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The economic evaluation of an antibiotic checklist as antimicrobial stewardship intervention

Frederike V. van Daalen[1]*, Brent C. Opmeer[2], Jan M. Prins[1], Suzanne E. Geerlings[1] and Marlies E. J. L. Hulscher[3]

[1]Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; [2]Clinical Research Unit, Academic Medical Centre, University of Amsterdam, The Netherlands; [3]IQ healthcare, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands

*Corresponding author. Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Centre, University of Amsterdam, Room F4-132, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. Tel: +31-20-5666807; Fax: +31-20-6972286; E-mail: f.v.vandaalen@amc.uva.nl

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Objectives: An antibiotic checklist was introduced in nine Dutch hospitals to improve appropriate antibiotic use. We estimated the cost-effectiveness of checklist use.

Methods: We compared 853 patients treated with an antibiotic before checklist introduction (usual care group) with 1207 patients treated after introduction (checklist group). We calculated the change of costs between these groups per unit effect [incremental cost-effectiveness ratio (ICER)]: per extra patient receiving appropriate treatment; and per day reduction in length of hospital stay (LOS). We also calculated the benefit-to-cost ratio per day reduction in LOS. Finally, we estimated the number of checklists after which the expected benefits would compensate for costs in one hospital.

Results: The cost of checklist use per patient was €10.10. Of the usual care patients, 48.8% received appropriate antibiotic treatment compared with 67.5% of the checklist patients (+18.7%). The ICER was €54.01 (1010/18.7) per extra patient with appropriate treatment. In a model calculation the expected effect of appropriate antibiotic use was a reduction in LOS of 1.05 days, which was extrapolated to a reduction of 19.64 hospital days per 100 patients. The ICER was €51.43 (1010/19.64) per day reduction in LOS. The estimated benefit of a 1 day reduction was €611. The benefit-to-cost ratio was 11.9 (611/51.43) per day reduction in LOS, indicating a cost saving of €12 for every euro spent on checklist use. The benefits would compensate for costs after use of 11 checklists.

Conclusions: Efforts for further implementation of the antibiotic checklist can be justified by potential economic benefits.

Introduction

Worldwide antimicrobial stewardship programmes (ASPs) have been introduced in hospitals with the aims of improving antibiotic use and curbing antimicrobial resistance.[1,2] Many studies have been published describing the effectiveness of ASP interventions.[2,3] Some of these studies also evaluated the interventions in terms of economic outcomes. The quality of these economic evaluations, however, varies.[4,5] Analysis of the costs associated with ASP interventions is required to select efficient ASP strategies and underpin resource use.[6]

Recently we implemented an antibiotic checklist as a supporting tool for physicians in nine Dutch hospitals. The checklist aims to improve the quality of antibiotic use by reminding physicians of the most important steps in recommended appropriate antibiotic use.[7] We showed that, despite sub-optimal use of the checklist, more appropriate antibiotic use was achieved (Table 1).[7] It remained unclear, however, whether the antibiotic checklist was an efficient ASP strategy in terms of costs, and thus, whether further implementation should be supported.

The aim of the current study was to estimate costs associated with implementation and use of the antibiotic checklist, and to relate these to potential benefits in terms of more appropriate antibiotic use and reduced use of healthcare resources.

Materials and methods

Study design, setting and participants

We performed an economic analysis alongside a stepped wedge cluster randomized trial evaluating the impact of an antibiotic checklist on length of hospital stay and the appropriateness of antibiotic use.[7] The study design involved random and sequential crossover of clusters from usual care to intervention. The total study period lasted from November 2014 until September 2015. Figure 1 illustrates which periods supplied data on

Table 1. Performance per checklist item and total performance of appropriate antibiotic treatment

Checklist item	Performance (%) usual care (*N* = 853)	Performance (%) checklist use (*N* = 1207)	Comparison difference (%)	OR*	95% CI	*P*
1. Take at least two sets of blood cultures before starting antibiotic therapy	46.5	70.4	+23.9	3.2[a]	2.6–4.0	<0.001
2. Take specimens for cultures from suspected sites of infection	46.6	50.5	+3.9	1.2[b]	0.9–1.5	0.3
3. Prescribe systemic antibiotic treatment according to the local antibiotic guideline	45.6	55.8	+10.2	1.5[c]	1.2–1.8	<0.001
4. Adapt dose and dosing interval of systemic antibiotics to renal function	34.0	44.6	+10.6	1.4[d]	0.8–2.3	0.2
5. Document the indication for the antibiotic treatment in the case notes or electronic medical record	87.0	90.0	+3.0	1.6[e]	1.1–2.1	0.006
6. Adapt therapy when culture results become available	33.7	41.8	+8.1	1.5[f]	1.0 to 2.1	0.03
7. Switch from intravenous to oral antibiotic therapy after 48–72 h	56.2	66.8	+10.6	1.5[g]	1.2–2.0	0.003
Total performance of appropriate antibiotic treatment (QI sum score >50%)	48.8	67.5	+18.7	2.4[h]	2.0–3.0	<0.001

*After correction for the same covariates as in the clinical trial,[7] namely:
[a]Adjusted for sex, MEWS (modified early warning score), type of diagnosis, antibiotics started at emergency department versus ward.
[b]Adjusted for type of diagnosis.
[c]Adjusted for antibiotic last 30 days, type of diagnosis, community- versus hospital-acquired infection.
[d]Adjusted for sex.
[e]Adjusted for type of diagnosis, community-acquired versus hospital-acquired infection.
[f]Adjusted for community-acquired versus hospital-acquired infection.
[g]Adjusted for age, type of diagnosis, community-acquired versus hospital-acquired infection, antibiotics started at emergency department versus ward.
[h]Adjusted for community-acquired versus hospital-acquired infection, antibiotics started at emergency department versus ward.

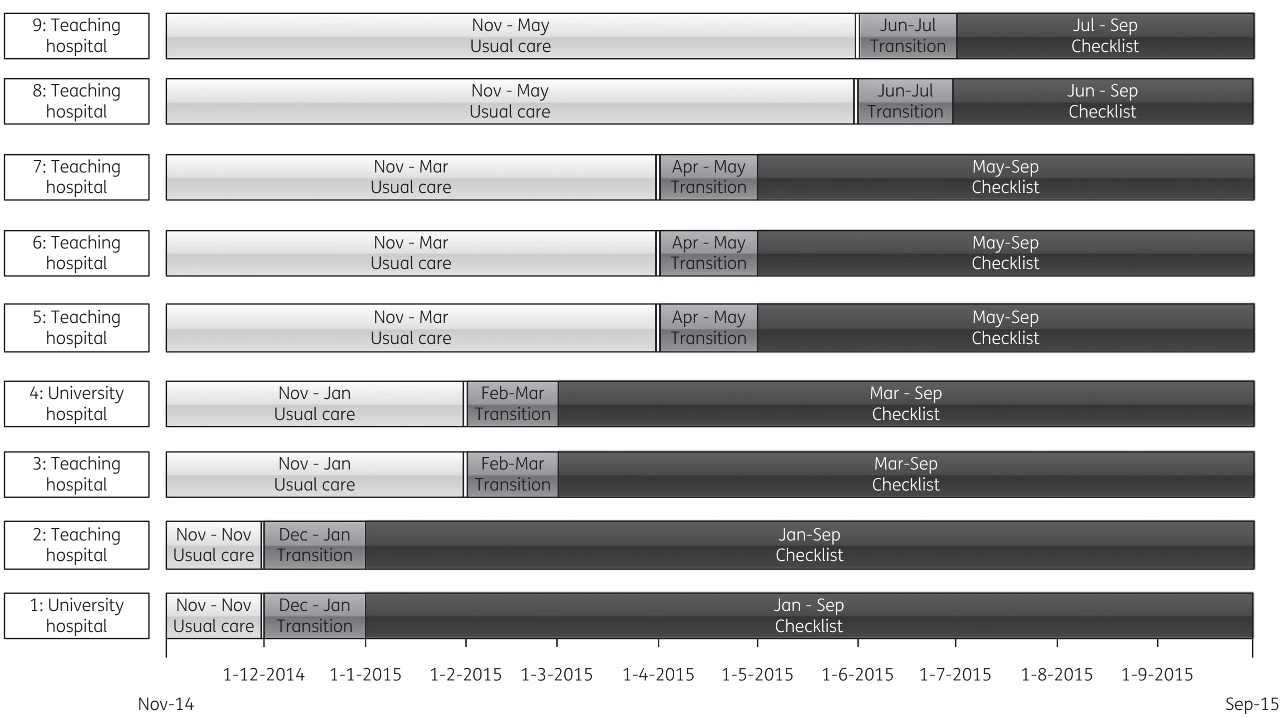

Figure 1. The stepped wedge design.

patients with usual care and which on patients treated with the use of the antibiotic checklist. Clusters were defined by hospitals. Two university and seven teaching hospitals were included, and in each hospital at least one surgical, one non-surgical and the emergency department participated. In short, 2060 patients were included in the mixed models evaluating the appropriateness of antibiotic use, of whom 853 were included in the usual care group and 1207 in the checklist group. In the clinical evaluation we distinguished between fully completed ($n = 993$) and partly completed

($n = 214$) checklists. For this economic evaluation we did not distinguish between these two groups because we believe this has little effect on the costs. Two researchers collected all data required for the evaluation of the effectiveness of the checklist in the nine participating hospitals.[7] All analyses were performed centrally.

Intervention and implementation strategies

The antibiotic checklist was based on seven validated generic quality indicators (QIs) that define appropriate antibiotic use in the treatment of bacterial infections in the hospital.[8,9] According to this definition, the appropriateness of antibiotic use includes several elements, beginning with the performance of cultures before starting antibiotics and ending with the early switch from intravenous to oral therapy if possible, as shown in the left column of Table 1.[7–9] We performed a barrier survey to identify barriers to the uptake of this checklist among physicians and we used their comments to adapt it.[10] We started with a measurement of usual care without checklist use in each hospital. This measurement was followed by a transition period, in which introduction of the antibiotic checklist was prepared and no data were collected. The checklists were displayed in printed format in all working places at the participating departments. For each participating ward we organized a briefing on appropriate antibiotic use including feedback on current antibiotic use by showing data from the usual care measurement of their own hospital. Furthermore, we distributed posters and laminated pocket versions to remind physicians about the checklist. On all materials we referred to the web site we designed (www.abchecklist.nl), which provided additional information and e-learning materials about appropriate antibiotic use. These interventions were organized by a project team consisting of the study coordinator (F. V. van D.) and at least two physicians per hospital, of whom at least one was a supervisor.

Physicians working on the participating wards were asked to complete checklists for all eligible patients during the intervention period. One member of the project team visited the participating departments weekly to supply the checklists and to remind the physicians to use them.

Cost analysis

Costs associated with the antibiotic checklist were incurred at three levels: development of the checklist and implementation strategy (development costs), implementation of the checklist in the participating departments in each hospital (implementation costs), and use of the checklist for an individual patient (operational costs). Development costs were based on time to develop the checklist including the performance of the barrier survey,[10] and time to develop supporting materials including a web site, e-learning materials, briefings, posters and laminated pocket versions. These development costs could not be assigned to one hospital and were therefore equally split over the nine participating hospitals.

Implementation costs included materials (printing costs of supporting materials and boxes) and time spent on checklist introduction at the participating departments. The study coordinator spent time on planning, distributing materials, giving briefings and travelling. The local supervisor spent time on planning, distributing materials, informing colleagues and the Board of Directors about the project, and attending a briefing. Physicians working in the participating departments spent time on attending a briefing and performing the e-learning.

Operational costs were split into costs directly associated with checklist use (stage 1) and costs associated with direct changes in healthcare use due to complying with checklist items (stage 2). Operational costs stage 1 included all net additional costs caused by checklist use, namely printing costs of the checklist, time spent on completing a checklist by the physician, and time spent on weekly visits on the wards to support use of the checklist by the local supervisor. Operational costs stage 2 concerned differences in costs between usual care and care with checklist use. These differences in costs were calculated based on an increase in culture performance, in changes from broad-spectrum to narrow-spectrum treatment, and in switches from intravenous to oral therapy in the first 3 days of antibiotic therapy.

The analysis included costs in 2015 euros. We used the invoices of our effectiveness study to calculate printing and material expenses.[7] Salary costs for research staff and healthcare professionals and antibiotic costs were based on sources of the National Health Care Institute,[11,12] inflated where appropriate. Culture costs were based on Dutch reference prices.[13]

Assumptions

In this economic analysis we assumed that the operational costs of checklist use were equal for all completed checklists. Concerning the operational costs stage 2, differences in costs caused by changes from broad-spectrum to narrow-spectrum treatment were based on the five most common changes in therapy in our clinical trial, and differences caused by changes from intravenous to oral antibiotic treatment were estimated by the five most prescribed antibiotics. Changes in healthcare due to complying with other items on the checklist (prescribe systemic antibiotic treatment according to the local antibiotic guideline, adapt dose and dosage interval of systemic antibiotics to renal function, and document the indication for antibiotic treatment) were assumed not to cause changes in costs.

Measures of effectiveness

The economic evaluation was based on two different measures of effectiveness: the QI sum score and length of hospital stay of the patient. The QI sum score indicated appropriate antibiotic use.[8] It was calculated in two steps. First, we assessed the performance per patient per QI (yes/no) with computerized algorithms (in SPSS syntax)[8] in which the collected patient data were entered. When a QI did not apply to a patient, this QI was excluded from further analysis for that specific patient. Table 2 explains per QI when the QI was applicable to a patient, and how correct performance was defined. Second, we calculated the QI sum score for each patient by dividing the number of performed QIs by the number of QIs that applied to that specific patient. QI sum scores were converted into a binary variable, defining inappropriate (QI sum score $\leq$50%) and appropriate (QI sum score $>$50%) antibiotic use. As algorithms were used for all calculations, the appropriateness of antibiotic treatment of each patient was evaluated in the same manner.

The second measure expressed the effect of the intervention in terms of length of hospital stay. A previous study showed that a higher QI sum score was associated with a reduced length of hospital stay for the patient.[14] Our study could not directly demonstrate a decrease in length of stay as a result of checklist use, but did show—as the previous study[14]—that an increase in QI sum score was associated with a reduction in length of stay.[7] In 32% of the checklist answers indicating appropriate care it was not actually provided[7] (meaning that not each patient in whom a checklist was used received more appropriate antibiotic treatment), which could explain the lack of effect of checklist use on length of stay. At group level, however, the appropriateness of antibiotic use did increase significantly (Table 1). When assuming that this increase at group level can be achieved at patient level (with each completed checklist), length of stay can be affected. We therefore used a model-based approach to indirectly derive the potential impact of checklist use on length of stay as a consequence of a higher QI sum score at patient level (Figure 2). In this model-based calculation we first estimated the difference in length of stay between patients with inappropriate and appropriate antibiotic use. We separated patients with usual care and patients with checklist use (Figure 3) as they comprised a different mix of patients: while the usual care group was a random sample of hospitalized patients treated with intravenous antibiotics, patients in the checklist group were shown to be more complicated cases.[7] Within the usual care as well as within the checklist group, a higher QI sum score was associated with a reduction in length of stay (Figure 3). Subsequently the mean of these two

Table 2. Definitions of quality indicators included in the antibiotic checklist

Checklist item	Applicable to	The algorithm considered the item correctly performed if
1. Take at least two sets of blood cultures before starting antibiotic therapy	all patients	at least two sets of blood cultures were performed in the last 3 days before start of antibiotic therapy
2. Take specimens for cultures from suspected sites of infection	patients with a suspected site of infection from which a culture can be taken	cultures from the suspected site of infection were taken in the last 3 days before start of antibiotic therapy
3. Prescribe systemic antibiotic treatment according to the local antibiotic guideline	patients under empirical antibiotic therapy, with a suspected site of infection for which a guideline is available	prescription was the correct type of antibiotic (or antibiotic combination) according to the Dutch guidelines (http://www.swab.nl/guidelines). Patient characteristics including allergies, pregnancy and previous ESBL infection were taken into account. Note: the local antibiotic guidelines of the participating hospitals were all in line with these Dutch guidelines
4. Adapt dose and dosing interval of systemic antibiotics to renal function	patients with impaired renal function treated with an antibiotic that should be dosed according to the renal function	plasma creatinine was checked in the last 3 days before start of antibiotics, and dosage was adjusted according to the Dutch guidelines (http://www.swab.nl/guidelines), taking into account three categories of impaired renal function: glomerular filtration rate 30–50, 10–30 or <10 mL/min/1.72 m^2
5. Document the indication for the antibiotic treatment in the case notes or electronic medical record	all patients	the indication for antibiotic treatment was documented either as the reason for admission or in the conclusion section in the patient's medical files
6. Adapt therapy when culture results become available	patients with a positive culture	the patient received a treatment that was in accordance with the resistance pattern of the cultured microorganism, regardless of whether antibiotic therapy was changed or not. If possible, antibiotics were chosen from a group of recommended narrow-spectrum antibiotics[8]
7. Switch from intravenous to oral antibiotic therapy after 48–72 h	patients who were haemodynamically stable, had no fever, had a normal white blood count ($4–12\times10^9$/L), were able to take oral medication, had no signs of malabsorption and no exclusion diagnosis[8]	intravenous antibiotic therapy was switched to oral therapy between 0 and 72 h after start of antibiotic treatment

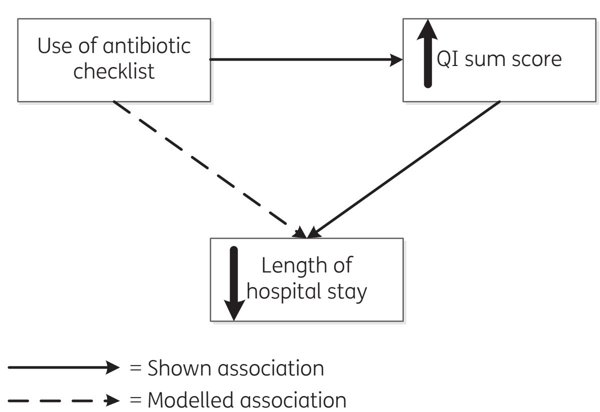

Figure 2. The association triangle between checklist use, QI sum score and length of hospital stay.

differences was assumed to represent the effect of appropriate antibiotic use on length of hospital stay per patient. Then, to translate this into an effect of checklist use on length of stay, we used the observed difference in appropriate antibiotic use between the usual care group and the checklist group.[7] We multiplied the percentage of extra patients with appropriate antibiotic use in the checklist group with the effect of appropriate antibiotic use on length of stay, resulting in an estimated reduction in length of stay with checklist use per 100 patients.

Neither admission to, nor length of stay in, the ICU changed with more appropriate antibiotic treatment according to the QIs.[7,9] Therefore, these parameters were not included in this analysis.

Effectiveness analyses

This economic analysis was performed from a hospital perspective as the costs of checklist implementation are of particular interest to hospital management.

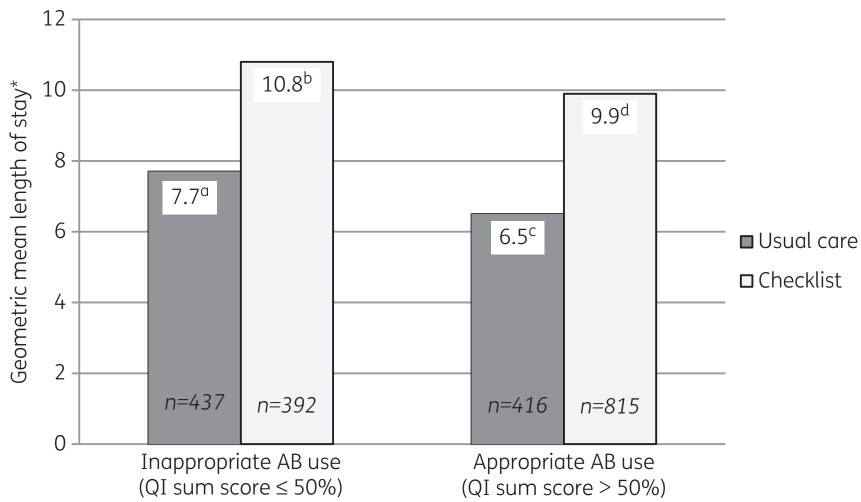

Figure 3. The association between appropriate antibiotic treatment and length of stay (days). The geometric mean length of stay was corrected for the same covariates as in the clinical trial,[7] namely: age, comorbidity, type of diagnosis, community-acquired versus hospital-acquired infection, antibiotics started at emergency department versus ward, and three interaction variables (checklist + anticancer chemotherapy, checklist + admission at a university medical centre, checklist + surgical ward). [a]95% CI 6.3–9.3; [b]95% CI 9.3–12.6; [c]95% CI 5.4–7.9; [d]95% CI 8.6–11.5. AB, antibiotic.

(a) ICER per extra patient who received appropriate antibiotic treatment

$$\frac{\text{Operational costs of the use of 1 checklist} \times 100}{\text{(\% of patients with appropriate antibiotic use in the checklist group)} - \text{(\% of patients with appropriate antibiotic use in the usual care group)}}$$

(b) ICER per day reduction in length of hospital stay

$$\frac{\text{Operational costs of the use of 1 checklist} \times 100}{\text{(\% of patients with appropriate antibiotic use in the checklist group)} - \text{(\% of patients with appropriate antibiotic use in the usual care group)} \times \text{expected effect on length of stay per patient with appropriate antibiotic use}}$$

(c) Benefit-to-cost ratio per day reduction in length of stay

$$\frac{\text{Cost savings as a consequence of a reduction in length of stay of 1 day}}{\text{Operational costs to achieve a reduction in length of stay of 1 day (=ICER per day reduction in length of hospital stay)}}$$

Figure 4. Calculated ratios.

The first cost-effectiveness analysis evaluated the operational costs of checklist use associated with the increase in patients with appropriate antibiotic use (QI sum score >50%). We calculated the incremental cost-effectiveness ratio (ICER) per extra patient who received appropriate antibiotic treatment (Figure 4a).

The second cost-effectiveness analysis evaluated the operational costs of checklist use associated with the model-based reduction in length of stay as a consequence of more appropriate antibiotic use, wherefore we calculated the ICER per day reduction in length of hospital stay (Figure 4b).

After calculating the ICER for this second cost-effectiveness analysis, the benefit-to-cost ratio was calculated based on the unit cost for 1 day of hospitalization (Figure 4c). A ratio <1 indicated that more costs were incurred than saved by checklist use, whereas a ratio >1 indicated that the costs associated with checklist use were more than compensated by the cost savings.

In case checklist use was cost-saving for operational costs, we also estimated the number of checklists after which the expected benefits would compensate for implementation costs in one hospital, assuming that each completed checklist equally contributed to a reduction in length of stay.

Table 3. Development costs

Category	Item that was developed	By whom	Time spent on the exercise (h)	Average costs per hospital (€)	Total costs (€)
Checklist	checklist (including barrier analysis)	study coordinator	464	938	8438
		infectious disease specialist	18	111	999
Supporting materials	web site	study coordinator	19	39	350
		supplier	NA	7	59
	e-learning	study coordinator	5	10	91
		infectious disease specialist	1	6	55
		technician	1.5	8	75
	briefings	study coordinator	18	36	327
	posters	study coordinator	18	36	327
	laminated pocket versions	study coordinator	18	36	327
Total (€)				1227	11048

NA, not applicable.

Table 4. Implementation costs per hospital, including 3–4 participating departments

Category	Costs to be calculated	Time spent on the exercise (h)	Average costs per hospital (€)	Range of costs per hospital (€)
Materials	printing laminated pocket versions	NA	54	30–78
	printing posters	NA	29	19–38
	yellow boxes	NA	43	32–54
Activities of study coordinator	planning	1–2	25	18–32
	spreading materials	0.5–1	14	9–18
	giving briefings	0.75–1	16	14–18
	travelling	1–2	25	18–32
Activities of local supervisor	planning	1–2	83	55–111
	spreading materials	0.5–1	39	23–55
	informing colleagues and board of directors	1–1.5	69	55–83
	attending a briefing	0.25	14	14
Activities of physicians working at the wards	residents attending a briefing	0.25	141	84–197
	specialists attending a briefing	0.25	278	139–416
	residents performing e-learning	0–0.3	123	0–245
	specialists performing e-learning	0–0.3	255	0–510
Total (€)			1208	510–1901

NA, not applicable.

All analyses for patient-level data were carried out in IBM SPSS Statistics, version 23.0. For costs and cost-effectiveness analyses Microsoft Excel 2010 was used.

Results

Cost analysis

Development costs were €11048 in total and €1227 per hospital after equally splitting the costs over the nine participating hospitals (Table 3).

Table 4 shows the implementation costs. The range in the fifth column indicates the variation between the participating hospitals. A minimum of 15 residents and 10 specialists worked on the wards versus a maximum of, respectively, 35 and 30 per hospital, which caused variation in the amount of supporting materials and the total amount of time spent on activities by the physicians. The number of wards participating in the trial was three or four per hospital, which caused variation in the time spent on briefings by the study coordinator and time spent on informing colleagues by the local supervisor. The geographic location of the hospitals is responsible for the variation in time spent on travelling by the study coordinator.

Briefings of approximately 15 min were given during a set meeting (e.g. the morning report) at which all involved physicians were assumed to be present. Performance of the e-learning was voluntarily and completion was not registered. We assumed that it took 20 min to perform the e-learning. Therefore, the time spent on the e-learning ranged between 0 (the physician did not perform the e-learning) and 20 min (the physician performed the total e-learning), explaining the time range of 0–0.3 h shown in Table 4.

Table 5. Operational costs per checklist

Category	Costs to be calculated	Average costs per checklist (€)	Range of costs per checklist (€)
Stage 1	printing expenses	0.1	0.12
	5 min spent on completing the checklist by the physician	3.5	2–5
	0.5–1 h/month spent on reminders by the local supervisor	0.8	0.5–1.0
Stage 2	blood cultures	14.2	10.5–17.9
	change from broad-spectrum to narrow-spectrum therapy	−2.5	−7.3 to 2.4
	switch from intravenous to oral therapy	−6	−10 to −2
Total (€)		10.1	−4.2 to 24.4

The fifth column in Table 4 presents the range of costs if either none or all of the physicians performed the e-learning. We assumed that on average 50% of the physicians voluntarily performed the e-learning, explaining the average costs presented in the fourth column in Table 4. Implementation costs were estimated at €1208 for an average hospital.

Operational costs are presented in Table 5. Stage 1 costs were estimated at €4.40 per checklist. The most important cost driver was the time the physician spent on completing the checklist, which was approximately 5 min per checklist. The range of these costs was caused by differences in salary of residents and specialists. Time spent on reminders by the local supervisor was divided over 55 checklists per month, as 5354 eligible patients were included in 106 intervention months.[7] We rounded up the number of patients because we excluded some patients for the effectiveness study who did not have to be excluded for checklist use outside the study. Operational costs stage 2 were based on an average increase of performed sets of blood cultures of 0.4 (performance of other cultures did not increase significantly), a reduced duration of broad-spectrum antibiotics with an average of 0.39 days, and a reduced duration of intravenous antibiotic treatment with an average of 0.35 days per checklist. The most beneficial change from broad-spectrum to narrow-spectrum treatment in the top five was the change from ceftriaxone intravenously to ciprofloxacin orally, and the most unprofitable change was from cefuroxime intravenously to ciprofloxacin intravenously. The range in Table 5 illustrates the difference between the most beneficial and the most unprofitable change. The top five of the most prescribed antibiotics were amoxicillin, amoxicillin/clavulanic acid, cefuroxime, ciprofloxacin and flucloxacillin, of which the intravenous-to-oral switch to ciprofloxacin was the most beneficial, and the intravenous-to-oral switch to flucloxacillin was the least beneficial. Again the range in Table 5 illustrates the difference between the most and least beneficial change. Operational costs stage 2 were estimated at €5.70 per checklist. Thus, the total operational costs of checklist use were estimated at €10.10 per checklist.

Cost-effectiveness

In the usual care group 48.8% received appropriate antibiotic treatment compared with 67.5% in the checklist group (Table 1),[7] hence there were 18.7% more patients with appropriate antibiotic use in the checklist group. Operational costs were €1010 per 100 patients. The ICER was €54.01 (1010/18.7) per extra patient who received appropriate antibiotic treatment.

The mean difference in length of stay between patients with appropriate and inappropriate antibiotic use is presented in Figure 3. In the baseline group the patients with inappropriate antibiotic use had a length of stay 1.2 days (16.1%) longer compared with the patients with appropriate antibiotic use (16.2%; 95% CI 6.0%–26.2%), while in the intervention group the patients with inappropriate antibiotic use had a length of stay 0.9 days (8.3%) longer compared with the patients with appropriate antibiotic use (8.3%; 95% CI 1.0%–17.7%). Thus, the expected effect of appropriate antibiotic use was a reduction in length of stay of 1.05 days. Per 100 patients, 18.7 extra patients received appropriate antibiotic use in the checklist group compared with the usual care group, which was extrapolated to a reduction in length of stay of 19.64 hospital days per 100 patients (18.7×1.05). The ICER was €51.43 (1010/19.64) per day reduction in length of hospital stay.

The cost of 1 day of hospitalization at an acute care department in the Netherlands varied between €526 and €696 in 2015.[11] The average benefit of a 1 day reduction in length of stay was €611 and the costs to achieve a 1 day reduction were €51.43. The benefit-to-cost ratio was 11.9 (611/51.43) per day reduction in length of hospital stay, indicating a cost saving of €12 for every euro spent on use of the checklist.

In our model calculation, length of stay was reduced by 19.64 days per 100 checklists, so in monetary units the hypothetical savings were 0.1964×€611=€120 per checklist, assuming that each checklist contributed equally to a reduction in length of stay. Costs included operational costs of €10.10 per checklist and average implementation costs of €1208 per hospital. The theoretical number of checklists after which benefits would compensate for costs was 11 [costs: €111.1 (11×€10.10)+€1208=€1319.1 versus savings: (11×€120)=€1320].

Discussion

In the present study, we estimated costs associated with development, implementation and use of an antibiotic checklist from a hospital perspective. Development costs were €11048 in total, implementation costs were on average €1208 per hospital, and operational costs were €10.10 per checklist. The ICER was €54.01 per extra patient with appropriate antibiotic treatment. In a model-based approach the costs to reduce length of hospital stay by 1 day were estimated at €51.43. After using the checklist in 11 patients, the initial implementation costs would be offset by cost savings resulting from more appropriate antibiotic use and reduced length of stay.

Due to the complexity of passing costs associated with developing the antibiotic checklist on to outcomes, development costs have not been included in the cost-effectiveness analyses.[15] Assigning the development costs only to the nine hospitals that participated in the clinical trial is a very conservative approach, as the checklist is now available online and can be used by others. For example, the antibiotic checklist has already been used in a hospital in Aruba, an island in the Caribbean.[16] If, however, we were also to include development costs in the calculation of the threshold where expected benefits compensate for costs in one hospital, including only nine hospitals, the turning point after which savings compensate for costs would not be 11 but rather 23 completed checklists, which is still a remarkably low number. Implementation costs have also been approached conservatively. We assumed that 50% of the physicians voluntarily performed the e-learning. However, this is most probably an overestimation, as during the intervention period the web site was visited (on average) twice a day.

Several other ASP interventions have been economically evaluated, of which most are said to be cost-effective.[4,5,17–21] The heterogeneity of interventions and outcomes complicates direct comparison of studies.

When looking at the type of interventions that have been evaluated for cost-effectiveness, it is remarkable that, to our knowledge, the antibiotic checklist is the only intervention that can be implemented in any moderately developed hospital, as it does not require the presence of infectious disease specialists or experts.[17–21]

Our study has several strengths. An economic analysis is required to complete the evaluation of an implementation strategy,[6] and we used our own primary data in this evaluation. In contrast to previous cost-effectiveness analyses of ASP interventions,[5] we provided full insight into costs incurred by the intervention by including personnel costs and costs of implementation activities. Furthermore, our cost analysis includes implementation costs of hospitals of different sizes, which helps to translate the results to other settings.

Our study also has limitations. The model-based approach is a limitation as the validity of the model depends on assumptions and input. We assumed that checklist use would result in a reduction in length of stay when used as intended.[7] We simplified the definition of appropriate antibiotic use by collapsing the measure into binary variables (inappropriate and appropriate), which is an artificial cut-off point: in reality the QI sum score can vary between 0% and 100%. It is possible that length of stay is more affected when increasing the QI sum score from 0% to 60% than from 50% to 60%. The assumed association between appropriate antibiotic use and length of stay should therefore be interpreted as an average effect. In addition, we did not include potential adverse effects of checklist use. Although we did not receive any feedback from the participants about adverse consequences, it cannot be ruled out that less attention was being paid to other relevant checklists or measures during antibiotic checklist use. Finally, the choice of a hospital perspective has narrowed the economic perspective of our analysis,[4,5] and a societal perspective would had been more in line with the previously emphasized economic consequences of antimicrobial resistance at a societal level.[22–24]

In conclusion, the results of this economic evaluation, which distinguished development, implementation and operational costs, suggest that implementation of this antibiotic checklist can be a cost-effective antimicrobial stewardship strategy. In the future, hospitals aiming to implement this antibiotic checklist should be aware that decision makers will be mostly interested in operational costs, as these are the main cost driver in the long run. This cost analysis can be used to anticipate associated costs, depending on their own setting. It shows that up-front investment is low and operational costs are about €10 per checklist.

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Transparency declarations

None to declare.

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