in the past, having renal failure, having chronic obstructive pulmonary disease, history of heart failure and suffering from diabetes all have an odds ratio significantly higher than 1. This means that people with these comorbidities have a higher odds on mortality than people without these comorbidities, after suffering an acute myocardial infarction.

Both in-hospital mortality and 30-day mortality can be used to assess the performance of a hospital, but the assessments of these two are not the same. The in-hospital mortality is biased and favors hospitals with shorter lengths of stays (28). For that reason, 30-day mortality is deemed more appropriate and will be used in this thesis.

# Research methods

## Data collection

The hospital specific data used in this study will be collected from an open panel database of the IGJ. The dataset called 'Basisset Medisch Specialistische Zorg Kwaliteitsindicatoren ziekenhuizen' (Base data Medical Specialistic Care Quality indicators hospitals) is used for the observations about the hospital related variables in the analysis. The IGJ gathers information about a great number of variables concerning 20 different care processes across all Dutch hospitals and private clinics. One observation is the mortality after PCI of 1 hospital in 1 year, with additional variables that are part of the process revolving PCI-treatments. These additional variables, that are published by the IGJ, are door-to-balloon time in minutes, door-to-needle time in minutes, percentage of patients that receive cardiac rehabilitation after a STEMI, number of interventional cardiologists that are working in the hospital and the total number of patients with a PCI. It is not known, however, whether the interventional cardiologists are working parttime or fulltime. For the remainder of this thesis, it is assumed that the reported interventional cardiologists are working fulltime. There are 30 hospitals in the Netherlands that perform PCI-treatments. The study period covers seven years, from 2013 to 2019, which leads to a total of 210 observations.

However, this dataset focusses only on the care processes and fails to report relevant patient characteristics, even though these are major outcome predictors. Therefore, the data of the demographic characteristics of the patients in the municipalities that the respective hospitals are in, are retrieved from the database of Centraal Bureau van de Statistiek (Central Bureau of Statistics). These characteristics are i) the percentage males in the population of the municipality each hospital is in, ii) the percentage of the population aged 65-80 and iii) the percentage of the population aged 80+. This information is available for every municipality for all years during the study period, which also leads to 210 observations, corresponding with the number of observations that are retrieved from the IGJ dataset. In the absence of patient-specific data, which would have delivered the most insights during the data analysis, this allows for a certain adjustment for age and sex.

Information about the comorbidities in the municipalities the hospitals are in, is retrieved from the 'Gezondheidsmonitor' (Health monitor), an inquiry by the Rijksinstituut Volksgezondheid en Milieu (RIVM, institute of public health and environment), since this information, as well as the demographic characteristics, is missing in the dataset of the IGJ. In the Gezondheidsmonitor a comorbidity is defined as the presence of one of more chronic conditions. The RIVM performs the inquiry once every four years to register the presence of comorbidities in the Dutch population. The only year for which the results are published during the study period is 2016, leading to only 30 observations within the 2013-2019 study period.

## Data cleaning

Before starting the statistical analysis, the data needs to be cleaned. The criteria for inclusion in this research are 1) hospitals reporting the 30-day mortality after PCI treatment for STEMI 2) the availability of 30-day mortality data between 2013 and 2019. Before 2013, mortality rates following all types of PCI-treatments are reported, not specifically after PCI-treatments in STEMI-patients. Therefore, it is not known how many patients with a STEMI have received a PCI and what the subsequent 30-day mortality is. For this reason, data before 2013 was not included in this analysis.

The dataset does not contain a variable that describes the experience and skills of the interventional cardiologists. In order to approximate this experience level, the number of patients is divided by the number of interventional cardiologists for each hospital in each year. The underlying assumption is a positive correlation between the skills and experience levels of interventional cardiologists and the number of PCI-treatment performed (23).

Another potential issue is missing data. This risk is present in three variables: 1) door-to-needle time, 2) door-to-balloon time and 3) the percentage of patients that received cardiac rehabilitation after PCI-treatment. To solve this problem, the door-to-needle and door-to-balloon time are combined into the door-to-PCI time in this analysis, since the mean of the door-to-needle and the door-to-balloon time differed only two minutes. However, even after this adjustment, there is still some missing data of the door-to-PCI time. The traditional missing data methods, like data deletion and mean imputation, are not applied in this analysis, considering the substantial bias and lack of power that these methods produce (29). Literature suggests that either multiple imputation or maximum likelihood estimation should be used to analyze datasets with missing data (29). However, these methods are very complex and require thorough background knowledge of the model and impact of the different variables on the missing data. This elaborate background knowledge is not known based on the available data and literature of this thesis. For that reason, the method of interpolation is used in this analysis to impute the missing data. This method uses the available data to identify the trend that best suits the datapoints. The missing values are subsequently based on this trend. Despite the fact that interpolation represents the true data less precisely, this method allows for missing data imputation with less bias than data deletion or mean imputation, and without the complex model and elaborate background knowledge required for multiple imputation and maximum likelihood estimation. It is not possible that more than 100% of the patients with a STEMI receive cardiac rehabilitation. For that reason, the interpolation values are capped at 0% and 100%.

Interpolation is not possible for the data about comorbidities, since there is only one value known per hospital. Comorbidities mostly are chronic diseases. The prevalence of chronic diseases hardly changes over a few years' time span. Therefore, the value of comorbidities in 2016 will not differ much from the values in surrounding years. For that reason, the value of the respective hospitals in 2016 is imputed in all other years.

### Standardization

Several hospitals have merged during or before the study period. Due to these mergers, there are hospitals that operate in multiple municipalities. This plays an important role for the demographic information of the patients, because this data is collected on the municipality level. If the merger happened during the study period, in all cases there was only one hospital that performed PCI-treatments before the merger. Therefore, the observations do not need to be combined during the study period, as the reported number of this one location can be used in the analysis. This assumes that the PCI's are still performed in the same hospital as before the merger. For the hospitals that have merged before the start of the study period, it is not known which location performs the PCI-treatments. In the dataset of the IGJ the data of the merged hospital is reported yearly in a single observation. Since the demographic characteristics of the patients are collected on the municipality level, and some hospitals have locations in different municipalities, there are multiple observations yearly for the demographic variables. These multiple observations need to be combined into one observation, in order to include them into the analysis. This combined observation is the weighted average of the demographic characteristics of the different municipalities. The weight is the population of the various municipalities. This way potential bias due to incorrect means, leading to lower content validity, is prevented.

## Conceptual model

To get an overview of the relationships between the variables, a Direct Acyclic Graph (DAG) is drawn. This graph consists of the outcome variable, the dependent variable, the independent variables and arrows that depict the possible associations. The arrows indicate possible impacts of one variable on another. Only when it is proven that there is no significant association between two variables, no arrow is drawn. In all other cases, there may be a relevant relationship and hence the arrow is included.  However, these arrows can only go one way and cannot point back at themselves through another variable.

Drawing a DAG helps identifying possible bias through confounding, intermediates and colliders. This way one can make sure that the results are adjusted for the right variables and bias is prevented as much as possible.

Based on the variables described previously, the following DAG can be drawn.

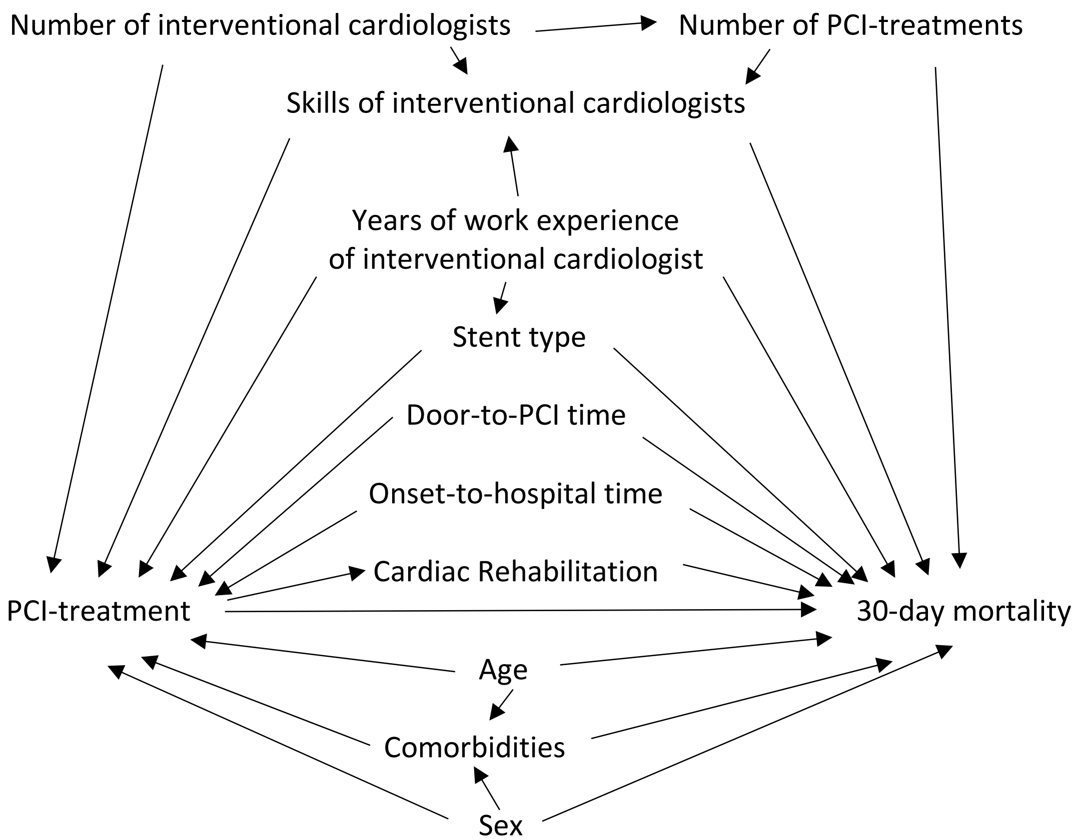


*Figure 1. Direct acyclic graph (DAG) of the variables that are associated the relation between PCI-treatment and 30-day mortality.*

Based on the DAG and availability of data, the independent variables that are included in the regression equation are the following:

- Door-to-PCI time
- The number of interventional cardiologists in the hospital
- The number of STEMI patients per year that receive a PCI-treatment in the hospital
- Experience of interventional cardiologists
- The percentage of patients that receive cardiac rehabilitation after PCI-treatment for a myocardial infarction
- For each hospital and their respective municipality populations: the percentage of males, the percentage of the population aged 65-80 and the percentage of population aged 80+

Some factors are not or only limitedly included in the analysis due to the lack of available information. These are:

- Comorbidities of the patients
- Type of stent used in PCI
- Onset-to-hospital time
- The number of years an interventional cardiologist has worked

The fact that these variables are not part of the analysis, changes the regression results. The results now present a less complete picture than the situation where these variables would be included, because the variables that cannot be included due to missing information are associated with a higher or lower mortality after a PCI (8,12,24,30). Additionally, as can be seen in the DAG, confounding bias is present when the results are not adjusted for these missing variables. The presence of comorbidities, a longer onset-to-hospital time and the use of a bare metal stent instead of a new-generation drug-eluting stent are associated with a higher mortality rate after suffering a STEMI (8,12,30). For that reason, it would lead to an overestimation of the other variables, when these three variables are not included in the analysis. In the first two decades of their career, the mortality rate of the treatments performed by that interventional cardiologists declines. In the third decade the mortality stabilizes and in the last decade it increases (24). Therefore, not including the total years of work experience of an interventional cardiologist can lead to either positive or negative biased results, due to varying mortality rates. Subsequently, the incomplete results alter the interpretation of the analysis. It leads to a less representative and biased result, and therefore a lower content validity.

## Empirical strategy

Answering the research questions requires two separate analyses. The first intends to identify whether there is variation in 30-day mortality after PCI-treatment between hospitals in the Netherlands. The second focuses on adjusting the variation using the data provided by the IGJ and additional data about characteristics of the patients in the various regions. This analysis allows to see which variables are the main cause of the variation between hospitals, or proves that the variation found in the first analysis, cannot fully be explained with the variables included in this thesis.

## First analysis

In order to identify which hospitals are above or below the average 30-day mortality, several steps are required.

1) The first step is to calculate the mean mortality in each year. This overall mean mortality of a certain year is subsequently compared with the 30-day mortality per hospital in that same year.

2) The next step is to determine the deviation of the hospital specific mortality from the overall mean mortality in that year for each consecutive year from 2013 to 2019.

3) The overall deviation of the different hospitals is calculated by taking the mean of the hospital specific deviation from the overall mean mortality, combining all deviations of a hospital in the period 2013-2019. This provides a value that indicates the performance of a hospital compared to the overall mean regarding 30-day mortality after PCI-treatment for a myocardial infarction.

4) After calculating the 95% confidence intervals, the hospitals with a statistically significant high or low 30-day mortality can be identified. A 95% confidence interval can be calculated by adding 1,96 *standard deviation to the mean (upper bound) and subtracting 1,96*standard deviation from the mean (lower bound) (31). The standard deviation of the mean of the hospital specific deviation is used for calculating the 95% confidence intervals. When one is calculating the difference between two variables, the difference is considered significant when the confidence interval is entirely above or below zero.

## Second analysis

The second analysis focusses on identifying which variables are associated with a higher or lower mortality rate. A regression analysis will be performed to identify these variables. In total three regressions will be performed: a main regression analysis, a regression analysis with comorbidities and a subgroup regression analysis. The regression produces regression equation as follows:

$$Y_o = ß_0 + ß_1 * v_1 + ß_2 * v_2 + ß_3 * v_3 + ß_4 * v_4 + ß_5 * v_5 + ß_6 * v_6 + ß_7 * v_7 + ß_8 * v_8 + ß_9 * v_9$$

Where:

$Y_o$ = the outcome variable 30-day mortality

$ß_0$ = the constant

$ß_{1\text{-}9}$ = regression coefficients of the independent variables

$v_1$ = Door-to-PCI time

$v_2$ = Number of interventional cardiologists working in the hospital

$v_3$ = Number of STEMI-patients that receive PCI-treatment in the hospital

$v_4$ = Experience of interventional cardiologists

$v_5$ = Percentage of patients that receive cardiac rehabilitation after PCI-treatment for myocardial infarction

$v_6$ = Percentage of males in the municipality population

$v_7$ = Percentage of the municipality population aged 65-80

$v_8$ = Percentage of municipality population aged 80+

$v_9$= Percentage of STEMI-patients that receive cardiac rehabilitation

$ß_9$ and $v_9$ are only part of the regression equation in the regression analysis with comorbidities and the subgroup analysis.

The outcomes of the regression analysis are the regression coefficients of the different variables. These coefficients indicate the association of each variable with the mortality rate. If a variable has a positive regression coefficient, that variable is associated with a higher 30-day mortality, and vice versa. This way not only the negative factors are identified but also the success factors, providing the hospitals with more precise information and insights on how they can improve their medical treatment.

### *Comorbidities*

A second regression analysis is performed for comorbidities because of the limited number of observations. This separate regression analysis is performed because there is data available and comorbidities are an important outcome determinant after suffering a myocardial infarction. All variables that are included in the main regression analysis are also included in this additional regression analysis. Two regression analyses are performed: i) a regression with the data from 2016, the only year in which information about comorbidities in the population of the municipality the hospital is in, is available and ii) a regression with imputed comorbidities data.

### *Subgroup regression*

Lastly a subgroup regression analysis is performed. The hospitals are divided into two groups, one with the academic hospitals and one with the peripheral hospitals. In general, academic hospitals treat more complicated patients than peripheral hospitals. This may lead to case-mix differences between academic and peripheral hospitals. This case-mix can lead to higher mortality numbers in academic hospitals, because of their more complicated patient population. For that reason, an additional regression analysis is performed, in which the hospitals are divided into two groups, based on the fact whether it is an academic hospital or not, again with the same variables as are used in the earlier analyses. This way some of the case-mix bias may be prevented.

These analyses combined can now be used to answer the second part of the research question, by identifying which variables are associated with a high 30-day mortality rate.

# Results

## Data

Of the 30 hospitals that perform PCI-treatments in the Netherlands, 27 are included in this analysis. The 3 hospitals that are not included, did not report the mortality after the PCI-treatment as 30-day mortality, or did not report the 30-day mortality between 2013 and 2019. The mean time between arrival in the hospital and the PCI was 24,16 minutes. The standard deviation is 8,03, indicating a broad spread in reported times between the hospitals. This broad spread is also evident in the reported 30-day mortality and the number of patients with a PCI-treatment. The mean percentage of patients with a STEMI that receives cardiac rehabilitation is 75,92% with a standard deviation of 26,89. The data that is used in the analysis is depicted in table 1.

| | MEAN | STANDARD DEVIATION |
|---|---|---|
| **HOSPITALS** | 27 | |
| **30-DAY MORTALITY (%)** | 2,32 | 0,96 |
| **TIME DOOR-TO-PCI (MINUTES)** | 24,16 | 8,03 |
| **NUMBER OF PATIENTS WITH PCI** | 347,40 | 125,79 |
| **NUMBER OF INTERVENTIONAL CARDIOLOGISTS** | 5,80 | 1,33 |
| **HEART REHABILITATION (%)** | 75,92 | 26,89 |
| **SEX (% MALES)** | 49,37 | 0,75 |
| **AGE 65-80 (%)** | 12,63 | 2,49 |
| **AGE 80+ (%)** | 4,24 | 0,98 |

*Table 1. Characteristics of the hospitals. The reported means are the means of all hospitals in all years of the study period.*

As can be seen in Figure 2, the mean 30-day mortality rate after a PCI as treatment for a STEMI fluctuates around 2,3% ± 0,5%. This shows that there is variation in 30-day mortality between the different years during the study period, but that there is also large variation between the hospitals in the different years. There is no clear trend visible, indicating that the 30-day mortality has hardly changed during the study period, neither the mean nor the variation between hospitals within a year.

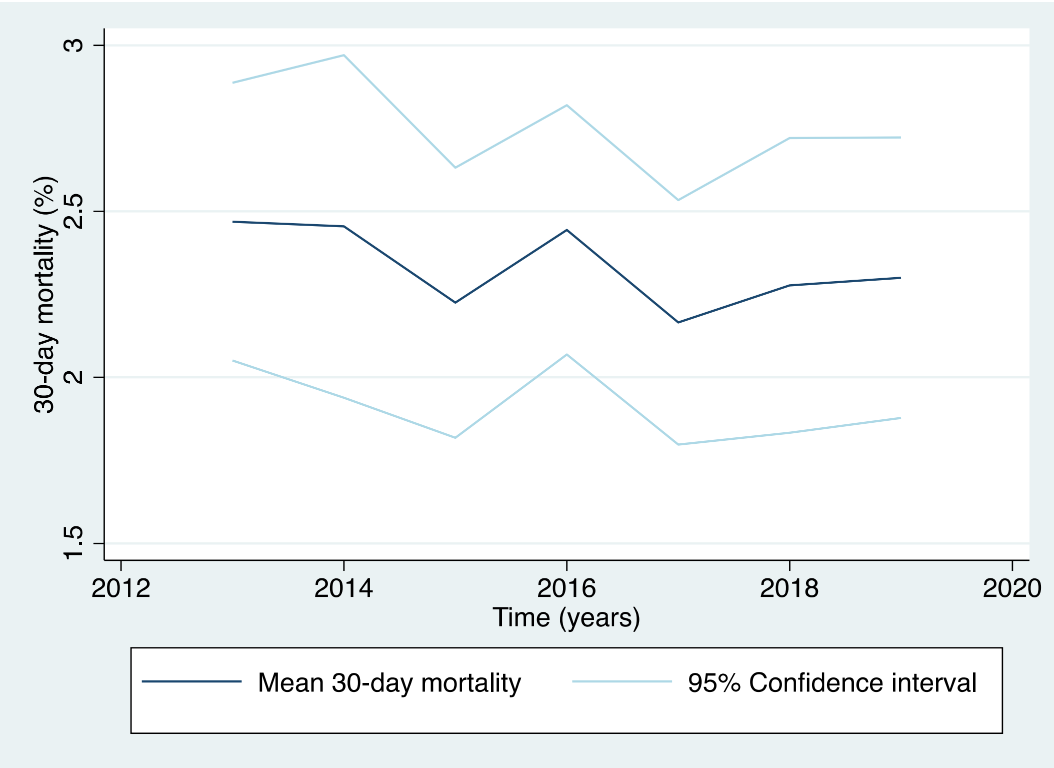


*Figure 2. Development of mean 30-day mortality through time.*

Figure 3 describes the mean number of patients that underwent a PCI after suffering a STEMI during the study period, showing possible changes throughout the years. In 2013 there was a relatively large number of patients that underwent a PCI compared to later years. This high mean is remarkable, especially because in 2013 there were two hospitals that reported, respectively, 43 and 24 treated STEMI with a PCI, as can be seen in figure 7, leading to the large confidence interval in that year. After 2014 the number of patients shows a negative trend with only in 2016 and 2017 slightly more patients than in surrounding years. The two hospitals with a low reported number of patients in 2013 are geographically far from the hospitals with a STEMI population of 600-800 patients. Therefore, the relatively high mean in 2013 cannot be explained by patient spread in the years thereafter. The 95% confidence interval has gotten smaller from 2013 to 2015 and remained similar in the subsequent years, but still shows a large variation in number of patients between the hospitals in the different years.

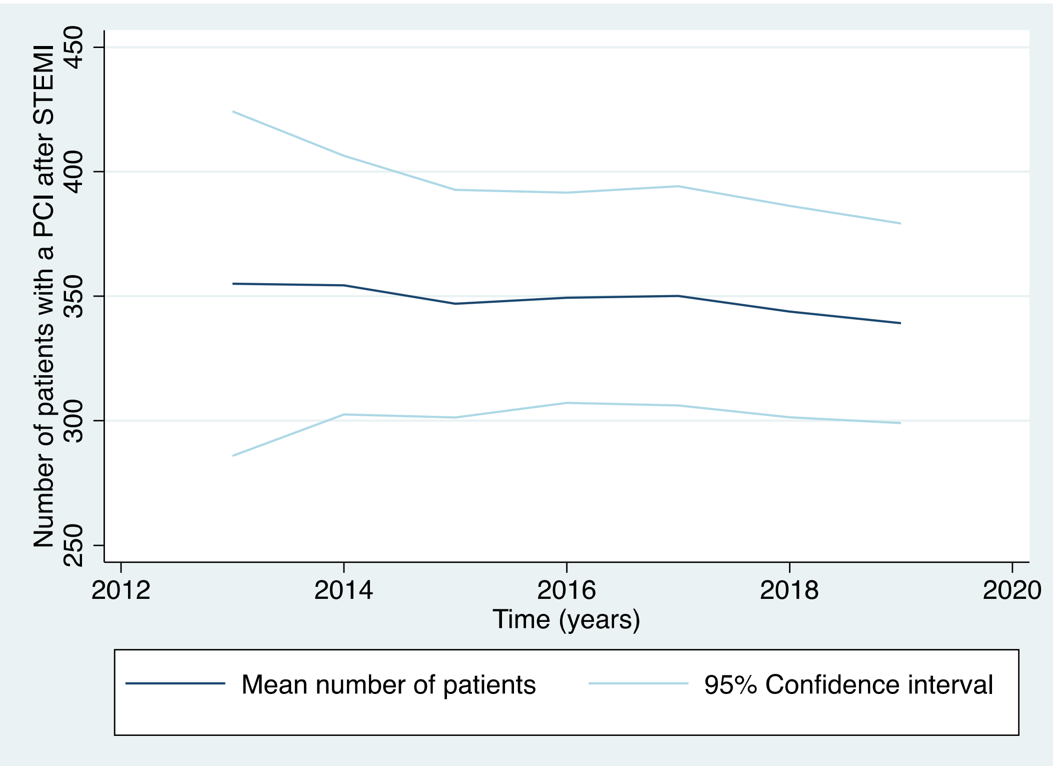


*Figure 3. Development of mean number of patients per hospital through time.*

During the first years of the study period the door-to-PCI time declined rapidly (figure 4). However, from 2017 the decline flattened. The 95% confidence interval shows that there exists variation between the hospitals in door-to-PCI time, but this variation is not as substantial as for the 30-day mortality or the total number of patients with a PCI after STEMI. As can be seen in figure 5, a longer door-to-PCI time is associated with a higher 30-day mortality. For that reason, it would be interesting to see why the decline has stopped in 2017. This goes beyond the scope of this thesis but is something worth investigating in future research.

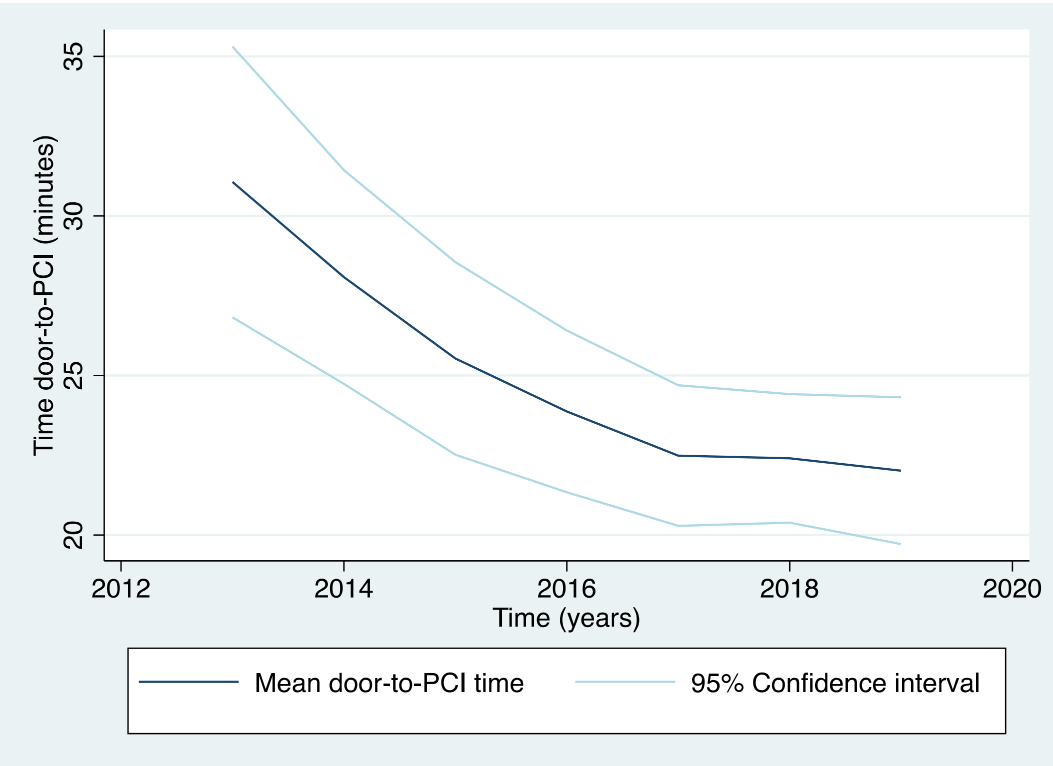


*Figure 4. Development of door-to-PCI time through time.*

The difference between the longest and shortest door-to-PCI time (figure 5) is almost 50 minutes. This is a substantial difference given the fact that with every minute the coronary artery is obstructed, more necrosis of myocardial tissue occurs because it spends more time in ischemia (4). There are two outliers visible that are reported door-to-PCI times of 6 and 8 minutes. These numbers are what ZorgSaam Zeeuws-Vlaanderen reported to the IGJ in two consecutive years, without distinctive explanation why these two numbers are 10 minutes shorter than the reported door-to-PCI times in the surrounding years. This most likely has been a reporting error by the hospital. Furthermore, the fitted line shows an association between a longer door-to-PCI time and a higher 30-day mortality.

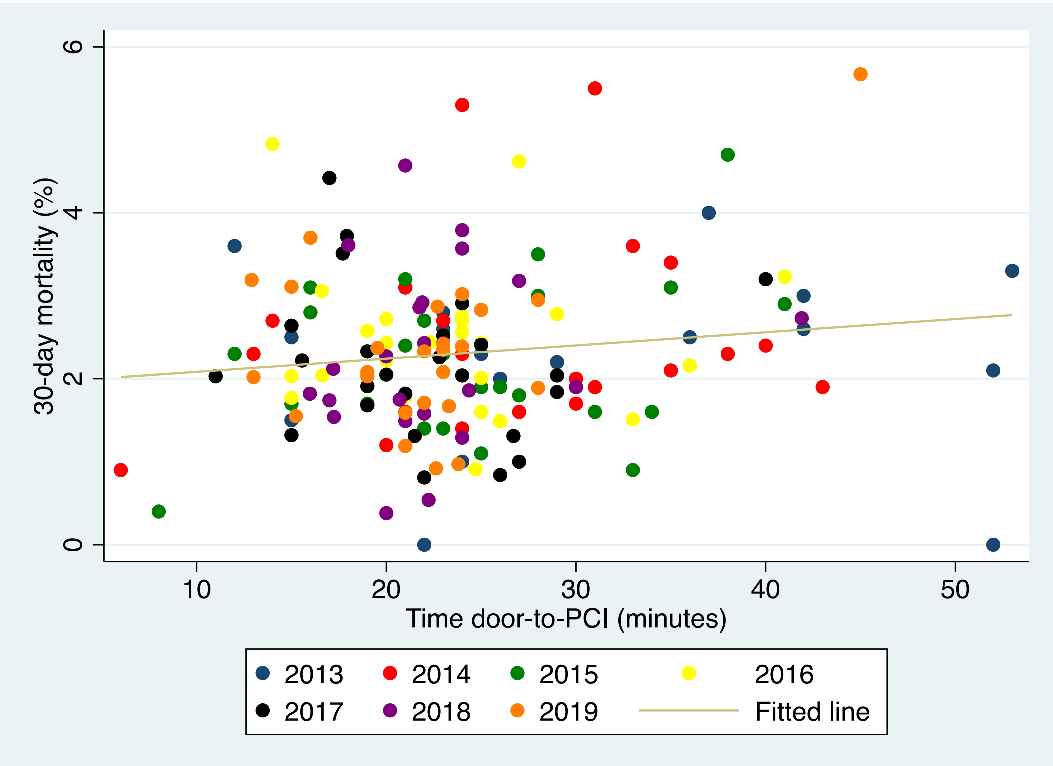


*Figure 5. Scatterplot door-to-PCI time and 30-day mortality with fitted line.*

In Figure 6, there are the two outliers at the bottom left of the graph. These two datapoints show that two hospitals in 2013 have treated close to zero patients. The hospitals started performing PCI-treatments in 2013. That may be an explanation for the low number of patients. Furthermore, the fitted line shows that a higher number of patients with a PCI in a hospital is associated with a higher 30-day mortality.

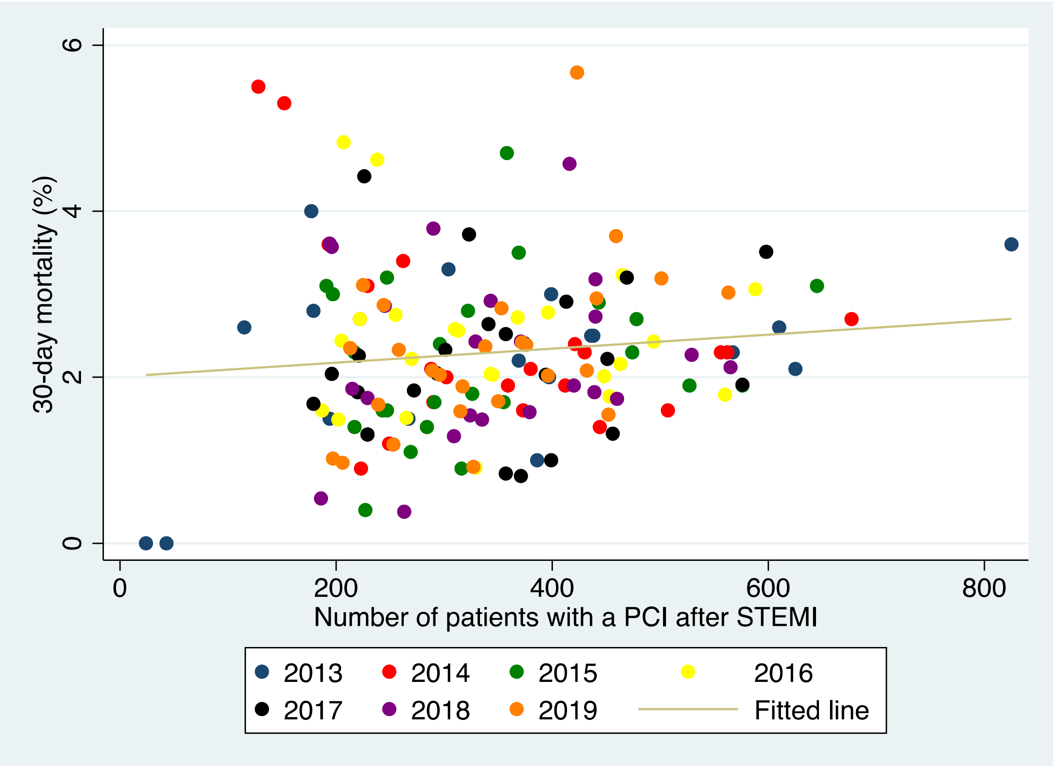


*Figure 6. Scatterplot of number of patients per hospital and 30-day mortality with fitted line.*

There are two observations that are noteworthy about the datapoints in Figure 7. Firstly, there are multiple datapoints with a 0% cardiac rehabilitation. Amphia Ziekenhuis and Maasstad Ziekenhuis do not offer a cardiac rehabilitation program, leading to a score of 0% of patients that receive cardiac rehabilitation in the hospital after a STEMI. Both hospitals refer their patients to other clinics for the rehabilitation but have no information about how many patients receive the cardiac rehabilitation. Secondly, the fitted line shows that a higher percentage of patients with cardiac rehabilitation is associated with a lower 30-day mortality, as would be expected based on existing literature (27). This would mean that it would be useful to investigate the possibilities to implement this program and enlist as many patients as possible after a PCI.

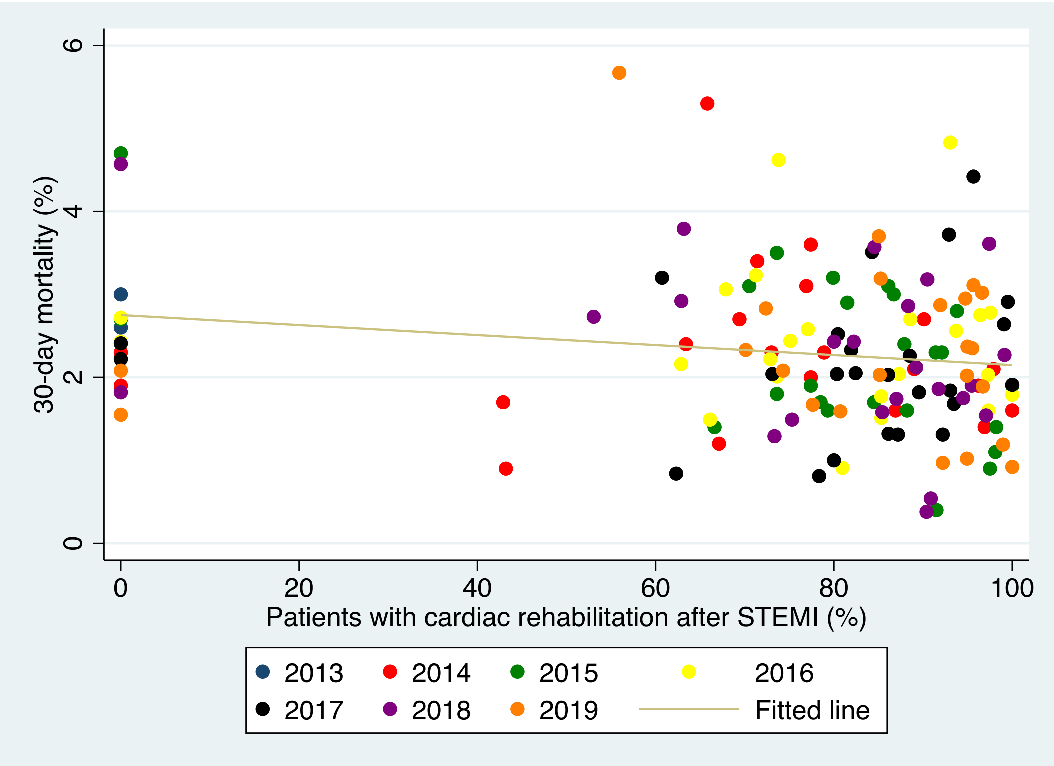


*Figure 7. Scatterplot of percentage of patients that receive cardiac rehabilitation after STEMI and 30-day mortality with fitted line.*

## First analysis

Of the 27 hospitals in this analysis, only two hospitals had a significantly higher, and two hospitals had a significantly lower 30-day mortality than average in the period 2013-2019. The two hospitals with a higher than average 30-day mortality were Treant Zorggroep and Catharina Ziekenhuis (table 2a). The two hospitals with a lower than average 30-day mortality were AMC and Canisius-Wilhelmina Ziekenhuis (table 2b). This shows that there exists variation in 30-mortlity after a PCI-treatment for patients with a myocardial infarction between Dutch hospitals.

| HOSPITALS WITH 30-DAY MORTALITY BELOW AVERAGE | 30-DAY MORTALITY COMPARED TO AVERAGE | 95% CI |
|---|---|---|
| **AMC** | -1.10** | -1.44, -0.77 |
| **CANISIUS-WILHELMINA ZIEKENHUIS** | -1.04** | -1.64, -0.43 |
| **VUMC** | -0.76 | -2.17, 0.65 |
| **LUMC** | -0.71 | -2.41, 0.99 |
| **ZUYDERLAND MC** | -0.60 | -1.90, 0.70 |
| **ST. ANTONIUS ZIEKENHUIS** | -0.46 | -1.20, 0.28 |
| **NOORDWEST-ZIEKENHUISGROEP** | -0.36 | -1.41, 0.69 |
| **ELISABETH-TWEESTEDEN ZIEKENHUIS** | -0.24 | -1.05, 0.58 |
| **RIJNSTATE ZIEKENHUIS** | -0.22 | -0.69, 0.25 |
| **HAGAZIEKENHUIS** | -0.19 | -0.58, 0.20 |
| **UMC ST RADBOUD** | -0.17 | -1.20, 0.28 |
| **MUMC** | -0.14 | -0.96, 0.68 |
| **AMPHIA ZIEKENHUIS** | -0.10 | -0.48, 0.27 |
| **MEDISCH SPECTRUM TWENTE** | -0.10 | -0.79, 0.59 |
| **VIECURI** | -0.06 | -0.38, 0.26 |
| **MEANDER ZORGGROEP** | -0.04 | -1.03, 0.94 |

*Table 2a. Hospitals with 30-day mortality below average. Mean 30-day mortality per hospital compared to average overall 30-day mortality. ** indicates a significant result.*

| HOSPITALS WITH 30-DAY MORTALITY ABOVE AVERAGE | 30-DAY MORTALITY COMPARED TO AVERAGE | 95% CI |
|---|---|---|
| **Erasmus MC** | 0.02 | -1.48, 1.53 |
| **Tergooi** | 0.10 | -1.34, 1.55 |
| **UMC Utrecht** | 0.10 | -0.42, 0.62 |
| **MCL** | 0.10 | -0.49, 0.70 |
| **Jeroen Bosch Ziekenhuis** | 0.33 | -0.14, 0.79 |
| **ZorgSaam Zeeuws-Vlaanderen** | 0.35 | -1.30, 1.99 |
| **Haaglanden MC** | 0.41 | -0.75, 1.57 |
| **Catharina Ziekenhuis** | 0.71** | 0.23, 1.19 |
| **Maasstad Ziekenhuis** | 0.72 | -0.38, 1.82 |
| **UMCG** | 0.90 | -0.17, 1.97 |
| **Treant Zorggroep** | 1.43** | 0.52, 2.33 |

*Table 2b. Hospitals with 30-day mortality above average. Mean 30-day mortality per hospital compared to average overall 30-day mortality. ** indicates a significant result*

## Second analysis

As can be seen in table 3, all independent variables were statistically significant except for the percentage of municipality population aged 65-80 and the percentage of patients that receive cardiac rehabilitation. Being a male, having an age of 80 years or higher, higher number of patients in a hospital and a longer door-to-PCI time are all associated with an increased 30-day mortality. More interventional cardiologists and more patients per interventional cardiologists are variables that are associated with a decreased 30-day mortality. This means that, in order to decrease their 30-day mortality after a PCI as treatment for a STEMI, hospitals should employ more interventional cardiologists, make sure these interventional cardiologists are skilled by performing many treatments and shorten the door-to-PCI time. Based on the regression coefficients, increasing the total number of interventional cardiologists is associated with the largest decrease in 30-day mortality. One additional interventional cardiologist is associated with a decrease in 30-day mortality of 0,630 percentage-points. The number of patients, patients per interventional cardiologists and door-to-PCI time are associated with a small difference in 30-day mortality. However, when there are large numbers of patients or differences in time, the small differences in 30-day mortality can become more substantial in absolute terms. The total number of patients cannot be decreased by hospitals. To decrease the total number of patients with a STEMI, for example a government funded prevention campaign would be needed. Investing in a cardiac rehabilitation program is as not useful for lowering 30-day mortality after PCI as treatment for a STEMI, based on this analysis. However, it may have benefits in helping patient return to their normal life after suffering a life-threatening event such as a STEMI, by education about risk factors and provision of psychological support  (26).

Therefore, despite that this analysis suggests that cardiac rehabilitation not effective in lowering the 30-day mortality, it can still be useful.

| 159 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| **MALE SEX** | 0,303*** | 0,068 – 0,538 |
| **AGE 65-80** | -0,019 | -0,120 – 0,082 |
| **AGE 80+** | 0,291*** | 0,050 – 0,532 |
| **NUMBER OF PATIENTS** | 0,010*** | 0,004 – 0,016 |
| **NUMBER OF INTERVENTIONAL CARDIOLOGISTS** | -0,630*** | -0,958 – -0,301 |
| **PATIENTS PER CARDIOLOGIST** | -0,062*** | -0,097 – -0,027 |
| **TIME DOOR-TO-PCI** | 0,037*** | 0,019 – 0,056 |
| **CARDIAC REHABILITATION** | -0,003 | -0,008 – 0,003 |
| **CONSTANT** | -11,519* | -22,298 – 1,261 |

*Table 3. Regression results primary regression: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

When comorbidities are added to the analyses, the interpretation of the results remains the same as the results depicted in table 3. The presence of comorbidities is not significantly associated with a lower or higher 30-day mortality after PCI as treatment for a STEMI. This contradicts earlier literature, in which the presence of comorbidities is associated with a higher mortality rate after a STEMI (12). Either the earlier studies presented incorrect results, or the data from the Gezondheidsmonitor of 2016, interpolated in the other years of the study period, is not representative for the presence of comorbidities in the patients that undergo a PCI as treatment for a STEMI.

The R-squared of the regression described in table 3 and 4 was 24%, indicating that the variables in this model explain only 24% of the variation in 30-day mortality. This is in line with the interpretation that the comorbidities based on the Gezondheidsmonitor are not a good predictor of patients' comorbidities, since the R-squared remains the same after adding an extra variable to the analysis.

| 159 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| **MALE SEX** | 0.303*** | 0.067, 0.538 |
| **AGE 65-80** | -0.011 | -0.117, 0.095 |
| **AGE 80+** | 0.301*** | 0.056, 0.546 |
| **NUMBER OF PATIENTS** | 0.010*** | 0.004, 0.016 |
| **NUMBER OF INTERVENTIONAL CARDIOLOGISTS** | -0.607*** | -0.949, -0.264 |
| **PATIENTS PER CARDIOLOGIST** | -0.060*** | -0.096, -0.024 |
| **TIME DOOR-TO-PCI** | 0.039*** | 0.020, 0.058 |
| **CARDIAC REHABILITATION** | -0.002 | -0.008, 0.003 |
| **COMORBIDITIES** | -0.014 | -0.072, 0.044 |
| **CONSTANT** | -10.360* | -22.188, 1.468 |

*Table 4. Regression results imputed comorbidities regression: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

Table 5a and 5b describe the results of the subgroup analysis. The results of the group with peripheral hospitals are almost the same as in table 3 and 4; male sex, age of 80 years and higher, higher number of patients and a longer door-to-PCI time have a statistically significant association with a higher 30-day mortality. The confidence level of an age of 80 years or higher decreased from p<0.01 to p<0.05. A higher number of interventional cardiologists and more patients per interventional cardiologist are associated with a significantly lower 30-day mortality. This means that peripheral hospitals should focus especially on employing more interventional cardiologists, since one additional interventional cardiologist is associated with a decrease of the 30-day mortality after a PCI as treatment for a STEMI with 0,606%-point.

In the group with academic hospitals only a higher percentage of people in the municipality population with an age of 65-80 years is associated with a significantly higher 30-day mortality. The presence of at least one comorbidity in the municipality population is significantly associated with a lower 30-day mortality. This result is not what would be expected based on existing literature (12).

| 124 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| MALE SEX | 0.398*** | 0.115, 0.681 |
| AGE 65-80 | -0.033 | -0.177, 0.111 |
| AGE 80+ | 0.341** | 0.014, 0.668 |
| NUMBER OF PATIENTS | 0.010*** | 0.003, 0.016 |
| NUMBER OF INTERVENTIONAL CARDIOLOGISTS | -0.606*** | -0.984, -0.227 |
| PATIENTS PER CARDIOLOGIST | -0.057*** | -0.095, -0.019 |
| TIME DOOR-TO-PCI | 0.038*** | 0.013, 0.062 |
| CARDIAC REHABILITATION | -0.003 | -0.009, 0.003 |
| COMORBIDITIES | 0.001 | -0.066, 0.067 |
| CONSTANT | -15.478** | -29.657, -1.299 |

*Table 5a. Regression results peripheral hospitals: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

| 35 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| MALE SEX | -0.898 | -2.229, 0.432 |
| AGE 65-80 | 0.453** | 0.035, 0.872 |
| AGE 80+ | 0.060 | -0.361, 0.481 |
| NUMBER OF PATIENTS | 0.020 | -0.026, 0.065 |
| NUMBER OF INTERVENTIONAL CARDIOLOGISTS | -0.827 | -3.010, 1.444 |
| PATIENTS PER CARDIOLOGIST | -0.077 | -0.383, 0.230 |
| TIME DOOR-TO-PCI | 0.027 | -0.029, 0.084 |
| CARDIAC REHABILITATION | -0.009 | -0.039, 0.021 |
| COMORBIDITIES | -0.584** | -1.031, -0.136 |
| CONSTANT | 62.657* | -3.719, 129.034 |

*Table 5b. Regression results academic hospitals: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

# Discussion

## Relevance and study aim

The aim of this research was to improve the efficiency of the treatment of a STEMI with a PCI by increasing the effectiveness of this treatment. This is achieved by investigating whether there exists variation in 30-day mortality between the hospitals in the Netherlands after a PCI as treatment for a STEMI, and which factors are associated with a higher or lower 30-day mortality. The scientific relevance of this research follows from the existence of a serious medical and societal problem in the Netherlands that requires solving, most notably the fact that the decline of the myocardial infarction mortality has flattened, remaining around 3 death per 10.000 inhabitants (1).

## Main results

There exists variation in 30-day mortality after PCI-treatment for a STEMI in Dutch hospitals. Of the 27 hospitals in this analysis, two had a significantly higher and two a significantly lower 30-day mortality than average. The cause for this variation needs to be determined, in order to lower the mortality rate after PCI-treatments for STEMIs. Having an age of 80 years or higher, being male, a larger number of patients with a PCI in a hospital and a longer door-to-PCI are all factors that are associated with a higher 30-day mortality. More interventional cardiologists and more patients per interventional cardiologists are factors that are associated with a lower 30-day mortality. Having an age between 65 and 80 years, more patients with cardiac rehabilitation and the presence of comorbidities are not significantly associated with a lower or higher 30-day mortality. With this information, hospitals can accurately improve their policy in order to lower their 30-day mortality after a PCI-treatment for a STEMI, by employing more interventional cardiologists, ensuring the interventional cardiologists perform enough PCIs yearly to maintain and improve their skills and shortening the time-to-PCI time. When the hospitals are divided into subgroups based on the fact whether they are an academic hospital or a peripheral hospital, the interpretation of the result of the regression of the subgroup of peripheral hospitals is the same as in the two prior analyses. The results of the subgroup of academic hospitals shows that age is significantly associated with a significantly higher 30-day mortality and that the presence of comorbidities is associated with a significantly lower 30-day mortality.

## Validity and reliability

There are some limitations to the statistical analysis. Firstly, not all hospitals in the Netherlands that perform PCI-treatments are included in the analysis. If a hospital didn't report the 30-day mortality after a PCI as treatment for a STEMI or the reported data wasn't between 2013 and 2019, the hospital was excluded from the analysis, as was the case for 3 of the 30 hospitals. While this reduces the overall external validity of the study results due to the fact that not all hospitals that perform PCI-treatments for STEMI's are included in the analysis, the majority of hospitals that perform these treatments in the Netherlands are included. Hence, the results of the analysis can still be considered as representative for all patients that undergo a PCI-treatment in Dutch hospitals as treatment for a STEMI.

Additionally, there is no information about case-mix available. Age, sex and comorbidities are associated with the outcome of a myocardial infarction and the probability of success of such treatments (12). Therefore, the mortality rate in hospitals in areas with a high rate of people with these additional characteristics may be overestimated. If a larger percentage of the hospital's population has a comorbidity, the expectation is that more people will pass away after suffering a STEMI. Hence, when there is no option to adjust for these factors, bias may occur. One approach to correct for this information void is to use the data collected at the CBS population registry. Since people with a myocardial infarction are brought to the nearest hospital, the CBS data can be used to remove some of this bias, in case the municipality has a high average age or a high proportion of men. While this removes the influence of the age and sex, the bias by comorbidities remains. The Gezondheidsmonitor provides information about the total presence of comorbidities in the municipality the hospital stands in. It is not reported which comorbidities are present in the population, only what percentage of the population has at least one chronic condition. This data is collected once every four years. This leads to limited availability of data about the comorbidities. This means that there is only data available for 2016, providing 30 datapoints. If the comorbidities before imputation were included in the main regression, the power of the analysis would have decreased dramatically. If the missing data was imputed using interpolation or mean imputation, results with a low reliability would come from the analysis because of the high number of imputed data. To prevent this from interfering with the main regression results, the comorbidities were not included in the main analysis, but an additional analysis was performed given the importance of comorbidities as outcome determinant. The content validity of the analysis results is limited due to the non-specific comorbidities that are reported in the Gezondheidsmonitor. The reliability of this additional analysis is low due to the high number of imputed observations. On the other hand, the information about the hospital processes that are reported to the IGJ is available in all years during the study period for all hospitals. This strengthens the validity and reliability of the analysis, because future research with the methods used in this thesis will produce similar results as this thesis.

Besides, there is limited information available about the PCI-treatment processes in the hospitals, the infarction-to-hospital time and how long an interventional cardiologist has been performing PCIs. Specifics on how the PCI-treatment was performed, the type of stent used, experience levels of the interventional cardiologists and how long it took the patient to arrive in the hospital, are important determinants for the outcome of the treatment and potential mortality thereafter (8,12,16,24,30). As this data is not available, these factors cannot be included in the second analysis. Consequence is that only a part of the situation revolving around the treatment of a STEMI using a PCI is clarified. This is especially relevant for hospitals in the rural areas with a low population density. The distances between hospitals in these regions may be larger, which leads to longer onset-to-hospital times in these regions. A longer onset-to-hospital time is associated with a higher mortality after STEMI (8). Therefore, the association of the variables that were included in the analysis with 30-day mortality after a PCI as treatment for a STEMI may be overestimated. Additionally, a new-generation drug-eluting stents was developed during the study period. This new-generation stent has better mortality rate outcomes than bare metal stents or early-generation drug-eluting stents. If a hospital still uses the old stent mainly, either an early-generation drug-eluting stent or a bare metal stent, can that lead to a higher 30-day mortality (30). Now that the variable about the type of stent used is not included in the analysis due to missing information, the associations of the variables that were included in the analysis with 30-day mortality may be overestimated. Due to the possible overestimation of the included variables and the resulting bias, and the confounding bias as identified in de DAG, the content validity of the results is limited.

When a patient with a myocardial infarction is presented at the ER of a hospital that does not perform PCI’s, this patient needs to be transferred to a hospital that does perform a PCI. This additional travel time increases the period between onset and treatment. Therefore, it has a possible association with the outcome of the PCI-procedure (8), because a longer occlusion time means more myocardial necrosis (4). However, this variable is not included in the analysis in this thesis due to missing data. This is because only in 2013 and 2014 it was reported which hospitals received referred patients. Of the 27 hospitals that are included in this thesis, only four hospitals did not receive any referred patients. Because of the combination of the two previously mentioned factors and the limited validity of including this variable due to low number of observations, this variable was excluded from the analysis, despite its likely association with the 30-day mortality after PCI-treatment. However, the fact that only 4 out of 27 hospitals did not receive referred patients suggests that the impact of this missing information may be limited.

There are two datapoints that are outliers because of their low number of treated patients. These two outliers occur in two hospitals in their first year of performing PCI-treatments. It is conceivable that the hospital did not start with performing this intervention on 1 January, but only in October for example. That explains the low number of treated patients in those two instances. The two outliers have an extraordinarily low 30-day mortality, potentially because the patients with complicated comorbidities were treated in a hospital that is more experienced with PCIs. The hospitals with the outliers have a large impact on the regression results due to the low 30-day mortality, as can be seen in table 7 in the Appendix. That would lead to biased results, and therefore a lower content validity. For that reason, they were excluded from the rest of the analysis.

A noteworthy fact about the registration of the data is about the cardiac rehabilitation. In the inquiry of the IGJ hospitals have to report the total number of patients with a STEMI that have been discharged home or to a nursing home and the number of patients that have received cardiac rehabilitation after a STEMI. However, this number of total patients with a STEMI that were discharged home or to a nursing home, was significantly less than the number of patients with a STEMI that have underwent a PCI-treatment. The number of patients that passed away after PCI is far less than the difference between these two reported numbers. This was the case in many hospitals in all years of the study period. There was no clear reason to be found about why there was a discrepancy between the number of patients with a STEMI reported at the cardiac rehabilitation question and the number of patients with a PCI-treatment after a STEMI. At the same time, there is no clear reason to expect a negative impact on the validity.

## Recommendation

Firstly, there are some recommendations for the IGJ. At the moment they publish the dataset about quality indicators of hospitals, but report nothing about the patient characteristics. Potential reasons for not reporting these features are privacy or too much workload for the hospitals. However, these characteristics are important for a fair comparison between hospitals, because a higher age or more male patients can lead to a higher 30-day mortality, based on the regression results and existing literature (12). Therefore, a solution needs to be found which provides useful information about the age and sex of the patient population with a STEMI of the hospitals that is not privacy sensitive and with low workload for the hospitals. Furthermore, there needs to be clarification about the reason why there is a large discrepancy between the total number of patients with a STEMI in the cardiac rehabilitation question and the total number of patients with a STEMI that have received a PCI.

Secondly, there are some recommendations for the hospitals in order to improve their 30-day mortality. Based on the results of this research, hospitals should hire more interventional cardiologists, while making sure that the skills are maintained and improved by a high annual caseload of PCIs per interventional cardiologists. In addition, hospitals can shorten the door-to-needle time. This may be achieved by shortening the distance between the emergency room and the operation room or improving preparation procedures aimed at decreasing the time needed to prepare for a PCI.

Finally, there are some recommendations for future research. As seen in figure 4, the decreasing door-to-needle time has suddenly flattened in 2017. With every minute that the coronary artery is occluded, more cardiac tissue goes into necrosis (4). That is why it is worth investigating why the downward trend has stopped and how the trend will develop in coming years. Additionally, future research needs to be performed i) with the variables that were not included in the analysis due to missing information, for example the type of stent used, more specific and complete information about the comorbidities of the patients, skill and experience level of the interventional cardiologists and the time it took the patients to get to the hospital, ii) with a larger sample, for example by a longer study period and inclusion of all hospitals that perform PCI-treatments in the Netherlands. Inclusion of all hospitals is possible in the future, because all hospitals have to report the 30-day mortality to the IGJ starting from 2020, and iii) that looks into the costs of employing more interventional cardiologists and shorting the door-to-PCI time, and whether the lower mortality leads to higher medical expenses due to more chronic patients.

Concluding, there are hospital specific quality indicators that are associated with a higher or lower 30-day mortality after a PCI as treatment for a STEMI. A higher number of patients that have received a PCI and a longer door-to-PCI time are associated with a higher 30-day mortality. A larger number of interventional cardiologists and a larger number of PCI-treatments per interventional cardiologists are associated with a lower 30-day mortality. However, the model used in the statistical analysis only explains the variation in 30-day mortality partly and the sample was too small for a proper subgroup analysis. The analysis in this thesis should be investigated in the future with a larger sample and include all variables that are revolving around the treatment of a STEMI with a PCI, allowing better research about success and failure factors in hospitals processes regarding treating a STEMI with a PCI.

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# Appendix

Table 6 presents a more elaborate overview of the characteristics of the hospitals that are included in the analysis than table 1, because in this table the mean outcomes are reported per hospital instead of combined. The variable ‘years reported’ shows in how many years during the study period a hospital has reported its 30-day mortality after a PCI as treatment for a STEMI.

| Hospital | Years reported | 30-day mortality (%) | % male | % 65-80 | % 80+ | Number of Patients | Number of Cardioligists | Patients Per cardiologist | Cardiac rehabilitation (%) | Door-to-PCI time (minutes) |
|---|---|---|---|---|---|---|---|---|---|---|
| AMC | 6 | 1,21 (0,33) | 49,42 (0,14) | 9,42 (0,37) | 2,73 (0,05) | 343 (58,78) | 7,33 (0,52) | 47,04 (9,38) | 82,66 (13,77) | 24,28 (1,34) |
| Amphia Ziekenhuis | 7 | 2,23 (0,42) | 49,05 (0,16) | 12,81 (0,56) | 4,54 (0,10) | 497,14 (63,41) | 6 (0) | 82,86 (10,57) | 0 (0) | 19,39 (3,77) |
| Canisius-Wilhelmina Ziekenhuis | 5 | 1,25 (0,47) | 48,27 (0,18) | 11,52 (0,40) | 3,64 (0,05) | 193,2 (14,77) | 4 (0) | 48,3 (3,69) | 94,95 (2,97) | 22,94 (2,58) |
| Catharina Ziekenhuis | 7 | 3,04 (0,5) | 51,19 (0,17) | 11,96 (0,01) | 4,6 (0,08) | 628,43 (103,36) | 7,57 (0,53) | 84,03 (19,17) | 76,4 (9,37) | 15,2 (2,23) |
| Elisabeth-Tweesteden Ziekenhuis | 7 | 2,1 (0,91) | 49,77 (0,06) | 12,13 (0,55) | 3,74 (0,13) | 235,43 (21,91) | 5 (0) | 47,09 (4,38) | 85,46 (8,62) | 23,12 (2,2) |
| Erasmus MC | 4 | 2,32 (0,98) | 49,29 (0,02) | 11,1 (0,18) | 4,08 (0,10) | 435,75 (26,7) | 7,25 (0,96) | 61,07 (10,77) | 82,02 (14,2) | 29,5 (4,36) |
| Haaglanden MC | 7 | 2,75 (1,3) | 47,98 (0,13) | 15,97 (0,50) | 6,27 (0,05) | 190,57 (49,37) | 4,43 (0,53) | 42,72 (8,78) | 90,09 (12,06) | 27,16 (7,47) |
| HagaZiekenhuis | 7 | 2,14 (0,37) | 49,46 (0,10) | 10,4 (0,46) | 3,66 (0,15) | 473,14 (104,33) | 6,29 (0,95) | 78,52 (27,21) | 85,99 (10,77) | 31,86 (10,04) |
| Jaroen Bosch Ziekenhuis | 7 | 2,66 (0,45) | 49,34 (0,07) | 12,71 (0,82) | 3,91 (0,13) | 328 (24,22) | 5 (0) | 65,6 (4,48) | 85,51 (13,48) | 25,77 (13,91) |
| LUMC | 3 | 1,58 (0,53) | 48,59 (0,02) | 10,47 (0,55) | 3,43 (0,06) | 378,33 (20,6) | 6,67 (0,58) | 57,11 (6,85) | 86,83 (2,78) | 16,67 (6,66) |
| MCL | 7 | 2,44 (0,56) | 49,47 (0,20) | 12,59 (0,90) | 4,44 (0,05) | 363,43 (16,31) | 6 (0,82) | 61,77 (10,36) | 82,53 (8,77) | 25,43 (2,64) |
| MUMC | 6 | 2,18 (0,75) | 47,99 (0,08) | 15,02 (0,55) | 5,25 (0,14) | 243,33 (41,49) | 7,17 (0,41) | 33,99 (5,9) | 80,98 (6,56) | 28,67 (4,8) |
| Maasstad Ziekenhuis | 7 | 3,05 (1,14) | 49,26 (0,04) | 10,91 (0,28) | 4,14 (0,11) | 394,14 (27,84) | 6,71 (0,49) | 59,06 (6,97) | 0 (0) | 29,71 (10,83) |
| Meander Zorggroep | 6 | 2,27 (0,9) | 49,22 (0,06) | 10,42 (0,54) | 3,53 (0,05) | 292,67 (23,82) | 4 (0) | 73,17 (5,96) | 79,17 (11,85) | 21,67 (1,86) |
| Medisch Spectrum Twente | 7 | 2,23 (0,77) | 50,83 (0,13) | 12,79 (0,55) | 4,03 (0,11) | 452,86 (14,66) | 6 (0) | 75,48 (2,44) | 80,35 (12,67) | 14,71 (1,7) |
| Noordwest-ziekenhuis-groep | 6 | 1,95 (0,94) | 49,32 (0,40) | 14,6 (0,88) | 4,4 (0,13) | 322,17 (17,38) | 5,5 (0,55) | 59,02 (6,38) | 82,29 (21,43) | 21,9 (5,61) |
| Rijnstate Ziekenhuis | 7 | 2,11 (0,47) | 49,54 (0,09) | 13,15 (0,61) | 4,39 (0,21) | 554 (26,1) | 5,14 (0,38) | 108,28 (10,05) | 99,39 (1,27) | 22,14 (2,49) |
| St. Antonius Ziekenhuis | 5 | 1,92 (0,67) | 49,66 (0,09) | 14,32 (1,49) | 3,06 (0,21) | 372,8 (35,63) | 7 (0,71) | 53,84 (8,14) | 96,21 (1,31) | 26,4 (7,92) |
| Tergooi | 6 | 2,41 (1,45) | 48,92 (0,12) | 14,32 (0,16) | 5,39 (0,13) | 271,83 (62,57) | 4,67 (0,52) | 58 (11,56) | 73,13 (7,01) | 21,67 (2,07) |
| Treant Zorggroep | 4 | 3,83 (0,64) | 49,6 (0,07) | 15,42 (0,50) | 5,03 (0,22) | 199,75 (26,47) | 4 (0) | 49,94 (6,62) | 76,5 (7,33) | 33 (4,32) |
| UMC St Radboud | 4 | 2,13 (0,6) | 48,34 (0,12) | 11,63 (0,38) | 3,65 (0,06) | 220 (18,24) | 6 (0) | 36,67 (3,04) | 84,87 (12,9) | 22,94 (2,2) |
| UMC Utrecht | 6 | 2,45 (0,59) | 48,72 (0,18) | 7,58 (0,15) | 2,57 (0,05) | 218,83 (21,66) | 5,33 (0,52) | 41,5 (6,65) | 90,5 (1,85) | 22,87 (0,8) |
| UMCG | 7 | 3,23 (1,12) | 49,72 (0,25) | 9,2 (0,81) | 3,2 (0,18) | 442,43 (18,71) | 6,86 (0,38) | 64,69 (4,4) | 61,59 (12) | 40,7 (2,68) |
| Vumc | 3 | 1,49 (0,64) | 49,53 (0,04) | 9,73 (0,06) | 2,7 (0) | 346,33 (49,81) | 6,67 (1,15) | 52,57 (9,22) | 79,35 (5,63) | 22,33 (0,58) |
| VieCuri | 6 | 2,25 (0,31) | 50,03 (0,05) | 15,23 (0,74) | 4,82 (0,23) | 324,83 (32,15) | 4,5 (0,55) | 73,3 (13,29) | 85,43 (8,8) | 22,42 (6,36) |
| Zorgsaam Zeeuws-Vlaanderen | 7 | 2,68 (1,75) | 49,69 (0,04) | 17,64 (0,79) | 5,96 (0,23) | 213,71 (15,07) | 4 (0) | 53,43 (3,77) | 83,05 (39,49) | 13,29 (4,54) |
| Zuyderland MC | 5 | 1,68 (1,11) | 49,44 (0,05) | 16,19 (0,80) | 5,78 (0,27) | 259,4 (9,66) | 8,8 (0,45) | 29,53 (1,54) | 86,62 (11,1) | 27,2 (6,5) |

*Table 6. Characteristics of included hospitals. Reported number are mean (standard deviation).*

Table 7 and 8 present the regression results of i) the regression with two outliers with a low number of patients and ii) the regression with the comorbidities before imputation, respectively. As table 7 shows, the results with the two outliers are very different from the regression results without the two outliers, as is presented in table 3. In the regression analysis with the outliers the door-to-PCI time, male sex and age of 80+ are associated with an increased 30-day mortality with p<0,10. Only the door-to-PCI time is significantly associated with a decreased 30-day mortality, with p<0,01. The results of the regression with comorbidities before imputation, shown in table 8, show that only male sex is significantly associated with an increased 30-day mortality. That only this variable is significantly associated, is due to low number of observations leading to broader confidence intervals.

| 161 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| MALE SEX | 0.226* | -0.030, 0.482 |
| AGE 65-80 | -0.020 | -0.130, 0.091 |
| AGE 80+ | 0.244* | -0.020, 0.508 |
| NUMBER OF PATIENTS | 0.005 | -0.001, 0.012 |
| NUMBER OF INTERVENTIONAL CARDIOLOGISTS | -0.310* | -0.647, 0.027 |
| PATIENTS PER CARDIOLOGIST | -0.027 | -0.063, 0.009 |
| TIME DOOR-TO-PCI | 0.025*** | 0.006, 0.045 |
| CARDIAC REHABILITATION | -0.002 | -0.008, 0.004 |
| CONSTANT | -8.574 | -21.449, 4.300 |

*Table 7. Regression results with the two outliers of hospitals with a low number of patients: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

| 24 OBSERVATIONS | COEFFICIENT | 95% CONFIDENCE INTERVAL |
|---|---|---|
| MALE SEX | 1.097*** | 0.521, 1.673 |
| AGE 65-80 | -0.073 | -0.373, 0.228 |
| AGE 80+ | 0.371 | -0.088, 0.831 |
| NUMBER OF PATIENTS | 0.001 | -0.020, 0.023 |
| NUMBER OF INTERVENTIONAL CARDIOLOGISTS | -0.593 | -1.855, 0.669 |
| PATIENTS PER CARDIOLOGIST | -0.033 | -0.148, 0.082 |
| TIME DOOR-TO-PCI | 0.053* | -0.002, 0.107 |
| CARDIAC REHABILITATION | -0.010 | -0.024, 0.004 |
| COMORBIDITIES | -0.026 | -0.146, 0.095 |
| CONSTANT | -47.492*** | -77.456, -17.529 |

*Table 8. Regression results comorbidities before imputation: coefficients with 95% confidence interval. *** p<0,01, **p<0,05, *p<0,10*

Figures 8-12 show scatterplots of the individual associations of the variables that were included in the analysis put against the 30-day mortality. This association is indicated by the fitted line. This fitted line in figure 8 implies that the 30-day mortality decreases with a higher number of interventional cardiologists employed by a hospital. In figure 9, it shows that a higher percentage of the municipality population with an age of 65-80 years is associated with a higher 30-day mortality. In figure 10, it shows that a higher percentage of the municipality population with an age of 80 years and higher is associated with a higher 30-day mortality. As the line in figure 10 is steeper than in figure 9, this association seems stronger. In figure 11, it shows that a higher percentage of the municipality population with a male sex is associated with a higher 30-day mortality. Lastly, in figure 12, it shows that more patients per interventional cardiologist is slightly associated with a higher 30-day mortality. This seems to contradict the outcome of the regression analyses.

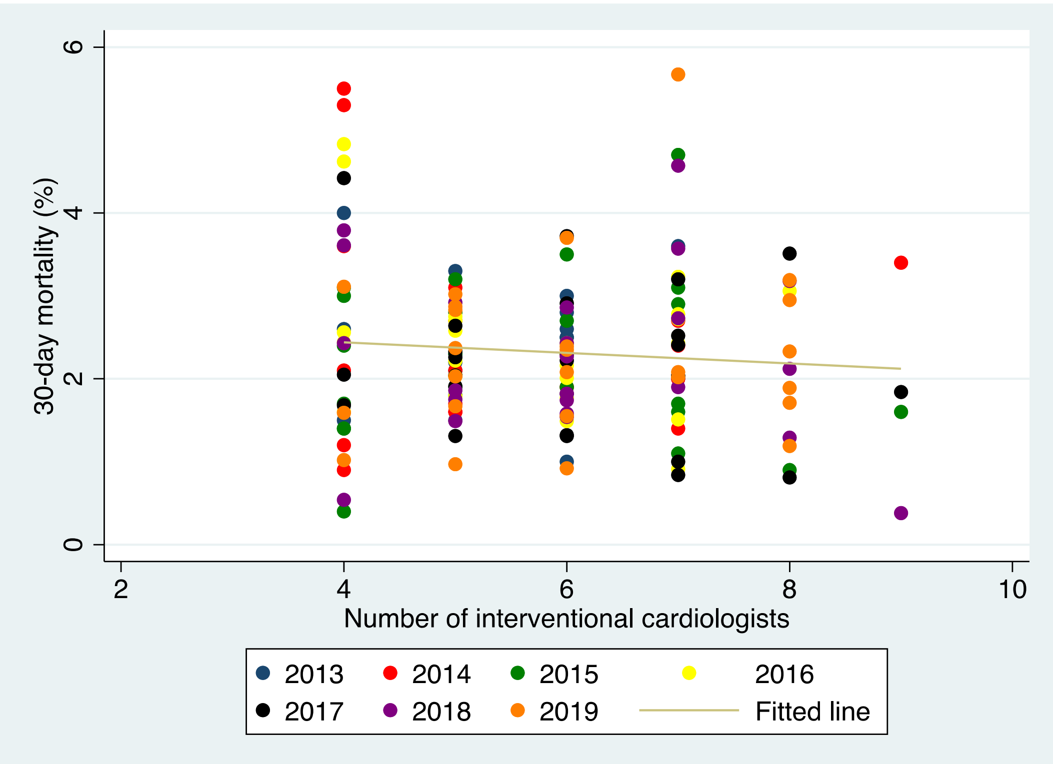


*Figure 8. Scatterplot of number of interventional cardiologists employed by the hospital and 30-day mortality with fitted line.*

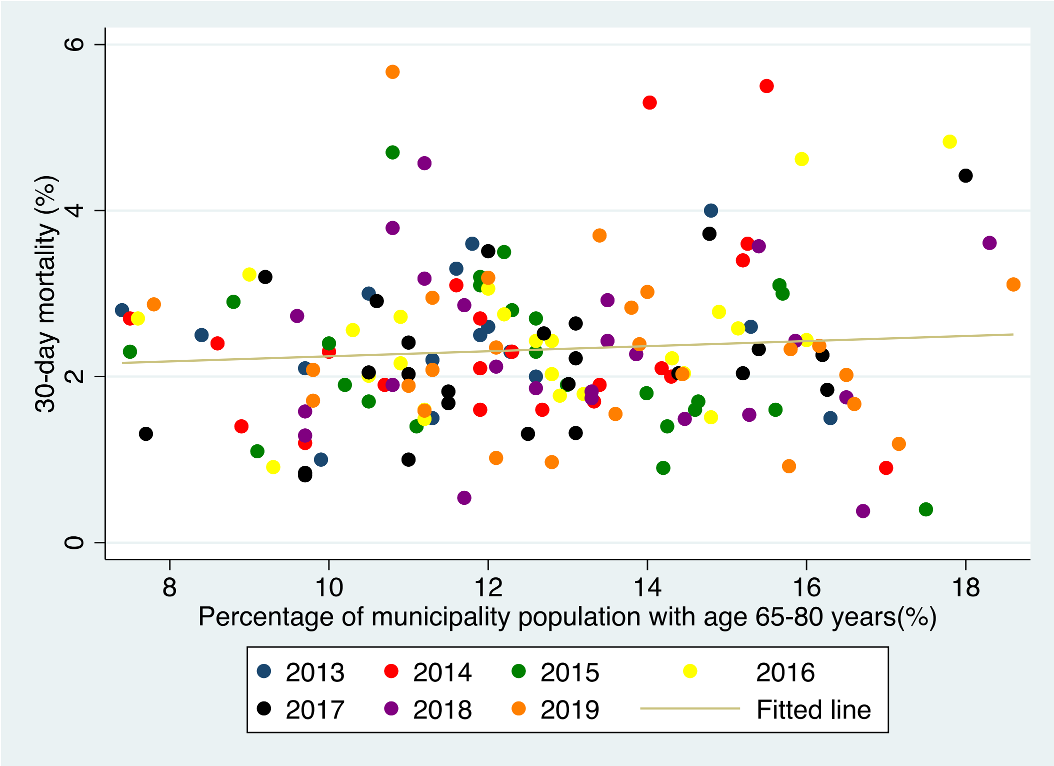


*Figure 9. Scatterplot of percentage of the population of the municipality the hospital is in with an age between 65 and 80 years, and 30-day mortality with fitted line.*

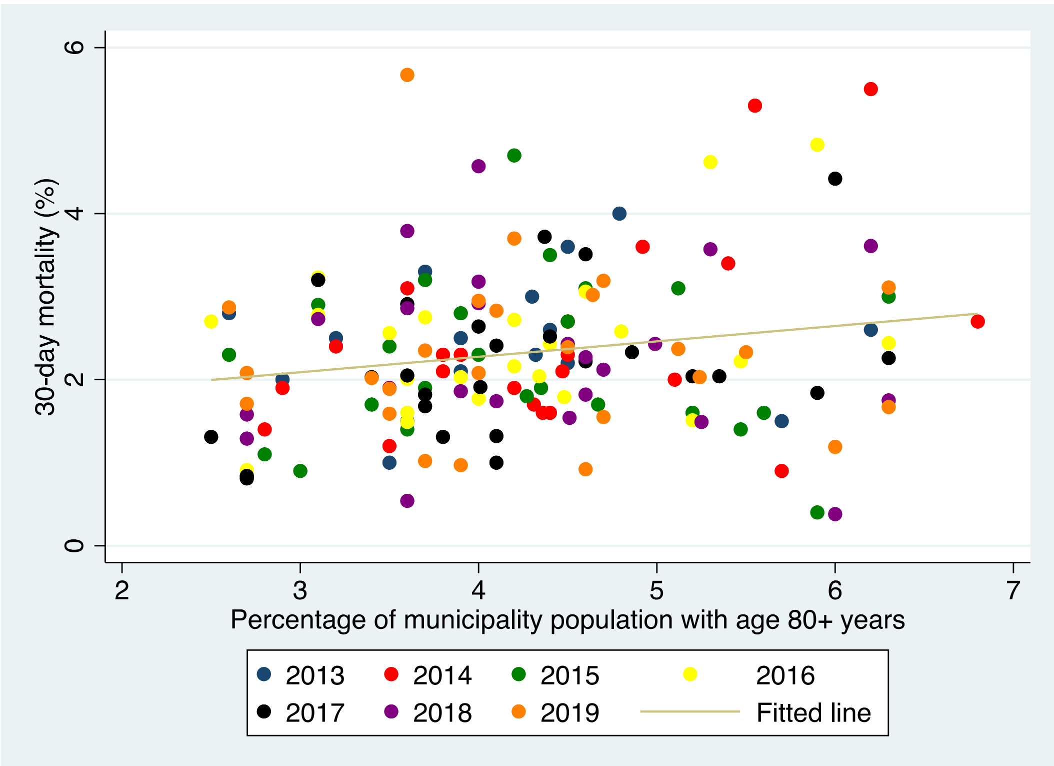


*Figure 10. Scatterplot of percentage of the population of the municipality the hospital is in with an age of 80 years and higher, and 30-day mortality with fitted line.*

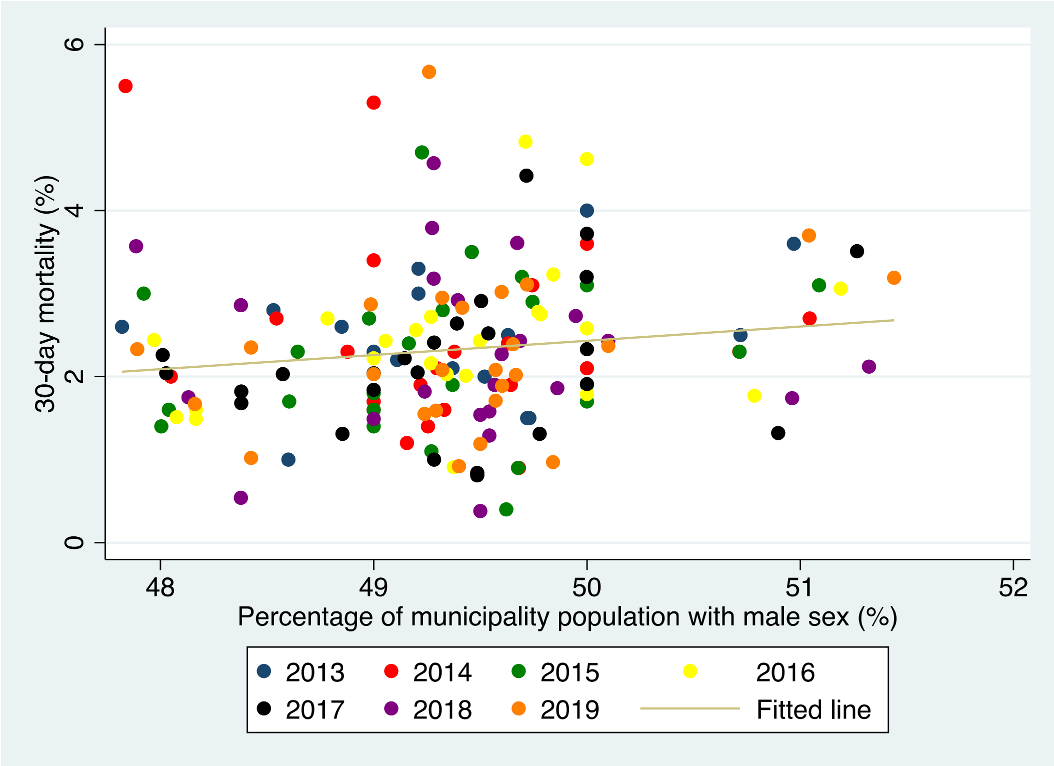


*Figure 11. Scatterplot of percentage of the population of the municipality the hospital is in with a male sex and 30-day mortality with fitted line.*

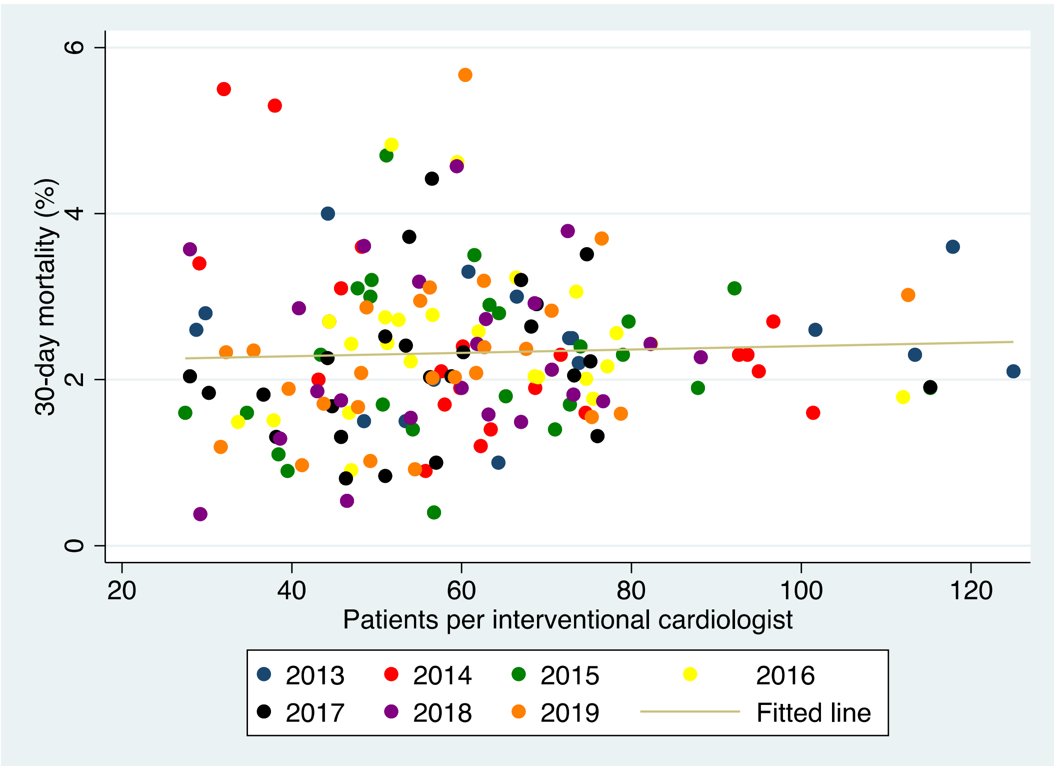


*Figure 12. Scatterplot of percentage of patients per cardiologists and 30-day mortality with fitted line.*