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Technische Universität Berlin

6th HTAi

The cost-effectiveness of coronary stents in AMI patients under real world conditions: Results from Germany

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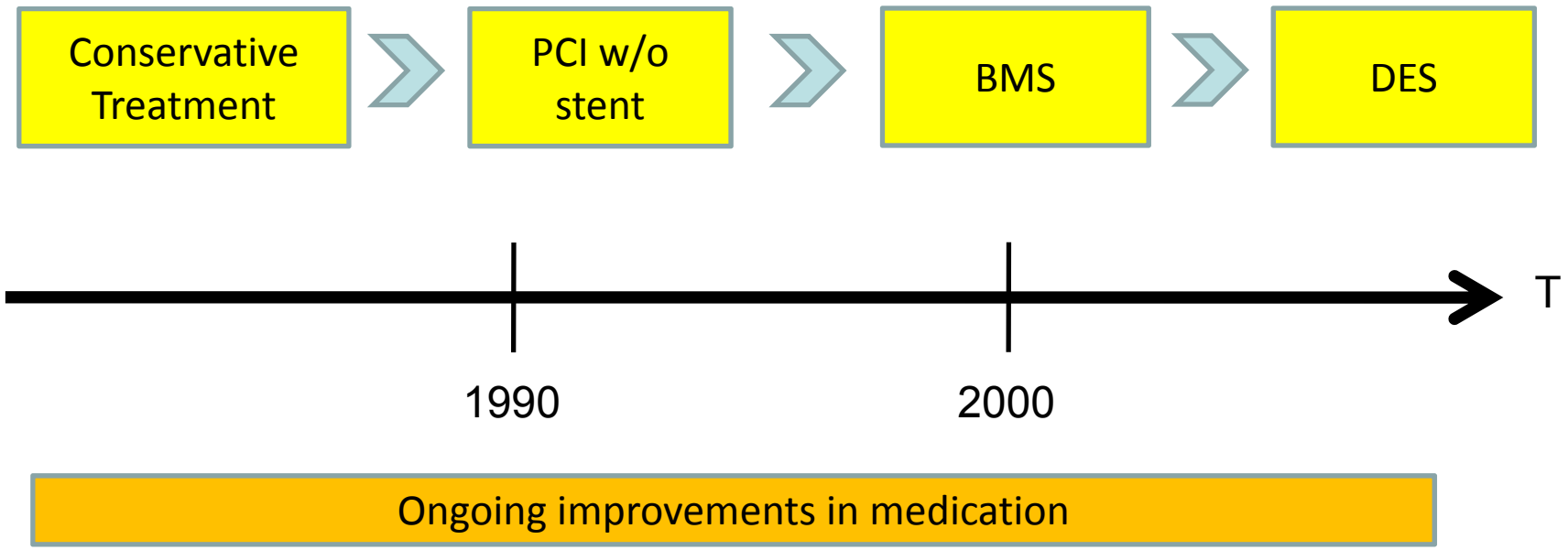
Innovations in the treatment of Acute Myocardial Infarction



⇒ Increasing expenditures are observable in the Western countries

⇒ Are innovative technologies associated with higher survival rates and higher or lower costs?

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Coronary artery stenting shows few clinical benefits: results from a systematic review of randomised clinical trials.

Meads C, Cummins C, Stevens A; International Society of Technology Assessment in Health Care. Meeting.

Annu Meet Int Soc Technol Assess Health Care Int Soc Technol Assess Health Care Meet. 1999; 15: 113.

Department of Public Health and Epidemiology, The University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.

OBJECTIVE/PURPOSE: The literature on coronary artery stents was reviewed to evaluate the clinical and cost effectiveness of routine stanting compared to percutaneous transluminal coronary angioplasty (PTCA) alone, medical treatment and coronary artery bypass grafting (CABG) in the treatment of native coronary artery disease. METHODS: Medline, BIDS ISI, Embase and the Cochrane library databases were searches for randomized controlled trials (RCTs) of coronary artery stent use and for economic evaluations of coronary artery stents. Meta-analyses were carried out in the Cochrane Collaboration Review Manager 3.0 and Metaview software. Cost utility was estimated using data from the largest RCT, EUROQOL was used to estimate utility and costs were based on local NHS tariffs for treatment. RESULTS: Eleven RCTs compared stents to PTCA in three main subgroups of patients - with new lesions, with chronic coronary occlusion or following myocardial infarction (MI). No trials compared stents to medical treatment or CABG. For the eleven RCTs the clinical outcome measures of incidence of death, MI, repeat revascularization (CABG or repeat PTCA), event free survival and angina free survival with follow up for one year or less are reported. There was a reduced risk of the need for repeat PTCA and target vessel revascularization in the stent group compared to the PTCA group but no evidence that stents reduce the risk of death, MI or need for CABG. For the stent group there was also a small increased chance of being angina free and of no adverse event occurring during the one year follow up period. Cost utility estimation showed the increase in QALYs from PTCA to stent to be very small (0.04 QALYs per person) and the additional cost per QALY gained of Pounds 23,000 if a single stent is used and if two stents per person are used of Pounds 41,500. (Sensitivity analysis range for single stent of Pounds 12,000 - Pounds 58,000). CONCLUSIONS: The evidence suggests that there are some small clinical advantages but the QALYs gained from stent insertion is very similar to that from PTCA. More research on long term outcomes is essential.

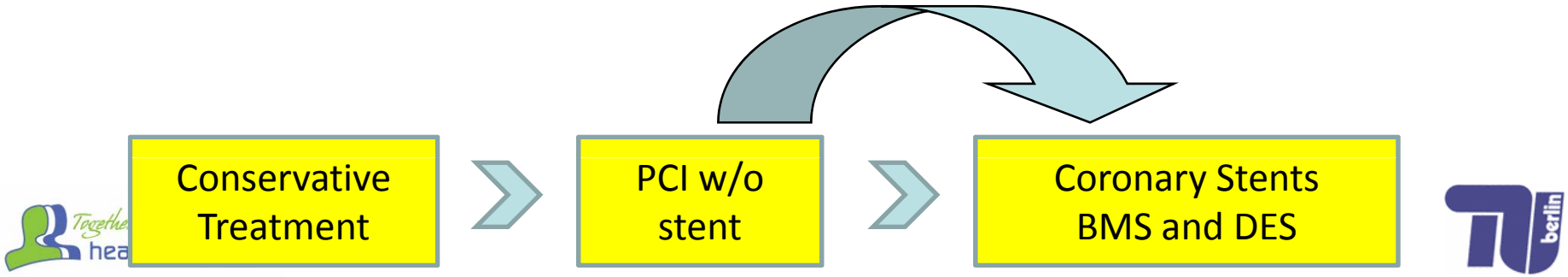
Publication Types:
- Meeting Abstracts

Keywords:
- Angina Pectoris
- Angioplasty, Transluminal, Percutaneous Coronary
- Aorta, Thoracic

Assessing the value of innovations

- Cutler (2007) measured the lifetime costs and benefits of PTCA vs. no-PTCA for the treatment of AMI in the US, based data from 1986 to 2003/4 using patient-level data
- We take a similar approach for measuring the value of innovations in AMI technology
  - To account for changes in AMI medication, we use a simultaneous patient cohort from 2004 and 2005
- First analysis: Comparing PCI with and without stenting, further analysis will follow

Hypothesis: Cost-effectiveness of PCI w/o stent > stent implantation



Dataset

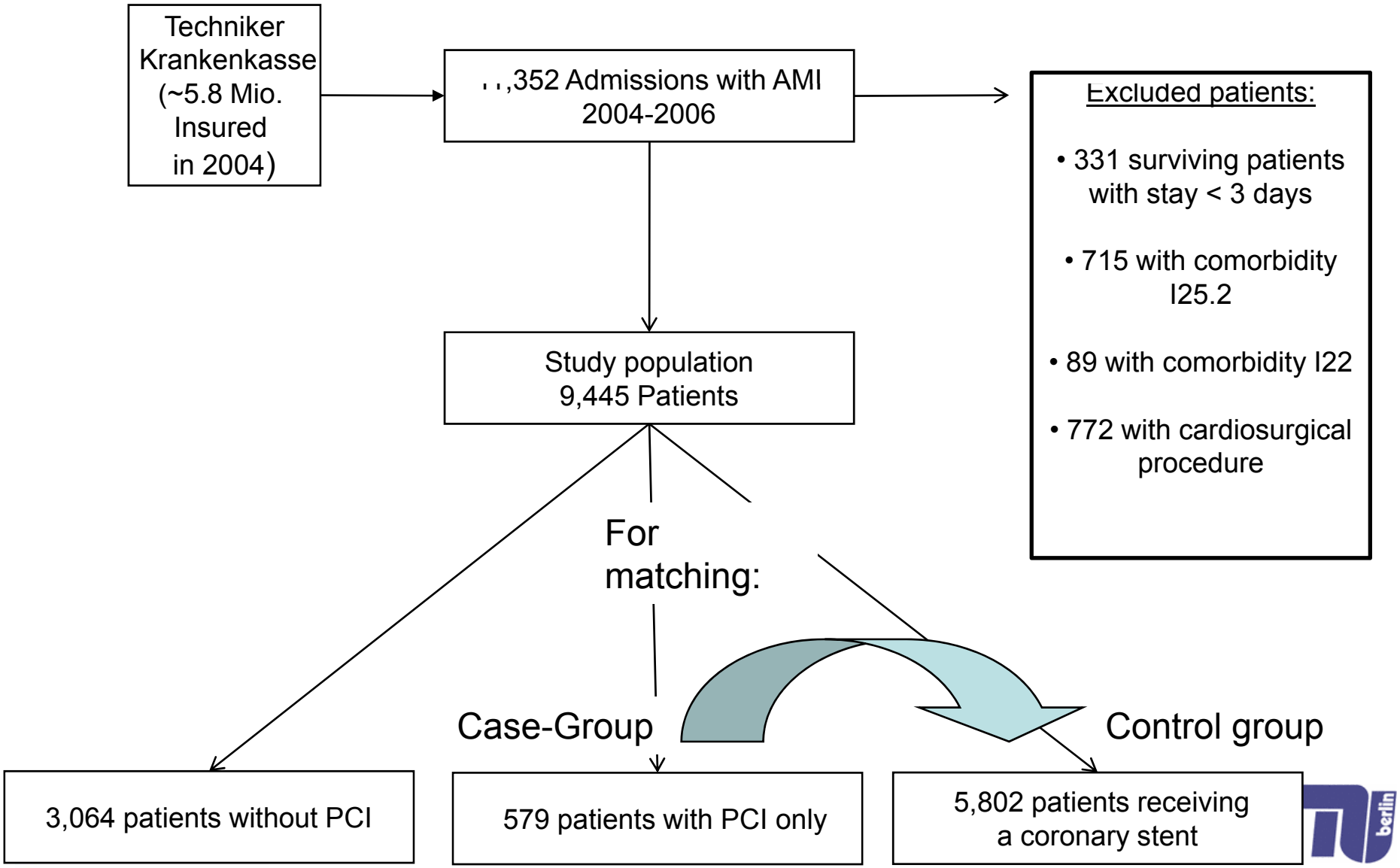
- We use data from a German sickness funds for index admissions with AMI in 2004 and 2005
- The dataset guarantees the follow-up of at least one year
- To define costs, we take the payers' perspective
- Information in the hospital-data-set contains all implemented procedures (OPS-codes), co-morbidities (ICD 10), all follow-up admissions and payments to the hospital
- Information about mortality is taken directly from the fund's general insured data
- Costs consists of all inpatient payments

⇒Target measure of the analysis will be the ICER after one year

Methods

- To account for treatment selection bias -> propensity score matching, derived from logistic regression models (dependent variable = received treatment)
- 1:1 perfect matching with replacement; elimination of heterogeneity is measured by standardized difference D (Austin 2008)
- To adjust for comorbidities -> ICD 10 Adaptation of the Ontario AMI Mortality Prediction Rules (Vermeulen et al. 2007)
- Information on age, gender, year, insurance status and several other procedures, risk factors that can be derived from the data are included in the dataset including several interaction terms
- To deal with uncertainty -> sensitivity analyses and bootstrapping

Study population



Pro ensit Matching

- **All patients receiving either PCI only or a coronary stent are included in the analysis (579 with PCI only and 5,802 with a coronary stent).**
- **Regression model for propensity score is based on a theoretical model and for detecting interactions FSR (Boos et al. 2008)**
  - Age, gender, insurance status, dummies employment status, dummy for year 2004
  - Ontario mortality prediction rules variables and other risk factors
  - To do: Add hospital characteristics and geographical information, random-intercept model
- **Threshold for matching was set at 0.05%**
  - **Sensitivity Analysis: 0.01%**
- **Matched population consists of 538 patients in each group**

Regression model for ro ensit matching

Variable	Parameter Estimate	Std.-Error	p-Value
Intercept***	1.9419	0,1971	<0.0001
Age < 50 years	0.0563	0.1747	0.7474
Age 50 - 59 years	0.0670	0.1529	0.6613
Age 65 - 74 years***	0.3693	0.1405	0.0086
Age >= 75 years	-0.2276	0.1559	0.1443
Female	-0.0104	0.1385	0.9404
AMI in 2004***	-0.7256	0.0916	<0.0001
Voluntary insured**	0.4886	0.2274	0.0317
Self-Employed	-0.3392	0.2923	0.2458
Employed*	0.3004	0.1569	0.0556
Voluntary x Employed	-0.3588	0.2804	0.2007
Family exists	-0.0241	0.1040	0.8168
Insured through husband/wife	-0.3292	0.2419	0.1735
Shock	-0.1688	0.2081	0.4174
Diabetes with complications	0.000659	0.1635	0.9968
Congestive Heart Failure	-0 0737	0 1157	0 5240
Cerebrovascular Disease***	-0.7018	0.1984	0.0004
Cancer	-0.0506	0.2847	0.8589
Pulmonary Edema	0.1761	0.3512	0.6161
Acute Renal Failure	-0.2243	0.2845	0.4305
Chronic Renal Failure*	-0.2644	0.1423	0.0632
Cardiac Dysrhythmias	0.0649	0.1182	0.5832
STEMI**	0.2346	0.0978	0.0164
Coronary heart disease***	0.3736	0.1285	0.0036
Diabetes without complications	0.1732	0.1512	0.2521
Elevated level of lipoproteins	0.0901	0.0925	0.3301
Excessive smoking	0.0237	0.1209	0.8449
Hypertension	0.0722	0.0984	0.4324
Reference Case:	60-65 year old retired w.o. family,	relevant comorbidities & risk factors	c-value: 0.644

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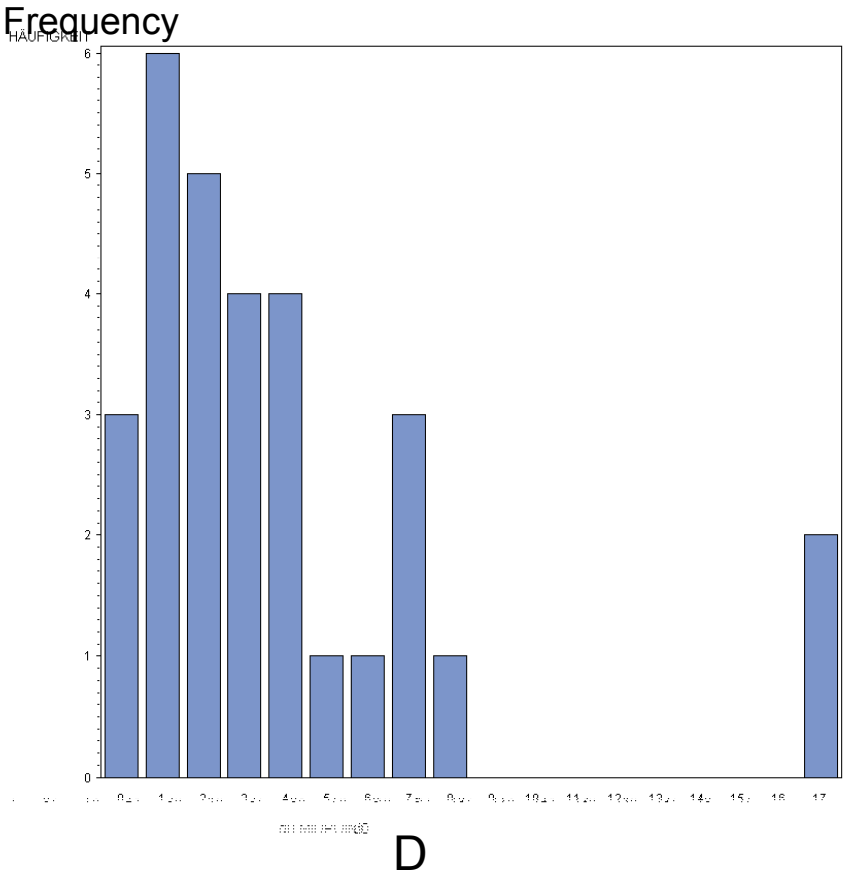
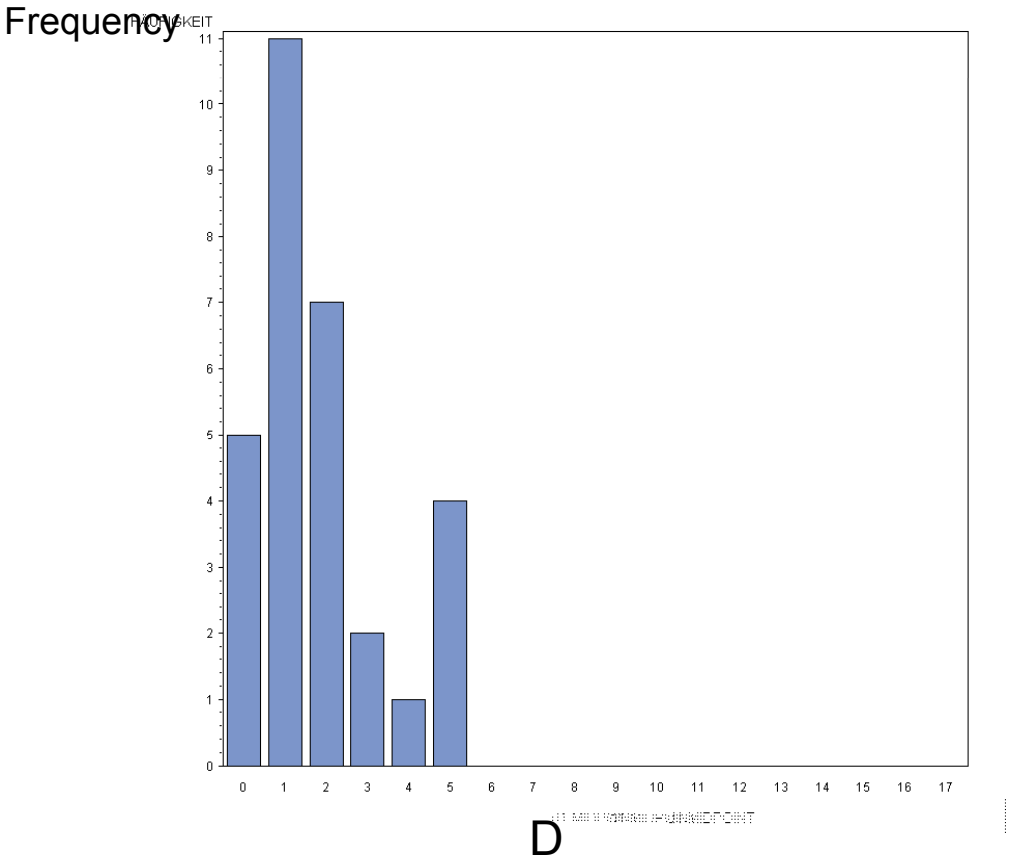
- Logit model
  - Dependent variable: Stent implantation (0/1)
  - Calculation of predicted probability for each patient
  - Reference patient:
    - 60-65 years old
    - retired, without family, obligatory insured
    - no Ontario Index comorbidities
    - no further risk factors

Standardized differences before and after matching



Before matching



After matching

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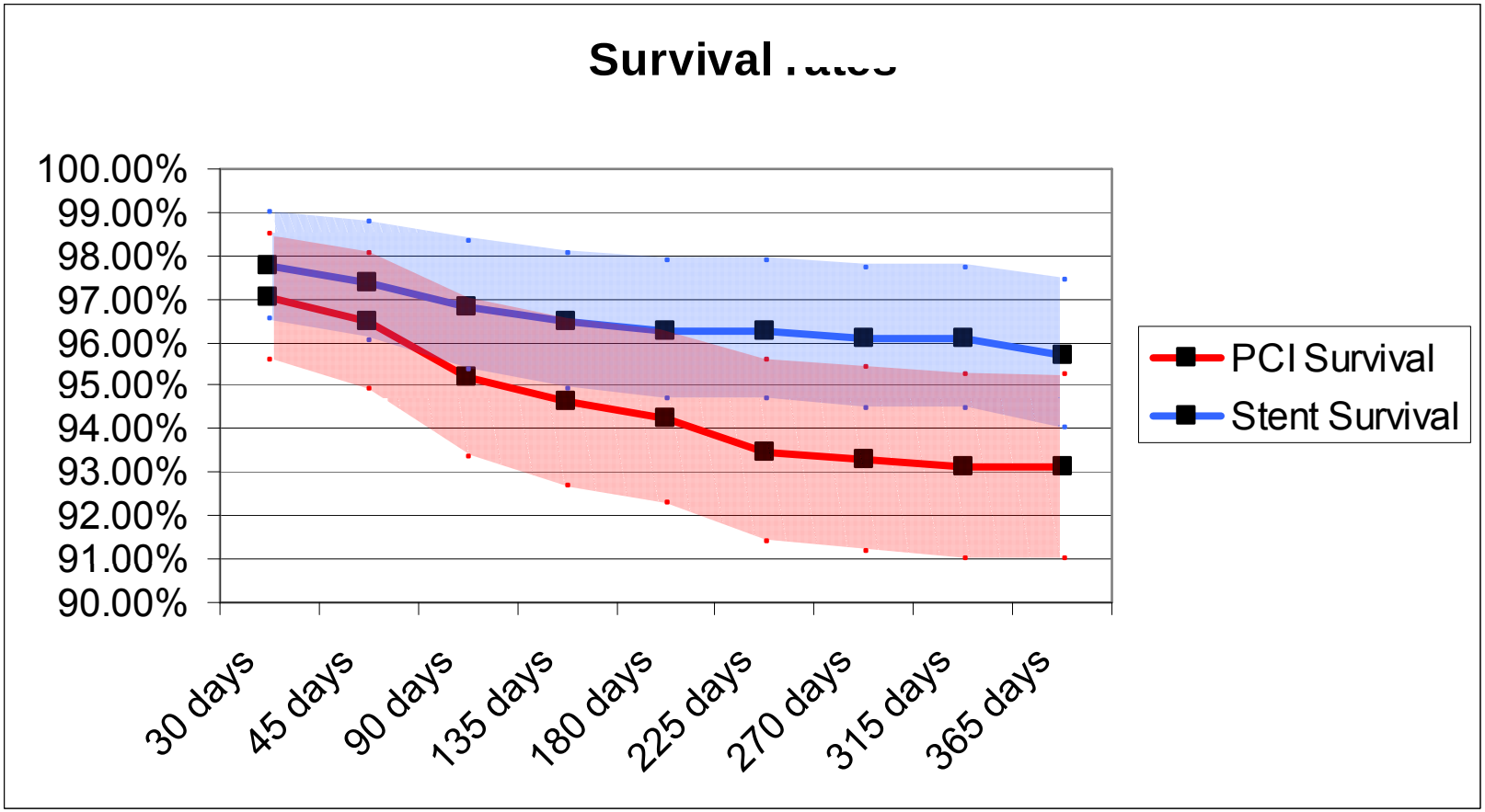
Variable	PCI Group: Mean / %	Stent Group: Mean / %	Stand. Difference
Age	64.2541	62.186	18.39
Age < 50 years	13.30%	15.60%	2.30
Age 50 - 59 years	21.24%	24.25%	3.01
Age 60 - 64 years	19.17%	17.27%	1.90
Age 65 - 74 years	25.56%	30.20%	4.64
Age >= 75 years	20.73%	12.69%	8.04
Female	16.75%	14.18%	2.57
AMI in 2004	63.04%	45.67%	17.37
Employed	29.19%	36.30%	7.11
Self-Employed	5.70%	5.95%	0.25
Retired	57.69%	50.21%	7.48
Family exists			2.51
Voluntary insured			5.54
Insured through husbar			0.94
Shock			1.29
Diabetes with complic			1.79
Congestive Heart Fa			1.77
Cerebrovascular Dise			3.13
Cancer			0.50
Pulmonary Edem			0.25
Acute Renal Failure	2.94%	1.86%	1.08
Chronic Renal Failure	13.13%	9.08%	4.05
Cardiac D¸srh¸thmias	19.86%	19.15%	0.71
Elevated level of lipoproteins	52.86%	56.95%	4.09
Excessive smoking	18.48%	20.23%	1.75
Hypertension	65.80%	67.03%	1.23
Coronary Artery disease	85.32%	89.71%	4.39
STEMI	68.57%	72.80%	4.23
Received intensive treatment	10.88%	17.63%	6.75
Received Lysis	2.59%	2.74%	0.15
Propensity Score	88.83%	91.14%	48.20

Characteristics before matching

Variable	PCI Group Mean / %	Stent group Mean / %	Stand. Difference
Age	62.3044	61.5314	7.21
Age < 50 years	14.68%	16.54%	1.86
Age 50 - 59 years	26.02%	26.95%	0.93
Age 60 - 64 years	17.84%	16.54%	1.30
Age 65 - 74 years	29.18%	28.18%	1.00
Age >= 75 years	12.27%	11.15%	1.12
Female	12.64%	14.31%	1.67
AMI in 2004	46.65%	46.28%	0.37
Employed	34.94%	39.22%	4.28
Self-Em			2.05
Ret			4.83
Family			3.02
Voluntar			1.68
Insured throug			1.49
Sh			0.00
Diabetes with			0.93
Congestive H			2.78
Cerebrovasc			2.04
Cancer	1.12%	1.49%	0.37
Pulmonary Edema	1.30%	1.30%	0.00
Acute Renal Failure	1.12%	1.67%	0.55
Chronic Renal Failure	8.36%	9.11%	0.75
Cardiac Dysrhythmias	17.84%	16.91%	0.93
Elevated level of lipoproteins	59.85%	54.65%	5.20
Excessive smoking	18.03%	20.45%	2.42
Hypertension	66.17%	65.06%	1.11
Coronary Artery disease	93.31%	90.52%	2.79
STEMI	74.35%	73.42%	0.93
Received intensive treatment	14.13%	19.14%	5.01
Received Lysis	1.49%	3.90%	2.41
Propensity Score	91.38%	91.38%	0.00

Characteristics after matching

Effects



- Survival rates are higher in Stent group
- Nevertheless, CIs are overlapping

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Effects and Uncertainty

- **Higher survival rates in the stent group**
- **But: Not significant at the 95% level**
- **To account for uncertainty, we carried out several sensitivity analyses**
  - **Matching at upper and lower 95% CI of propensity score**
  - **Threshold value for matching lowered to 0.01%**
    - **including sensitivity analysis for CI**

    ⇒ CI are overlapping as well

    ⇒ Higher survival rates in Stent group
  - **With a certain probability, higher survival rates can be expected in the group that received a coronary stent**

⇒ Higher survival rates in the PCI group are rather improbable

⇒BUT not impossible

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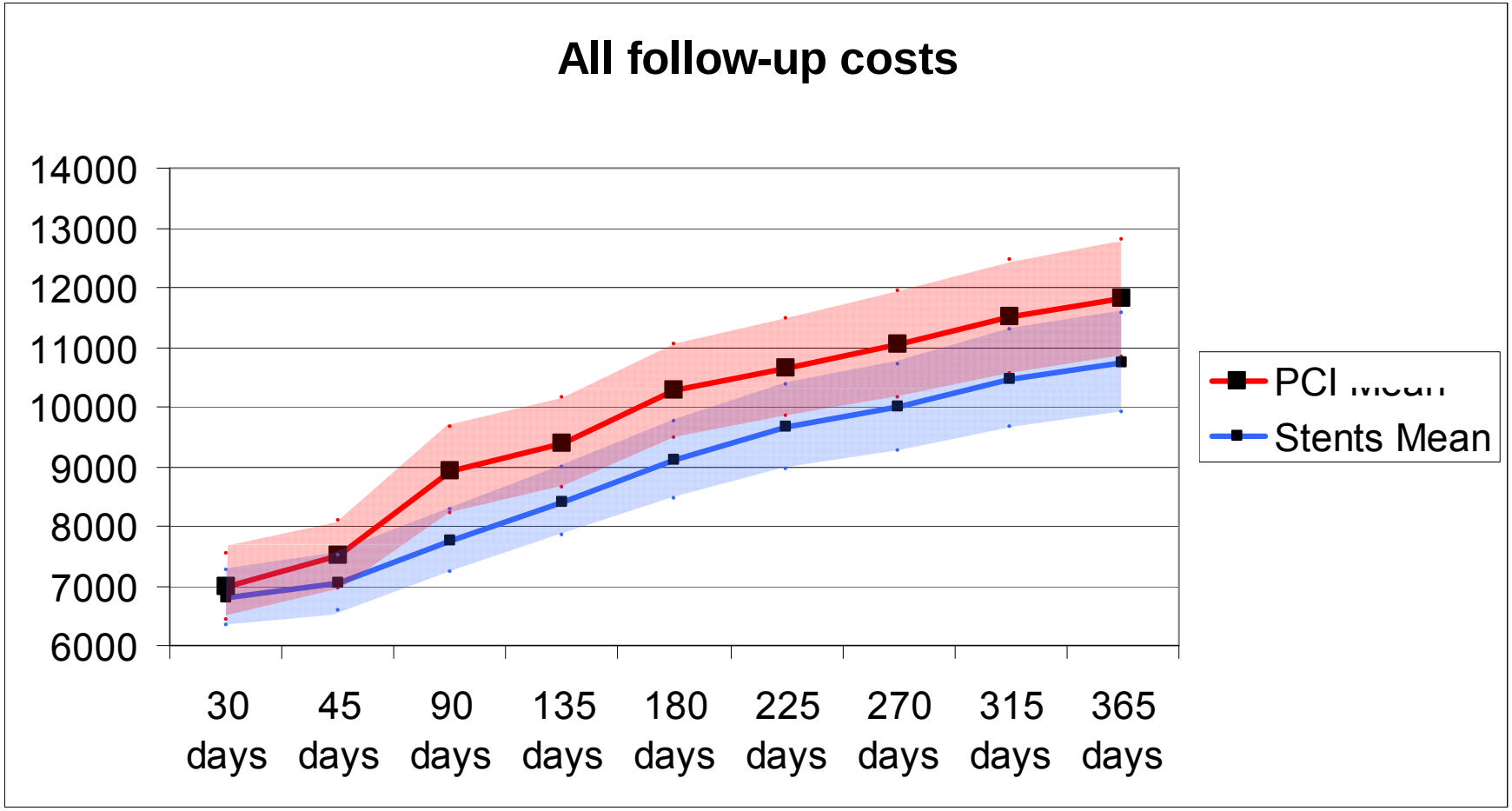
Costs


All follow-up costs
14000
13000
12000
11000
10000
9000
8000
7000
6000
30 days
45 days
90 days
135 days
180 days
225 days
270 days
315 days
365 days
PCI Mean
Stents Mean

Sensitivity analysis for costs

- **Sensitivity analysis:**
  - **Matching at upper and lower 95% CI limit of propensity score**
  - **Threshold value for matching lowered to 0.01%**
    - $\Rightarrow$ **Overlapping is similar to baseline matching**
    - $\Rightarrow$ **Mean costs are higher in the PCI group, but difference is not significant**
    - $\Rightarrow$ **Equality of costs may not be refused**

Combining Costs and Effects

- Mean Costs and Mean Effects

Δ All costs	Δ Survival Rate	ICER
825.29	-3.46%	-23,852 €

- Negative ICER due to higher survival rates in the stent group

  ⇒implies **stenting as a dominant strategy**

- BUT: As CI for both costs and effects are overlapping, uncertainty about this result

  ⇒Bootstrapping

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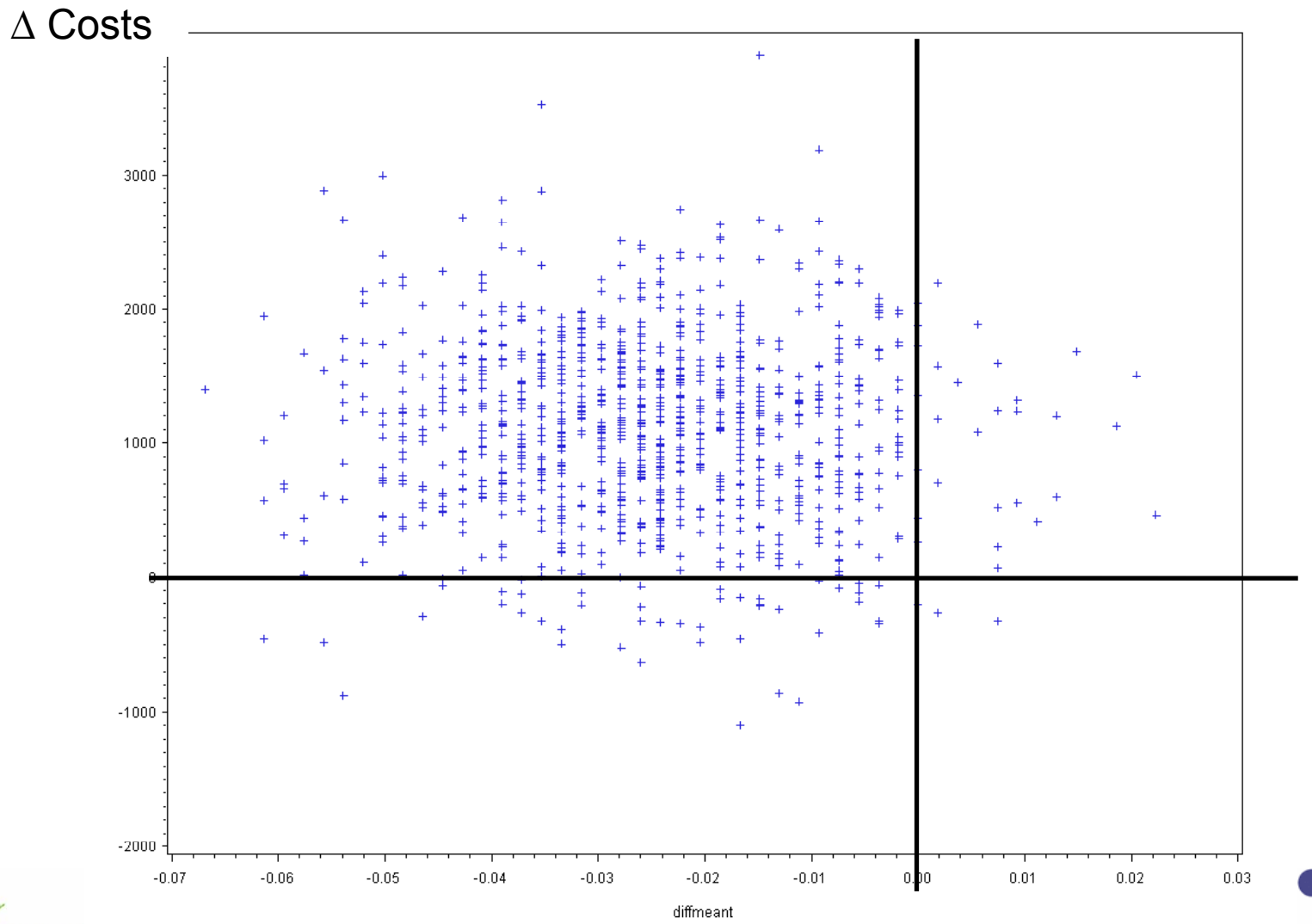
Bootstrap analysis, total costs: 1,000 replications



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Discussion (I)

- Regarding the effect on survival
  - stenting > PCI w/o stenting (comparing means)
  - CI only slightly overlapping
- Effects on costs are not unambiguous
  - Costs in Stent group are more likely to be lower
  - BUT: CI are overlapping
- Regarding the ICER

  $\Rightarrow$ The case of PCI w/o stent being dominant is rather improbable
  Much more likely: PCI w/o stent is dominated by stenting

Discussion and implications

- In general, data suggests that - with a high probability - stents are able
  - to save lives after AMI
  - save costs
- If this holds, this innovative technology can be seen as a dominant technology:
  - on the one hand, it is more effective than the predecessor *and*
  - it is able to decrease public spending
- In this case, innovative technologies seem to have a positive value for society

  $\Rightarrow$ Results are not necessarily transferable to other technologies

Limitations and assessment challenges

- Propensity score may only be as good as information available in the dataset to fulfill conditional independence assumption
- Considered costs do not comprise out-patient expenditures
- We cannot disentangle effects resulting from medication and different health technologies

  $\Rightarrow$ But: All patients are at least “exposed” the same medication.

- Follow-up periods are rather short, we do not consider lifetime costs and effects as Cutler does
- There is no distinction between different types of coronary stents

$\Rightarrow$ Further analysis should go more into detail

$\Rightarrow$ Larger population would be needed to disentangle the effects of different technologies

Outlook and to dos

- In a next step, hospital characteristics (and geographical information) are to be included in propensity scores (random effect-model) as they might influence treatment decision

  ⇒ Might have an effect on conditional independence assumption and therefore on validity of propensity matching

- Further outcome measures might clarify the effects of different technologies including data on medication

  ⇒ Major Adverse Coronary Events

  ⇒ further data are requested

- Analysis will be expanded to
  - Conservative treatment vs. PCI w/o stent
  - BMS vs. DES

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Thanks to the audience!

- Further information available at:

  www.mig.tu-berlin.de

- Further information on the European Health Technology Institute on Socio-Economic Research is available at:

  www.ehti.info

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