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Quasi-experimental evidence on the effectiveness of heart attack treatment in Germany

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Quasi-experimental evidence on the effectiveness of heart attack treatment in Germany

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Quasi-experimental evidence on the effectiveness of heart attack treatment in Germany

Abstract

Objective. *To examine the causal effect of percutaneous transluminal coronary angioplasty (PTCA) in comparison to conservative treatment methods on mortality.*

Data Sources. *We use a full sample of administrative hospital data from Germany for the years 2005 to 2007.*

Study Design. *To account for non-random treatment assignment of PTCA, instrumental variable approaches are implemented that aim to randomize patients into getting PTCA independent of heart attack severity. Instruments include differential distances to PTCA hospitals and regional PTCA rates.*

Principal Findings. *Our results suggest a 4.5 percentage point mortality reduction for patients who have access to PTCA compared to patients receiving only conservative treatment. We relate mortality reduction to the additional costs for this treatment and conclude that PTCA treatment is cost-effective in lowering mortality for AMI patients at reasonable cost-effectiveness thresholds.*

Conclusions. *Our local average treatment effect results suggest that PTCA treatment could be beneficial, at least for the group that did not receive PTCA because the nearest hospital did not provide PTCA.*

Key Words. *Acute myocardial infarction, instrumental variables, mortality*

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Introduction

In the year 2015, nearly 51,000 people (6% of all deaths) died from acute myocardial infarction (AMI) in Germany.[1] Although a decline in deaths is observable – in 2002 over 69,000 people died from a heart attack – AMI remains one of the most common causes of death in Germany. In the US, heart diseases are the leading cause of death, too. In 2015 114,000 people (4% of all deaths) died from AMI in the United States.[2] The cause of AMI is a blood clot which blocks a coronary vessel. AMI patients are treated either with thrombolytic drugs which aim to dissolve the blood clot or with invasive revascularization techniques. Revascularization (REVAS) encompasses coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA).

This paper investigates whether invasive AMI treatment options reduce mortality compared to a conservative therapy. Assessing treatment options for AMI patients is of interest for several reasons. First, AMI treatment has substantial welfare implications because AMI displays high mortality rates and treating it can substantially extend life. Second, assessing AMI patients allows us to focus on a large part of the health system, as AMI is one of the most common reasons for hospital admissions in countries like the US or Germany. The German population which is considered in this paper is large enough to detect even small impacts of the treatment on hospital mortality. Third, application of AMI treatments displays strong regional differences. This regional variation in health care use might reflect inefficiencies if they do not mirror differences in medical need.[3] Fourth, there is a lack of evidence on the effectiveness of AMI treatment options. Although randomized controlled trials provide evidence for the effectiveness of REVAS,[4] there are only a few quasi-experimental studies[5-8]

which assess whether this effectiveness is practically realized, i.e. whether external validity exists. We discuss how we extend these studies below.

There are empirical challenges to this analysis: patients who get invasive treatment options are not directly comparable to patients who get conservative treatment. The first group is often younger and healthier, may have lower AMI severity and may differ in unobserved factors from patients who do not get the invasive treatment. Differences in outcomes among AMI patients who are treated differently may be attributable to unobserved factors, resulting in biased estimates of the effectiveness of alternative treatments outside randomized controlled trials.[6] In consequence, existing observational studies have used instrumental variable techniques to attempt to identify patients who are similar in terms of health status and other unobserved factors but who for some reason receive different AMI treatment.

We follow the instrumental variable (IV) approach introduced by McClellan, McNeil, and Newhouse.[6] The authors use the difference between the distance of the closest hospital offering invasive treatment options to the patient and the closest hospital treating AMI patients regardless of whether invasive treatments are available (differential distance) as instrument. The authors find a 5 percentage point (pp) reduction in mortality, but this reduction occurs already prior to the REVAS intervention which is reflected in the 1-day mortality. The authors therefore conclude that reduced mortality is not due to REVAS, but is instead attributable to high-volume hospitals that - in addition to offering REVAS - generally have better facilities. Cutler[9] uses the same instrument and Medicare data as McClellan, McNeil, and Newhouse[6]. He has the advantage of being able to follow patients for up to 17 years, but only those AMI patients admitted in 1986-1988. He finds an one year additional life expectancy for REVAS patients at a cost of around $ 40,000 and concludes that REVAS is highly cost-effective. Sanwald and Schober[8] examine the effect for patient's treatment at a PTCA

hospital with an Austrian dataset from 2002 to 2011. They find a 9.5 pp reduction in 3-year mortality for patients treated in a PTCA hospital. Stukel et al.[5] use a slightly different approach, i.e. they take regional REVAS rates as instrument.

We contribute to the literature in the following ways: We are the first to execute the analysis with German data. Ethnic, geographic, and socioeconomic characteristics differ markedly between countries, and, hence, the effect of REVAS could also differ between countries. Second, we are the first who use comprehensive data from the unselected, complete hospital population of an industrialized nation to analyze the impact of PTCA treatment. Third, existing literature uses data from 1995 and older; since that time REVAS techniques have likely improved and more patients are treated with REVAS (see Appendix B for further details). One exception is the study of Sanwald and Schober[8] who use data from 2002 to 2011 but with a much smaller sample size and a different focus, namely on the effect of an admission to a hospital with a catheterization laboratory. Additionally, we shed some light on the issue whether the REVAS effect comes from the procedure itself or from the higher case volume. Finally, we conduct cost-effectiveness exercise that contributes to the literature analyzing whether technological change in heart attack treatment is worth it.[7]

Data

We use a full sample of all hospital inpatients in Germany from 2005 to 2007 provided by a large health insurance group. It is an administrative data set which must be generated by every hospital for insurance billing purposes according to German law requirements (§21 KHEntgG; hospital remuneration law). The data set includes patient characteristics, e.g. age, sex, admission and discharge date, main and secondary diagnoses and procedure codes, and the ZIP code of the patient's residence. The data set also contains hospital characteristics, e.g.

hospital identifier, ownership type, and whether it is a university hospital. The hospital identifier allows us to add the address of the hospital from another data source. Because we only have patient resident ZIP codes, we geo-coded the hospital addresses and the centroids of the ZIP codes and calculate the distance for every ZIP code to the chosen hospital and to the surrounding hospitals.

We focus on patients with AMI. AMI is an acute event characterized by an interruption of blood flow to a part of the heart due to the occlusion of arteries. The main goal of treatment is to limit immediate damage to the heart by restoring blood flow and providing the heart muscle with adequate oxygen as soon as possible. There are three options for treating AMI patients. Medical management often includes thrombolytic drugs, alongside with supportive care, in order to dissolve blood clots caused by AMI. An alternative to thrombolysis is using surgery. REVAS encompasses CABG and PTCA. The main difference between CABG and PTCA is that PTCA is a minimally invasive procedure and CABG is an open-heart surgery. CABG is less common than PTCA or thrombolytic drugs.[10] CABG and PTCA are preceded by cardiac catheterization, a diagnostic procedure to identify the affected artery (compare Appendix B for further background information).

We use diagnosis and procedure codes from a German definition handbook for inpatient quality indicators.[11] We include patients who are coded with the main diagnosis of a ST-elevated myocardial infarction (STEMI, diagnosis codes I21.0–I21.2) or a Non-ST-elevated myocardial infarction (NSTEMI, diagnosis code I21.3). Patients with a subsequent MI or unspecified MI are not included. On the basis of the procedure codes we are able to determine the invasive treatment options, i.e. whether the patient received a PTCA or a CABG. In the final sample, we do not include patients with a CABG (N = 27,128). PTCA and CABG are both invasive treatments for the heart attack treatment but only 5% of the patients get a CABG. To

determine the single effect of PTCA compared to medical treatment instead of the mixed effect of PTCA and CABG compared to medical treatment we exclude CABG patients.

Further exclusions are as follows: Patients under the age of 19 are excluded (N = 54). We delete patients with missing patient characteristics (N = 589) and patients with invalid ZIP codes (N = 6,816). We also exclude patients with a travel time exceeding 60 minutes to the chosen hospital (N = 15,488). It is unlikely that these patients had their heart attack at home but were on holiday, traveling etc. We exclude patients who have an ambulatory status and do not stay in the hospital (N = 1,408). We further remove patients who are coded with transfer as the reason for discharge (N = 126,455). This means that they were transferred to another hospital after their hospital stay. For the transferring hospital we cannot measure the outcome of the patient. We drop patients who are treated in hospitals with less than 10 cases (N = 1,719). We assume that these hospitals do not treat AMI patients and, therefore, do not belong in the sample. We end up with a sample of 406,281 patients treated in 1,292 hospitals.[a]

The main variable of interest is PTCA which is specified as 1 if the patient received a PTCA and 0 if not. As outcome measure we use in-hospital mortality. We extract this information from the variable discharge reason which can have the following main specifications: treatment ended regularly, discharge to nursing home or rehab hospital, or death.[b] We recoded this variable as mortality which is 1 if patient died in hospital and 0 otherwise. In-hospital mortality of AMI patients is a widely used outcome parameter (e.g. Cutler, 2007; McClellan, McNeil, and Newhouse, 1994).

We define a PTCA hospital as a hospital which treats more than 10 patients with PTCA per year.[c] Using this definition we are able to calculate the distances from the patient's residence ZIP code to the closest hospital which treats AMI patients and the closest PTCA hospital. We calculate the difference of both variables which we use as an instrument (see Section 3).

The decision whether a patient receives a PTCA is not independent from other health characteristics which also influence the outcome. For this reason we control for further patient characteristics. We include age, sex, and admission reason. We include a binary variable whether the admission was on a weekend or holiday, and a binary variable whether the admission was at night. These variables should capture the effect of "off-hour" admission because some literature has found that the mortality risk can increase during this time.[12,13] We use the Charlson Comorbidity Index (CCI) to control for further comorbidities besides the AMI.[14] The CCI consists of 17 comorbidities which are coded as binary variables. The first Charlson diagnosis is myocardial infarction. We set this diagnosis to "0" because all of our patients have it as main diagnosis. To construct the index, the comorbidities are weighted and summed up. The higher the index number, the more ill the patient is besides the main diagnosis of AMI.

Due to the different mortality rates of the two AMI types, we add a control variable for AMI type, which is 1 if the patient has a NSTEMI and 0 if the patient has a STEMI. We add a binary variable "city" which indicates whether patients live in an urban or rural area. We also include year dummies to capture any changes during the years. At the hospital level we control for ownership type (public, not-for-profit or for-profit), and university hospital.

We add federal state control variables to capture differences between federal states. We include purchasing power per inhabitant and the unemployment rate in every ZIP code of the year 2005.[15-19] These two variables capture socioeconomic differences between ZIP codes. Additionally, we include the minimum time to an AMI hospital to control for further structural differences between ZIP codes.

Table 1 shows descriptive statistics for the whole sample and the sample divided by the method of treatment, i.e. whether the patient receives a PTCA or not. 48% of all patients in

our sample receive a PTCA. The average unadjusted mortality rate is 12.3%. It is 6.3% for patients who receive a PTCA and 17.9% for patients without. Patients are on average 70 years old. Patients who get a PTCA have an average age of 65 and, hence, they are nearly nine years younger than patients who do not get a PTCA. On average 8% of the patients have a CCI of 5 or higher. This share is much lower in the group of patients who get a PTCA (4.0%) compared to patients who do not get a PTCA (11.4%).

[Insert Table 1 around here]

Methods

To measure the effect of PTCA on mortality, we regress our binary outcome variable, y_{ih}, "death", which is 1 if patient *i* died in hospital *h*, on a binary variable, $PTCA_{ih}$, which indicates whether the patient received a PTCA (1) or not (0). We also control for further patient characteristics, x_{ih}, and hospital characteristics, k_h. The specification is shown in equation (1). We estimate the equation on patient level. Standard errors are clustered at the hospital level.

$$y_{ih} = \alpha_0 + \beta_1 PTCA_{ih} + \boldsymbol{x}'_{ih}\boldsymbol{\beta}_A + \boldsymbol{k}'_h\boldsymbol{\beta}_A + \varepsilon_{ih} \quad (1)$$

Our administrative data set has detailed information on patient characteristics. Nevertheless, detailed socioeconomic characteristic and clinical parameters are missing. Hence, we cannot assume that we are able to control for all patient characteristics that are correlated with the decision whether a patient receives a PTCA or not. The reason for this is that patient groups with and without PTCA differ significantly, e.g. patients who receive PTCA are younger and healthier and therefore have a lower risk of death (see Table 1). The patient selection bias may occur not only in observable but also in unobservable characteristics which are captured

in the error term. If unobserved healthier patients get the PTCA who inherently also have a lower mortality rate, this will lead to an overestimation of the PTCA effect in absolute terms.

To exclude problems with unobserved patient heterogeneity we use an instrumental variable (IV) approach. Therefore, we need an instrument which is highly correlated with the likelihood of receiving a PTCA but has no effect on mortality. We follow the work of McClellan, McNeil, and Newhouse[6] and Newhouse and McClellan[20] who estimate the local average treatment effect of undergoing REVAS. The authors showed that the differential distance between the nearest REVAS hospital and the nearest hospital was strongly correlated with the probability of getting a PTCA treatment but uncorrelated with observable indicators of quality. The differential distance has become a widely applied instrument to study different treatment effects in medical care.[21,22]

We use differential time as an instrument and define it as the driving time to the closest PTCA hospital minus the driving time to the closest hospital which offers AMI treatment. For this instrument it is irrelevant which hospital the patient has chosen in reality. The differential time is 0 if the closest hospital is already a PTCA hospital and greater than 0 if the closest hospital offers no PTCA treatment option. Figure A1 in Appendix A shows how the differential distance varies within Germany and a descriptive statistic by differential time is shown in Table 2. Therefore, we build two groups; the first group has a differential time of 0 and the second group has a differential time greater than 0. The instrument should divide the patients into two groups which should not differ in their patient characteristics but in the probability of receiving a PTCA. It is perceivable that the first group has a slightly lower unadjusted probability of death and has a higher share of patients who receive a PTCA (57.9% vs. 39.8%), i.e. patients who have a PTCA hospital as the closest hospital have an 18 pp higher likelihood to receive a PTCA than patients who live further away. The minimum time to a hospital which

treats AMI patients is still similar for both groups (10.5 and 10.8 minutes) but the minimum time to a PTCA hospital is much higher for the second group (22.4 minutes). Hence, it is obvious that the differential distance is a crucial factor whether the patient is treated in a PTCA hospital and receives a PTCA.

Differential time is a valid instrument if patients do not choose their place of residence based on the availability of hospital resources. This is not a testable criteria but Table 2 shows that the characteristics of patients who live close to a PTCA hospital and patients who live further away are balanced. This is also assumed for the unobservable characteristics. Due to the large sample size the differences between the patient characteristics are nearly all statistically significant but the magnitudes of the differences are rather small. One exception is the distribution of urban and rural residence with a difference of more than 5%. This difference is rather caused by different hospital structures in rural and urban areas. The second exception is the different distribution of admission reason. On the one hand, this is a coding issue, because AMI patients are generally emergency cases and in our data set it is only possible to account for administrative emergencies, i.e. all patients are coded as emergencies if they reached the hospital without a doctor's referral. This is not comparable to a medical emergency. On the other hand, patients with admission reason transfer are usually patients who are transferred to a PTCA hospital. Patients who have as closest hospital a PTCA hospital need no transfer into a PTCA hospital. We account for the differences in admission status and rural and urban areas by including the variables in the regression and execute separate regressions for each group in robustness checks.

The second requirement for a valid instrument is that the instrument must not be correlated with another (unobserved) variable which is also correlated with the outcome. For example,

if PTCA hospitals are also better in the follow-up care of patients, the effect of PTCA is still overestimated in absolute terms.[9]

[Insert Table 2 around here]

We apply the IV regression in the established two-step procedure. In the first-stage equation (equation (2)), we regress our endogenous variable PTCA on all covariates and our instrument differential time (DT). In the second-stage equation (equation (3)), we use the fitted values of PTCA from equation (2) to estimate the causal effect of PTCA on mortality.

$$PTCA_{ih} = \pi_0 + \boldsymbol{x}'_{ih}\boldsymbol{\pi}_1 + \boldsymbol{k}'_h\boldsymbol{\pi}_2 + \gamma_2 DT_{ih} + \nu_{ih} \quad (2)$$

$$y_{ih} = \alpha_0 + \beta_2 \widehat{PTCA}_{ih} + \boldsymbol{x}'_{ih}\boldsymbol{\beta_B} + \boldsymbol{k}'_h\boldsymbol{\beta}_B + \varepsilon_{ih} \quad (3)$$

With IV regression we only measure a local average treatment effect (LATE).[23] In our case, it is the effect for patients who receive a PTCA because they live close to a PTCA hospital but would not get a PTCA if they lived further away (compliers).

Results

Regression coefficients of the linear probability model (LPM) are shown in Table 3. The complete regression results are shown in Table A1 in Appendix A. In a bivariate regression of PTCA on mortality (model (1)) we find an 11.7 pp reduction in mortality for PTCA patients compared to patients with a conservative therapy. If we add further patient and hospital characteristics the effect slightly decreases to 10.2 pp (model (4)). Because of unobserved patient characteristics the OLS coefficients are biased and, hence, we turn to our IV results. Our instrument differential time highly correlates with our endogenous variable PTCA. The first-stage F-statistic is 353 if we use the model with all covariates (model (8)). Further, we can

reject the null hypothesis of the Durbin-Wu-Hausman test that PTCA is exogenous ($p < 0.01$). Hence, we conclude that IV regression is necessary and we have a strong instrument.

[Insert Table 3 around here]

The IV coefficients are smaller in absolute terms than the OLS coefficients. Even though the coefficients are not directly comparable because they measure different treatment effects (ATT vs. LATE), the reduction in absolute terms is in line with the basic idea that unobserved patient characteristics may influence the PTCA treatment decision. If (unobserved) healthier patients get a PTCA, the PTCA coefficient will decrease in absolute terms in an IV specification. In the bivariate specification, we find a 4.5 pp reduction in mortality for PTCA patients (model (5)). After adding the covariates, the effect of PTCA on mortality stays constant at 4.5 pp (model (8)).

In a robustness check we also use a similar instrument to Stukel et al.[5], i.e. the regional PTCA rates. We specify the instrument as the share of PTCA patients in a 4-digit ZIP code area. Regional PTCA rates may serve as an effective instrumental variable because prognostic factors for AMI mortality, such as mean AMI severity, are similar between regions that have very different PTCA rates.[5] Additionally, in Appendix B we demonstrate that there is much variation in PTCA rates across German regions establishing that the range of variation spanned by the IV approximates the average effect in the population quite well.[20] The causal effect of PTCA in this IV specification is a 4.8 pp reduction in mortality in the full model (Table 3, model (12)). Even though this is slightly higher than the effect obtained when using differential time as instrument, there is no statistically significant difference between the two effects. This is investigated with a tentative test that checks whether the coefficient of one instrument lies within the 95% confidence interval of the other instrument.

To get more specific insights in the PTCA effectiveness, we split the sample into different subgroups (Table 4). In Table 4 every regression includes all covariates of the full model of Table 3. Due to different availability of rescue services and PTCA possibilities in urban and rural areas, we specify different regressions for these regions in order to rule out the possibility that the PTCA effect is only driven by PTCA hospitals in cities. Patients living in rural areas benefit even more from a PTCA than patients living in urban areas. This could be due to the effect that the differential time differs between urban and rural areas and has a higher variance in rural areas. In our sample we have patients with different admission statuses, namely regular admissions, emergencies and transfers from other hospitals. As outlined in Section 3 we can only distinguish administrative emergencies but no medical emergencies. Nevertheless, we specified a regression only with coded emergency cases. The PTCA effect increases in absolute terms. For patients with admission reason transfer it is not possible to calculate the real value for the instrument because the patients have been in another hospital before. In a robustness check we exclude these patients from the sample. The PTCA effect also increases in this case. For both regressions on the admission status the conclusions drawn from the main results remain the same. For the effectiveness of PTCA it does not matter whether the patient has been admitted at day or night time – the coefficients of PTCA for day and night are nearly identical. Our instrument differential time uses the patient's residence ZIP code to calculate the distance to the hospitals. During the day it may be the case that the patient is not at home when the heart attack occurs, and, hence, there might be a measurement error in the instrumental variable. At night it is more likely that the patient is at home. As both coefficients are comparable, we outrule the possibility of a measurement error in our instrumental variable during the day. The advantage of PTCA is greater for patients over the age of 65. The reason for this is that younger patients may have less severe heart attacks and the benefit of

PTCA is less important. A diverse effect is identified for different AMI types. Patients with a ST-elevated myocardial infarction benefit much more from a PTCA than patients with a Non-ST-elevated myocardial infarction.

[Insert Table 4 around here]

Former literature[6] could not detect whether the PTCA effect comes from the procedure itself or whether it is for example hospital's case volume or hospital's specialization. We want to shed some light on this issue. Figure 1 shows the distribution of hospital case volume for all hospitals and separately for hospitals with and without PTCA possibility. It is obvious that PTCA hospitals treat much more patients in general, i.e. there are only a few hospitals above 250 cases per year which do not offer PTCA treatment. This is one reason why the effect of PTCA and case volume are difficult to separate. We want to check whether the PTCA effect also exists in hospitals with lower case volumes. We specify a regression for patients treated in hospitals with less than 400 cases up to a case volume with less than 150 cases. The effect of PTCA decreases if the hospitals with the highest case volume are excluded from the sample but the effects are still highly significant (Table 4). For hospitals with a case volume below 150 cases, the PTCA effect becomes insignificant. Taken together, it can therefore be concluded that the PTCA effect is not only driven by hospitals with the highest case volume.

[Insert Figure 1 around here]

As another robustness check we follow Bound, Jaeger, and Baker[24] and do a placebo regression. Therefore, we randomly assign our instrument values to the patients. Hence, the instrument should have no explanatory power for the endogenous variable. Our first-stage F-statistic reduces below one and the results do change completely.

We find a 4.5 pp reduction in mortality for patients treated with PTCA. This is a sizable effect. Nevertheless, the additional PTCA costs must be in an appropriate proportion to these benefits. Due to the limited resources in the health system it is necessary to spend money only on treatments which have an adequate cost-benefit ratio. Therefore, we calculate the minimum number of years which a patient must live in perfect health in order to make PTCA cost-effective. We have 195,705 patients who get a PTCA in our sample during 2005 and 2007. 8,826 deaths are avoided through this intervention. PTCA costs are € 1,600 above the costs of conservative treatment. This amounts to € 315 million in additional costs for all PTCA patients within this period.[d]

For the calculation a value of a quality adjusted life year (QALY) has to be assigned. The thresholds are between US$ 50,000 to US$ 100,000 (approx. € 35,700 to € 71,400[e]) in the US and between £ 20,000 to £ 30,000 (approx. € 28,500 to € 42,800) in the UK.[25] The total benefit of the PTCA results from the multiplication of the number of avoided deaths, the value of a QALY and the additional number of years lived. The benefit must be higher than the additional costs. Therefore, we calculate the minimum number of years lived in perfect health to make PTCA cost-effective and set the PTCA benefit equal to the additional PTCA costs. The PTCA patients must therefore live at minimum 0.5 to 1.2 additional years in perfect health so that PTCA is cost-effective. Cutler[9] finds that PTCA patients have a 1.1 years additional life expectancy. Hence, our results indicate that PTCA is also a cost-effective intervention.

Conclusion

This paper investigates whether the use of PTCA for AMI leads to a reduction in mortality compared to conservative therapy. We use administrative hospital data of a full sample of all inpatients in Germany from 2005 to 2007. Due to the challenge of unobserved patient

heterogeneity we use an instrumental variable approach. As an instrument we use the differential time of the closest hospital to the patient offering PTCA treatment and the closest hospital treating AMI patients regardless of whether PTCA treatment is available in our basic specification. We find a 4.5 pp reduction in mortality for patients receiving PTCA treatment compared to conservative treatment. We measure the effect for AMI patients who receive a PTCA because they live relatively close to a PTCA hospital but who would not have gotten a PTCA had they lived further away (local average treatment effect). These estimates on the marginal returns to care are the most relevant ones because they give the effect for people who would be affected by a policy decision.[26]

In a robustness check, we apply another IV specification and measure the treatment effect of an alternative population, defined as patients who get a PTCA in regions with higher PTCA rates but would not have gotten a PTCA in regions with lower PTCA rates. The regional IV predicts a wide range of PTCA rates, as the share of PTCA procedures for AMI treatment is below 35% in some regions and above 65% in others. For this IV approach we find a 4.8 pp reduction in mortality for patients who were treated with PTCA compared to conservative therapy in the most conservative specification. This effect is similar to the effect in our main specification. In contrast to McClellan, McNeil, and Newhouse[6], we find that the PTCA effect is not only driven by hospitals with the highest case volume. This might reflect the improvement of PTCA techniques and that PTCA is performed sooner after hospital admission than in the past. Both aspects are associated with lower mortality rates.[10,27,28]

It cannot completely be ruled out that the PTCA effect includes other factors which are better within PTCA hospitals and lead to a better outcome, e.g. the follow-up care of patients. The effect of PTCA would then decrease. Nevertheless, our robustness checks indicate that the procedure itself substantially contributes to the treatment outcome.

What policy conclusions can be drawn from our results? To answer this question, one needs to keep in mind that our IV estimates only reflect the effect for patients who are affected by the instrument and need a careful interpretation as discussed above. Our results suggest the diffusion of PTCA treatment in Germany may be worthwhile and that providing patients' access to PTCA could be beneficial. Applying simple back-of-the-envelope calculations, we find that PTCA is cost-effective at reasonable cost-effectiveness thresholds, if the patients live for a minimum of 0.5 to 1.2 years in perfect health after the PTCA.

Notes

a. Generally, we observe a unique identifier for hospitals in our data set but for some hospitals the identifier stands for two or more hospital locations. In this case, we checked which location offers AMI treatment at all and in case two or more locations offer AMI treatment, we assign the patients to the closest hospital location. With this procedure we ended up with 30 more hospitals in the data set than without splitting the hospital locations. The results remain essentially the same when we compare results with and without splitting the hospital locations.
b. Another specification of the variable discharge reason is "discharge to another hospital" but these patients have been excluded beforehand.
c. We also defined a PTCA hospital with 5, 24 (i.e. 2 PTCA per month), and 48 cases (i.e. 4 PTCA per month) per year. The results do not change.
d. For 2007, we have accounting data for the AMI patients available. We take the weighted average for patients with and without PTCA which results in € 1,600 additional costs for PTCA. This is 1.4 times higher than treatment without PTCA and comparable with the study of Soekhlal et al.[29] in the Netherlands.

e. We use exchange rates of the year 2007, i.e. for the US $ 1.4 per euro and for the UK £ 0.7 per euro.

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Tables

Table 1: Descriptive statistics of AMI patients

	All Patients		Patients with PTCA		Patients w/o PTCA		Difference
	Mean	SD	Mean	SD	Mean	SD	
	(1)	(2)	(3)	(4)	(5)	(6)	(5)-(3)
Dependent variable							
Mortality	0.123	0.329	0.063	0.243	0.179	0.384	0.116 ***
Endogenous regressor							
PTCA	0.482	0.500	1.000	0.000	0.000	0.000	
Instrument							
Differential time	6.232	9.063	4.270	7.451	8.055	9.999	3.785 ***
Control variables							
Age	69.717	13.436	65.171	12.483	73.942	12.901	8.770 ***
Male	0.614	0.487	0.709	0.454	0.527	0.499	-0.182 ***
Admission reason: Emergency	0.639	0.480	0.657	0.475	0.621	0.485	-0.036 ***
Admission reason: Transfer	0.099	0.299	0.099	0.298	0.100	0.300	0.001
Non-ST-elevated MI	0.488	0.500	0.376	0.485	0.591	0.492	0.215 ***
CCI: 1-2	0.401	0.490	0.399	0.490	0.404	0.491	0.005 ***
CCI: 3-4	0.175	0.380	0.117	0.321	0.229	0.420	0.112 ***
CCI: >=5	0.079	0.269	0.040	0.197	0.114	0.318	0.074 ***
Winter	0.339	0.473	0.333	0.471	0.344	0.475	0.011 ***
Weekend/holiday admission	0.245	0.430	0.233	0.423	0.256	0.437	0.023 ***
Night admission	0.248	0.432	0.241	0.428	0.254	0.436	0.013 ***
City	0.723	0.447	0.736	0.441	0.711	0.453	-0.025 ***
Year 2006	0.330	0.470	0.332	0.471	0.329	0.470	-0.004 **
Year 2007	0.351	0.477	0.365	0.481	0.338	0.473	-0.026 ***
Ownership: not-for-profit	0.351	0.477	0.290	0.454	0.408	0.492	0.118 ***
Ownership: for-profit	0.144	0.351	0.161	0.367	0.128	0.334	-0.033 ***
University hospital	0.095	0.294	0.150	0.357	0.044	0.206	-0.106 ***
Minimum time to hospital	10.649	6.331	10.820	6.359	10.489	6.300	-0.331 ***
Purchasing power per inhabitant	18.370	3.990	18.564	4.133	18.189	3.844	-0.375 ***
Unemployment rate	8.507	4.594	8.508	4.708	8.507	4.486	-0.002
Number of patients	406,281		195,705		210,576		

Note: We control also for different federal states. * p<0.10, ** p<0.05, *** p<0.01. CCI - Charlson Comorbidity Index.

Table 2: Descriptive statistics by differential time

Differential time	0 min		> 0 min		Differences
	Mean	SD	Mean	SD	
Mortality	0.119	0.324	0.126	0.332	0.007 ***
PTCA	0.579	0.494	0.398	0.489	-0.181 ***
Differential time	0.000	0.000	11.578	9.524	11.578 ***
Age	69.587	13.470	69.828	13.406	0.241 ***
Male	0.618	0.486	0.612	0.487	-0.006 ***
Admission reason: Emergency	0.695	0.460	0.590	0.492	-0.105 ***
Admission reason: Transfer	0.054	0.227	0.138	0.345	0.083 ***
Non-ST-elevated MI	0.487	0.500	0.489	0.500	0.002
CCI: 1-2	0.399	0.490	0.404	0.491	0.005 ***
CCI: 3-4	0.174	0.380	0.175	0.380	0.001
CCI: >=5	0.077	0.266	0.080	0.272	0.004 ***
Winter	0.339	0.473	0.338	0.473	-0.001
Weekend/holiday admission	0.252	0.434	0.240	0.427	-0.013 ***
Night admission	0.261	0.439	0.237	0.425	-0.024 ***
City	0.757	0.429	0.695	0.461	-0.062 ***
Year 2006	0.336	0.472	0.326	0.469	-0.010 ***
Year 2007	0.368	0.482	0.337	0.473	-0.031 ***
Ownership: not-for-profit	0.323	0.468	0.375	0.484	0.053 ***
Ownership: for-profit	0.141	0.348	0.146	0.353	0.004 ***
University hospital	0.094	0.291	0.097	0.295	0.003 ***
Minimum time to hospital	10.456	6.152	10.815	6.475	0.359 ***
Purchasing power per inhabitant	18.988	4.279	17.840	3.642	-1.148 ***
Unemployment rate	8.781	4.750	8.273	4.442	-0.508 ***
Number of patients	187,596		218,685		

Note: We control also for different federal states. * p<0.10, ** p<0.05, *** p<0.01. CCI - Charlson Comorbidity Index.

Table 3: Regression results

a) LPM

	(1)	(2)	(3)	(4)
PTCA	-0.1165***	-0.0983***	-0.1023***	-0.1019***
	(0.0023)	(0.0025)	(0.0023)	(0.0023)
Patient characteristics	No	Yes	Yes	Yes
Hospital characteristics	No	No	Yes	Yes
Socioeconomic characteristics	No	No	No	Yes
Federal state indicators	No	No	No	Yes
R-squared	0.031	0.091	0.092	0.093
Number of patients	406,281	406,281	406,281	406,281
Number of hospitals	1,292	1,292	1,292	1,292

b) IV (instrument: differential time)

	(5)	(6)	(7)	(8)
PTCA	-0.0454***	-0.0486***	-0.0504***	-0.0451***
	(0.0100)	(0.0088)	(0.0089)	(0.0098)
Patient characteristics	No	Yes	Yes	Yes
Hospital characteristics	No	No	Yes	Yes
Socioeconomic characteristics	No	No	No	Yes
Federal state indicators	No	No	No	Yes
R-squared	0.020	0.086	0.087	0.087
First-stage F-statistic	210.081	281.658	349.745	352.852
Test for endogeneity (p-value)	0.000	0.000	0.000	0.000
Number of patients	406,281	406,281	406,281	406,281
Number of hospitals	1,292	1,292	1,292	1,292

c) IV (instrument: share of PTCA patients)

	(9)	(10)	(11)	(12)
PTCA	-0.0575***	-0.0570***	-0.0606***	-0.0480***
(SE)	(0.0056)	(0.0058)	(0.0061)	(0.0058)
Patient characteristics	No	Yes	Yes	Yes
Hospital characteristics	No	No	Yes	Yes
Federal state indicators	No	No	No	Yes
Socioeconomic/structural indica	No	No	No	Yes
R-squared	0.023	0.088	0.088	0.087
First-stage F-statistic	1305.759	1349.476	1165.124	1498.715
Test for endogeneity (p-value)	0.000	0.000	0.000	0.000
Number of patients	406,281	406,281	406,281	406,281
Number of hospitals	1,292	1,292	1,292	1,292

Notes: Clustered standard errors (at the hospital level) in parantheses; * p<0.10, ** p<0.05, *** p<0.01.

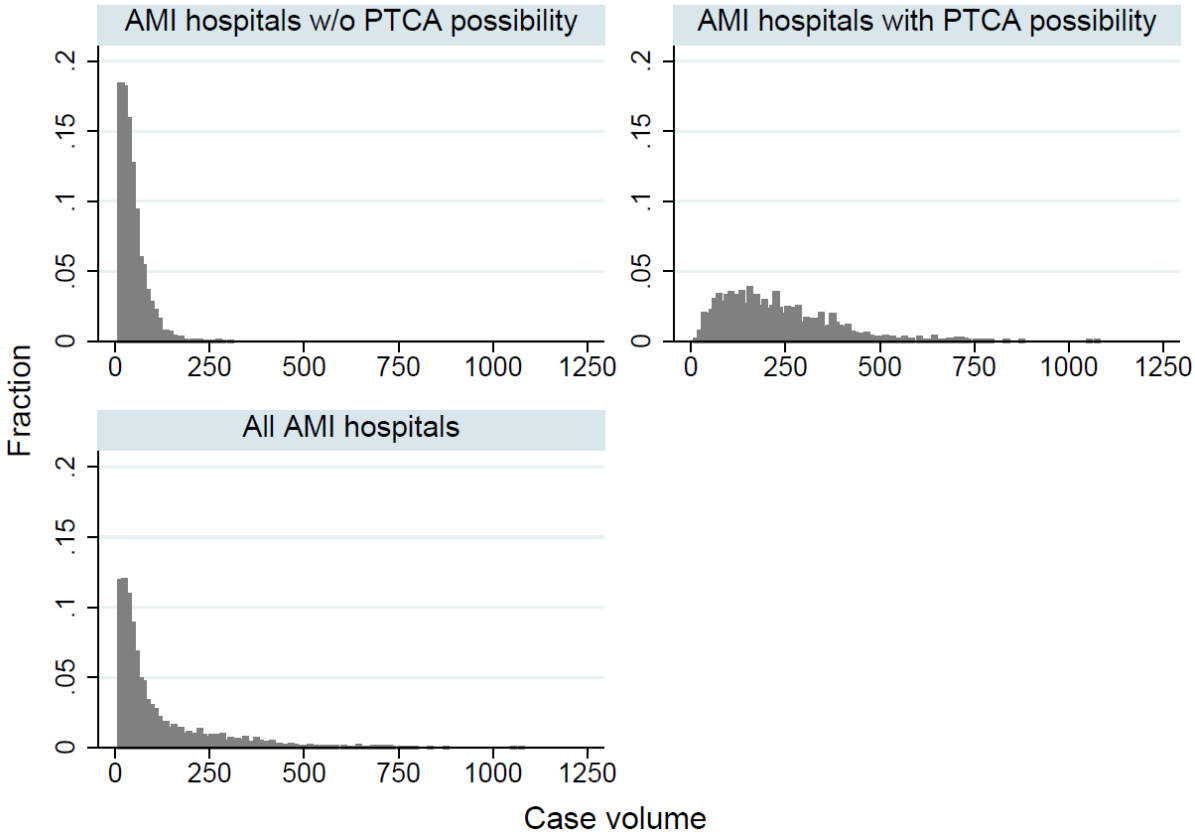
Table 4: Robustness regressions for different subgroups

	OLS		IV		First-stage	Test for endogen.	Number of	Number of
	Coefficient	S.E.	Coefficient	S.E.	F-statistic	(p-value)	patients	hospitals
Basic model	-0.1019 ***	0.0023	-0.0451 ***	0.0098	352.8525	0.0000	406,281	1,292
Regional area								
Rural area	-0.0990 ***	0.0038	-0.0766 ***	0.0169	200.4305	0.1828	112,440	799
Urban area	-0.1035 ***	0.0026	-0.0213 **	0.0108	211.8138	0.0000	293,841	1,137
Admission status								
Emergency	-0.1284 ***	0.0027	-0.0581 ***	0.0106	569.8578	0.0000	259,399	1,256
w/o Transfers	-0.1152 ***	0.0023	-0.0534 ***	0.0092	545.7250	0.0000	365,961	1,286
Admission time								
Day time	-0.0980 ***	0.0023	-0.0458 ***	0.0103	295.7826	0.0000	305,450	1,292
Night time	-0.1166 ***	0.0032	-0.0464 ***	0.0141	523.5723	0.0000	100,831	1,261
Age								
Age < 65 years	-0.0563 ***	0.0022	-0.0206 ***	0.0071	261.6932	0.0000	129,471	1,254
Age >= 65 years	-0.1158 ***	0.0027	-0.0541 ***	0.0134	378.9362	0.0000	276,810	1,292
AMI type								
Non-ST-elevated MI	-0.0592 ***	0.0018	-0.0219 *	0.0127	291.3082	0.0045	198,174	1,290
ST-elevated MI	-0.1440 ***	0.0036	-0.0576 ***	0.0115	349.6927	0.0000	208,107	1,292
Case volume								
Case volume < 400 cases	-0.1031 ***	0.0024	-0.0387 ***	0.0092	519.7764	0.0000	332,583	1,261
Case volume < 350 cases	-0.1022 ***	0.0025	-0.0380 ***	0.0091	591.0795	0.0000	301,457	1,239
Case volume < 300 cases	-0.1006 ***	0.0026	-0.0359 ***	0.0093	611.0190	0.0000	265,729	1,208
Case volume < 250 cases	-0.0981 ***	0.0028	-0.0390 ***	0.0094	642.9564	0.0000	225,682	1,168
Case volume < 200 cases	-0.0955 ***	0.0033	-0.0278 ***	0.0105	561.8094	0.0000	186,862	1,109
Case volume < 150 cases	-0.0970 ***	0.0038	-0.0131	0.0146	363.3696	0.0000	146,892	1,038
Placebo regression			-0.1353	0.2925	6.7857	0.9090	406,281	1,292

Notes: Clustered standard errors (at the hospital level) used; * p<0.10, ** p<0.05, *** p<0.01. All regressions are estimated with all covariates of the full standard regression model.

Figures

Figure 1: Distribution of case volume



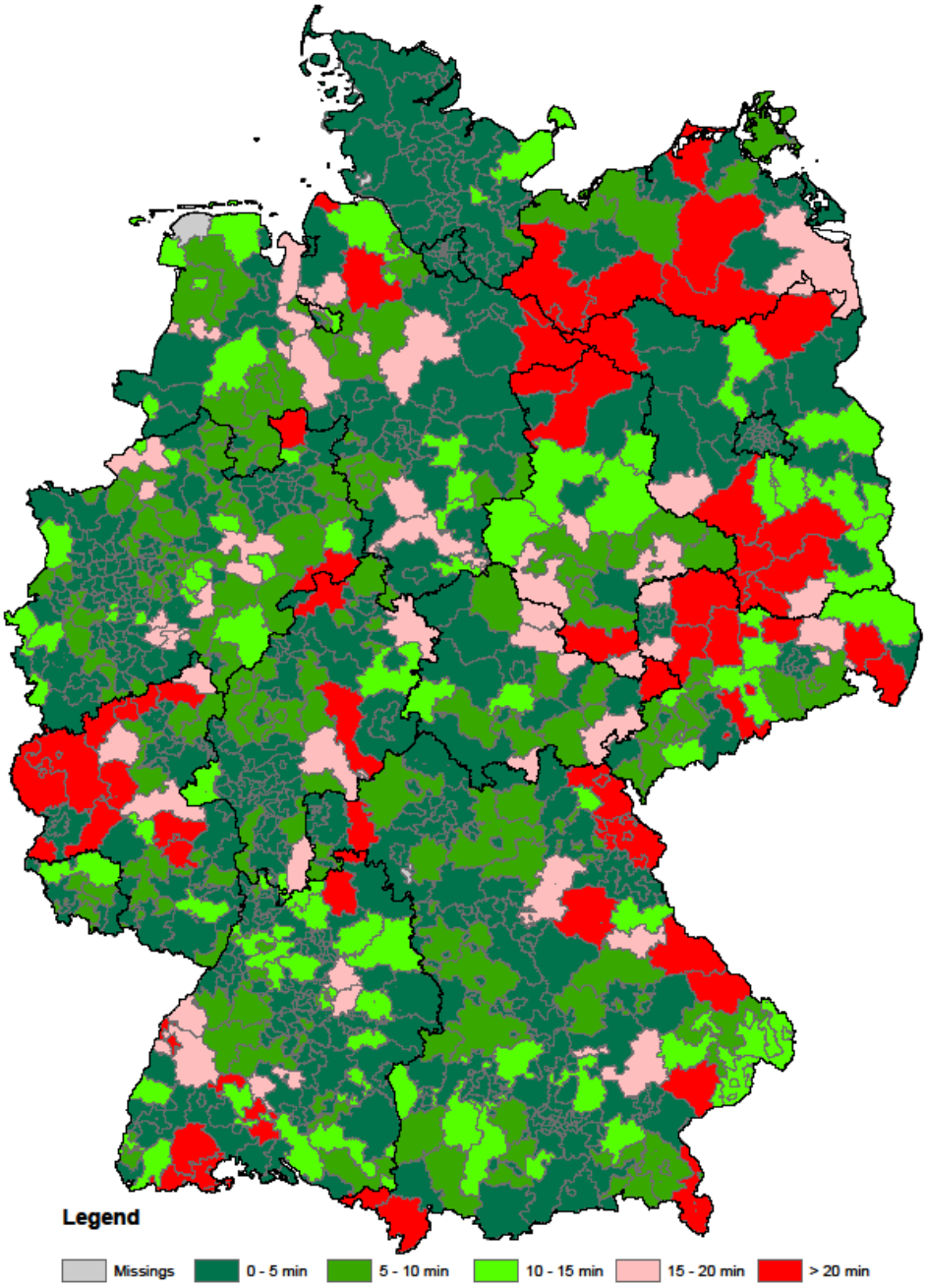
Appendix A Additional tables and figures

Table A1: Regression results (instrument: differential time)

	OLS				IV			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
PTCA	-0.1165***	-0.0983***	-0.1023***	-0.1019***	-0.0454***	-0.0486***	-0.0504***	-0.0451***
	(0.0023)	(0.0025)	(0.0023)	(0.0023)	(0.0100)	(0.0088)	(0.0089)	(0.0098)
Age		0.0044***	0.0045***	0.0045***		0.0049***	0.0049***	0.0049***
		(0.0001)	(0.0001)	(0.0001)		(0.0001)	(0.0001)	(0.0001)
Male		0.0010	0.0008	0.0012		-0.0036**	-0.0037***	-0.0037**
		(0.0012)	(0.0012)	(0.0012)		(0.0015)	(0.0014)	(0.0015)
Admission reason: Emergency		0.0220***	0.0205***	0.0200***		0.0207***	0.0199***	0.0197***
		(0.0018)	(0.0018)	(0.0018)		(0.0018)	(0.0018)	(0.0018)
Admission reason: Transfer		-0.0052	-0.0084*	-0.0100**		-0.0048	-0.0064	-0.0079*
		(0.0047)	(0.0044)	(0.0044)		(0.0043)	(0.0042)	(0.0041)
Non-ST-elevated MI		-0.1216***	-0.1225***	-0.1224***		-0.1142***	-0.1147***	-0.1138***
		(0.0018)	(0.0018)	(0.0018)		(0.0022)	(0.0023)	(0.0023)
CCI: 1-2		0.0058***	0.0051***	0.0047***		0.0089***	0.0085***	0.0084***
		(0.0017)	(0.0017)	(0.0017)		(0.0018)	(0.0018)	(0.0018)
CCI: 3-4		0.0230***	0.0221***	0.0216***		0.0305***	0.0301***	0.0304***
		(0.0026)	(0.0026)	(0.0026)		(0.0029)	(0.0030)	(0.0030)
CCI: >=5		0.0476***	0.0465***	0.0457***		0.0586***	0.0581***	0.0584***
		(0.0036)	(0.0035)	(0.0034)		(0.0041)	(0.0041)	(0.0042)
Winter		0.0027**	0.0027**	0.0027**		0.0032***	0.0032***	0.0032***
		(0.0011)	(0.0011)	(0.0011)		(0.0011)	(0.0011)	(0.0011)
Weekend/holiday admission		0.0135***	0.0134***	0.0136***		0.0154***	0.0154***	0.0156***
		(0.0012)	(0.0012)	(0.0012)		(0.0013)	(0.0013)	(0.0013)
Night admission		0.0062***	0.0059***	0.0060***		0.0074***	0.0072***	0.0074***
		(0.0013)	(0.0013)	(0.0013)		(0.0013)	(0.0013)	(0.0013)
City		-0.0000	0.0001	0.0026		-0.0014	-0.0015	0.0011
		(0.0025)	(0.0025)	(0.0026)		(0.0024)	(0.0024)	(0.0025)
Year 2006		0.0050***	0.0053***	0.0054***		0.0033**	0.0035**	0.0034**
		(0.0014)	(0.0014)	(0.0014)		(0.0014)	(0.0014)	(0.0014)
Year 2007		0.0111***	0.0115***	0.0116***		0.0082***	0.0084***	0.0081***
		(0.0015)	(0.0015)	(0.0015)		(0.0015)	(0.0015)	(0.0016)
Ownership: not-for-profit			-0.0074***	-0.0110***			-0.0033	-0.0080***
			(0.0026)	(0.0027)			(0.0026)	(0.0026)
Ownership: for-profit			0.0013	-0.0015			-0.0015	-0.0045
			(0.0037)	(0.0038)			(0.0037)	(0.0038)
University hospital			0.0276***	0.0261***			0.0150***	0.0123**
			(0.0049)	(0.0047)			(0.0052)	(0.0049)
Minimum time to hospital				0.0002				-0.0001
				(0.0001)				(0.0001)
Purchasing power per inhabitant				-0.0000				-0.0006**
				(0.0003)				(0.0003)
Unemployment rate				0.0009***				0.0006**
				(0.0003)				(0.0003)
Constant	0.1793***	-0.1156***	-0.1130***	-0.1185***	0.1451***	-0.1700***	-0.1687***	-0.1648***
	(0.0021)	(0.0056)	(0.0059)	(0.0098)	(0.0051)	(0.0106)	(0.0109)	(0.0126)
Federal state indicators	No	No	No	Yes	No	No	No	Yes
R-squared	0.031	0.091	0.092	0.093	0.020	0.086	0.087	0.087
First-stage F-statistic					210.0809	281.6580	349.7454	352.8525
Test for endogeneity (p-value)					0.0000	0.0000	0.0000	0.0000
Number of patients	406,281	406,281	406,281	406,281	406,281	406,281	406,281	406,281
Number of hospitals	1,292	1,292	1,292	1,292	1,292	1,292	1,292	1,292

Notes: Clustered standard errors (at the hospital level) in parantheses; * p<0.10, ** p<0.05, *** p<0.01.

Figure A1: Differential time 2007



Appendix B Background information

Cardiovascular diseases are the most frequent cause of death in Germany and other developed countries. Within this group AMI patients have a high share of deaths.[30] In recent decades, however, a considerable reduction in AMI mortality rates can be observed in industrial countries.[31-34] Public health and medical literature attributes these improvements to a reduction of classical risk factors like smoking or hypertension or by better secondary prevention (e.g. long term drug therapy with statins, aspirin, etc.).[31,32,34] However, improved AMI treatment like the expanded use of REVAS is considered as main cause for this development.[31,34]

Additionally, it is also plausible that the REVAS techniques itself have improved. This is reflected in medical guidelines. In 1987, i.e. the year of the data from the study of McClellan, McNeil, and Newhouse[6], REVAS was rarely used on the first day of hospital admission. This has changed. It is now recommended to perform REVAS as soon as possible, i.e. within 12 hours of symptoms' onset or rather within 2 hours from the first medical contact.[10] This more timely use is strongly associated with lower mortality rates.[27,28]

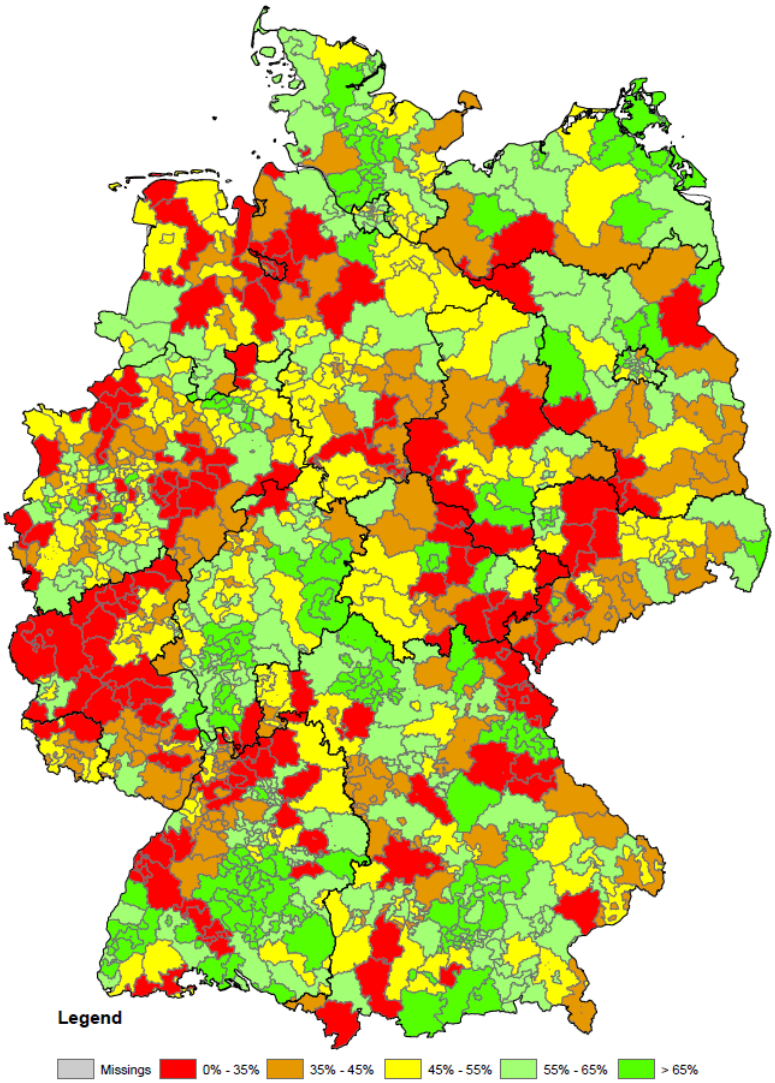
The advantage of REVAS over conservative AMI treatment has been documented in several clinical trials. In general, randomized controlled trials (RCTs) find that patients treated with REVAS have better outcomes than patients treated with thrombolytic drugs.[4] However, RCTs have been criticized because although they have high internal validity, they have shortcomings in external validity.[20] This is because RCTs are often executed under optimal conditions unachievable in the real world. Moreover, RCTs focus on narrow treatment comparisons and special patient populations, therefore, their results are often insufficient to shape health policy. [6] With administrative data it is possible to detect the effect of REVAS on mortality in the whole population.

In recent years, REVAS has been increasingly used in Germany and in other developed countries. In Germany, the application of REVAS more than doubled between 1996 and 2004.[35] About 48.1% of AMI patients were treated with PTCA methods in Germany in 2009.[30] Germany is first in the number of PTCAs per 100,000 inhabitants and second for CABG amongst OECD countries.[36] At the same time, large regional variation occurs within Germany.[36] Figure B1 illustrates that the share of PTCA procedures for AMI treatment is below 35% in some regions, for example in parts of west Rhineland-Palatinate or parts of Lower

Saxony, but already above 65% in others, for example in east Hesse and parts of Baden-Württemberg.

AMI is of increasing economic importance. For example, € 1.40 billion were spent on heart attack treatment in Germany in 2004, whereas by 2008 the total was already € 1.87 billion.[37] Annual growth in real terms was about 5.5%. Increasing AMI costs cannot be explained by a rising number of heart attacks, because AMI overall incidence and AMI hospital incidence remained relatively constant in recent years.[30] Similar trends of increasing heart attack spending have been observed in other developed countries, like the US. Cutler and McClellan[7] suggest that technological change, i.e. the extension of REVAS methods to more patients, is the main reason for the increasing costs.

Figure B1: Share of PTCA patients 2007



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