Redesigning cardiovascular healthcare: patient and professional perspectives on value

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PART ONE

COMPARING GUIDLINE RECOMMENDATIONS TO REAL WORLD CARE PATTERNS - NATIONAL AND REGIONAL MYOCARDIAL INFARCTION CARE ANALYSIS THROUGH CLAIMS DATA

CHAPTER II

NON ST ELEVATION MYOCARDIAL INFARCTION IN THE NETHERLANDS: ROOM FOR IMPROVEMENT!

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Abstract

Aim

To analyse NSTEMI care in the Netherlands and identify modifiable factors to improve NSTEMI healthcare.

Methods

This retrospective cohort study analysed hospital and pharmaceutical claims data of all NSTEMI patients in the Netherlands in 2015. The effect of PCI during hospitalisation on 1-year mortality was investigated in the cohort alive 4 days after NSTEMI. The effect of medical treatment on 1-year mortality was assessed in the cohort alive 30 days after NSTEMI. The effect of age, gender and co-morbidities was evaluated. PCI during hospitalisation was defined as PCI within 72 hours after NSTEMI and optimal medical treatment was defined as the combined use of an aspirin specie, P2Y12-inhibitor, statin, beta-blocker and ACE-inhibitor/AT-2-receptor blocker, started within 30 days after NSTEMI.

Results

Data from 17,997 NSTEMI patients (age 69.6(SD=12.8) years, 64% male) were analysed. In patients alive 4-days after NSTEMI, 43% of patients had a PCI during hospitalisation and 1-year mortality was 10%. In the cohort alive 30-days after NSTEMI, 47% of patients had optimal medical treatment at 30-days and 1-year mortality was 7%.

PCI during hospitalisation (OR 0.42; 95%CI 0.37-0.48) and optimal medical treatment (OR 0.59; 95%CI 0.51-0.67) were associated with a lower 1-year mortality.

Conclusion

In Dutch NSTEMI patients, use of PCI during hospitalisation and optimal medical treatment is modest. As both are independently associated with a lower 1-year mortality, this study provides direction on how to improve NSTEMI healthcare quality in the Netherlands.

Abbreviations

ACE-/AT2-inhibitors	Angiotensin Converting Enzyme / Angiotensin II receptor -inhibitors
CI	Confidence Interval
DBC	Diagnose Behandel Combinatie
DIS	DBC Informatie Systeem
GIP	Geneesmiddelen Informatie Project
NSTEMI	Non ST-elevation Myocardial Infarction
OR	Odds Ratio
PCI	Percutaneous Coronary Intervention
P2Y12	Thienopyridine receptor blockers
SMD	Standardized Mean Difference
STEMI	ST-elevation Myocardial Infarction
ZINL	Zorginstituut Nederland

Introduction

Improvements in early recognition and revascularisation significantly decreased mortality after myocardial infarction over the last decades(1-3). This reduction in mortality, however, is especially achieved in ST-elevation myocardial infarction (STEMI) patients. Unfortunately, non ST-elevation myocardial infarction (NSTEMI) mortality rate did not decline over the last years (4, 5).

Most recent European and American guidelines emphasize that the use of an early invasive strategy, as well as optimal medical therapy contribute to a better long term survival after NSTEMI (both evidence class 1, level A)(2, 3, 6). The European guidelines even indicate them as performance measures of NSTEMI-care, based on various large meta-analyses and randomized controlled trials(7, 8). Recently, Hall et al. demonstrated that optimal use of guideline-indicated care for NSTEMI was associated with greater survival gain(9). However, in Hall's study the adherence rate was suboptimal indicating that survival can potentially be improved.

This recent study illustrates that large-scale monitoring of guideline indicated care adherence is crucial to provide insight on how to improve NSTEMI care, ultimately resulting in improved survival.

The National Healthcare Institute (Zorginstituut Nederland, ZINL) has an advisory role to the Dutch government with the primary objective to improve Dutch national healthcare. For this purpose, ZINL has access to all Dutch patients' claims data in the Netherlands. The use of these claims data has been proven to reflect the real clinical data and to be correct and adequate in prior studies(10-12). The current study is performed in close collaboration with ZINL and aims to analyse NSTEMI care in the Netherlands and identify modifiable performance factors to analyse and improve the quality of NSTEMI healthcare in the Netherlands.

Methods

Hospital claims are sent to patient's insurance companies and subsequently collected in the central database of the insurance companies in the Netherlands. The use of this type of data has been validated in previous studies(11). The National Healthcare Institute has access to both clinical- and pharmaceutical claims databases and can access data on a patient level, which can be linked but is anonymous (Figure 1).

Study Population

This is a retrospective cohort design study. Three cohorts were used for analysis, as shown in Figure 2.

- The entire study cohort comprises all Dutch patients above 18 years old who were admitted with a NSTEMI (diagnosis code 0320.11.205) in 2015. Only the first infarction during the study period was used for analysis. Patients who died on the first day of admission with the diagnosis of NSTEMI were excluded, in order to evaluate the effect of the different treatments.
- A sub-cohort, "NSTEMI-4days alive", comprises all patients alive 4 days after NSTEMI. This cohort was used to evaluate the effect of PCI during hospitalisation on 1-year mortality.
- A second sub-cohort, "NSTEMI-30 days alive", comprises all patients alive 30 days after NSTEMI. This cohort was used to evaluate the effect of medication use at 30 days on 1-year mortality.

Outcome Measures: Baseline Characteristics

Age, gender, co-morbidities and 1-year mortality were evaluated for all patients alive at 4 days and 30 days. For each patient, the absence or presence of diabetes mellitus, hypercholesterolemia and obstructive pulmonary disease (COPD/asthma) at the time of infarction was determined based on medication use, 180 days before admission. Diabetes mellitus was defined as use of glucose lowering medication (code A10XX, oral antidiabetics or insulin), hypercholesterolemia as use of any form of cholesterol lowering medication (code C10XX, all forms of cholesterol lowering medication) and obstructive pulmonary disease as use of any inhalation medication (code R03XX, all forms of inhalation medication).

These types of medication had to be used at least 180 days prior to the admission to qualify a patient as having the specified comorbidity.

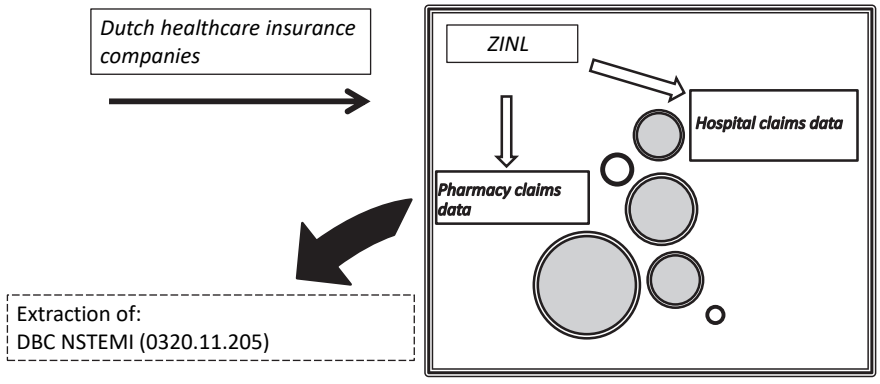

Figure 1: Data collection.

All healthcare claims from the Dutch healthcare insurance companies are stored and collected by the National Healthcare institute (ZINL). This includes hospital claims data as well as pharmacy claims data. Dara are available for analysis when approved (Figure 1). From each dataset from different years, the claims for NSTEMI -care can be collected for all patients (Figure 2) but also specific patient cohorts.

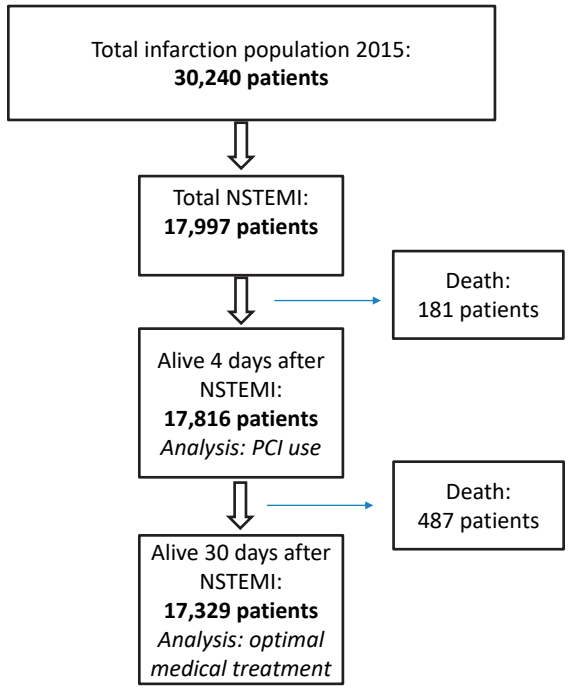

Figure 2: NSTEMI patient cohort.

PCI Treatment

In the "NSTEMI-4days alive" cohort, the effect of PCI within 4 days of the diagnosis on mortality was evaluated (figure 2) in all patients alive at 4 days. The cut-off of 4 days was based on European and American guidelines which recommend an invasive strategy, meaning coronary angiography, within the first 72 hours, which is the acute or semi-acute phase of the infarction. (6, 13). PCI at a later moment for instance after 7- or 30 days , were not analyzed as this was not deemed 'acute phase' of the NSTEMI.

Optimal Medical Treatment

In the "NSTEMI-30 days alive" cohort, the effect of complete optimal medical treatment on mortality was evaluated (figure 2). Optimal medical treatment after NSTEMI was defined as the combined use of an aspirin specie, a P2Y12- inhibitor, a statin, a beta-blocker and an ACE-/AT2-inhibitor. Fulfilled prescriptions of each of these were collected from the pharmacological database (GIP database).

Statistical Analysis

Data are presented as absolute numbers and as a proportion of the total population. Proportion comparisons were done by a X^2 test. Multivariate logistic regression analysis was done to understand the relation between 1-year mortality as dependent variable and independent variables: gender, age, diabetes, hypercholesterolemia, obstructive pulmonary disease, PCI treatment and optimal medical treatment use. To assess the relation of treatment (PCI/optimal medical treatment) and 1-year mortality, propensity score matching was applied.

Statistics: Propensity Score Matching

Patients were matched 1-to-1 using caliper matching. This procedure ensures an optimal balance of covariates between the treatment and the reference group. Age, gender and co-morbidities were analyzed as risk factors and used for matching. When assessing effectiveness of PCI and optimal medical treatment, interference of the added effect of the other (respectively optimal medical treatment or PCI when assessing the effect of optimal medical treatment) was unwanted and thus corrected for in all propensity score analyses. With propensity score matching a treatment and a reference cohort were created with a comparable load of risk factors.

Matching was done specifically for PCI and a second time specifically for optimal medical treatment. (Appendix A). Statistics were done with R statistical program version 3.3.2 (x64), R packages MatchtIt and tableone and SAS™ (SAS Institute, Cary, NC, USA.). For all tests, a P-value <0.05 was considered statistically significant.

Ethical Considerations

This research uses pseudo anonymous and encrypted patient data. Dutch law states that prior ethical review and approval is not necessary.

Results

Study Population

In 2015, a total of 30,240 myocardial infarction patients were admitted to Dutch hospitals. In 60% of them it concerned NSTEMI patients (N=17,997). Average age was 69.6 (SD=12.8) years. In total, 64% of the NSTEMI patients were male and 1-year mortality was 11% (Table 1)

In the first 4 days 181 patients died. The sub-cohort of "NSTEMI-4days alive" consisted of 17,816 patients (Table 1, NSTEMI 4 days). Average age was 69.5 (SD=12.7) years with 64% being male and 1-year mortality in this cohort was 10%.

Additionally, in the following 26 days 487 patients died. This sub-cohort, "NSTEMI-30 days alive" consisted of 17,329 patients (Table 1, NSTEMI 30 days). Average age was 69.2 (SD=12.7) years, with 64% being male. The 1-year mortality in this cohort was 7%. Co-morbidities were frequent in all cohorts, and equally distributed (P=NS, table 1).

Table 1. Patient Characteristics

	NSTEMI	NSTEMI 4 days	NSTEMI 30 days	P-value
Total patients (N)	**17,997**	**17,816**	**17,329**	
Age (average, SD)	69.6(12.8)	69.5(12.7)	69.2(12.7)	NS
Male (N, %)	11,518(64%)	11,388(64%)	11,089(64%)	NS
Diabetes (N, %)	3,779(21%)	3,765(21%)	3,610(21%)	NS
Hypercholesterolemia (N, %)	7,739(43%)	7,632(43%)	7,375(43%)	NS
Obstructive Pulmonary disease (N, %)	2,880(16%)	2,793(16%)	2,691(16%)	NS
1-year mortality	1,980(11%)	1,781(10%)	1,285(7%)	<0.001

NSTEMI = total non ST-elevation myocardial infarction population.

NSTEMI 4 days = non ST-elevation myocardial infarction patients alive at 4 days.

NSTEMI 30 days = non ST-elevation myocardial infarction patients alive at 30 days.

PCI Treatment (NSTEMI-4days alive)

In the "NSTEMI-4days alive' sub cohort (N= 17,816), PCI within the first 72 hours (3 days) was performed in 43% of patients. Of interest, PCI treatment was performed in 35% of the female NSTEMI patients as compared to 47% of the male NSTEMI patients (P<0.001).

Medication Use (NSTEMI-30 days alive)

Table 2 displays medication use at 30 days in the "NSTEMI-30 days alive" cohort (N=17,329). In this subgroup, the percentage of patients with complete "optimal medical treatment" was 47% at 30 days. Aspirin-specie use was 91%, P2Y12-inhibitors use 76%, statin use 85%, bètablocker use 74% and ACE/AT-2 inhibitor use 75%.

Effect of PCI on Mortality (NSTEMI-4days alive)

Table 3 displays the predictors of 1-year mortality in the "NSTEMI-4days alive" cohort (N=17,816). The following predictors add significantly to increased mortality: increasing age (OR 1.09; 95% CI 1.08-1.09), male gender (OR 1.27; 95% CI 1.14-1.42), diabetes mellitus (OR 1.51; 95% CI 1.34-1.70), and obstructive pulmonary disease (OR 1.52; 95% CI 1.37-1.71).

Noticeably, PCI treatment within 4 days (OR 0.42; 95% CI 0.37-0.48) is associated with a substantial lower 1-year mortality.

Table 2. NSTEMI-30 days alive cohort: medication use at 30 days.

Total complete optimal medical treatment use	**8,144(47%)**
Aspirin species	15,769(91%)
P2Y12-inhibitor	13,170(76%)
Statin	14,729(85%)
Bètablocker	12,823(74%)
ACE/AT-2-inhibitor	12,996(75%)

ACE/AT-2 = angiotensin converting enzyme/ angiotensin II -receptor inhibitor;

NSTEMI-30 days = non ST-elevation myocardial infarction alive at 30 days.

Table 3. Multivariate logistic regression of predictors of 1-year mortality in the subcohort of non-ST-elevation myocardial infarction patients alive at 4 days.

Factor	**Odds ratio**	**95%-confidence interval**	**P-value**
Age (increase by 1 year)	1.09	1.08-1.09	<0.001
Male gender	1.27	1.14-1.42	<0.001
Diabetes mellitus	1.51	1.34-1.70	<0.001
Hypercholesterolemia	1.11	0.99-1.23	NS
Obstructive Pulmonary disease	1.52	1.37-1.71	<0.001
PCI during hospitalisation	0.42	0.37-0.48	<0.001

NSTEMI = non ST-elevation myocardial infarction; PCI = percutaneous coronary intervention

Table 4. Multivariate logistic regression of predictors of 1-year mortality in the subcohort of non ST-elevation myocardial infarction patients alive at 30 days.

Factor	Odds ratio	95%-confidence interval	P-value
Age (increase by 1 year)	1.08	1.08-1.09	<0.001
Male gender	1.21	1.07-1.37	<0.01
Diabetes mellitus	1.54	1.34-1.76	<0.001
Hypercholesterolemia	1.23	1.08-1.39	<0.01
Obstructive Pulmonary disease	1.61	1.40-1.85	<0.001
Complete optimal medical treatment	0.59	0.51-0.67	<0.001
PCI during hospitalisation*	0.52	0.45-0.60	<0.001

NSTEMI = non ST-elevation myocardial infarction; PCI = percutaneous coronary intervention

* = In the patients alive at 30 days, the effect of PCI within 3 days was equally calculated to correct for it and to use this variable in propensity score matching (see Methods section)

Effect of Medication on Mortality (NSTEMI-30 days alive)

Predictors for 1-year mortality in the "NSTEMI-30 days alive" sub cohort (N=17,329) are shown in Table 4. In line with the entire study cohort, the following predictors add significantly to increased mortality: increasing age (OR 1.08; 95% CI 1.08-1.09), male gender (OR 1.21; 95% CI 1.07-1.37), diabetes mellitus (OR 1.54; 95% CI 1.34-1.76), hypercholesterolemia (OR 1.23; 95% CI 1.08-1.39) and obstructive pulmonary disease (OR 1.61; 95% CI 1.40-1.85). Importantly, complete "optimal medical treatment" (OR 0.59; 95% CI 0.51-0.67) is associated with a substantial lower 1-year mortality.

Propensity Score Matched Cohort

Propensity score matching was performed in both cohorts; 14,364 patients could be matched in case of PCI and 13,038 patients could be matched in case of optimal medical treatment. After matching the standardised mean differences (SMDs) of nearly all covariates was less than 0.1.

The effect of PCI and the effect of optimal medical treatment, when compared with a reference group with a nearly identical mix of covariates, was significant ($p < 0.001$), stressing that both PCI treatment within 4 days and optimal medical treatment are both significantly associated with increased survival for the Dutch NSTEMI population (Appendix A).

Discussion

The current study analyses NSTEMI care in the Netherlands through hospital and pharmaceutical claims data. The main findings can be summarized as; NSTEMI patients are predominantly older, male patients. The use of PCI within 4 days of hospitalisation and " complete optimal medication treatment-use" within 30-days after NSTEMI is both modest, but both significantly lower 1-year mortality in these patients. Non-use of both factors is independently associated with increased mortality, which suggests that through present study, NSTEMI healthcare quality can be improved in the Netherlands.

The current call for awareness for a wider use of PCI within 4 days of admission after NSTEMI and "optimal medical treatment-use" is in line with the recommendations in the ESC guidelines(3). Furthermore, it is congruent with a recently published study by Hall et al. analyzing over 400,000 hospital survivors of a NSTEMI in England and Wales, in order to investigate whether improved survival associated with the use of NSTEMI guideline-indicated treatments(9).

In this somewhat older cohort (2003-2013), Hall et al. demonstrate that guideline-indicated treatment is associated with improved survival that persisted over the longer term. An invasive coronary strategy was found to have the most comprehensive and persistent impact on survival. This is consistent with the finding of the current study where PCI treatment for NSTEMI substantially reduces 1-year mortality with an OR of 0.42.

A potential argument for non-use of PCI in NSTEMI patients in daily practice may be that the beneficial effect of PCI is less in the elderly with more comorbidities and complications are more prominent in this group. Interestingly, Couture et al. found that especially in older patients with more comorbidities a more invasive strategy should be considered (14). With the NSTEMI cohort in our study having a similar profile and low PCI rate, this can be an important finding to improve on in the Netherlands. This issue was indeed also raised in a very recent registry by Hoedemaker et al. evaluating treatment patterns of NSTEMI patients in 23 non-PCI centers in the Netherlands.

In this registry, the majority of high risk patients underwent angiography at a non-PCI center. Despite guideline recommendation only a quarter of these high risk patients was transferred to a PCI center within 1 day(15).

Apart from early PCI, the present study also underlines the importance of "optimal medical treatment-use" implemented within 30 days after NSTEMI. Where Hall et al reported on recipes at discharge, the current study reveals which medication is collected at pharmacies up to 30 days after NSTEMI.

Since primary non-adherence of prescribed medication has reported to be very common in patients with ischemic heart disease(16), we think that the current results provide additional insight in the significance of secondary prevention medication use after NSTEMI, especially since mortality differences were already observed within the first year. Accordingly, a conjoint effort of cardiologists and patients is warranted to improve medication adherence after NSTEMI.

The current study confirms the findings by Hall et al and extends them to the entire Dutch population with additional insights in the impact of secondary prevention medication truly collected at pharmacies. Interestingly, the method of data collection substantially differs between the two studies. In particular, Hall et al reported on data gathered from national clinical audits.

Data collection for audits, however, is time consuming and expensive. We want to stress the need for new effective ways of evaluating healthcare as a key element in healthcare innovation. The use of claims data has been proven correct and adequate in prior studies(10, 11). National claims data provide a good representation of "the real world setting" in contrast to the common single centre registries in NSTEMI studies(17-22). Furthermore, it has the advantage of coming with a low administrational load, costs, an absence of reporting bias and it provides easy follow-up of patients being treated in more than one hospital.

Some limitations should nonetheless be considered when interpreting the results. First the study uses a non-randomized design with observational data. The addition of propensity score matching however, strengthens the results(23).

Second, this study only assessed PCI treatment in the acute phase of the infarction; an effect of PCI on mortality after the acute phase of NSTEMI was not calculated. Identically, the effect of bypass surgery (CABG) on mortality after NSTEMI was not calculated. Third, the level of clinical detail is limited such as completeness of revascularization or infarct size. Common used risk scores (e.g. Global Registry of Acute Coronary Events (GRACE) risk score) cannot be applied as well. Potentially there could have been a bias from patients, registered as NSTEMI, who did not meet all the criteria of myocardial infarction and therefore should have been classified as unstable angina. For our study we however rely on the correctness of registration of Dutch cardiologists. Equally, used definitions for comorbidities are only determined through medication use prior to the infarction and not clinical data. Equally, used definitions for comorbidities are only determined through medication use prior to the infarction and not clinical data. Likewise, clinical details on differences between male and female PCI rates lack from financial claim data. Fourth, although mortality data are available, the cause of death is not specified. Fifth, the pharmaceutical claims data only represent the collected medication, not the consumed medication.

Furthermore, it remains unclear if medication was contra-indicated or not prescribed. And lastly, further randomized trials are needed to validate the healthcare benefit of PCI during hospitalization and optimal medical treatment.

Future perspectives

The use of financial claims data in the medical field is a relatively novel and modern way of analyzing healthcare. It provides insight in where healthcare quality can be improved, both for clinicians and patients as well as for healthcare managers, insurance companies and policy makers on a national level. Particular attention should go to a wider use of PCI within 4 days of admission for NSTEMI as well as to patient, doctor and financial factors contributing to medication adherence. Financial claims data can again be used to monitor the impact of such initiatives.

Conclusion

The present study analyzed hospital and pharmaceutical claims data of more than 17,000 NSTEMI patients in the Netherlands. PCI use during hospitalization and "optimal medical treatment" both are moderately applied in this patient group but are independently associated with a lower 1-year mortality.

These findings importantly suggest that attention for a wider use of PCI during hospitalization and particular attention for "optimal medical treatment" prescription by cardiologists and its use by patients, may substantially improve outcome after NSTEMI.

Conflict of interest

None.

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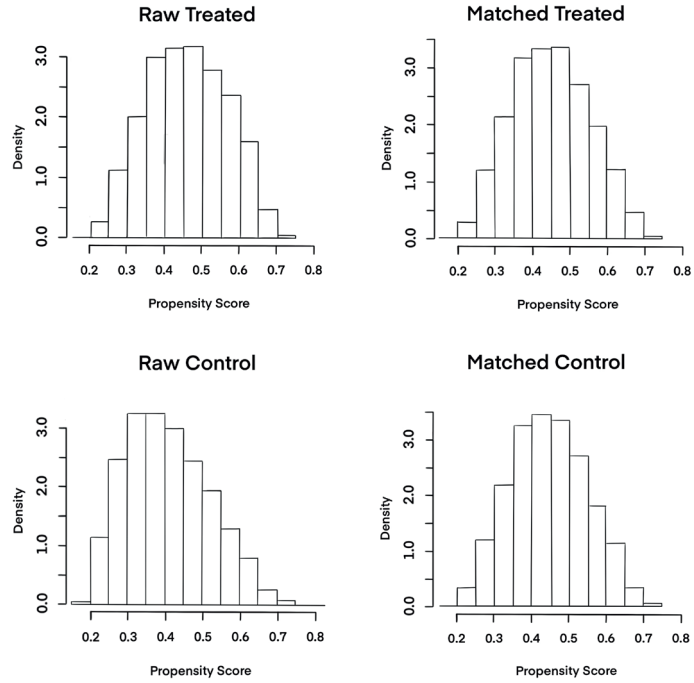
Appendix A: propensity score matching for PCI during hospitalisation and complete optimal medical treatment-use.

Part 1: PCI

To assess the effect of PCI during hospitalisation on 1-year mortality, a treatment (PCI) and a reference group with an identical balance of covariates were created. This was done by calculating propensity scores with the R programming language and logistic regression on covariates: age, gender, use of diabetes mellitus medication in year before NSTEMI, use of medication for obstructive pulmonary disease in the year before NSTEMI and use of medication for hypercholesterolemia in year before NSTEMI.

With the R package 'MatchIt' patients were matched 1:1 based on corresponding propensity scores and a caliper of 0.9. Of the patients, 14,368 were matched. After matching the histograms of propensity scores of optimal medical treatment and reference group were nearly identical.

With the R package 'tableone' we checked if standardized mean differences (SMD) between the PCI and the reference group were comparable. Before propensity score matching (unadjusted table), age and sex were unevenly distributed between the reference and PCI group. After propensity score matching (adjusted table), all variables were evenly distributed; nearly all SMDs were < 0.1.



Unadjusted (before propensity scoring)	Reference Group	PCI group	SMD
Patients (N=)	10,172	7,644	
Age (Mean (SD))	71.69(12.91)	66.48(11.89)	0.420
Male (Mean(SD))	0.59(0.49)	0.71(0.46)	0.243
Diabetes Mellitus (Mean(SD)	0.23(0.42)	0.19(0.39)	0.109
Hypercholesterolemia (Mean(SD))	0.46(0.50)	0.39(0.49)	0.129
Obstructive Pulmonary Disease (Mean(SD))	0.18(0.38)	0.13(0.34)	0.121

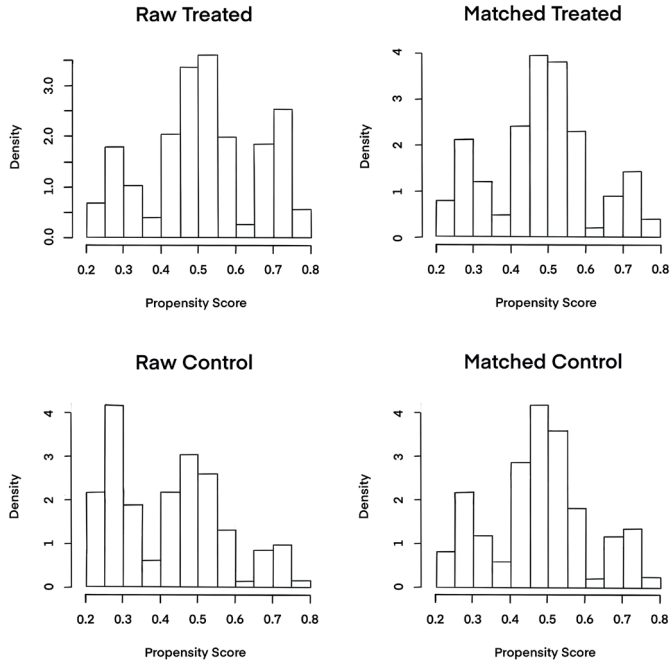
Adjusted (after propensity scoring)	Reference Group	PCI group	SMD
Patients (N=)	7,184	7,184	
Age (Mean (SD))	67.87 (12.29)	67.54 (11.40)	0.028
Male (Mean(SD))	0.69 (0.46)	0.70 (0.46)	0.021
Diabetes Mellitus (Mean(SD)	0.20 (0.40)	0.19 (0.39)	0.034
Hypercholesterolemia (Mean(SD))	0.42 (0.49)	0.41 (0.49)	0.018
Obstructive Pulmonary Disease (Mean(SD))	0.14 (0.35)	0.13 (0.34)	0.026

With a paired T test we evaluated the effect difference on 1-year mortality. The effect difference of PCI treatment was significant ($P < 0.001$). Effect size: In this total group of 14,368 matched patients, the 1-year mortality was 7.7%. In the PCI group 1-year mortality was 4.6%, in the reference group 1-year mortality was 10.9%.

Part 2: Complete optimal medical treatment (OMT)

To assess the effect of complete optimal medical treatment on 1-year mortality, a treatment (optimal medical treatment) and a reference group with an identical balance of covariates were created. This was done by calculating propensity scores with the R programming language and logistic regression on covariates: age, gender, use of diabetes mellitus medication in year before NSTEMI, use of medication for obstructive pulmonary disease in the year before NSTEMI, use of medication for hypercholesterolemia in year before NSTEMI and PCI during hospitalisation.

With the R package 'MatchIt' patients were matched 1:1 based on corresponding propensity scores and a caliper of 0.5. Of the patients, 13,456 were matched. After matching the histograms of propensity scores of (optimal medical treatment) treatment and reference group were nearly identical.



With the R package 'tableone' we checked if standardized mean differences (SMD) between the optimal medical treatment and the reference group were comparable. Before propensity score matching, noticeably patients with hypercholesterolemia and having had a PCI during hospitalisation were unevenly distributed amongst the reference and OMT group. After propensity score matching, nearly all SMDs for used variables were < 0.1.

Unadjusted (before propensity scoring)	Reference Group	OMT group	SMD
Patients (N=)	9,303	8,026	
Age (Mean (SD))	70,07(13.03)	68.11(12.23)	0.156
Male (Mean(SD))	0.62(0.49)	0.67(0.47)	0.102
Diabetes Mellitus (Mean(SD)	0.18(0.39)	0.24(0.43)	0.137
Hypercholesterolemia (Mean(SD))	0.35(0.48)	0.51(0.50)	0.323
Obstructive Pulmonary Disease (Mean(SD))	0.16(0.37)	0.15(0.36)	0.036
PCI during hospitalisation (Mean(SD))	0.33(0.47)	0.57(0.50)	0.497

Adjusted (after propensity scoring)	Reference Group	OMT group	SMD
Patients (N=)	6,728	6,728	
Age (Mean (SD))	69.32 (12.40)	68.01 (12.59)	0.105
Male (Mean(SD))	0.64 (0.48)	0.65 (0.48)	0.004
Diabetes Mellitus (Mean(SD)	0.21 (0.41)	0.23 (0.42)	0.054
Hypercholesterolemia (Mean(SD))	0.47 (0.50)	0.44 (0.50)	0.068
Obstructive Pulmonary Disease (Mean(SD))	0.16 (0.36)	0.16 (0.37)	0.011
PCI during hospitalisation (Mean(SD))	0.45 (0.50)	0.49 (0.50)	0.075

With a paired T test we evaluated the effect difference on 1-year mortality. The effect difference of optimal medical treatment was significant (P < 0.001). Effect size: In the total group of 13,456 matched patients, the 1-year mortality was 6.7%. In the optimal medical treatment group it was 5.1% and in the reference group it was 8.6%.