Effect of an antibiotic checklist on length of hospital stay and appropriate antibiotic use in adult patients treated with intravenous antibiotics: a stepped wedge cluster randomized trial

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A B S T R A C T

Objectives: Quality indicators (QIs) have been developed to define appropriate antibiotic use in hospitalized patients. We evaluated whether a checklist based on these QIs affects appropriate antibiotic use and length of hospital stay.

Methods: An antibiotic checklist for patients treated with intravenous antibiotics was introduced in nine Dutch hospitals in a stepped wedge cluster randomized trial. Prophylaxis was excluded. We included a random sample before (baseline), and all eligible patients after (intervention) checklist introduction. Baseline and intervention outcomes were compared. Primary endpoint was length of stay (LOS), analysed by intention to treat. Secondary endpoints, including QI performances, QI sum score (performance on all QIs per patient), and quality of checklist use, were analysed per protocol.

Results: Between 1 November 2014 and 1 October 2015 we included 853 baseline and 5354 intervention patients, of whom 993 (19%) had a completed checklist. The LOS did not change (baseline geometric mean 10.0 days (95% CI 8.6–11.5) versus intervention 10.1 days (95% CI 8.9–11.5), p = 0.8). QI performances increased between +3.0% and +23.9% per QI, and the percentage of patients with a QI sum score above 50% increased significantly (OR 2.4 (95% CI 2.0–3.0), p < 0.001). Higher QI sum scores were significantly associated with shorter LOS. Discordance existed between checklist-answers and actual performance.

Conclusions: Use of an antibiotic checklist resulted in a significant increase in appropriateness of antibiotic use, but not in a reduction of LOS. Low overall checklist completion rates and discordance between checklist-answers and actual provided care might have attenuated the impact of the checklist. F.V. van Daalen, Clin Microbiol Infect 2017;e1

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Introduction

Better use of antibiotic agents is necessary to control antimicrobial resistance (AMR) [1,2]. There is considerable room for improvement in antibiotic use, as 30–50% of antibiotic prescriptions in hospitals are indicated to be unnecessary or inappropriate [3]. Appropriate antibiotic use has been associated with better outcomes at the patient level, such as a decreased length of hospital stay [4–8] which is an important outcome measure to reflect recovery time of patients and to define hospital costs [8].

Antibiotic Stewardship Programs (ASP) have been introduced in hospitals to measure and improve appropriate use of antibiotics [9]. Most ASP interventions are performed during antibiotic treatment, with few focusing on prescribers at the moment of antibiotic prescribing [4,9,10]. An antibiotic checklist could be functional to embed appropriate antibiotic use in daily practice, as checklists have been shown to be useful tools for improving health care in different settings [11,12].

In previous studies we developed generic quality indicators (QIs) to define and measure appropriate antibiotic treatment in adult patients with a suspected bacterial infection [13,14]. Treatment according to these QIs was associated with a shorter length of hospital stay [8]. Based on these QIs we developed an antibiotic checklist [15]. Our aim was to analyse the effect of the introduction of this antibiotic checklist on outcomes at the patient level, including length of hospital stay, admission to ICU, and mortality, and on appropriate antibiotic treatment defined by the generic QIs.

Methods

Study design and participants

We evaluated the introduction of the antibiotic checklist in a multicentre stepped wedge cluster randomized trial, comparing outcomes before and after its introduction. The full study protocol is reported elsewhere [16]. Fig. 1 presents the study design in detail. The stepped wedge design was considered to be the most suitable because of the cross-sectional control between, and the longitudinal control within, hospitals, and because in the end all hospitals used the checklist, which was favourable as the checklist was unlikely to cause harm [8,17,18]. Clusters were defined by hospitals. Hospitals were eligible if they were willing to be randomly assigned to a time point of checklist introduction, and if at least one surgical, one non-surgical, and the emergency department (ED) were willing to participate. The ICU and the paediatric department were excluded, as the QIs do not apply to these populations. Twelve hospitals were approached by the researchers (SG, FVD) to take part. The ICU and the paediatric department were willing to participate relative to the number of patients on the list. For each hospital we determined a minimum number of third eligible patient —depending on the number of patients required for inclusion relative to the number of patients on the list.

Introduction of the antibiotic checklist. The antibiotic checklist is based on generic QIs that define appropriate antibiotic use in the treatment of bacterial infections in the hospital [13,14]. We determined the barriers towards the uptake of this checklist among physicians and used their comments to adapt it [15]. The antibiotic checklist is divided into two bundles (Fig. S1, supporting information). The first bundle (five items) has to be completed at the moment of prescribing IV antibiotics. The second bundle (two items) has to be completed during the course of treatment, at the latest after 72 hours of treatment.

During the transition period, which took place 1 month preceding the start of checklist use in each hospital, introduction of the antibiotic checklist was prepared and no data were collected. The checklists were displayed in printed form at all working places at the participating departments. Other interventions were organized to stimulate use of the checklist, such as education, feedback on current antibiotic use showing baseline data from the department’s own hospital, and reminders (Table S1, supporting information) [15]. The education material was sent by email to all participating physicians at the start of the intervention period. These interventions were organized by a project team consisting of the study coordinator (FVD) and at least two physicians per hospital.

Physicians were asked to complete checklists for all eligible patients during the intervention period. If the first bundle was completed at the ED, the checklist was to be taken to the ward with the patient. It was the physicians’ responsibility to use the checklist each time an antibiotic was started. The project team visited the participating departments weekly to supply the checklists and to remind the physicians to use the checklist. In one university hospital the start of the intervention coincided with the rotation of residents, and an extra presentation was given on their first working day. In other hospitals these rotations occurred during the intervention period and new residents were informed by email and during the weekly visits of the project team.

Randomization and masking

Participating hospitals were randomly allocated to four sequential time points by an independent data manager using ALEA software version release 4.0 for randomization in clinical trials. Masking of physicians and researchers was not possible. Patients were unaware of the study.

Procedures

Baseline measurement (baseline group). Eligible patients admitted between 1 November 2014 and 1 month before introduction of the checklist at that hospital were considered as baseline patients. For each hospital we determined a minimum number of patients that should be included, based on the power calculation and the randomization order of the hospital in the stepped wedge trial.

To identify eligible patients, in each hospital a list was generated by the local hospital pharmacy from the computerized medication ordering system of all patients treated with IV antibiotics. This list was structured by date, and we included every second or every third eligible patient —depending on the number of patients required for inclusion relative to the number of patients on the list.
Post introduction measurement (intervention group). Eligible patients admitted after introduction of the checklist and before 1 October 2015 were considered as the intervention group. Likewise, we used the list of all patients with prescribed IV antibiotics per hospital, but for the intervention group we included all eligible patients. In this way we were able to perform both an intention-to-treat analysis (including the complete intervention group) and a per-protocol analysis (including only those patients in the intervention group with a completed checklist), as illustrated in Fig. 2. If eligible patients were hospitalized more than once during the intervention period, we included all admissions.

Data collection

Case notes and electronic medical records were reviewed to collect the data, which were entered into a certified online data entry system (OpenClinica). Two researchers collected the data in all hospitals, using a logbook that was developed before start of data collection. We distinguished the following four patient groups:

- Baseline group (1)
- Intervention group, consisting of:
  - Eligible patients with a completed checklist; (2)
  - Eligible patients with a partially completed checklist; (3)
  - Eligible patients without a checklist. (4)

For all patients, we recorded length of stay and patient characteristics, including age, sex, Charlson comorbidity index [19], clinical condition as assessed by the Modified Early Warning System [20], current use of anti-cancer chemotherapy, use of antibiotics during the previous 30 days, type of diagnosis, community- or hospital-acquired infection, ward of admission, and location of start

![Fig. 1. Study design and trial profile. Red colour indicates baseline period, green colour indicates intervention period. B = number of baseline patients, CC = number of patients with completed checklist, PC = number of patients with partially completed checklist, NC = number of patients without a checklist.](image)

102 excluded completed checklists
- 20 oral antibiotic treatment
- 17 hospitalisation at ICU
- 15 unclear for which patient the checklist was completed
- 11 double checklist for the same patient and the same treatment
- 10 participation in another study focused on antibiotic use
- 9 transfer from another hospital
- 7 antibiotics used as prophylaxis or < 24 hrs of treatment
- 6 hospital stay < 24 hrs
- 5 therapy started at a non-participating department
- 2 patient < 18 years

62 excluded partly completed checklists
- 21 therapy started at a non-participating department
- 9 unclear for which patient the checklist was completed
- 8 double checklist for the same patient and the same treatment
- 8 hospital stay < 24 hrs
- 8 antibiotics used as prophylaxis or < 24 hrs of treatment
- 4 participation in another study focused on antibiotic use
- 4 hospitalisation at ICU
- 3 oral antibiotic treatment

Analysed:
- Intervention: 5354
  - Completed checklist: 993
  - Partly completed checklist: 214
  - No checklist: 4147
- Baseline: 853

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of antibiotic treatment (ED or ward), as these characteristics were suggested to be potential confounders for length of stay in our previous studies [7,8].

Data concerning secondary outcomes, including data to calculate QI performance [16], total antibiotic use (both IV and oral treatment), admission and duration of ICU stay, mortality, and readmission, were only collected for all baseline patients (1) and for patients with a (partially) completed checklist (2 and 3). For patient groups 2 and 3 we documented the answers to all items on the checklists.

**Outcomes**

Primary endpoint was length of hospital stay (LOS) per patient in days. LOS in community-acquired infections was defined as the number of days between admission and discharge. In hospital-acquired infections, LOS was defined as the number of days between start of antibiotic treatment and discharge.

Secondary endpoints were appropriate antibiotic treatment according to the generic QIs, defined by a score per QI (yes/no per QI) and a sum score of all QIs per patient [7,8], and total antibiotic use defined by days of therapy (DOT) per single antibiotic agent. Other secondary endpoints at patient level were ICU admission, duration of ICU stay in days, in-hospital mortality, mortality in the first 30 days after discharge, and readmission within 30 days with an infection.

To investigate the quality of checklist use, secondary endpoints at implementation level were the completion rate of checklists [21,22] and discordance between 'YES'-answers on the checklist indicating appropriate care and actual provided care, as ticking the 'YES'-box might not always mean actual performance of that checklist-item [23].

**Statistical analysis**

To adjust for the time steps of the stepped wedge and for clustering in the data, we used mixed models to compare the primary outcome, LOS, before and after introduction of the checklist. The core model included the clusters (hospitals) as a random effect and the time in months as a fixed effect. To adjust the estimated (difference in) LOS for other factors associated with LOS, for each analysis several covariates were considered and selected as follows: the core model was extended with each single covariate. Covariates with a significant univariate effect (p < 0.1) on the outcomes were included in the multivariate model. Thereafter we excluded covariates without an effect (p > 0.1) in the multivariate model (backward selection). Tested covariates included the potential confounders mentioned in the ‘data collection’ section. We also explored whether clinically relevant subgroups of patients were associated with a longer or shorter LOS and, if so, interaction variables were included in the model to account for these differences. We used the Akaike’s Information Criterion as a parameter for the goodness-of-fit for the model. According to the intention-to-treat principle, we compared the geometric mean of LOS of the baseline group (1) with the geometric mean of the total intervention group (2, 3, and 4). In addition, the baseline group (1) was compared with the intervention group with a completed checklist (2), reflecting a per protocol approach (Fig. 2).

For secondary outcomes we evaluated differences between the baseline group (1) and the checklist groups (2 and 3). QI performance was calculated for each patient by algorithms [14]. We used mixed models to compare the proportions of appropriate antibiotic treatment according to the generic QIs. The patient’s QI sum score was calculated by the performance on all QIs for a patient according to the information from the electronic medical records, divided by the number of QIs that applied to that specific patient. In a mixed model analysis we compared the percentage of patients with a QI sum score >50% in the baseline and the checklist group [8]. Furthermore, we determined whether the association between a higher QI sum score and a reduced length of stay—as described previously [8]—also existed in our baseline and checklist patients with a mixed model analysis.

Mixed models were also used to compare the DOTs per 100 patient-days and per 100 admissions. For outcomes with a relatively low incidence that varies between hospitals (including ICU admission, duration of ICU stay, in-hospital mortality, mortality in the first 30 days after discharge, and readmission within 30 days), we could not use mixed model analyses, as groups have been compared and adjusted for hospitals. Therefore descriptive statistics assessed those secondary outcomes.

To evaluate the quality of checklist use we also used descriptive measures. The completion rate was expressed as the percentage of eligible patients for whom the checklist was fully completed. Discordance between ‘YES’-answers indicating appropriate care
and actual provided care was expressed by the percentage of ‘YES’-answers on the checklists that could not be confirmed by information from the electronic medical records.

**Sample size**

Previous studies showed that appropriate antibiotic use reduces LOS by approximately 10-15% [7,8]. We performed extensive simulation analyses, where hypothetical data were generated according to the stepped wedge design, by varying macro parameters for baseline values and before/after differences for LOS, intra-class correlation coefficients, number of clusters, and number of patients per cluster. Each simulated dataset was analysed with a mixed effects model. We estimated that 1620 patients would be needed to show a 13% reduction in LOS, assuming a type I error of 0.05, a type II error of 0.2, and an intra-cluster correlation coefficient of 0.2. To identify a significant difference in LOS in the per protocol analysis (Fig. 2), a minimum of 810 patients was required in both the baseline group and the complete checklist group.

For the power analysis we used IBM SPSS Statistics, version 23.0.

**Results**

Between 1 November 2014 and 1 June 2015, 853 patients were included in the baseline group. Between 1 January and 1 October 2015, 5354 patients were enrolled in the intervention group: 19% had a completed checklist, 4% had a partially completed checklist, and 77% had no checklist (Fig. 1). Baseline, transition, and intervention periods took place as planned in all hospitals (Fig. 1). Patient characteristics are listed in Table 1.

In an intention-to-treat analysis 853 baseline patients were compared with 5354 intervention patients. Three subgroups of patients with a completed checklist were associated with a longer LOS: patients admitted to a university hospital, those hospitalized at a surgical ward, and those currently treated with anti-cancer chemotherapy (Table S2, supporting information). Independently, these three factors did not affect LOS, but as an interaction variable with a completed checklist, they all had a significant effect on LOS (Table S3, supporting information). The geometric mean of LOS was 10.0 days in the baseline group (95% CI 8.6–11.5) versus 10.1 days in the total intervention group (95% CI 8.9–11.5) (p 0.8), while adjusting for age, comorbidity, type of diagnosis, community- or hospital-acquired infection, antibiotics started at ED or ward, and the interaction variables.

In a per-protocol analysis we compared LOS of 853 baseline patients and 993 intervention patients with a completed checklist. Adjusted for the same covariates and interaction variables as in the intention-to-treat analysis, the geometric mean of LOS of the baseline group was 10.1 days (95% CI 8.5–12.0), which is similar to the LOS of the checklist group (10.4 days (95% CI 9.1–12.0), p 0.6).

For the secondary outcomes we compared the baseline group with the patients with a (partially) completed checklist (n = 1207). Scores per QI and QI sum scores were higher in the patients with a checklist compared with baseline (Table 2). The increase of QI performance varied between +3.0% and +23.9%, and this was significant for five of the seven QIs. The percentage of patients with a QI sum score above 50% was also significantly higher in the checklist group compared with the baseline group (OR 2.4 (95% CI 2.0–3.0), p < 0.001). In the baseline group and the patients with a partially completed checklist together (n = 2600), a higher QI sum score was significantly associated with a shorter length of hospital stay (Fig. 2).

DOTs, admission to- and LOS at the ICU, mortality, and readmission rates were similar across the study groups (Table 3). For 23% of all eligible patients a checklist was used, of whom 19% had a fully, and 4% had a partially completed checklist. The percentage of patients with a (partially) completed checklist per hospital varied between 18.3% and 31.6%. The total number of checklist-items answered with ‘YES’ was 5020. In 32% the ‘YES’-answer (1628/5020) was discordant with information from the electronic medical records.

**Discussion**

In the present study the use of an antibiotic checklist for in-hospital antibiotic treatment did not result in a shorter length of

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**Table 1**

Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Baseline N = 853a</th>
<th>Intervention N = 5354b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed checklists N = 993</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex, male</td>
<td>445 (52.2)c</td>
<td>557 (56.1)c</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>69.1 (17)</td>
<td>66.9 (17)</td>
</tr>
<tr>
<td>Infection, community-acquired/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hospital-acquired</td>
<td>656 (76.9)/197 (23.1)</td>
<td>742 (74.8)/251 (25.2)</td>
</tr>
<tr>
<td>Type of diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>221 (25.9)</td>
<td>233 (23.5)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>133 (15.6)</td>
<td>174 (17.5)</td>
</tr>
<tr>
<td>Skin and soft tissue infection</td>
<td>99 (11.6)</td>
<td>85 (8.6)</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>95 (11.1)</td>
<td>80 (8.0)</td>
</tr>
<tr>
<td>Other infections</td>
<td>108 (12.7)</td>
<td>184 (18.5)</td>
</tr>
<tr>
<td>Two diagnoses</td>
<td>82 (9.6)</td>
<td>106 (10.7)</td>
</tr>
<tr>
<td>More than two possible diagnoses</td>
<td>115 (13.5)</td>
<td>131 (13.2)</td>
</tr>
<tr>
<td>diagnosis not covered by guideline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson comorbidity index, median (IQR)</td>
<td>1.0 (0-2)</td>
<td>1.0 (0-2)</td>
</tr>
<tr>
<td>Received antibiotics &lt;30 days before</td>
<td>306 (36.0)</td>
<td>424 (42.7)</td>
</tr>
<tr>
<td>start of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic started at the emergency department</td>
<td>369 (43.3)</td>
<td>525 (52.9)</td>
</tr>
</tbody>
</table>

a Missing data in <3 patients.
b Missing data in <6 patients.
c Numbers are n (%) unless otherwise indicated. Percentages were calculated with the denominator excluding missing cases.
However, antibiotics were used more appropriately according to generic quality indicators (QIs) after introduction of the antibiotic checklist. In addition, a higher QI sum score was associated with a shorter LOS, which is in line with previous results [7,8]. Further analysis showed a first probable reason for these conflicting conclusions, as 32% of the checklist-answers indicating appropriate care were not in line with actual provided care. The checklists with discordant answers might have disrupted the impact of the checklist on LOS, as it is obviously not ticking the ‘YES’-boxes that leads to reduction in length of stay, but performance according to the QIs.

Few other studies report exact numbers of discordance between indicated appropriate care and actual provided care [23]. The most successful checklist studies do not discuss discordance at all [11,12,24], but it has previously been suggested as an explanation for the absence of effects [25,26]. In 101 hospitals in Canada, for example, use of the WHO surgical safety checklist did not have the expected effect on comorbidity and mortality rates [25]. The most likely explanation was that the actions on the checklist were not actually performed [25,26]. While this explanation is only a suggestion in the Canadian study, we actually measured it in the current project.

A second explanation for the absence of effect on LOS in the group with a completed checklist might be indication bias, as the checklist seemed to be predominantly used in more complicated cases. The geometric mean of LOS in patients with a completed checklist and admitted to a university hospital, hospitalized at a surgical ward, or currently treated with anti-cancer chemotherapy, was more than 3 days longer than in patients without a checklist (Tables S2 and S3). We have statistically corrected for this and for the absence of effects [25,26].

### Table 2
Score per quality indicator (QI) and QI sum score

<table>
<thead>
<tr>
<th>QI</th>
<th>Baseline N = 853</th>
<th>Checklist N = 1207</th>
<th>Comparison</th>
<th>OR[^a]</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blood cultures</td>
<td>46.5</td>
<td>70.4</td>
<td>+ 23.9</td>
<td>3.2[^b]</td>
<td>2.6 to 4.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Cultures of suspected site of infection</td>
<td>46.6</td>
<td>50.5</td>
<td>+ 3.9</td>
<td>1.2[^c]</td>
<td>0.9 to 1.5</td>
<td>0.3</td>
</tr>
<tr>
<td>3. Guideline adherence</td>
<td>45.6</td>
<td>55.8</td>
<td>+ 10.2</td>
<td>1.5[^d]</td>
<td>1.2 to 1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4. Adjustment to renal function</td>
<td>34.0</td>
<td>44.6</td>
<td>+ 10.6</td>
<td>1.4[^e]</td>
<td>0.8 to 2.3</td>
<td>0.2</td>
</tr>
<tr>
<td>5. Documented antibiotic plan</td>
<td>87.0</td>
<td>90.0</td>
<td>+ 3.0</td>
<td>1.6[^f]</td>
<td>1.1 to 2.1</td>
<td>0.006</td>
</tr>
<tr>
<td>6. Adapt therapy when culture results become available</td>
<td>33.7</td>
<td>41.8</td>
<td>+ 8.1</td>
<td>1.5[^g]</td>
<td>1.0 to 2.1</td>
<td>0.03</td>
</tr>
<tr>
<td>7. IV-oral switch</td>
<td>56.2</td>
<td>66.8</td>
<td>+ 10.6</td>
<td>1.5[^h]</td>
<td>1.2 to 2.0</td>
<td>0.003</td>
</tr>
<tr>
<td>QI sum score &gt;50%</td>
<td>48.8</td>
<td>67.5</td>
<td>+ 18.7</td>
<td>2.4[^i]</td>
<td>2.0 to 3.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

[^a]: Based on generalized linear mixed models, taking covariates into account.  
[^b]: Adjusted for sex, Modified Early Warning Score, type of diagnosis, antibiotics started at emergency department vs. ward.  
[^c]: Adjusted for type of diagnosis.  
[^d]: Adjusted for antibiotic use in last 30 days, type of diagnosis, community- vs. hospital-acquired infection.  
[^e]: Adjusted for sex.  
[^f]: Adjusted for type of diagnosis, community- vs. hospital-acquired infection.  
[^g]: Adjusted for community- vs. hospital-acquired infection.  
[^h]: Adjusted for age, type of diagnosis, community- vs. hospital-acquired infection, antibiotics started at emergency department vs. ward.  
[^i]: Adjusted for community- vs. hospital-acquired infection, antibiotics started at emergency department vs. ward.

Fig. 3. Association between quality indicator sum score and length of stay. *: Adjusted for age, comorbidity, type of diagnosis, community- vs. hospital-acquired infection, antibiotics started at emergency department vs. ward, and interaction variables checklist + anti-cancer chemotherapy, checklist + admission at a University Medical Centre, checklist + surgical ward. **: The upper quartile is the reference quartile.
Further analysis of discordant instructions for adjustment to renal function and IV-oral switch. Medical record with links to digital antibiotic guidelines and to introduction of a checklist has been stressed [26, 29, 30], for them. As the importance of supporting activities added to the electronically, might have discouraged prescribers from using from the ED to the ward and the checklists not being available were developed with an international panel [13], our results may Dutch hospitals. Although the generic QIs included in the checklist evaluating parameters as completion and discordance between intervention period enabled identification of indication bias in the checklist group. Finally, we demonstrated the importance of evaluating parameters as completion and discordance between checklist-answers and actual performance.

Our study has some limitations. The checklist was only tested in Dutch hospitals. Although the generic QIs included in the checklist were developed with an international panel [13], our results may not be completely generalizable to all other hospitals. Moreover, only teaching and university hospitals participated. Furthermore, the low rate of checklist completion is remarkable. Our implementation strategy appeared to have important limitations, such as the lack of a reminder each time an antibiotic was started. During the weekly visits by the project team the physicians often acknowledged they had forgotten the checklist ‘in the heat of the moment’. Also logistic barriers, such as the transport of checklists from the ED to the ward and the checklists not being available electronically, might have discouraged prescribers from using them. As the importance of supporting activities added to the introduction of a checklist has been stressed [26, 29, 30], for example a checklist for reassessing intravenous antibiotic therapy after 3 days in combination with advice from an infectious disease specialist had much more impact than simply distributing the checklist [29], additional activities might have resulted in higher completion scores. However, our completion score of 19% is comparable with the measured score of 20% in the first period of a surgical safety checklist implementation study [21]. Other studies mentioned completion scores that are self-reported by hospitals, which appear to be much higher than real-life completion [22, 25] or do not present completion rates at all [12, 24].

In future, the checklist could be included in the electronic medical record with links to digital antibiotic guidelines and to instructions for adjustment to renal function and IV-oral switch. Further analysis of discordant ‘YES’-answers per QI could illustrate where to focus for further implementation. Also the economic perspective of the antibiotic checklist introduction should be considered.

In conclusion, introduction of the antibiotic checklist resulted in significantly improved quality of IV antibiotic use in the hospital as defined by the generic QIs. Unfortunately, LOS was not affected, presumably as a result of indication bias, low overall checklist completion rates, and high discordance rates between checklist-answers indicating appropriate care and actual provided care. Improving the quality of checklist use is necessary to conclude whether implementation of the antibiotic checklist is the most optimal way to improve the quality of antibiotic use among prescribers of antibiotics in the hospital.

**Transparency declaration**

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**Appendix A. Supporting information**

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cmi.2017.01.019.

**References**


Table 3

<table>
<thead>
<tr>
<th>Other secondary endpoints</th>
<th>Baseline N = 853*</th>
<th>Checklists N = 1207*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of therapy per 100 patient-days without adjustment for covariates</td>
<td>84</td>
<td>79</td>
</tr>
<tr>
<td>Days of therapy per 100 patient-days with adjustment for covariates</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td>Days of therapy per 100 admissions without adjustment for covariates</td>
<td>827</td>
<td>837</td>
</tr>
<tr>
<td>Days of therapy per 100 admissions with adjustment for covariates</td>
<td>951</td>
<td>941</td>
</tr>
<tr>
<td>ICU admission</td>
<td>31 (3.6)</td>
<td>50 (4.1)</td>
</tr>
<tr>
<td>Geometric mean of LOS at ICU (95% CI)</td>
<td>2.32 (1.5-3.5)</td>
<td>2.61 (1.8-3.8)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>54 (6.3)</td>
<td>64 (5.3)</td>
</tr>
<tr>
<td>Mortality -30 days after discharge</td>
<td>33 (4.2)</td>
<td>39 (3.4)</td>
</tr>
<tr>
<td>Readmission -30 days after discharge</td>
<td>98 (12.3)</td>
<td>123 (10.8)</td>
</tr>
</tbody>
</table>

Numbers are n (%) unless otherwise indicated. Percentages were calculated with the denominator excluding missing cases.

a Missing data on IC admission in three patients, on mortality <30 days after discharge in 10 patients, and on readmission <30 days after discharge in three patients.

b Missing data on IC admission in two patients, on mortality <30 days after discharge in eight patients, and on readmission <30 days after discharge in six patients.

Adjusted for comorbidity, type of diagnosis, community- vs. hospital-acquired infection, antibiotics started at emergency department vs. ward.

Adjusted for sex, MEWS, type of diagnosis, community- vs. hospital-acquired infection, antibiotics started at emergency department vs. ward.

No correction for covariates.

The percentages are calculated after exclusion of the patients who died in hospital.


