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Practice testing of generic quality indicators for responsible antibiotic use in nine hospitals in the Dutch–Belgian border area☆

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SUMMARY

Background: Inpatient quality indicators (IQIs) were previously developed to assess responsible antibiotic use.
Aim: Practice testing of these QIs in the hospital setting.
Method: This study was performed within a Dutch–Belgian border network of hospitals implementing the Infection Risk Scan (IRIS) point prevalence survey (PPS) as part of the i-4-1-Health project. Twenty out of 51 DRIVE-AB IQIs, including 13 structure and seven process IQIs, were tested. Data on structure IQIs were obtained through a web-based questionnaire sent to the hospital medical microbiologists. PPS data from October to December 2018 were used to calculate performance scores for the process QIs.
Findings: Nine hospitals participated. Regarding structure IQIs: the lowest performance scores were observed for recommendations for microbiological investigations in the guidelines and the use of an approval system for restricted antibiotics. In addition, most hospitals reported that some antibiotics were out of stock due to shortages. Regarding process IQIs: 697 systemic antibiotic prescriptions were used to calculate performance scores. The lowest score was observed for documentation of an antibiotic plan in the

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medical file (58.8%). Performance scores for IQIs on guideline compliance varied between 74.1% and 82.3% for different aspects of the antibiotic regimen (duration, choice, route, timing).

Conclusion: This multicentre practice testing of IQIs identified improvement targets for stewardship efforts for both structure and process aspects of antibiotic care (approval system for restricted antibiotics, documentation of antibiotic plan). These results can guide the design of future PPS studies and a more extensive evaluation of the clinimetric properties of the IQIs.

Introduction

In Europe, about a third of antibiotic prescriptions in the hospital setting are still considered inappropriate [1,2]. Antibiotic stewardship programmes aim at improving antibiotic use to optimize patient outcome and reduce unintended consequences (e.g. *Clostridioides difficile* infection, the development of resistance, increased healthcare costs) [3].

Monitoring the quality of hospital antibiotic use is a key element of an effective antibiotic stewardship programme and can be achieved using quality indicators which are valuable for assessing responsible antibiotic use and for visualizing variation in antibiotic use practices across different hospitals and regions [4,5]. Both are in turn important for identifying improvement targets for future stewardship efforts. Fifty-one quality indicators were previously developed by the DRIVE-AB project to assess the quality of antibiotic use in the inpatient setting [6]. The inpatient quality indicators (IQIs) were developed using a Delphi method combining evidence from the literature and multidisciplinary international stakeholder opinions. Altogether, the IQIs for responsible antibiotic use cover a wide range of 19 different themes (e.g. access–availability, evidence-based guidelines). These inpatient QIs are generic, i.e. intended to be universally applicable, regardless of infectious disease type, geographical or socio-economic setting. Thus far, there is a paucity of data on the implementation of these DRIVE-AB IQIs in clinical practice. Only a selection of the IQIs relevant for assessing empiric antibiotic sepsis therapy (i.e. eight out of a total of 51) has been evaluated in a single hospital in Belgium [7].

A low-threshold approach for implementing quality improvement projects is to join programmes that are already in place at the healthcare facility. An example is the infection risk scan (IRIS) that provides insights into the performance of infection control and appropriateness of antibiotic therapy, thereby identifying improvement potential [8]. IRIS is carried out using point-prevalence survey (PPS) data and has already been performed in several inpatient settings including hospitals in the Netherlands and the USA [8,9].

This study aims to test the generic DRIVE-AB IQIs for responsible antibiotic use and assess their value in identifying stewardship improvement targets in hospitals in the Dutch–Belgian border area.

Methods

Study design and setting

An observational cross-sectional multicentre study was performed to assess the first-time use of the DRIVE-AB IQIs in nine hospitals (three Belgian university hospitals, one Dutch university hospital, three Dutch teaching hospitals and two Dutch general hospitals) in the Dutch–Belgian border area using IRIS and participating in the i-4-1 Health project (Supplementary Table S1) [10,11]. The i-4-1 Health project is a European Union (EU) Interreg funded initiative with the aim of broadening the knowledge regarding antimicrobial resistance and use in different healthcare and veterinary settings in the cross-border region of Belgium and the Netherlands [11]. The IRIS tool measures several patient-, ward-, and care-related variables in a standardized way to assess the quality of infection control and antimicrobial use. The implementation of the IRIS in these nine hospitals is reported elsewhere [11]. Our study focused on the antibiotic therapy section of the IRIS. An overview of the included wards is shown in Supplementary Table S2.

Data collection

The DRIVE-AB inpatient quality indicators for responsible antibiotic use were developed using a RAND-modified Delphi method [6]. First, 70 distinct potential generic IQIs were identified by a systematic review of the literature. Then, the relevance of these IQIs to assess responsible antibiotic use in the patient setting was appraised by a multidisciplinary international stakeholder panel. This was done through two questionnaires and an in-between face-to-face consensus meeting. A total of 25 international stakeholders with diverse backgrounds (i.e. medical community, public health, patients, antibiotic research and development, regulators and governments) assessed the 70 distinct potential generic IQIs. Ultimately, 51 IQIs were selected in consensus [6]. A systematic review published during the preparations for this study concluded that the DRIVE-AB were the most comprehensive set of QIs for the inpatient setting [12].

Process and outcome IQIs that could not be measured in the PPS were excluded (Supplementary Figure S1). Ultimately, 20 IQIs were included: seven process IQIs, 12 structure IQIs, one IQI originally defined as process IQI was converted to a structure IQI (IQI-33) (Supplementary Table S3). A complete antibiotic plan was defined as including indication, name, doses/interval, route of administration, and duration or stop/review date [6]. An antibiotic formulary was defined as a list of antibiotics that facilitates restriction policies and the pharmacy's stock management [13]. A(n) (local) antibiotic (clinical) guideline was defined as 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances' [14].

Data for process IQIs were obtained from a PPS performed within all nine hospitals of the i-4-1 health project from October 2018 through the end of December 2018. For each hospital, only one set of PPS data was collected and used for the analysis. The PPS followed the methodology from the Global Point Prevalence Survey of Antimicrobial Consumption and resistance (GLOBAL-PPS) guidance [2,15]. All adult (aged ≥18 years) inpatients were asked to participate in the PPS. For all consenting patients, antibiotic prescription data were extracted retrospectively from the medical records and added in the IRIS digital registration form. All systemic antibiotic prescriptions were identified at 8.00 CET on the day of the PPS. Preferentially, minimally 50 patients per hospital ward and four wards per hospital were to be included. Data extraction from medical records was done by infection control practitioners and antibiotic prescriptions assessment was done by the medical microbiologist from the hospital involved with the PPS. The questions guiding the data extraction and assessment of the antibiotic prescriptions are shown in Supplementary Table S4. Appropriateness of prescriptions was assessed based on local guidelines or expert opinion. In each hospital, one single medical microbiologist that was not involved in the prescription decision assessed the antibiotic prescriptions. The results of the prescription assessments were discussed with the prescribing physicians to reflect on and identify potential stewardship targets. Prior to the PPS data collection, the staff members involved with the study from each hospital followed several training sessions and data validation visits were held to ensure high quality data.

Structure indicators were translated into a web-based questionnaire using Qualtrics (Provo, UT, USA). At the start of the PPS in October 2018, invitations to participate were sent to the medical microbiologists of the i-4-1-Health consortium who were involved in the PPS. For some questions medical microbiologists were asked to contact the hospital pharmacy to provide the more detailed answers possible. Participants received the questionnaire link by email. Alternatively, participants could schedule a phone meeting with one of the researchers (A.M.) to answer the questionnaire verbally.

Data analysis

Standard descriptive statistics in SPSS version 25 (IBM, Chicago, IL, USA) were used to analyse the compliance scores for structure and process IQIs. Potential room for improvement measures the sensitivity of a potential indicator to detect variability in the quality of care. It is expressed as 100% minus the compliance score [16]. Improvement potential was considered 'low' if the performance scores of all hospitals were >85% in agreement with others [17]. Missing data in the IRIS database were interpreted as not documented in the medical records. Missing data were included as a separate category in the analysis of compliance for the two IQIs on documentation (IQI-8 and IQI-9) but excluded from the analysis for the remaining IQIs.

Ethics

Written or verbal informed consent was obtained from patients and the medical microbiologists answering the questionnaire on the structure QIs. All patient data were processed anonymously. The study protocol was reviewed by the Medical Research and Ethics Committee of the University Medical Center Utrecht (Protocol Number 17–426C), the Medical Research and Ethics Committee of the Maastricht University Medical Center+ (METC 2017–0115 and METC 2017–0116) in the Netherlands and the Ethics Committee of the University Hospital Antwerp (B300210733784), the Ethics Committee of the University Hospital Ghent (B670201733428), and the Ethics Committee of the University Hospitals Leuven (S59580 BD1 and S61807) in Belgium.

Results

Process indicators

A total of 1551 patients from 32 wards in nine hospitals in the Dutch–Belgian border area were included in this study (Table I; Supplementary Table S2). This corresponds to an overall participation rate of 65.9%. Of those 1551 patients, 582 (37.5%) received at least one antibiotic, comprising of 336 (59.1%) in the Netherlands and 233 (40.9%) in Belgium. A total of 697 antibiotic prescriptions were used for process IQI evaluation. The most common indications for antibiotic treatment were community-acquired infection (CAI) (53.4%), hospital-acquired infection (HAI) (26.1%), and surgical prophylaxis (10.2%). A more detailed overview of indications is shown in Supplementary Table S5. The most frequently prescribed antibiotics were amoxicillin with β-lactamase inhibitor (18.1%), piperacillin with β-lactamase inhibitor (10.6%), cefuroxime (9.8%), ciprofloxacin (8.0%), and meropenem (6.0%). A summary of compliance scores for the process IQIs is shown in Table II.

With a score of 94.3%, the performance was highest for the QI on collecting specimens for diagnostics before antibiotic administration. Performance scores for QIs on guideline compliance varied between 74.1% and 82.3% for different aspects of the antibiotic regimen (including duration, choice, route, and timing).

Performance score was lowest for the QI on documenting a complete antibiotic plan in the medical file (58.5%) (IQI-8). The indication, dose and interval, and route were documented in 85.1%, 95.0%, and 94.2% of prescriptions, respectively. The duration of therapy and the date of stop or prescription review were documented in 65.9% and 71.0%, respectively.

Some assessments of the antibiotic prescriptions were based on expert opinion. When accounting for assessment based on expert opinion, which could be considered responsible use, compliance scores increased slightly (Table III).

Structure indicators

Information on structure IQIs was collected for nine hospitals. Seven questionnaires were completed electronically and two were completed during a phone call with one of the researchers (A.M.). Structure indicator performances are shown in Table III.

The highest compliance scores (nine out of nine hospitals) were observed for the IQIs on the availability of electronic evidence-based clinical guidelines (IQI-21) based on national guidelines (IQI-23) and antibiotic stewardship (ABS) pro-

Table I
Crude prevalence of antibiotic therapy (ATC code J01): results of the PPS IRIS-3

Patients and prescribing	No.
Total included patients	1551
Patients receiving antibiotics	569 (36.7%)
No. of prescribed antibiotics	697 (100%)
Belgium	299 (42.9%)
Netherlands	398 (57.1%)
Prescribed antibiotics per patient	
$N = 1$	427 (75.0%)
Belgium	177 (76.0%)
Netherlands	250 (74.4%)
$N = 2$	114 (20.0%)
Belgium	38 (16.3%)
Netherlands	76 (22.6%)
$N = 3$	22 (3.9%)
Belgium	9 (2.7%)
Netherlands	13 (5.6%)
$N = 4$	4 (0.7%)
Belgium	0
Netherlands	4 (1.7%)
$N = 5$	2 (0.4%)
Belgium	1 (0.4%)
Netherlands	1 (0.3%)
Mean (SD)	1.31 (0.6)
Belgium	1.34 (0.7)
Netherlands	1.29 (0.5)
Prescribed antibiotics per clinical indication[a]	
Community-acquired infection	372 (53.4%)
Belgium	176 (47.3%)
Netherlands	196 (52.7%)
Hospital-acquired infection	183 (26.1%)
Belgium	88 (48.1%)
Netherlands	95 (51.9%)
Surgical or medical prophylaxis	71 (10.2%)
Belgium	9 (12.7%)
Netherlands	62 (87.3%)
Other	19 (2.7%)
Belgium	16 (84.2%)
Netherlands	3 (15.8%)
Most frequently prescribed antibiotics	
Belgium	
Amoxicillin + β-lactamase inhibitor[b]	55 (18.4%)
Piperacillin + β-lactamase inhibitor[a]	47 (15.7%)
Meropenem	35 (11.7%)
Ceftazidim	17 (5.7%)
Azithromycin	16 (5.4%)
Netherlands	
Amoxicillin + β-lactamase inhibitor[b]	71 (17.8%)
Cefuroxime	64 (16.1%)
Ciprofloxacin	44 (11.1%)
Cefazolin	34 (8.5%)
Piperacillin + β-lactamase inhibitor[c]	27 (6.8%)

ATC, anatomical therapeutic chemical.
[a] $N = 52$ missing.
[b] Clavulanic acid.
[c] Tazobactam.

grammes (IQI-26). All nine hospitals also indicated the use of selective susceptibility reports by the microbiology laboratory (IQI-4) and at least yearly antibiotic use and antibiotic resistance surveillance (IQI-40). One hospital reported not having an appointed ABS team (IQI-29).

More variation in compliance was observed between hospitals on the organization of education sessions (i.e. target audience) (IQI-17), the presence of an antibiotic formulary (IQI-24), and a restricted antibiotic list (IQI-25) as well as on the frequency of audits (IQI-28) and guideline updates (IQI-22).

The lowest performance scores were observed for guideline recommendations for microbiological investigations (IQI-33) and for the use of an approval system for restricted antibiotics (IQI-25).

Six out of eight hospitals reported antibiotic shortages (IQI-1) in the period of the PPS (Table III). For one hospital, data on availability of antibiotics and restricted antibiotics was missing.

Discussion

This multicentre practice testing of IQIs identified improvement targets for stewardship efforts for both structure and process aspects of antibiotic care. Variable compliance scores were observed for 20 IQIs. The highest compliance scores were observed for structure indicators on the availability of evidence-based clinical guidelines, stewardship programmes, the use of selective susceptibility reports, and at least yearly antibiotic use and antibiotic resistance surveillance. All but one participating hospital reported having an appointed antibiotic stewardship team. The highest compliance scores were observed for process indicators on the collection of specimens before antibiotic administration. These high compliance scores illustrate almost optimal responsible use practices, and these IQIs are thus not useful to identify quality improvement and/or antibiotic stewardship targets in hospitals in the Dutch–Belgian border region. By contrast, IQIs with lower compliance scores offer more improvement potential.

Structure-related improvement targets at the hospital level included adding recommendations for microbiological investigations to the hospital guidelines and implementing an approval system for restricted antibiotics. A worrying finding was the presence of antibiotic shortages in a majority of hospitals. Antibiotics are the second type of drugs most affected by shortages in Europe [18]. Drug shortages have both clinical and financial consequences. Clinical consequences can include antibiotic substitutions (including substitutions with inferior antibiotics), drug rationing, medication error, delay of therapy, and switch in dosing. Financial consequences include more expensive alternative drugs, increased hospital cost, increased pharmacy/personnel cost, and increased costs for patients [19]. Both Belgium and the Netherlands have organizations that keep track of national drug shortages and, in the Netherlands, also provide options for substitutions [20,21]. Unfortunately, despite increasing concern and attention to the issue, shortages are increasing worldwide and became painfully visible during the SARS-CoV-2 pandemic [22–24]. Hospital pharmacists have developed solutions to obtain the missing antibiotics using their network, but ordering abroad invariably increases costs. Understanding the precise impact of the reported antibiotic

Table II
Compliance scores for process inpatient quality indicators (IQIs)

Quality indicators per theme		Results
Total antibiotic prescriptions		$N = 697$
Documentation		
IQI-8	An antibiotic plan[a] should be documented in the medical record at the start of the antibiotic treatment.	Documentation of complete antibiotic plan: 408 (58.5%) Product name documented: 697 (100%) Dose and interval documented: 659 (95.0%) Route documented: 657 (94.2%) Indication documented: 593 (85.1%) Stop or review date documented: 495 (71.0%) Duration documented: 436 (65.9%)
Dosing, interval		
IQI-11	Dosing and dosing interval of antibiotics should be prescribed according to guidelines.	Total compliance: 480 (89.4%)[b] Compliance with guideline: 424 (79.0%) Compliance with expert opinion: 56 (10.4%)
Duration		
IQI-14	Duration of antibiotic therapy should be compliant with guidelines.	Total compliance: 436 (81.1%)[b] Compliance with guideline: 398 (74.1%) Compliance with expert opinion: 38 (7.0%)
Microbiological diagnostics		348 (94.3%)[c]
IQI-32	Specimens for culture from suspected sites of infection should be collected before antibiotic administration.	
Route		
IQI-36	The route of administration of antibiotics should be compliant with guidelines.	Total compliance: 494 (92.0%)[b] Compliance with guideline: 438 (81.6%) Compliance with expert opinion: 56 (10.4%)
IQI-37	Antibiotic therapy in adult patients with sepsis should be started intravenously.[a]	2 (66.7%)
Timing		
IQI-45	Timeliness of administration of antibiotic therapy and prophylaxis should be compliant with guidelines.	Total compliance: 497 (92.5%)[b] Compliance with guideline: 442 (82.3%) Compliance with expert opinion: 55 (10.2%)

[a] A complete antibiotic plan was defined as including: indication, product name, doses/interval, route of administration, and duration or stop/review date [6].
[b] $N = 537$ were assessed for this indicator; see flow of assessment questions in Supplementary Table S4.
[c] Missing $N = 328$, only targeted antibiotic regimens, not empirical, were assessed for this indicator; see flow of assessment questions in Supplementary Table S4.

shortages on quality of care and healthcare expenses was beyond the scope of this study but should be prioritized in the future.

Process-related improvement targets included improving the documentation of an antibiotic plan in the medical records and guideline compliance for the duration of therapy and the choice of antibiotic prescriptions. An interesting finding is that the elements of an antibiotic plan or antibiotic regimen were documented heterogeneously. Indeed, the name of the antibiotic, and the dose, interval, and route of therapy were documented more frequently than the duration of treatment or the stop or review date for the prescription.

Documentation scores in our study were comparable with a previous Dutch study, and slightly higher than when compared to the prevalence found in two recent European PPS studies [2,17,25]. Our study points to a lower reporting of the duration of treatment or the stop or review date compared to other elements of the antibiotic plan. Regarding guideline compliance, more aspects (i.e. choice, dosing, duration, route, and timing) were explored in our PPS study compared with the literature. Indeed, the recent global PPS compliance with guidelines was limited to the choice of antibiotic, and compliance to guidelines was not assessed in the European PPS [2,25]. Collecting more detailed data on documentation practices and guideline compliance aspects is valuable for identifying specific improvement targets and narrowing the focus of future quality improvement efforts.

In our study, six out of 20 QIs were not helpful to identify improvement targets (IQI-4, -21, -23, -26, -29, and -40) for the Dutch–Belgian hospital setting. Previous work by Van den Bosch and colleagues assessed the clinimetric properties of 11 QIs (nine process and two structure IQIs) in daily clinical practice in

Table III
Compliance scores for structure inpatient quality indicators (IQIs)

Structure inpatient quality indicators per theme		Results (total $N = 9$ hospitals)
Access—availability		
IQI-1	Antibiotics from the antibiotic formulary[a] should not be out of stock at the healthcare facility.	Antibiotics out of stock (on day of questionnaire)[b]: **Yes ($N = 6$)**; antibiotic out of stock ordered abroad: • Yes ($N = 4$) • No ($N = 2$) **No ($N = 2$)** Antibiotics reported as out of stock: erythromycin, pheneticillin, clarithromycin, flucloxacillin, cefotaxime, aztreonam, benzylpenicillin (penicillin G), cotrimoxazole.
Antibacterial spectrum		
IQI-4	The microbiological laboratory should report individual selective susceptibility report (or antibiogram) adapted to local guidelines.	**Yes ($N = 9$)**
Education		
IQI-17	Educational sessions about practice guidelines should be organized for medical staff and should have a predetermined attendance target.	**Yes ($N = 6$)**; attendance target: • interns/residents $N = 1$ • new employees $N = 2$ • all prescribing physicians $N = 1$ • no predetermined attendance target $N = 2$ **No ($N = 3$)**
Evidence-based guidelines		
IQI-21	A local antibiotic guideline should be present at the healthcare facility.	**Yes ($N = 9$)** (electronic format): • Use of regional guidelines in $N = 2$
IQI-22	An evaluation whether an update should be considered for the local antibiotic guideline once a year.	Yes ($N = 6$), frequency of updates: • Continuously/depending on regional or national updates ($N = 4$) • Monthly ($N = 2$) **No ($N = 3$)**, frequency of updates: • Project-based ($N = 1$) • Every 2 years ($N = 1$) • Every 3 years ($N = 1$)
IQI-23	The local guidelines should correspond to the national guideline but should be adapted based on local resistance patterns.	**Yes ($N = 9$)**: • $N = 6$ Dutch hospitals mention SWAB guidelines • $N = 3$ Belgian hospitals mention BVIKM guidelines
Expertise and resources		
IQI-24	An antibiotic formulary[a] should be available and updated continuously at the healthcare facility.	Availability of antibiotic formulary[b]: **Yes ($N = 6$)**; frequency of updates: • Continuously ($N = 3$) • Monthly ($N = 1$) • Yearly ($N = 2$) • Every 3 years ($N = 1$) **No ($N = 2$)**
IQI-25	An approval system should be in place for prescriptions of restricted antibiotics at the healthcare facility.	Presence of list of restricted antibiotics[b]: **Yes ($N = 5$)**; approval system: • Yes ($N = 4$) • No ($N = 1$) **No ($N = 3$)** Examples of restricted antibiotics: meropenem, vancomycin, piperacillin/tazobactam, rifampicin, linezolid, moxifloxacin

Table III (*continued*)

Structure inpatient quality indicators per theme		Results (total $N = 9$ hospitals)
IQI-26	An antibiotic stewardship programme (antibiotic prescribing control programme and/or antibiotic prescribing policy) should be in place at the healthcare facility.	**Yes ($N = 9$)**
IQI-28	Audits of antibiotic use by the antibiotic stewardship team should be performed regularly at the healthcare facility.	Audits performed: **Yes ($N = 6$)**; by: • ABS team ($N = 5$) • microbiologist and infection control team ($N = 1$) **No ($N = 3$)**
IQI-29	A multidisciplinary antibiotic stewardship (ABS) team appointed by the healthcare facility management should have meetings at least twice a year and make a report with objectives and selected performance indicators.	Presence of an ABS team: **Yes ($N = 8$)** Names of ABS team: • Antibiotic stewardship team ($N = 1$) • A(ntibiotic)-team ($N = 3$) • Antibiotic policy group ($N = 2$) • Multidisciplinary infections team ($N = 1$) • Not specified ($N = 1$) Multidisciplinary composition of ABS team: • Yes ($N = 8$) Appointed by hospital management: • Yes ($N = 6$) • No ($N = 2$) Reports: • Yes ($N = 7$) • No ($N = 1$) **No ($N = 1$)**
Microbiological diagnostics		
IQI-33	Hospital guideline should recommend which specific microbiological investigations should be performed.[c]	**Yes $N = 3$** (e.g. pneumonia) **No ($N = 6$)**
Surveillance		
IQI-40	Surveillance of antibiotic use and resistance should be performed at least once per year at the healthcare facility.	**Yes ($N = 9$)**

SWAB, Dutch Working Party on Antibiotic Policy; BVIKM, Belgian Society for Infectiology and Clinical Microbiology.
[a] An antibiotic formulary was defined as a list of antibiotics that facilitates restriction policies and stock management by the pharmacy [13].
[b] Hospital pharmacy missing data for one hospital.
[c] Process IQI converted to a structure IQI.

22 hospitals in the Netherlands using PPS data collected in 2011–2012 [17]. Of the 11 tested QIs, seven showed sound clinimetric properties, and four presented unsatisfactory results.

To our knowledge, this study is the first international and multicentre practice testing of the DRIVE-AB generic IQIs for responsible antibiotic use to assess their value in identifying stewardship improvement targets. Our collaboration with the IRIS team allowed for the efficient use of resources for data collection (i.e. infection control practitioners and medical microbiologists). Furthermore, the practice testing of the IQIs together with the IRIS stimulated interdisciplinary collaboration on antibiotic use (i.e. infection control practitioners, medical microbiologists, prescribing physicians, and pharmacists) and involved reflections on local prescription practices through feedback reports. Targets for quality improvement efforts were successfully identified for both structure and process aspects of antibiotic care (i.e. approval system for restricted antibiotics, documentation of antibiotic plan). Using the standardized IQIs developed by the DRIVE project should facilitate informative comparisons over time both within and between different hospitals and reduce the large variation in measures and indicators of responsible antibiotic use described in the literature [26]. Indeed, the IQIs can be used as outcomes for future antibiotic stewardship intervention studies in the nine hospitals. As antibiotic use drives unintended consequences including side-effects and the development of resistance, stewardship interventions are important to improve individual patient outcomes and to safeguard antibiotic effectiveness for future patients.

The limitations of this study should be addressed. First, the use of only a subset of the 51 IQIs (i.e. 41%) was feasible. Indeed, not all IQIs could be assessed using a cross-sectional study design and we had to consider the limited timeframe and resources available for this study. However, despite the inclusion of only a subset of IQIs, several improvement potentials and targets were identified to guide future ABS implementation projects. Indeed,

the subset tested in this study should be seen as a first step or pilot study and the numbers of IQIs can be expanded in future PPSs. Second, patient participation differed across different wards and hospitals (Supplementary Table S2). The aim to include a minimum 50 patients per ward and four wards per hospital for statistical relevance could not systematically be achieved for all hospitals. This can be explained by the variation in size between the participating hospitals and wards. While it might have influenced the overall antibiotic prevalence it is not expected to have impacted the quality of the data used in our analysis. Another point is the assessment of the antibiotic prescriptions by the medical microbiologist. Intra-rater variability is expected to be small because the assessment was performed by only one person (not the prescriber) or, in larger hospitals, by a team. Furthermore, guidelines could differ between hospitals due to local epidemiology. Also, clinical experience can vary among microbiologists and it remains unclear how much inter-rater variability affected our dataset. The fact that the results of the assessments were fed back to the prescribing physicians should be considered a useful stewardship practice to improve the quality of antibiotic prescribing. Finally, the missing data across the reported results highlight the need for improving the data collection process and the need for a multidisciplinary collaboration for this type of study. Additional efforts should be undertaken to minimize missing data in the design of future PPS studies.

This work led to the following recommendations for future PPS studies: (i) use standardized tools to collect and report data (e.g. IRIS and the DRIVE-AB IQIs) to facilitate informative comparisons over time both within and between different hospitals; (ii) collect more detailed data on documentation practices and guideline compliance for different aspects of the antibiotic prescription (i.e. choice, dosing, duration, route, and timing); (iii) minimize missing data. Other recommendations for future work are (iv) to explore the impact of antibiotic shortages on quality of care and healthcare expenses and (v) to conduct additional evaluations of the clinimetric properties of the DRIVE-AB IQIs in different healthcare and geographical settings.

This multicentre practice testing of IQIs allowed identification of improvement targets for stewardship efforts for both structure and process aspects of antibiotic care in hospitals in the Dutch—Belgian border region. In addition, these results can guide the design of future PPS studies and a more extensive evaluation of the clinimetric properties of the IQIs.

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Author contributions

A.A.M., I.W., J.K and I.C.G. co-designed the study. A.A.M. sent the questionnaire and conducted the interviews. I.W., M.K. and J.K. led the data collection of the IRIS PPS. A.A.M, V.D and I.G. analysed the data and drafted the manuscript. All authors have critically reviewed and approved the final manuscript.

Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2022.07.030.

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