

Cost Reductions with Oral Step-Down Antibiotic Treatment by Causative Microorganism in Infective Endocarditis: A POET Trial Analysis

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SUMMARY OF KEY RESEARCH FINDINGS

The POET randomised clinical trial challenged the long-standing principle of the treatment of infective endocarditis by demonstrating that, in clinically stable patients with left-sided endocarditis, oral step-down treatment was non-inferior to conventional intravenous treatment.^{1,2} After a median follow-up of 5.4 years, the authors found that the composite outcome of all-cause mortality, unplanned cardiac surgery, embolic events, and relapse of bacteraemia remained lower in patients assigned to oral step-down treatment.³ This difference was mainly driven by a lower all-cause mortality.³ In a nationwide Phase IV study, the authors evaluated the effectiveness and safety of oral step-down treatment in routine clinical practice, demonstrating an association with fewer in-hospital bed-days, no increase in recurrent bacteraemia, and lower 6-month all-cause mortality.⁴ Beyond the clinical benefits, the authors found that oral step-down treatment reduced healthcare resource use, mainly through fewer hospital bed-days and lower antibiotic costs.⁵

WHAT CHALLENGE DOES THIS ADDRESS?

Streptococcus spp., *Enterococcus faecalis*, and *Staphylococcus aureus* cause more than 70% of all endocarditis cases, but require different antibiotic treatment regimens.^{2,6} These differences affect

Table 1: A partial cost analysis from a Danish hospital-provider perspective of the POET trial.^a

<i>Streptococcus</i> species	Conventional intravenous treatment (n=104)	Oral step-down treatment (n=92)	Difference^b
In-hospital bed-days after randomisation, per patient, ^c days (median)	16 (IQR: 14–19)	2 (IQR: 1–8)	14 (IQR: 13–14)
Costs for in-hospital bed-days after randomization, per patient, ^d EUR (mean)	15,256±5,342 EUR	4,099±4,509 EUR	11,157 EUR (95% CI: 9,786–12,514)
Outpatient visits, per patient, n (mean)	-	4.10±1.51	-
Costs for outpatient visits, per patient, EUR (mean) ^e	-	648±241 EUR	-
Antibiotic cost, per patient, EUR (mean) ^f	663±469 EUR	226±290 EUR	437 EUR (95% CI: 329–547)
Combined included costs, per patient, ^g EUR (mean)	15,919±5,497 EUR	4,974±4,478 EUR	10,946 EUR (95% CI: 9,544–12,326)
<i>Enterococcus faecalis</i>	Conventional intravenous treatment (n=46)	Oral step-down treatment (n=51)	Difference^b
In-hospital bed-days after randomisation, per patient, ^c days (median)	24 (IQR: 19–27)	3 (IQR: 1–8)	21 (IQR: 20–22)
Costs for in-hospital bed-days after randomisation, per patient, ^d EUR (mean)	20,657±5,299 EUR	5,102±6,100 EUR	15,555 EUR (95% CI: 13,23–17,786)
Outpatient visits, per patient, n (mean)	-	5.8±1.59	-
Costs for outpatient visits, per patient, EUR (mean) ^e	-	923±252 EUR	-
Antibiotic cost, per patient, EUR (mean) ^f	2,658±5,679 EUR	401±594 EUR	2,257 EUR (95% CI: 1,122–4,137)
Combined included costs, per patient, ^g EUR (mean)	23,315±7,901 EUR	6,426±5,998 EUR	16,888 EUR (95% CI: 14,128–19,800)
<i>Staphylococcus aureus</i>	Conventional intravenous treatment (n=40)	Oral step-down treatment (n=47)	Difference^b
In-hospital bed-days after randomisation, per patient, ^c days (median)	20 (IQR: 16–26)	3 (IQR: 2–12)	17 (IQR: 16–18)
Costs for in-hospital bed-days after randomisation, per patient, ^d EUR (mean)	18,459±6,024 EUR	7,144±7,829 EUR	11,315 EUR (95% CI: 8,388–14,127)
Outpatient visits, per patient, n (mean)	-	5±1.78	-
Costs for outpatient visits, per patient, EUR (mean) ^e	-	793±283 EUR	-
Antibiotic cost, per patient, EUR (mean) ^f	1,509±5,078 EUR	249±398 EUR	1,260 EUR (95% CI: 247–3,029)
Combined included costs, per patient, ^g EUR (mean)	19,968±7,868 EUR	8,187±7,959 EUR	11,781 EUR (95% CI: 8,467–15,051)

^aMedian with IQR values and means with SD (±) are given; 95% CIs were estimated by non-parametric bootstrapping with 10,000 resamples.

^bThis partial cost-analysis was conducted from a Danish hospital-provider perspective and included only in-hospital bed-days, outpatient follow-up visits, and medication costs from randomisation until completion of antibiotic treatment. Costs of home care, diagnostic evaluation including procedures and surgeries, and broader societal costs were not included. Cost estimates were not adjusted for inflation, because of the short time horizon.

^cRandomisation took place after the individual patient had reached the stabilisation criteria as defined in the POET trial.

^dThe cost per in-hospital bed-day was 879 EUR, based on cost data from 2023–2026. The costs for in-hospital bed-days were provided by the financial administration of the Department of Cardiology at Rigshospitalet, Capital Region of Denmark. The estimates represent the average daily cost of hospitalisation for a patient with infective endocarditis and include personnel costs and costs related to hygiene and infection control. Medication costs and costs related to cardiac surgery were not part of this estimate.

^eCosts per outpatient visit; the governmentally provided costs of outpatient visits of 159 EUR (2023–2026) were used.

^fCosts for antibiotics according to the Danish Medicines Agency (2011–2017).

^gInclude costs for in-hospital bed-days after randomisation, outpatient visits from randomisation and until completion of antibiotic therapy, and costs for antibiotics.

Differences in bed-days, outpatient visits, and associated costs, and costs for antibiotics between patients with infective endocarditis caused by *Streptococcus* species, *Enterococcus faecalis*, and *Staphylococcus aureus* randomised to conventional intravenous treatment compared with patients randomised to oral step-down antibiotic treatment.

IQR: interquartile range.

treatment duration, antibiotic costs, and length of hospitalisation, which may influence the cost savings achieved with oral step-down treatment. The authors performed a microorganism-specific cost analysis to determine whether the economic benefit of oral step-down treatment is consistent across the bacterial subgroups in the original POET cohort.¹

In this partial within-trial analysis of the POET trial, the authors assessed cost estimates in 380 clinically stable adults with left-sided endocarditis caused by *Streptococcus* spp., *E. faecalis*, and *S. aureus* treated with conventional intravenous treatment (190 patients) or oral step-down treatment (190 patients). The analysis was conducted from a Danish hospital-provider perspective and included costs from randomisation until completion of antibiotic treatment for in-hospital bed-days, outpatient visits, and antibiotic costs. Patients assigned to oral step-down treatment were discharged when clinically appropriate and followed twice weekly in the outpatient clinic.¹ Cost estimates were based on official Danish prices, and differences between treatment groups with 95% CIs were estimated using non-parametric bootstrapping (Table 1).

After randomisation, oral step-down treatment resulted in a mean combined saving per patient of 10,946 EUR (95% CI: 9,544–12,326) for endocarditis caused by *Streptococcus* spp., 16,888 EUR (95% CI: 14,128–19,800) for endocarditis

caused by *E. faecalis*, and 11,781 EUR (95% CI: 8,467–15,051) for endocarditis caused by *S. aureus* (Table 1). All bacterial subgroups showed cost savings, adding an economic perspective to the established clinical benefits of oral stepdown treatment across causative microorganisms.¹ Cost savings were primarily driven by shorter in-hospital stay (Table 1). After randomisation, the median difference in hospital bed-days was 14 days (interquartile range [IQR]: 13–14) per patient for streptococcal endocarditis, 21 days (IQR: 20–22) for *E. faecalis* endocarditis, and 17 days (IQR: 16–18) for *S. aureus* endocarditis (Table 1). Additional outpatient visits and antibiotic costs accounted only for a small proportion of total included costs per patient (Table 1).

RELEVANCE TO EUROPEAN PRACTICE

The largest per patient savings were observed in *E. faecalis* endocarditis. This is particularly relevant because these patients are often older, more comorbid, and more likely to have prosthetic heart valve infection, with prolonged hospitalisation contributing substantially to resource use.^{7,8} Oral step-down treatment can therefore reduce hospital stays and release hospital capacity in *E. faecalis* endocarditis. In *S. aureus* endocarditis, savings remained substantial despite the typically acute disease course and frequent need for cardiac surgery.^{2,9} Switching to oral

step-down treatment can therefore still provide cost savings in complex and critically ill patients once patients are clinically stable.

This partial within-trial cost analysis did not include post-discharge costs such as home care, rehabilitation, and productivity loss. It captured the hospital resources most directly affected by oral step-down treatment and provides microorganism-specific estimates of its economic impact from a healthcare provider perspective.

WHAT ARE THE NEXT STEPS FOR THE RESEARCH?

In conclusion, oral step-down treatment reduced in-hospital bed-days and provided both favourable clinical outcomes and health-economic benefits across streptococcal, *E. faecalis*, and *S. aureus* endocarditis. These findings provided a strong rationale for systematically identifying eligible patients and treating them with oral step-down therapy in accordance with current standard practice.

References

1. Iversen K et al. Partial oral versus intravenous antibiotic treatment of endocarditis. *N Engl J Med*. 2019;380(5):415-24.
2. Delgado V et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of endocarditis. *Eur Heart J*. 2023;44(39):3948-4042. Erratum in: *Eur Heart J*. 2023;44(45):4780. Erratum in: *Eur Heart J*. 2024;45(1):56.
3. Pries-Heje MM et al. Five-year outcomes of the Partial Oral Treatment of Endocarditis (POET) trial. *N Engl J Med*. 2022;386(6):601-2.
4. Pries-Heje MM et al. Clinical implementation of partial oral treatment in infective endocarditis: the Danish POETry study. *Eur Heart J*. 2023;44(48):5095-106.
5. Kader N et al. Costs of oral step-down antibiotic treatment versus intravenous hospital antibiotic treatment in patients with endocarditis: cost analysis from the POET randomized trial. *Circ Popul Health Outcomes*. 2026;DOI:10.1161/CIRCOUTCOMES.126.014059.
6. Tzoumas A et al. Epidemiological profile and mortality of infective endocarditis over the past decade: a systematic review and meta-analysis of 133 studies. *Am J Cardiol*. 2025;244:67-88.
7. Strange JE et al. Patient characteristics, microbiology, and mortality of infective endocarditis after transcatheter aortic valve implantation. *Clin Infect Dis*. 2023;77(12):1617-25.
8. Philip M et al.; EURO-ENDO Investigators. Clinical characteristics, management and outcomes of enterococcal infective endocarditis: an ancillary study from the ESC-EORP EURO-ENDO registry. *Eur Heart J Qual Care Clin Outcomes*. 2026;12(3):308-21.
9. Fowler Jr VG et al.; ICE Investigators. *Staphylococcus aureus* endocarditis: a consequence of medical progress. *JAMA*. 2005;293(24):3012-21.