

Cost-effectiveness-analysis of landiolol, an ultra-short-acting beta-blocker, for prevention of postoperative atrial fibrillation for the Germany health care system*

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* J Cardiothorac Vasc Anesth. 2019 Nov 9. pii: S1053-0770(19)31140-1. doi: 10.1053/j.jvca.2019.11.003. [Epub ahead of print]

Objectives

Postoperative atrial-fibrillation (POAF) is common among surgical patients and associated with a worse outcome. Atrial-fibrillation (AF) is the most frequent complication arising after coronary-artery-bypass-grafting (CABG) surgery, occurring in 30% of cases. The incidence of this complication is even higher after valve-replacement surgery (30–40%) and after compound operative procedures (40–60%). Beta-blockers reduce POAF and supraventricular tachycardia and have direct antiarrhythmic activity. Landiolol hydrochloride is an ultrashort-acting beta-blocker with high beta-1 receptor affinity and less blood-pressure lowering properties than other beta-blockers available for intravenous use in Germany. The present analysis aims to determine if perioperative treatment with Landiolol hydrochloride in cardiac surgical patients is cost-effective under the conditions of the German Diagnosis-Related-Groups health cost reimbursement system.

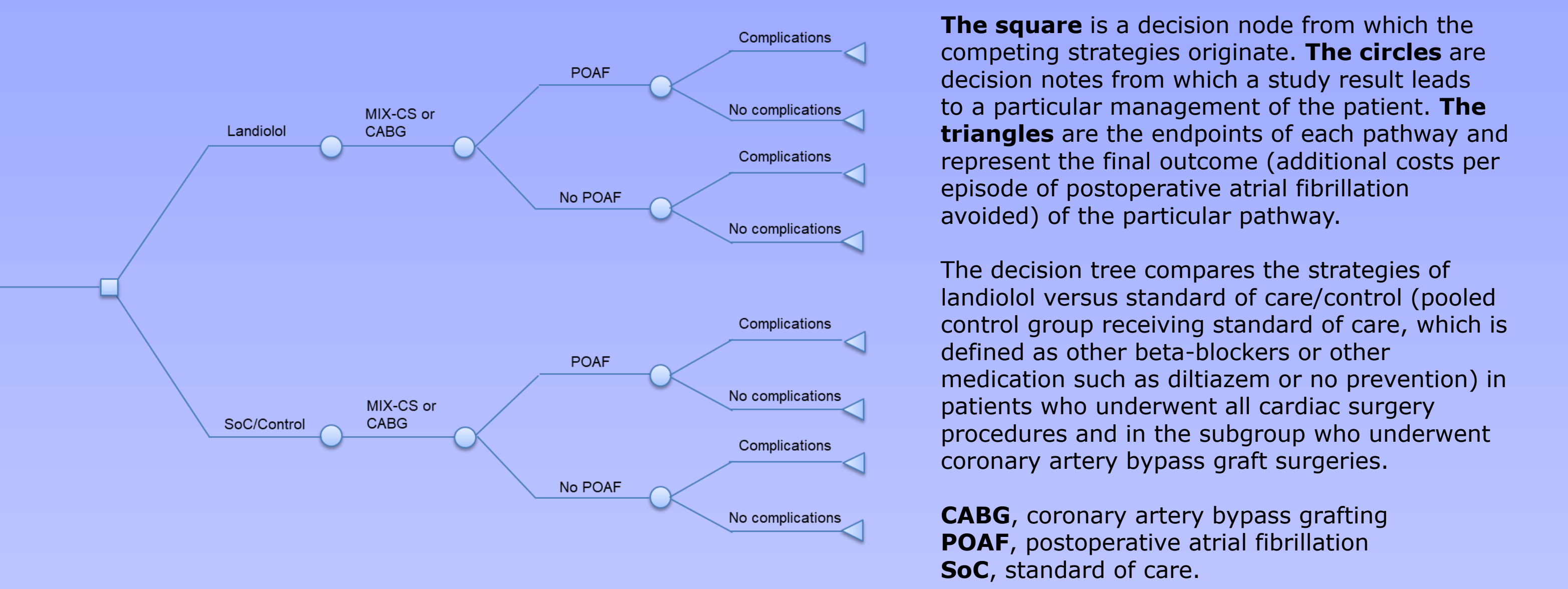
Methods

A decision-model was developed to reflect the cost-effectiveness of landiolol vs. standard-of-care (SoC) for the patient group

- with heterogenous mix of cardiac surgical procedures (MIX-CS) in general
- and for a subgroup of patients with coronary artery bypass grafting (CABG).

The model benefit is expressed in a reduction in POAF episodes and reduced complications. The model calculates total inpatient costs (incl. surgery, ICU, complication and re-hospitalisation) over the hospital-length-of-stay (LOS). Costs from published sources were used (2016 Euro) from the German hospital perspective. A one-way deterministic sensitivity-analysis accounts for uncertainty.

Fig. 1: Model Design



Source: own developed

Clinical Data

The economic model of Rapibloc (landiolol) was designed based on clinical trial data of the RCTs and the Meta-Analysis of Li et al. (2015). → 9 RCTs and 807 patients.

- The AF protecting effect of landiolol in the all-surgery patient population was:
- The meta-analysis included three trials, only presented as posters, which were excluded from the efficacy evaluation.
 - In addition, a publication from Sezai and colleagues (2015)
 - = 7 selected RCTs involving 622 patients
 - A Mantele-Haenszel fixed-effects model was used for meta-analysis. Risk ratios are shown with 95% confidence intervals
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- Landiolol was associated with a significant reduction of AF episodes after cardiac surgery (RR=0.35; 95% CI 0.25-0.48; P<0.001) compared with the control group. The incidence of POAF was 12.6% with landiolol and 36.0% for the control group.
 - The administration of landiolol in patients who underwent CABG showed comparable results (RR=0.36; 95% CI 0.25-0.52; P<0.001). AF occurred in 12.1% in the landiolol group and in 33.6% in the control group.

Fig. 2a: Forest plot comparing the protective effect after MIX-CS surgery of landiolol with control group.

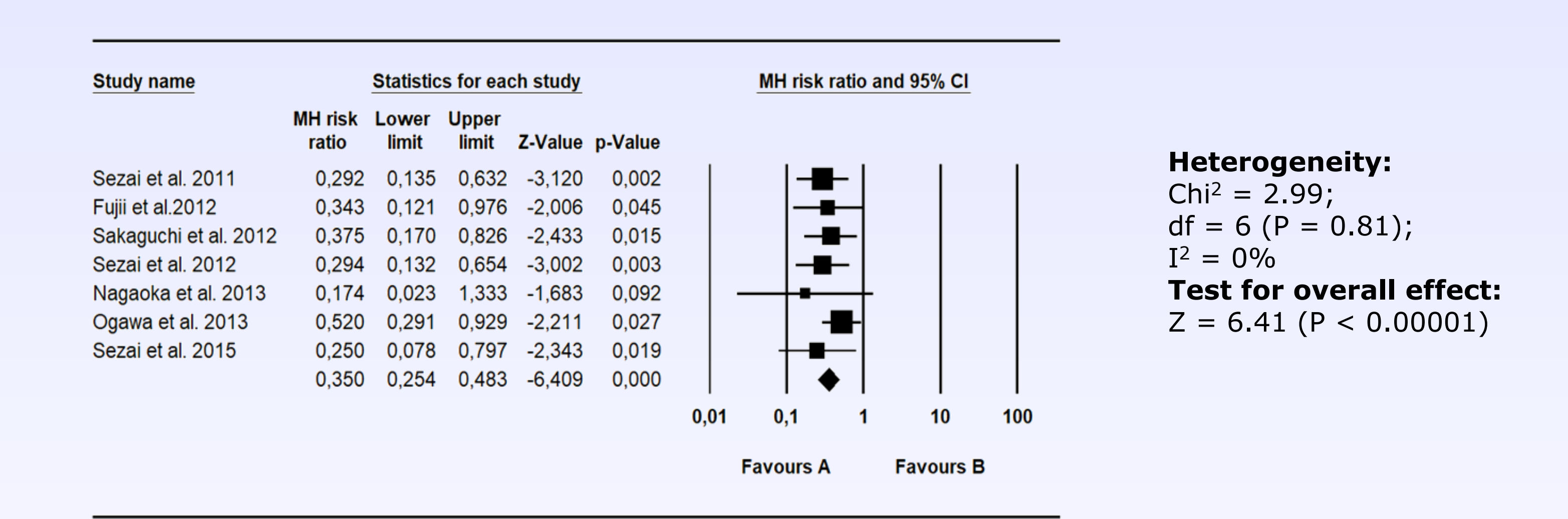
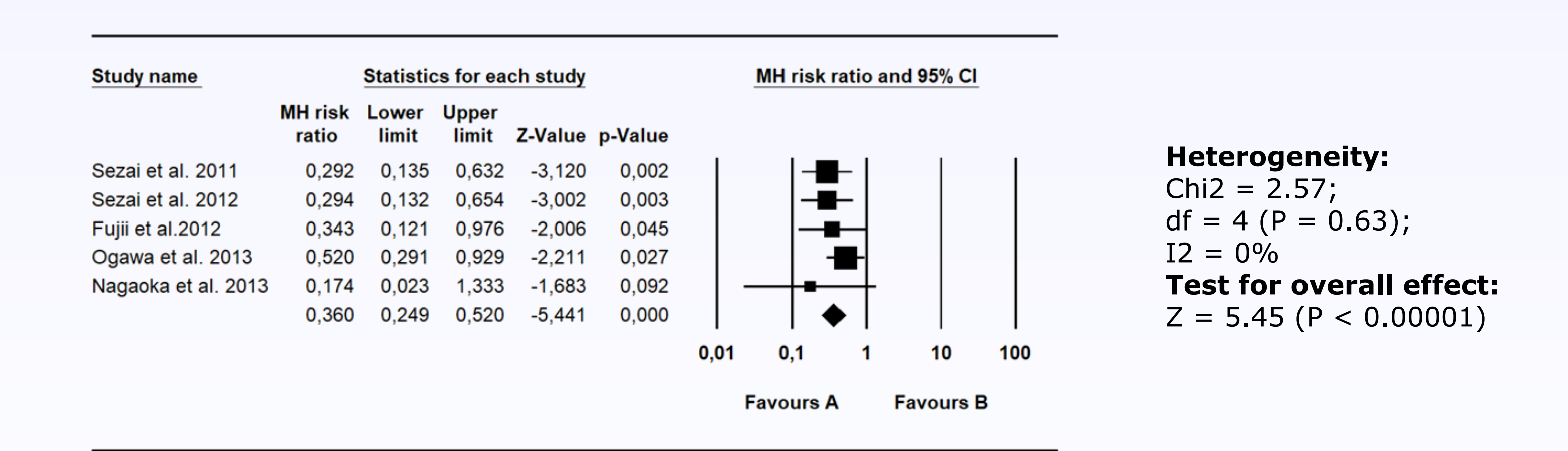


Fig. 2b: Forest plot comparing the protective effect after CSABG of landiolol with control group.



Source: own developed

Resource Use and Costs

Resource use data were derived via literature search including German data to reflect the German clinical practice. The CEA collects hospitalization costs due to cardiac surgery (including ICU costs), costs of complication and hospital readmission. Medication costs for POAF prevention are covered in the German G-DRG lump sum. All costs were derived from public price lists, tariff catalogues and the literature. When necessary, prices were adjusted to 2016 prices using the consumer price index. Due to the short time horizon of the model, discounting of costs is not necessary.

Results

The model benefit was expressed in a reduction of postoperative atrial-fibrillation (POAF) episodes and reduced complications. The model calculated total inpatient costs over the hospital-length-of-stay (LOS). Costs from published sources were used for the German hospital perspective.

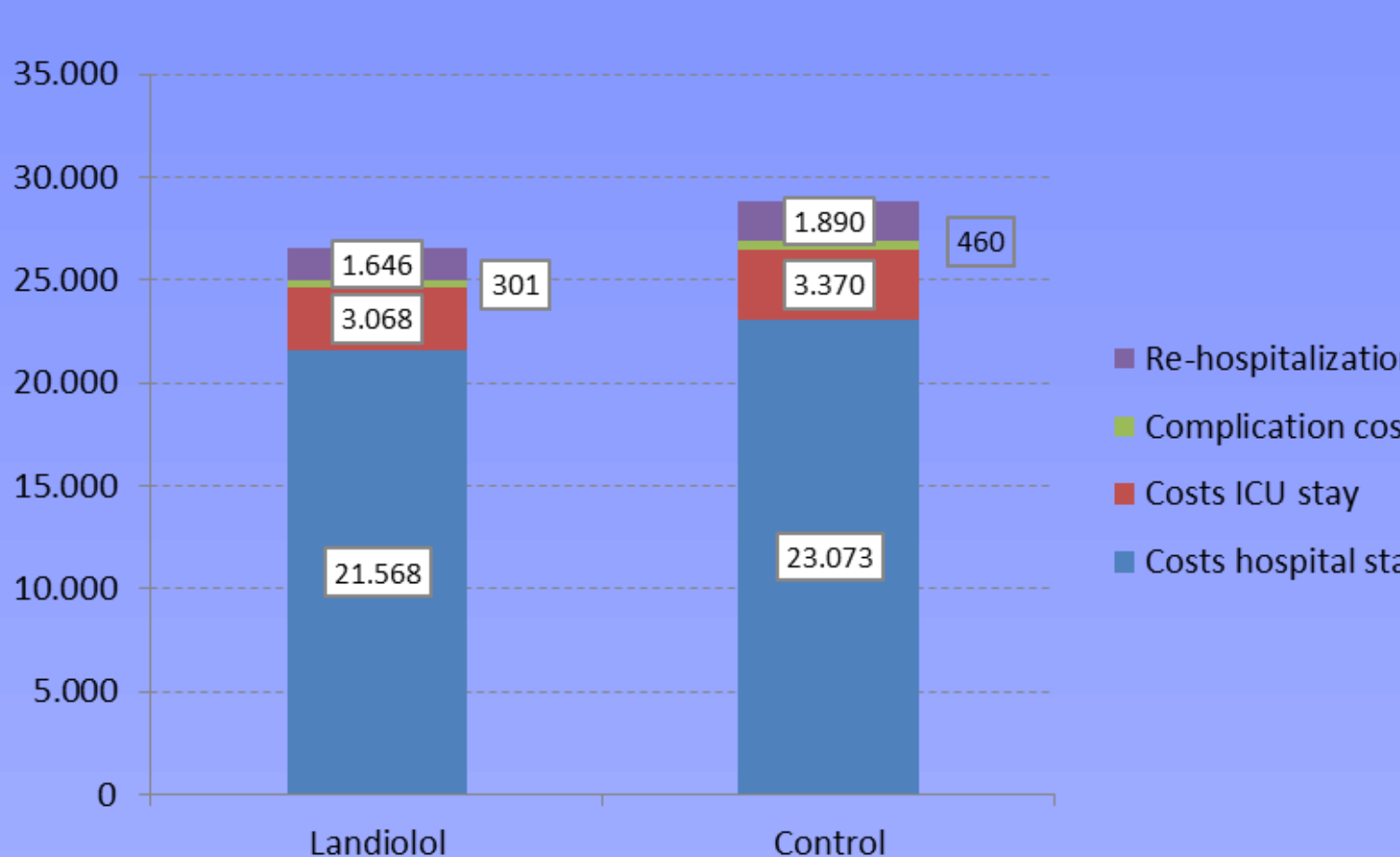
Tab. 1: Cost-effectiveness results, MIX-CS population

Cost Components	Landiolol	Control
Costs hospital stay	21.568	23.073
Costs ICU stay	3.068	3.370
Complication costs	301	460
Re-hospitalization	1.646	1.890
Total costs	26.583	28.793
Cost difference		2.209
POAF free patients	87.4%	64.0%
Difference in POAF onset		-23.4%
Additional costs/savings per POAF avoided (ICER)		-9.430

ICER= incremental cost effectiveness ratio

Source: own calculations

Fig 3: Cost results, MIX-CS population



In the MIX-CS population the average per patient costs in the landiolol group was estimated at 26,583 €. POAF occurred in 12.6% of cases. Compared to SoC, prevention with landiolol reduced costs by 2,209 € and reduces POAF by 23.4%. An in-depth analysis showed that the major proportion of cost reduction is associated with the reduced hospital length of stay (-1,505 €) followed by decreased ICU stay costs (-302 €). From the cost-effectiveness perspective landiolol dominated SoC; additional savings per POAF avoided amounted -9,430 €.

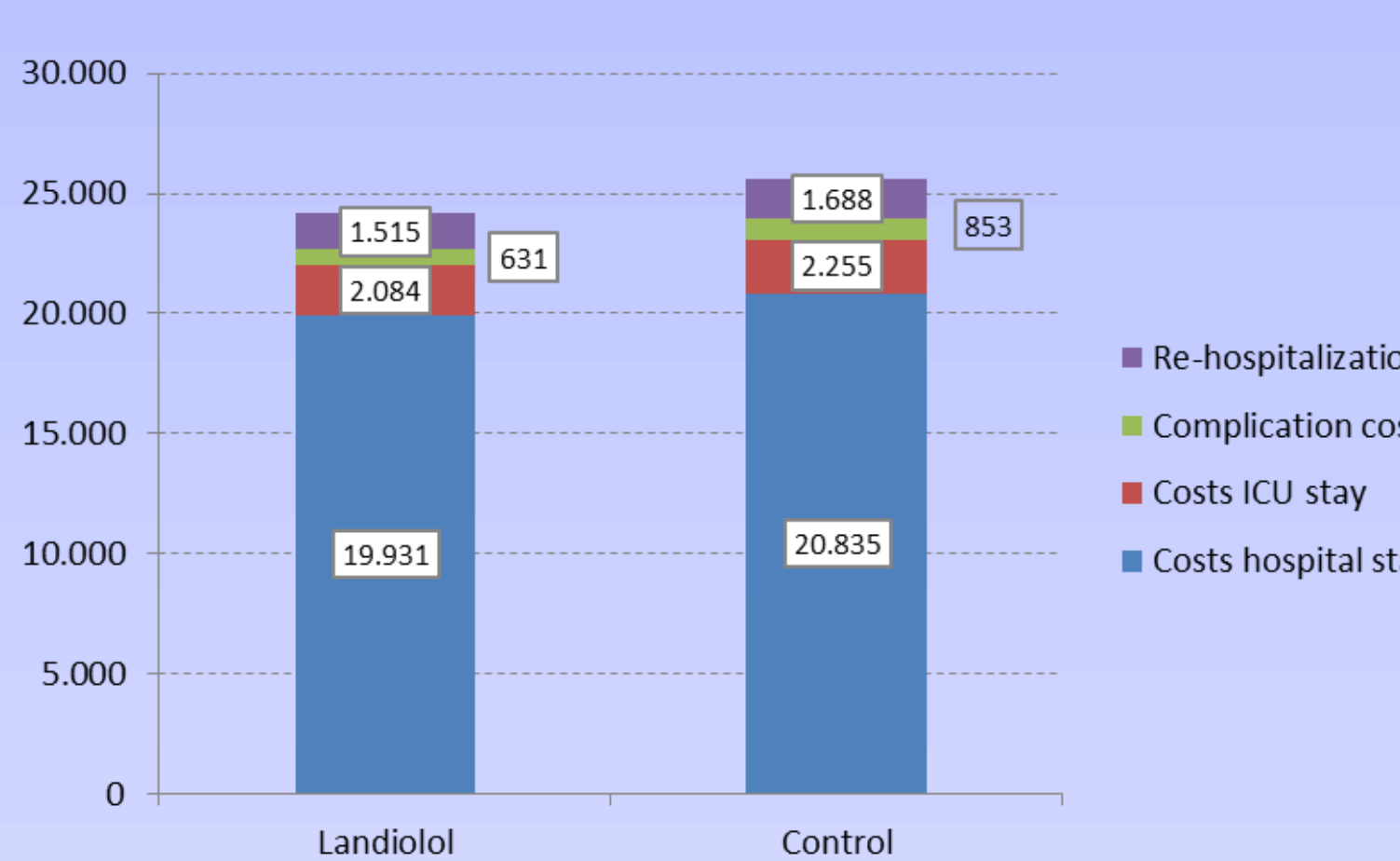
Tab. 2: Cost-effectiveness results, CABG population

Cost Components	Landiolol	Control
Costs hospital stay	19.931	20.835
Costs ICU stay	2.084	2.255
Complication costs	631	853
Re-hospitalization	1.515	1.688
Total costs	24.161	25.631
Cost difference		1.470
POAF free patients	87.9%	66.4%
Difference in POAF onset		-21.5%
Additional costs/savings per POAF avoided (ICER)		-6.840

ICER= incremental cost effectiveness ratio

Source: own calculations

Fig 4: Cost results, CABG population



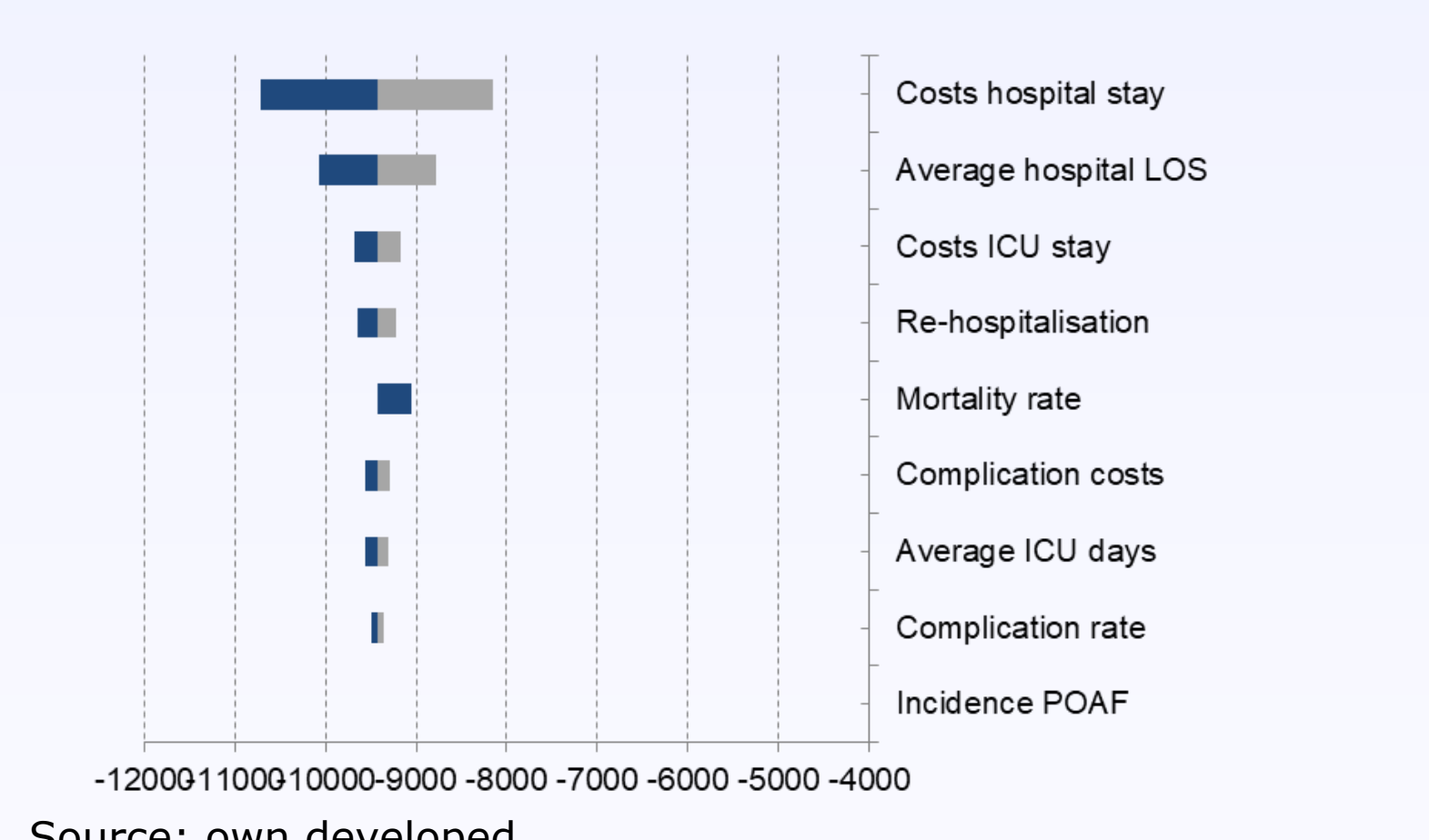
In the CABG population the average per patient costs in the landiolol group was estimated at 24,161 €. POAF occurred in 12.1% of cases. Compared to SoC, prevention with landiolol reduced costs by 1,470 € and reduces POAF by 21.5%. An in-depth analysis showed that the major proportion of cost reduction is associated with the reduced hospital length of stay (-904 €) followed by decreased costs to manage complications (-222 €). From the cost-effectiveness perspective landiolol dominated SoC; additional savings per POAF avoided amounted -6,840 €.

Sensitivity Analysis

Deterministic sensitivity analysis (SA) was carried out. For the MIX-CS population the generated ICERs ranged from -8,146 € to -10.715 €. Landiolol remains the dominant strategy in all variations of the SA. The variations with the highest magnitude of influence are costs hospital stay, hospital LOS and costs of ICU stay.

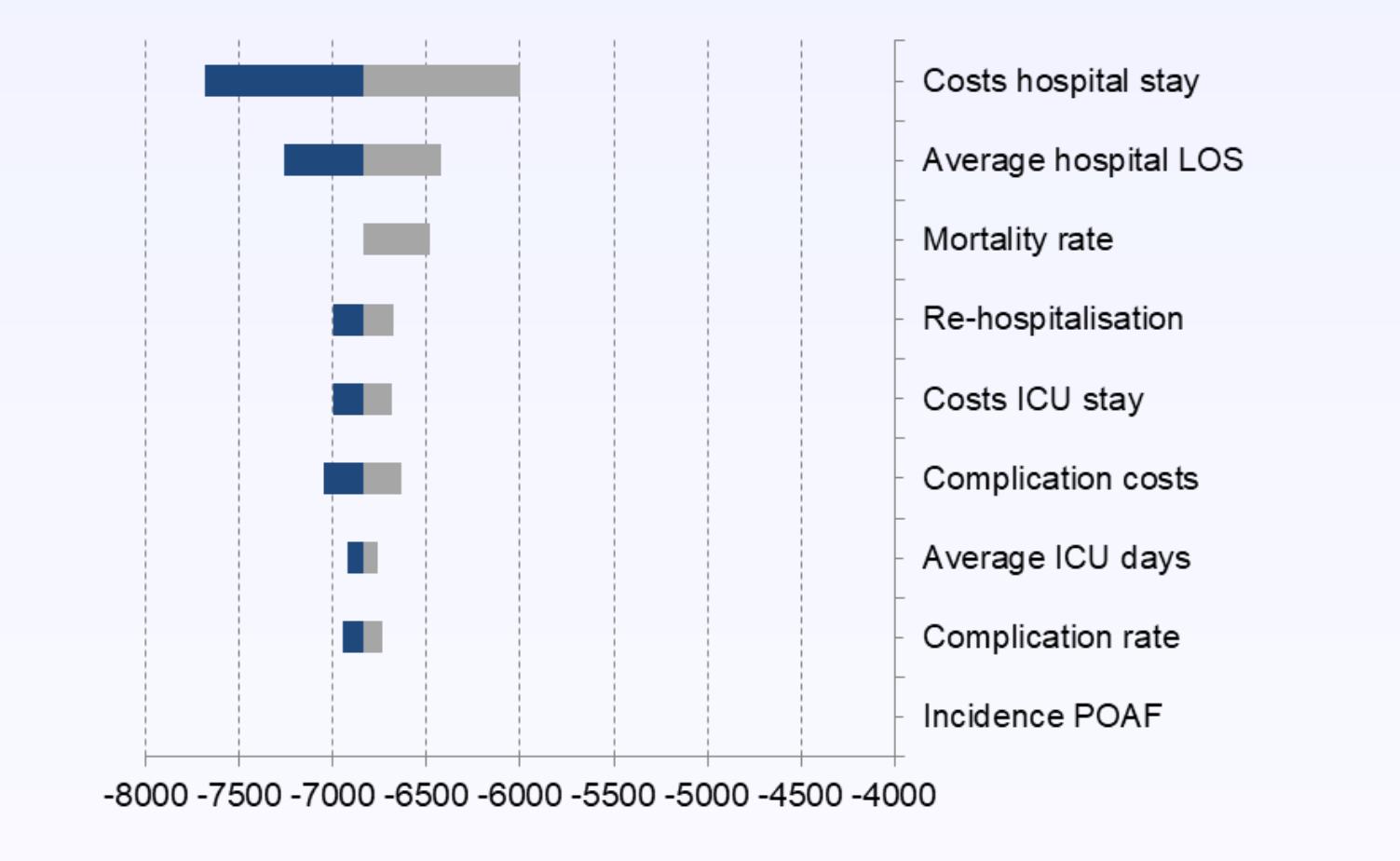
In the CABG subpopulation the ICERs of landiolol versus SoC ranged from -5,999 € to -7,682 €. Variations of costs hospital stay, hospital LOS and the mortality rate demonstrate the greatest influence. Landiolol represented the dominant strategy.

Fig. 4a: Deterministic SA, MIX-CS population



Source: own developed

Fig. 4b: Deterministic SA, CABG population



Conclusion

The results suggest that preventing POAF with landiolol is highly cost-effective. Further studies are needed whether a comparable reduction in POAF and associated cost-savings may be achieved using conventional intravenous beta-blockers or amiodarone.

References

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Additional Literature with the author

Funding: This study was funded by a grant from Amomed Pharma GmbH