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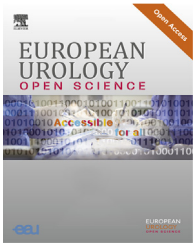

European Association of Urology

Prostate Cancer

Cost Effectiveness of Rectal Culture-based Antibiotic Prophylaxis in Transrectal Prostate Biopsy: The Results from a Randomized, Nonblinded, Multicenter Trial

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Abstract

Background: Culture-based antibiotic prophylaxis is a plausible strategy to reduce infections after transrectal prostate biopsy (PB) related to fluoroquinolone-resistant pathogens.
Objective: To assess the cost effectiveness of rectal culture-based prophylaxis compared with empirical ciprofloxacin prophylaxis.
Design, setting, and participants: The study was performed alongside a trial in 11 Dutch hospitals investigating the effectiveness of culture-based prophylaxis in transrectal PB between April 2018 and July 2021 (trial registration number: NCT03228108).
Intervention: Patients were 1:1 randomized for empirical ciprofloxacin prophylaxis (oral) or culture-based prophylaxis. Costs for both prophylactic strategies were determined for two scenarios: (1) all infectious complications within 7 d after biopsy and (2) culture-proven Gram-negative infections within 30 d after biopsy.

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Outcome measurements and statistical analysis: Differences in costs and effects (quality-adjusted life-years [QALYs]) were analyzed from a healthcare and societal perspective (including productivity losses, and travel and parking costs) using a bootstrap procedure presenting uncertainty surrounding the incremental cost-effectiveness ratio in a cost-effectiveness plane and acceptability curve.
Results and limitations: For the 7-d follow-up period, culture-based prophylaxis (n = 636) was €51.57 (95% confidence interval [CI] 6.52–96.63) more expensive from a healthcare perspective and €16.95 (95% CI –54.29 to 88.18) from a societal perspective than empirical ciprofloxacin prophylaxis (n = 652). Ciprofloxacin-resistant bacteria were detected in 15.4%. Extrapolating our data, from a healthcare perspective, 40% ciprofloxacin resistance would lead to equal cost for both strategies. Results were similar for the 30-d follow-up period. No significant differences in QALYs were observed.
Conclusions: Our results should be interpreted in the context of local ciprofloxacin resistance rates. In our setting, from a healthcare perspective, culture-based prophylaxis was significantly more expensive than empirical ciprofloxacin prophylaxis. From a societal perspective, culture-based prophylaxis was somewhat more cost effective against the threshold value customary for the Netherlands (€80.000).
Patient summary: Culture-based prophylaxis in transrectal prostate biopsy was not associated with reduced costs compared with empirical ciprofloxacin prophylaxis.

1. Introduction

Approximately 50 million men in Europe and the USA (9.6%) are diagnosed with prostate cancer at some point during their lifetime, making it the second most commonly diagnosed cancer and fifth leading cause of cancer mortality in men worldwide [1–3]. Given these numbers, prostate biopsy (PB), the standard procedure for the diagnosis, staging, and follow-up of prostate cancer, is commonly performed. Unfortunately, infection is a well-known complication of the procedure due to the often used transrectal approach, which can cause the introduction of enteric bacteria, particularly Enterobacterales, into the urinary tract, prostate, or bloodstream [4].

Various studies have demonstrated the clinical benefit of antibiotic prophylaxis with fluoroquinolones (FQs) for infectious complication rates in transrectal PB [5]. Recent studies, however, showed an increasing trend of postbiopsy infections from <1% to 6% due to a rise in FQ-resistant Enterobacterales [6–9]. Related to this, hospitalization rates for postbiopsy infection have also increased with rates reported up to 5.5% [10–12], leading to a relevant burden on patient's health and healthcare facilities [13–16].

Therefore, alternative strategies to reduce the risk of postbiopsy infection must be considered, such as rectal culture-based antibiotic prophylaxis [17,18], in which patients with FQ-susceptible rectal flora receive ciprofloxacin and those with FQ-resistant rectal flora receive alternative antibiotic prophylaxis based on rectal culture results. In a nonblinded multicenter randomized controlled trial (RCT), we showed that rectal culture-based antibiotic prophylaxis reduced postbiopsy infections, hospitalization, and therapeutic antibiotic use compared with empirical FQ prophylaxis [19]. In the present study, performed alongside our RCT, the cost effectiveness of the strategy was assessed, which provides additional information necessary when considering the switch from empirical to culture-based prophylaxis in clinical practice. In this economic evaluation, the higher cost of culture-based prophylaxis to a large population of men undergoing transrectal PB was weighed against a higher disease burden due to more frequent infectious complications associated with empirical prophylaxis from both a healthcare and a societal perspective.

2. Patients and methods

2.1. Study design

This empirical economic evaluation was performed alongside a nonblinded multicenter RCT on the effectiveness of rectal culture-based prophylaxis on the infectious complications of transrectal PB (ClinicalTrials.gov registration number: NCT03228108). The study was approved by the Medical Research Ethics Committee Nijmegen and the institutional review boards of the 11 participating hospitals, and it underwent an extra marginal review by the national Central Committee on Research Involving Human Subjects.

The study design, inclusion and exclusion criteria, and clinical outcome measures have extensively been reported elsewhere [19]. In summary, patients undergoing transrectal PB as part of the standard of care were included in 11 Dutch hospitals between April 2018 and July 2021. Patients were 1:1 randomized, and stratified for hospital and PB technique, to receive either the standard empirical prophylaxis, that is, ciprofloxacin (control group; CG), or the rectal culture-based prophylaxis (intervention group; IG). To direct antibiotic prophylaxis in the IG, a rectal swab was collected from each patient approximately 2–3 wk before PB. In Figure 1, a flowchart of the antibiotic prophylaxis regimens prescribed per group is depicted.

2.2. Outcome measures

The cost effectiveness of culture-based antibiotic prophylaxis (IG) in transrectal PB was compared with the standard of care, that is, empirical

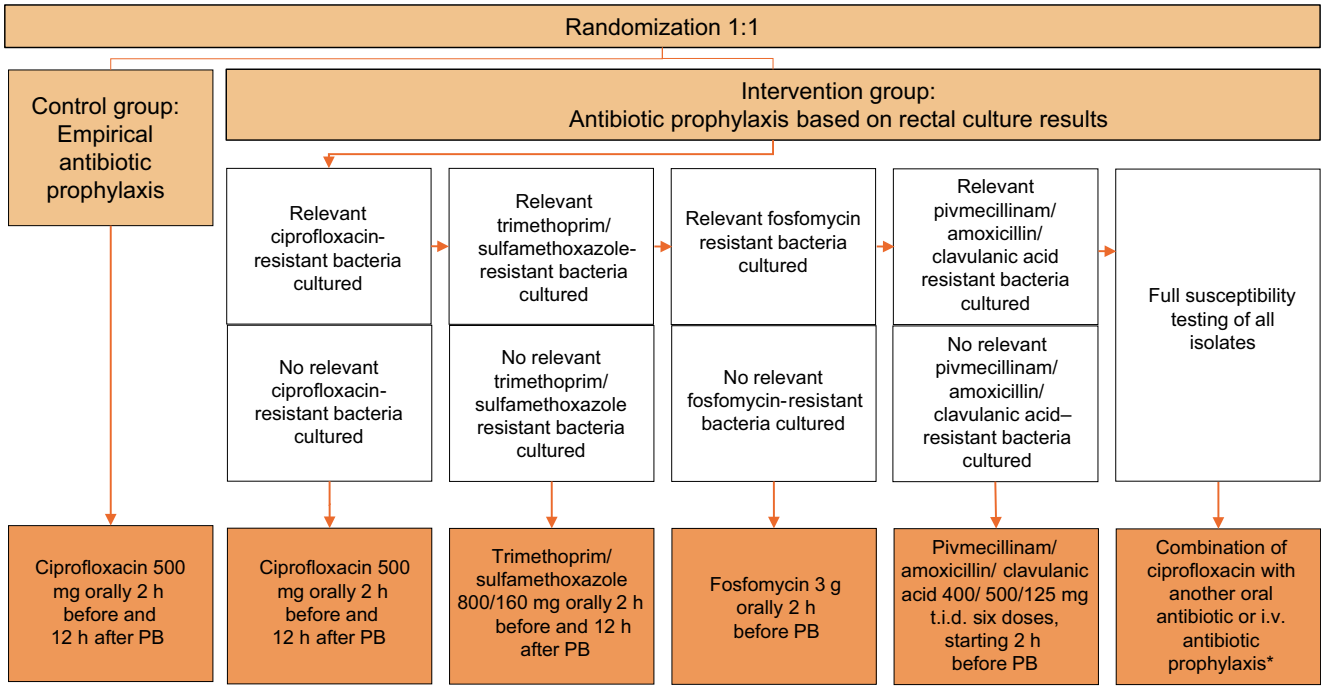

Fig. 1 – Flowchart of the antibiotic prophylaxis regimens prescribed per group. i.v. = intravenous; PB = prostate biopsy.

prophylaxis with oral ciprofloxacin (CG). The economic evaluation was performed from both a healthcare perspective including healthcare-related costs, and a societal perspective including healthcare-related costs plus patient-based cost from productivity losses within 30 d after biopsy, and travel and parking costs to the hospital. The economic evaluation was based on the general principles of a cost-utility analysis adhering to the Dutch guidelines for performing economic evaluations in healthcare [20]. Cost effectiveness was expressed in terms of cost per quality-adjusted life-years (QALYs) gained.

2.3. Cost analysis

The included healthcare-related and societal costs are depicted in Table 1. Healthcare consumption related to postbiopsy infection was measured prospectively on patient level. Data were collected from the hospital's electronic health record and by patient questionnaires, sent at baseline, and 7 and 30 d after biopsy. Productivity losses were assessed using the Productivity Cost Questionnaire (PCQ) of the Institute for Medical Technology Assessment, answered by patients at baseline, and 7 and 30 d after PB [21].

Costs were determined for two scenarios with different follow-up periods: (1) all infectious complications within 7 d after biopsy and (2) culture-proven infectious complications caused by Gram-negative bacteria (GNB) within 30 d after biopsy. These scenarios were chosen to increase the likelihood of capturing only and all infections attributable to transrectal PB.

Standard cost prices were determined per item of healthcare consumption (Table 1). The lowest reported price of antibiotics (including dispensing costs) was derived from the website of the Dutch National Healthcare Institute for medicine costs [22]. The cost price for the culture-based prophylaxis strategy was based on the tariffs for primary care diagnostics, set by the Dutch Healthcare Authority (NZA), an autonomous administrative authority falling under the Dutch Ministry of Health, Welfare, and Sport (VWS; tariff codes: 79991, 75043, 75045, and 70507). Assumptions made for the determination of the cost price of the culture-based prophylaxis strategy (based on own data) are depicted in the Supplementary material. Standard cost prices for the other items of healthcare consumption, and travel and parking costs were determined using Appendix 1 of the guideline for performing economic evaluations [20]. To estimate productivity losses, the friction cost method was applied [21]. All costs were calculated in Euros indexed at the year of PB (2018–2021).

2.4. Patient's health-related quality of life

To assess patient's health-related quality of life (QoL), the EQ-5D-5L questionnaire was sent to patients at baseline, and 7 and 30 d after PB [23]. QoL was determined at 7 d after biopsy (QALY7d), taking into account all EQ-5D-5L questionnaires filled in between 5 and 21 d after biopsy, and at 30 d after biopsy (QALY30d), taking into account all EQ-5D-5L questionnaires filled in between 22 and 37 d after biopsy. The EQ-5D-5L questionnaire comprises five domains of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ-5D-5L utility index was obtained by applying predetermined Dutch weights to the five domains providing a societal-based global quantification of patient's health status on a scale ranging from 0 (death) to 1 (perfect health) [23]. QALYs were calculated by multiplying the EQ-5D-5L utility index by the time period of evaluation (7 and 30 d) applying the trapezium rule, a method that calculates the area under the curve.

2.5. Statistical method

Demographic data of patients were depicted as median and interquartile range for continuous data, and number and percentage for categorical data. Costs were expressed as mean ± standard deviation and effects as mean ± robust standard error. Differences in total costs and QALYs were analyzed with a generalized linear model using a gamma distribu-

Table 1 – Cost prices in Euros, indexed at 2018 prices

	Cost price (€)
Healthcare-related costs	
Antibiotic prophylaxis (lowest reported price for the total duration of prophylaxis incl. dispensing costs)	
Ciprofloxacin 500 mg tablet	11.30
Trimethoprim/sulfamethoxazole 800/160 mg tablet	11.61
Fosfomycin 3 g granules for oral solution	15.90
Pivmecillinam/amoxicillin/clavulanic acid 400/500/125 mg tablet	34.13
Ciprofloxacin 750 mg tablet	11.59
Ceftazidime 1000 mg solution for intravenous infusion (including administration at **day care unit**)	368.29
Ceftazidime 2000 mg solution for intravenous infusion (including administration at day **care unit**)	370.64
Rectal culture-based prophylaxis strategy (**incl. time of healthcare professionals to collect the rectal swab, lab materials, and hands-on time of laboratory personnel excluding costs of prescribed antibiotics**)	72.56
Costs related to infectious complications after prostate biopsy	
Inpatient day	
General hospital	460.90
University hospital	667.94
Intensive Care Unit	1233.91
Outpatient visit	
General hospital	83.23
University hospital	169.59
Emergency room visit	269.46
General practitioner	
Standard consultation	34.33
Home visit	52.02
Telephonic consultation	17.69
Emergency ambulance transportation	637.77
Culture test	
Blood culture	40.02
Urine culture	47.26
Antibiotics (lowest reported price per day **excluding dispensing costs**)	
Amoxicillin 500 mg tablet	0.19
Amoxicillin/clavulanic acid 500/125 mg tablet	0.28
Azitromycin 500 mg tablet	0.38
Ceftazidime 2000 mg solution for intravenous infusion	25.46
Ceftriaxone 2000 mg solution for intravenous infusion	16.51
Cefuroxime 1500 mg solution for intravenous infusion	12.50
Ciprofloxacin 500 mg tablet	0.11
Fosfomycin 3 g granules for oral solution	4.72
Gentamicin 400 mg solution for intravenous infusion	11.89
Nitrofurantoin 400 mg tablet	0.60
Piperacillin/tazobactam 4000/500 mg solution for intravenous infusion	31.37
Tobramycin 120 mg solution for intravenous infusion	23.36
Trimethoprim/sulfamethoxazole 800/160 mg tablet	0.43
Dispensing costs	11.19
Social costs	
Productivity losses for patients within 30 d after biopsy	
Paid per hour	39.43
Unpaid per hour	14.56
Travel costs (extra visits for infectious complications)	
Parking	3.12
Cost per kilometer by car	0.20

incl. = including.

tion to deal with possible skewness and a tobit regression for EQ-5D utility scores. The EQ-5D-5L utility index at 7 and 30 d after biopsy was corrected for baseline. The incremental cost-effectiveness ratio (ICER) was estimated by dividing the difference in costs between the IG and CG by the difference in their effect (QALYs) in a bootstrap procedure with 1000 simulations. The EQ-5D contained missing data which were dealt with by multiple imputation. Cost data were complete. The bootstrap procedure was based on the imputed QALY data and the complete cost data. Cost and QALY data were randomly drawn in pairs with replacement. SPSS Statistics for Windows version 25.0 (IBM Corp, Armonk, NY, USA) and STATA version 16 were used.

3. Results

In total, 652 patients receiving empirical ciprofloxacin prophylaxis (CG) and 636 patients receiving culture-based prophylaxis (IG) were included in the final analysis. Eighteen patients participated twice for two different PB sessions. Patients' characteristics are depicted in Table 2. Ciprofloxacin-resistant bacteria were detected in 15.4% of the patients (n = 1288). In the IG, 13.3% therefore received alternative oral antibiotic prophylaxis (other than ciprofloxacin) and 0.5% received intravenous antibiotic prophylaxis. Infectious complications occurred in 4.3% (CG) and 2.5% (IG) of the patients within 7 d after biopsy (–1.8% reduction; 95% confidence interval [CI] –0.004 to 0.040). Of the patients, 3.4% (CG) and 1.4% (IG) had a Gram-negative infection within 30 d after biopsy (–2.0% reduction; 95% CI 0.001–0.039).

3.1. Costs

From a healthcare perspective, culture-based prophylaxis was significantly more expensive than empirical ciprofloxacin prophylaxis. From a societal perspective, costs of both strategies were not significantly different (Table 3).

The number needed to screen (and direct prophylaxis on rectal culture results) to prevent an infection amounted to 56 patients for the 7-d follow-up period and 77 patients for the 30-d follow-up period. Although for both follow-up periods, healthcare-related costs were lower in the IG due to reduced infectious complication rates, it did not compensate the cost of the culture-based prophylaxis strategy due to the rectal culture process, resulting in higher total costs per patient in the IG (Fig. 2).

3.2. Effects

Patients in the IG reported slightly, though insignificant, better QoL at 7 d after biopsy than the CG (Table 3). At 30 d after biopsy, patients in the IG reported slightly, though insignificant, worse QoL than the CG (Table 3).

3.3. Incremental cost-effectiveness ratio

Figure 3 shows the cost-effectiveness plane of the societal perspective based on 1000 bootstrapped simulations for the 7-d follow-up period. It can be inferred that the IG is slightly more expensive but also slightly more effective, with a point estimate of the ICER of €62.890. At a willingness to pay (WTP) threshold for a QALY gained of €80.000, the efficiency benchmark in the Netherlands, the acceptability of the culture-based prophylaxis strategy is 55.4%, meaning that at that particular WTP threshold, the IG is slightly preferred with regard to efficiency. At higher WTP thresholds for a QALY gained, the IG becomes more favorable.

3.4. Approaches to improve cost efficiency

One approach to narrow cost differences between both prophylaxis strategies is to reduce the cost of the rectal culture process. From a healthcare perspective, to equalize cost, the cost of the culture process should be reduced to approximately €24 (–68.2%) and €35 (–53.7%) for the 7- and 30-d

Table 2 – Patients' characteristics per group

	Total	Empirical prophylaxis	Culture-based prophylaxis
Number of patients, *n* (%)	1288	652	636
Hospital A	36 (2.8)	18 (2.8)	18 (2.8)
Hospital B	399	206 (31.6)	193 (30.3)
Hospital C	(31.0)	56 (8.6)	55 (8.6)
Hospital D	111	35 (5.4)	37 (5.8)
Hospital E	(8.6)	19 (2.9)	20 (3.1)
Hospital F	72 (5.6)	26 (4.0)	28 (4.4)
Hospital G	39 (3.0)	179 (27.5)	171 (26.9)
Hospital H	54 (4.2)	28 (4.3)	28 (4.4)
Hospital I	350	42 (6.4)	40 (6.3)
Hospital J	(27.2)	42 (6.4)	45 (7.1)
Hospital K	56 (4.3)	1 (0.2)	1 (0.2)
	82 (6.4)		
	87 (6.8)		
	2 (0.2)		
Age (yr), median (IQR)	69 (64–73)	68 (63–73)	69 (65–73)
Ciprofloxacin-resistant rectal flora, *n* (%)	196 (15.2)	102 (15.6)	94 (14.8)
Antibiotic prophylaxis used, *n* (%)			
Ciprofloxacin	1199	652 (100)	548 (86.2)
Trimethoprim/sulfamethoxazole	(93.1)		22 (3.5)
Fosfomycin	22 (1.7)		13 (2.0)
Pivmecillinam + **amoxicillin/clavulanic acid**	13 (1.0)		9 (1.4)
Ciprofloxacin + t**rimethoprim/sulfamethoxazole**	9 (0.7)		20 (3.1)
Ciprofloxacin + f**osfomycin**	20 (1.6)		14 (2.2)
Ciprofloxacin + p**ivmecillinam + a**moxicillin/clavulanic acid	15 (1.2)		7 (1.1)
	7 (0.5)		
Ciprofloxacin + Ceftazidime			2 (0.3)
Ceftazidime	2 (0.2)		1 (0.2)
	1 (0.1)		
Type of prostate biopsy, *n* (%)			
Random TRUSPB	449	221 (33.9)	228 (35.8)
TRUSPB with additional targeted (cognitive)	(34.9)	380 (58.3)	366 (57.5)
MRI-TRUS fusion guided PB	746		
Targeted MRI-TRUS fusion guided PB only	(57.9)	38 (5.8)	32 (5.0)
Targeted i**n-bore MRI-guided PB only**		13 (2.0)	10 (1.6)
	70 (5.4)		
	23 (1.8)		
Number of biopsy cores, median (IQR)	12 (10–13)	12 (10–14)	12 (10–13)
Histopathology positive for malignancy, *n* (%)	900 (69.9)	449 (68.9)	451 (70.9)
Age-adjusted Charlson Comorbidity Index, median (IQR)	3 (2–4)	3 (2–4)	3 (2–4)
History of diabetes mellitus, *n* (%)	120 (9.3)	49 (7.5)	71 (11.2)
Drug-induced immunosuppression, *n* (%)	31 (2.4)	15 (2.3)	16 (2.5)
Indwelling catheter in situ or intermittent catheterization (***n*** = 1266), ***n* (%)**	34 (2.7)	22 (3.4)	12 (1.9)
International Prostate Symptom Score (***n*** = 1253), **median (IQR)**	9 (5–16)	10 (5–16)	9 (5–16)
Baseline EQ-5D-NL (***n*** = 1100), **median (IQR)**	0.89 (0.84–1.00)	0.89 (0.83–1.00)	0.92 (0.85–1.00)

IQR = interquartile range; MRI = magnetic resonance imaging; PB = prostate biopsy; TRUSPB = transrectal ultrasound; TRUSPB = transrectal ultrasound-guided prostate biopsy.

follow-up periods, respectively. From a societal perspective, cost should be reduced to approximately €59 (–21.9%) and €67 (–11.3%) for the 7- and 30-d follow-up periods, respectively.

Another approach is to implement the strategy in geographic areas with higher rates of ciprofloxacin-resistant GNB or in patients at a high risk of harboring these bacteria in which the impact of culture-based prophylaxis will probably be higher. Extrapolating our data, every 5% increase in ciprofloxacin resistance leads to a 0.6% increased risk of postbiopsy infection, and costs per patient increase by €9.50 in a strategy using empirical ciprofloxacin prophylaxis. From a healthcare perspective, using a 7-d follow-up period, 40% ciprofloxacin resistance would lead to equal cost for both strategies (see the Supplementary material for more detailed information).

4. Discussion

We assessed the cost effectiveness of rectal culture-based prophylaxis in transrectal PB compared with the standard of care, that is, empirical prophylaxis with oral ciprofloxacin. When societal costs were taken into account, which is advised by the Dutch guidelines on economic evaluations in healthcare, empirical prophylaxis with ciprofloxacin was more or less equally efficient than culture-based prophylaxis. From a healthcare perspective, the cost of the rectal culture process—performed in all men undergoing transrectal PB—were not offset by the lower costs related to fewer infectious complications using culture-based prophylaxis, leading to an unfavorable conclusion from this perspective on the cost criterion of the culture-based prophylaxis strategy. This is in contrast to the conclusion that can be inferred from the positive results of our effectiveness trial [19]. However, no single criterion in itself is decisive for the adoption of any strategy. Besides, it should be noted that there are several approaches to improve the cost (efficiency) of culture-based prophylaxis that lead to a set of criteria pointing in the same direction (Supplementary material).

We performed the first experimental study on the cost effectiveness of culture-based prophylaxis in transrectal

Table 3 – Costs and effects per patient for the different prophylaxis strategies analyzed with a generalized linear model

	Empirical prophylaxis (CG)	Culture-based prophylaxis (IG)	ΔIG and CG; 95% CI
QALY_NL at 7 d **after biopsy corrected for baseline**	0.0173 ± 0.00004	0.0173 ± 0.00004	+0.00004; 95% CI –0.00008 to 0.0002
Health-related costs incl. all infectious complications ≤7 d	78.23 ± 16.43	129.80 ± 16.08	
			+51.57; 95% CI 6.52–96.63
Health-related costs + social costs incl. all infectious complications ≤ 7 days	132.74 ± 29.46	149.69 ± 21.29	
			+16.95; 95% CI –54.29 to 88.18
QALY_NL at 30 d **after biopsy corrected for baseline**	0.0748 ± 0.0003	0.0745 ± 0.0003	–0.0003; 95% CI –0.0012 to 0.0006
Health-related costs incl. Gram-negative infections ≤30 d	68.07 ± 15.59	108.33 ± 11.12	
			+40.26; 95% CI 2.74–77.78
Health-related costs + social costs incl. Gram-negative infections ≤30 d	116.10 ± 28.15	124.87 ± 18.90	
			+8.76; 95% CI –57.68 to 75.21

CG = control group; CI = confidence interval; IG = intervention group; incl. = including; QALY = quality-adjusted life-year.
Costs (€) were estimated with a generalized linear model with gamma distribution, expressed as mean ± standard deviation. Effects were analyzed using a tobit regression, expressed as mean ± robust standard error; 95% CIs for the difference in costs and effects between the IG and CG were determined.

PB alongside a multicenter RCT. Our results are in contrast with other studies based on a small number of patients from a single institution, or decision-analytic models in which the clinical impact of the prophylactic strategy was estimated mainly from cohort studies [24–26]. In these studies, the cost price of the rectal culture was relatively low, ranging from $13 to $25, compared with $77 in our study. In these previous studies, it was unclear how the cost price of the rectal culture was compiled and which cost components were included. In addition, our culture strategy could be optimized from a cost-efficiency perspective, which would result in a 58.3% cost reduction of the culture process. Then, at a WTP threshold for a QALY gained of €80.000, the IG acceptability is 52.5% for the 7-d follow-up period from a healthcare perspective (point estimate ICER €74.549). In this scenario, first we assess whether there is ciprofloxacin-resistant rectal flora, and only in case of ciprofloxacin resistance, the sensitivity to other antibiotics is determined (instead of determining both simultaneously). One should realize that, in this scenario, in case of ciprofloxacin-resistant rectal flora, the rectal culture takes 24–48 h longer, which should not be a problem with timely culture collection.

A limitation of our study was in the measurement of productivity losses. Owing to the short interval between the PCQ questionnaires (7 and 30 d), an (unwanted) overlap in the answers of the two measuring points was present in a considerably proportion of the patients with productivity losses [20]. Additionally, discrepant answers in some PCQ questionnaires were found with regard to the stated number of working days and hours, and the possible hours of productivity losses within the time interval. In these cases, the answers were corrected to the minimum amount of productivity loss to prevent overestimation.

A few remarks should be made: first, in our study, almost all patients in the culture-based prophylaxis group received oral antibiotic prophylaxis (99.5%), which positively influences the cost in this group. Intravenous and oral antibiotics are equally effective as prophylaxis, but intravenous antibiotics are more expensive [17]. Second, the generalizability of the results might be a concern because the cost effectiveness strongly relates to the effect of culture-based prophylaxis on postbiopsy infections and associated ciprofloxacin resistance rates of rectal GNB, which vary geographically. In addition, healthcare costs can vary geographically and between healthcare systems. Third, in our study, no significant differences in QALYs corrected for baseline were observed between patients in the CG and IG, which is partly due to the relatively low prevalence of infectious complications and the short interval of disease burden. One could debate about the use of QALYs in this setting. Every infection after PB is one too many, especially given the fact that PB is a diagnostic procedure that is in part performed in healthy patients without health gain from the procedure (in 30.1% of our patients, no malignancy was detected). Additionally, when interpreting our results, nonquantifiable effects must be kept in mind, such as the impact of the prophylactic strategy on antibiotic resistance rates. An advantage of culture-based prophylaxis is that it is targeted and has the potential to limit the selection of antibiotic resistance, thereby indirectly reducing healthcare-related costs in the long run, which are not included in our analysis. Last, the cost efficiency of rectal culture-based prophylaxis in transrectal PB should directly be compared against that of transperineal PB for which no cost-efficiency analysis has been performed till date.

5. Conclusions

In conclusion, from a societal perspective, the efficiency of rectal culture-based prophylaxis was comparable with that of empirical ciprofloxacin prophylaxis. From a healthcare perspective, rectal culture-based prophylaxis was more expensive than empirical prophylaxis at slightly, though insignificantly, better QoL. Our results should be interpreted in the context of local ciprofloxacin resistance rates and healthcare costs, which can be reduced when optimizing our rectal culture protocol.

***Author contributions*:** Sofie C.M. Tops had full access to all the data in

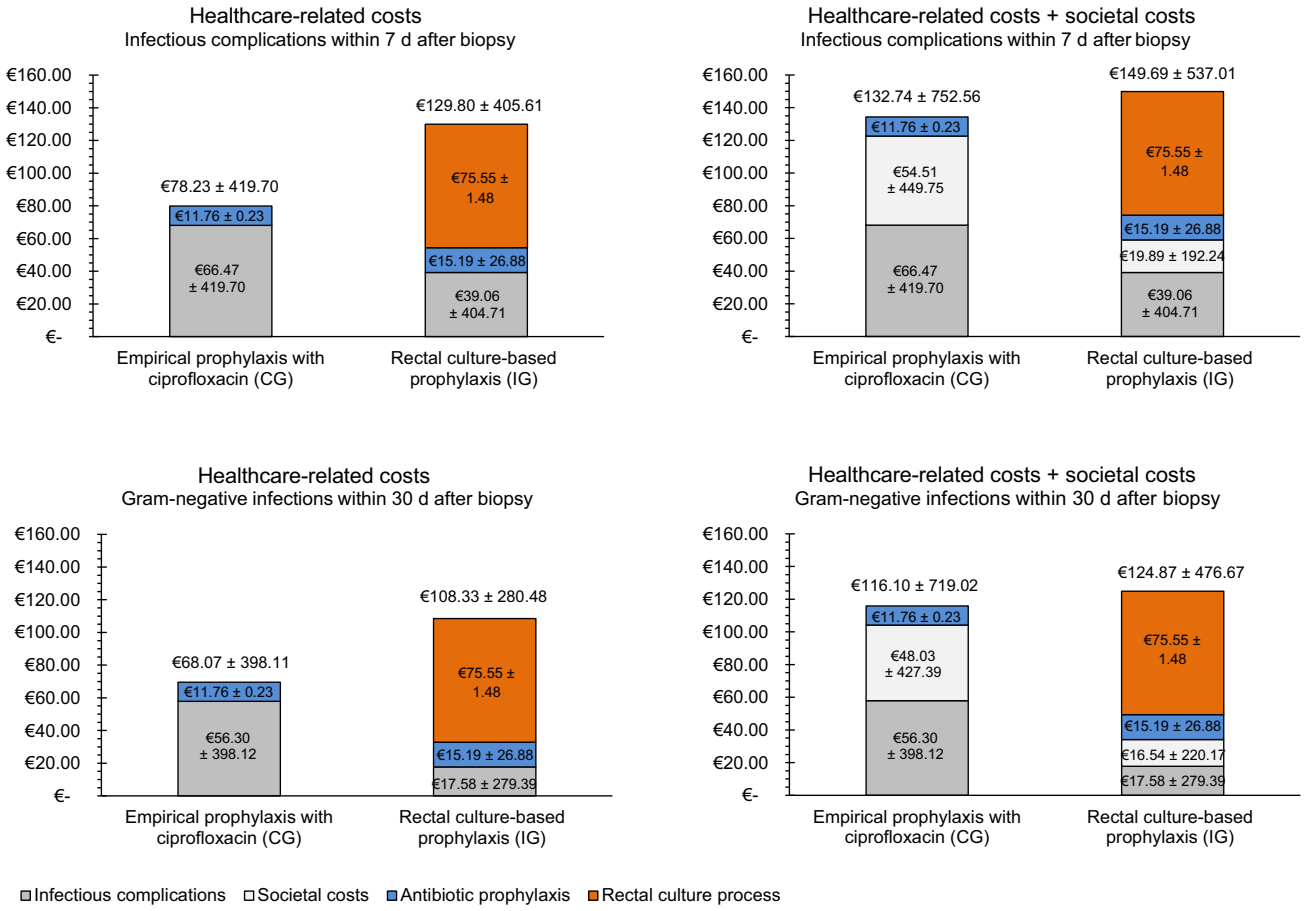

Fig. 2 – Overview of the costs per patient for the two different scenarios from healthcare and societal perspectives using descriptive statistics. CG = control group; IG = intervention group.

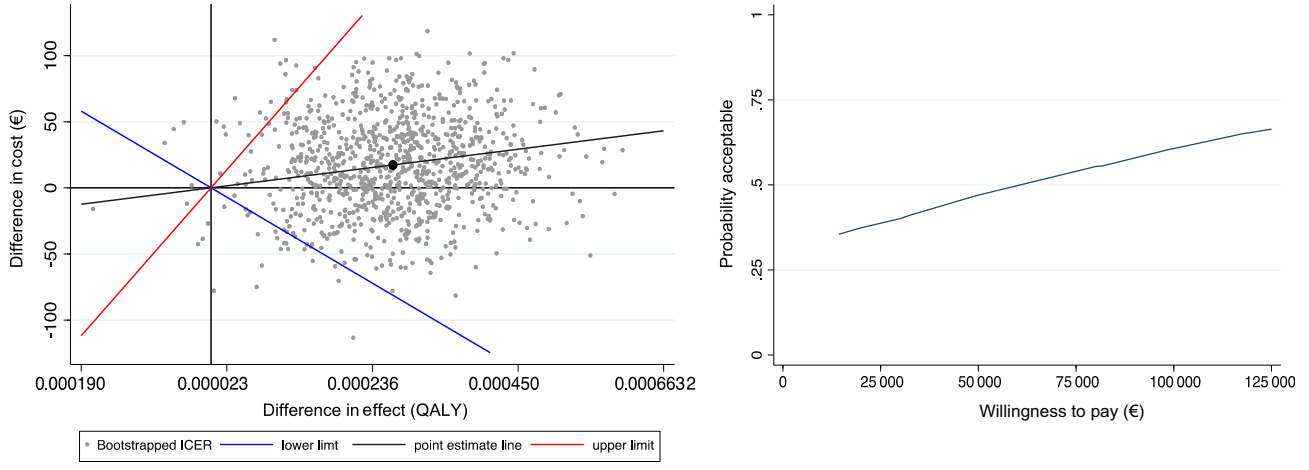

Fig. 3 – Cost-effectiveness plane of the culture-based prophylaxis strategy compared with a strategy with empirical ciprofloxacin prophylaxis (1000 bootstrapped replicates) and cost-effectiveness acceptability curve. ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.

the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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***Ethics statement*:** This study was approved by the Medical Research Ethics Committee Nijmegen (2017-3814), all 11 institutional review boards and underwent an extra marginal review by the Central Committee on Research Involving Human Subjects.

***Data sharing*:** The processed anonymized data will be made available following publication and approval by Heiman Wertheim of any formal request with a defined analysis plan. Data may be used only in the context of collaboration and after agreements are made about publication and authorship. Data may be used only for research questions for which our study group is not working on. For more information on this process, or to make a request, please send an e-mail to heiman.wertheim@radboudumc.nl.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2023.02.006.

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