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Measuring broad-spectrum antibiotic use in hospitals with established versus new indicators

ORIGINAL ARTICLE

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BACKGROUND

The target of a 30 % reduction in the use of broad-spectrum antibiotics in hospitals from 2012 to 2020 was not achieved, measured using the standard indicator of defined daily doses (DDD) per 100 bed days. We wished to investigate the reliability of the standard indicator and of selected alternative indicators for antibiotic use, and to determine the actual reduction in use.

MATERIAL AND METHOD

We included ten DDD-based indicators with adjustment for combinations of activity marker, admission category (inpatient vs. all admissions), and case mix, and evaluated these according to how each indicator correlated with antibiotic resistance in a self-developed model. We then calculated use of broad-spectrum antibiotics in hospitals for the period 2012–20 with indicators deemed valid, and compared these indicators with regard to change in use and

ranking of hospitals according to use. We used consumption rate (DDD per 1000 inhabitants per day) as an activity-neutral reference indicator (national and regional).

RESULTS

All the indicators for antibiotic use showed a strong correlation with resistance. For five indicators the correlation was statistically significant. Of these, the indicator that combined adjustment for the total number of admitted patients and case mix accorded best with the consumption rate (35.6 %). The same indicator also showed the largest reduction in use (29.3 %) and gave the most hospitals that achieved a reduction of at least 30 % (13 of 22).

INTERPRETATION

Combined adjustment for number of admitted patients and case mix represents a new, robust indicator for antibiotic use that is suitable for hospitals at all levels. The indicator can be used in parallel with the consumption rate, and consideration should be given to introducing the latter as the new standard indicator at national and regional level.

Main findings

The case mix index (average DRG weight per admission) was positively correlated with antibiotic use.

Additional adjustment for case mix improved accordance with the consumption rate.

The true reduction in the use of broad-spectrum antibiotics in hospitals in Norway in the period 2012–20 was close to 30 %.

Antimicrobial resistance is a threat to global public health and is driven mainly by use of antibiotics (1). One of the key goals of the 'Action Plan against Antibiotic Resistance in the Norwegian Health Service' was therefore to reduce the use of five selected groups of broad-spectrum antibiotics in Norwegian hospitals by 30 % between 2012 and 2020 (2). This goal was included in the clinical commissioning documents for hospitals in Norway. Neither the action plan nor the commissioning documents for the period in question specified which indicator should be used to evaluate whether the goal had been achieved; however, the Norwegian Directorate of Health used defined daily doses (DDD) per 100 bed days as their standard indicator (3).

In 2020, Norwegian hospitals used 31 % fewer DDD of broad-spectrum antibiotics than in 2012, but because the number of bed days also decreased by 19 % in the same period, the reduction in antibiotic use was only 15 % when measured as DDD per 100 bed days. The goal of a 30 % reduction was therefore extended until 2022, despite uncertainty over the reliability of the standard indicator (4, 5).

There is currently no international consensus on the most suitable indicator for monitoring and benchmarking antibiotic use in hospitals (6, 7), but the European Centre for Disease Prevention and Control (ECDC) uses the consumption rate (DDD per 1000 inhabitants per day) for surveillance of antibiotic use both in the community and in hospitals (8). This provides an activity-neutral, population-adjusted measure of antibiotic use and allows for comparisons across sectors and between countries. However, the consumption rate is considered unsuitable as an indicator of antibiotic use in individual hospitals (6). A key reason for this is that hospitals often treat patients from outside their own catchment areas, and the number of inhabitants within a hospital's catchment area will therefore not correspond exactly to their patient population.

Because the standard indicator 'DDD per 100 bed days' is affected by variation between hospitals and over time in the length of hospital stays, some have argued for the parallel use of indicators with other adjustment factors, typically DDD per admission (4, 5). Because increased patient complexity is associated with greater antibiotic use, it has also been suggested to use the economic surrogate marker case mix index (CMI) as an additional adjustment factor (7, 9).

Comparison of antibiotic use in hospitals is further complicated by differences in the use of day case admissions, which are defined as hospital admissions but not recorded as bed days. While antibiotics administered to day cases contribute to DDD in the numerator, day cases are not included in the denominator when calculating DDD per 100 bed days or per admission (4). Day cases comprise one-third of all patients admitted to Norwegian hospitals on average (10), and variation in the use of admission categories (inpatient or day case) for a small proportion of these patients could have a significant impact on calculated antibiotic use. To our knowledge, the effect of including day cases when adjusting for activity has not been investigated.

We wished to shed light on the actual reduction in use of broad-spectrum antibiotics in Norwegian hospitals in the period 2012–20 and to investigate whether there are suitable alternatives to the standard indicator. The study consisted of three parts: 1) establishment of a model for evaluating indicators of antibiotic use in hospitals, 2) validation of a selection of established and new DDD-based indicators with adjustment for various combinations of activity markers, admission categories, and case mix, and 3) calculation of national, regional and local use of broad-spectrum antibiotics in the period 2012–20 with valid indicators, and comparison of changes in use and hospital rankings with different indicators.

Material and method

Indicators

We evaluated ten indicators of antibiotic use in the hospital sector: five established (including the standard indicator) and five novel (Box 1 and Table 1). All were based on DDD, with adjustment for various activity markers (A =

number of bed days, B = number of admissions, C = number of patients). We distinguished between indicators that adjusted for inpatient admissions (A1, B1, C1) versus all admissions (B2, C2), i.e., both inpatient and day case admissions. A suffix (p) indicates additional adjustment for case mix.

Box 1 Included indicators of antibiotic use in hospitals. DDD = defined daily doses, CMI = case mix index (average DRG weight per admission).

Reference indicator

Indicator used for European surveillance of antibiotic use in the community and in hospitals (8). Used in the current study to establish a reference correlation and as an activity-neutral basis for comparison.

Consumption rate: DDD / 1000 inhabitants / day

Standard indicator

Indicator used to assess goal achievement in relation to the 'Action Plan against Antibiotic Resistance in the Norwegian Health Service' (2, 3).

A1: DDD / 100 bed days

Alternative indicators

A selection of previously described (7) and novel (this study) indicators.

A1p: DDD/100 bed days/CMI (7)
B1: DDD/inpatient admission (7)
B1p: DDD/inpatient admission/CMI (7)
B2: DDD/admission
B2p: DDD/admission/CMI
C1: DDD/inpatient (7)
C1p: DDD/inpatient/CMI
C2: DDD/patient
C2p: DDD/patient/CMI

Table 1

Evaluation of indicators of antibiotic use in hospitals. DDD = defined daily doses, CMI = case mix index (average DRG weight per admission). Designations indicate adjustment for activity (A = bed days, B = admissions, C = patients), admission category (1 = inpatient admissions, 2 = all admissions (both inpatient and day case admissions), and case mix (p).

Description of indicators			Evaluation and validation[1]	
Category and designation	Calculation of antibiotic use	Patient basis for adjustment	Pearson's *r*	*p*-value
Reference indicator				
Consumption rate	DDD / number of inhabitants × 1000 / 365	Population size	1.000	0.008

Description of indicators			Evaluation and validation[1]	
Category and designation	Calculation of antibiotic use	Patient basis for adjustment	Pearson's *r*	*p*-value
Standard indicator (3)				
A1	DDD / number of bed days × 100	Inpatient admissions	0.981	0.124
Alternative indicators				
A1 p	DDD / number of bed days × 100 / CMI	Inpatient admissions	1.000	0.013
B1	DDD / number of inpatient admissions	Inpatient admissions	0.999	0.027
B1 p	DDD / number of inpatient admissions / CMI	Inpatient admissions	0.994	0.069
B2	DDD / number of admissions	All admissions	0.989	0.096
B2 p	DDD / number of admissions / CMI	All admissions	0.992	0.079
C1	DDD / number of inpatients	Inpatient admissions	0.995	0.063
C1 p	DDD / number of inpatients / CMI	Inpatient admissions	0.998	0.043
C2	DDD / number of patients	All admissions	0.999	0.033
C2 p	DDD / number of patients / CMI	All admissions	0.999	0.023

[1]Based on the correlation between antibiotic use and resistance, with a highly significant reference correlation between regional consumption rates for piperacillin-tazobactam (ATC group J01CR05) and third-generation cephalosporins (J01DD) in hospitals and regional incidence rates of ESBL-producing E. coli in blood culture (2010–15) as a basis for comparison (see text). Indicators were considered valid if they showed a correlation between antibiotic use and resistance that was at least as strong as that shown by the standard indicator (A1).

To adjust for differences in patient complexity, we used the case mix index, calculated as the average diagnosis-related group (DRG) weight per admission (11). We assessed the validity of using the index for this purpose by analysing the correlation between the index and the use of broad-spectrum antibiotics measured in activity-adjusted DDD in 2019, which was the last year unaffected by COVID-19. In line with the Action Plan against Antibiotic Resistance in the Norwegian Health Service, we defined broad-spectrum antibiotics as the five

ATC groups J01CR (penicillins with an enzyme inhibitor), J01DC (second-generation cephalosporins), J01DD (third-generation cephalosporins), J01DH (carbapenems), and J01M (quinolones) (2).

Evaluation and validation

We wished to evaluate the indicators based on objective criteria, and assumed that there is a causal relationship between antibiotic use and resistance development, and that the resistance-driving effect of antibiotics is dose-dependent (6, 12, 13). Under optimal conditions, a reliable indicator will therefore show a strong correlation between the calculated use of a given antibiotic and the incidence of resistance to that same agent. The strength of this correlation will depend on the extent to which other factors contribute to variation in the incidence of resistance. Furthermore, the correlation will be strongest during periods of stable or increasing antibiotic use because the incidence of resistance declines slowly when antibiotic pressure is reduced (12).

On this basis, we established a reference correlation between the use of carefully selected antibiotics in Norwegian hospitals and the incidence of resistance to those same antibiotics. We based the reference correlation on the consumption rate, which was chosen as an activity-neutral reference indicator for antibiotic use (8), and required the correlation to be plausible, strong and statistically significant. In addition, the reference correlation had to be based on a period for which we had access to quality-assured data for the indicators in question (Table 1).

As a tentative reference correlation, we examined the relationship between regional consumption rates for piperacillin-tazobactam (TZP, ATC group J01CR05) and third-generation cephalosporins (3GC, ATC group J01DD) (TZP/3GC) in hospitals, and regional incidence rates of bacteraemia with extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli*. This correlation is plausible in that these agents select for ESBL (14, 15) and are associated with increased likelihood of ESBL bacteraemia in individuals with gut colonisation (16). We assumed that the use of TZP/3GC outside hospitals, and the use of other antibiotics, as well as the import and spread of ESBL, contributed in only a limited way to regional differences in the incidence of ESBL-*E. coli* bacteraemia. We calculated consumption rates and incidence rates using health regions as the population basis, treating the two northernmost regions with the smallest populations as one region ('Central-North') to reduce the margin of error. We selected a period (2010–15) where the consumption rate in hospitals was stable or increasing in all regions.

We then calculated antibiotic use with each of the indicators using the same data (number of DDD) as had been used to establish the reference correlation, and evaluated each indicator according to the strength of the correlation between regional use of TZP/3GC and regional incidence rates of ESBL-*E. coli* bacteraemia. Indicators that gave rise to a correlation at least as strong as the standard indicator DDD per 100 bed days (A1) were deemed valid.

Use of broad-spectrum antibiotics in hospitals

We calculated the annual use and the percentage change in use of the five groups of broad-spectrum antibiotics described in the Action Plan against Antibiotic Resistance in the Norwegian Health Service (2) (national, regional, and local, 2012–20) using the standard indicator and the alternative indicators that were deemed to be valid. As an activity-neutral basis of comparison (reference indicator), we calculated national and regional consumption rates. Finally, we ranked regional health authorities and acute hospitals based on their use of broad-spectrum antibiotics in 2020 calculated using valid indicators.

Data sources

We based our calculations of antibiotic use in hospitals on data for the sale of antibiotics to hospitals (Hospital Pharmacy Drug Statistics). The proportion of TZP/3GC that was administered in hospitals was calculated via comparison with total sales (Norwegian Institute of Public Health, Norwegian Drug Wholesale Statistics). Consumption rates were based on population figures (Statistics Norway), whereas antibiotic use with other indicators was calculated with the aid of activity data for somatic hospitals (Norwegian Directorate of Health, Norwegian Patient Registry). Incidence rates of ESBL-*E. coli* in blood culture were calculated using data from the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM).

Statistics

We used Excel 2016 for data processing and preparation of figures, and SPSS Statistics 26 for bivariate correlation analyses with calculation of correlation coefficients (Pearson's r) and significance level (two-tailed). We defined p-values <0.05 as statistically significant.

Ethics

All data were anonymous, and approval from an ethics committee or data protection officer was not required.

Results

Case mix and use of broad-spectrum antibiotics

A weak to moderate positive correlation was observed between the case mix index and activity-adjusted consumption, independent of activity marker and admission category (Figure 1). The correlation was statistically significant for three indicators (B1, B2, and C2).

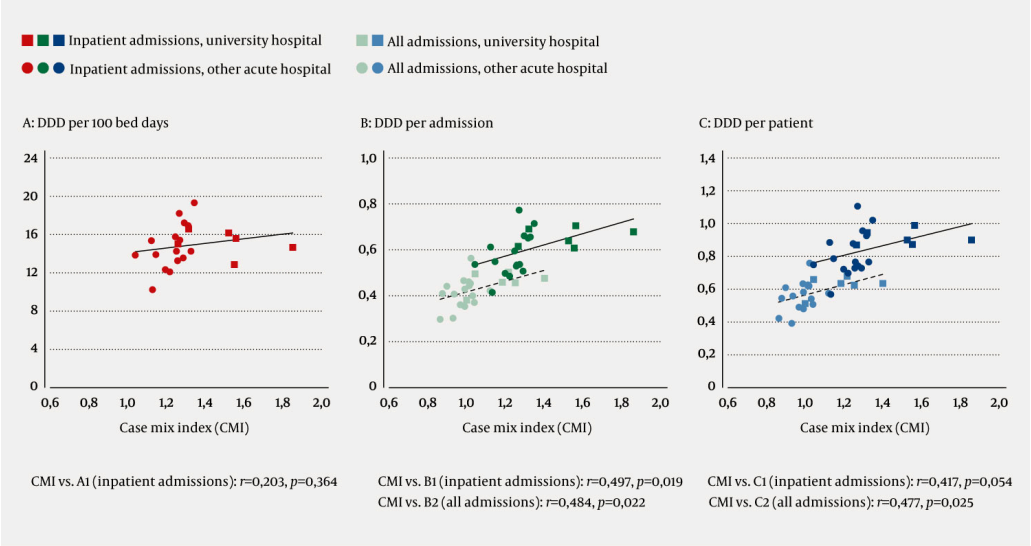

Figure 1 Correlation between the case mix index (average DRG weight per admission) and the use of broad-spectrum antibiotics in 22 acute hospitals in 2019 (activity-adjusted defined daily doses (DDD)).

Reference correlation

Sales to hospitals accounted for 89 % of all DDD of TZP/3GC sold in the period 2010–15. Within hospitals, the relative distribution of TZP and 3GC was 30 % and 70 %, respectively. Consumption rates for TZP/3GC were 0.202 DDD per 1000 inhabitants per day in the Western Norway health region, 0.178 in the South-Eastern Norway health region, and 0.144 in the 'Central-North' health region. The corresponding incidence rates of ESBL-*E. coli* bacteraemia were 16.0, 15.2 and 13.9 cases per million inhabitants per year. An almost perfect, highly significant correlation was observed between TZP/3GC consumption rate and ESBL incidence rate (Table 1).

Evaluation and validation

All indicators showed a strong correlation between calculated use of TZP/3GC in hospitals and the incidence rate of ESBL-*E. coli* bacteraemia, with the correlation statistically significant for five indicators (A1 p, B1, C1 p, C2, and C2 p) (Table 1). Additional adjustment for case mix strengthened the correlation between use and resistance for four of five indicators. All alternative indicators met the validation criterion.

Use of broad-spectrum antibiotics in hospitals

The national consumption rate for broad-spectrum antibiotics (reference indicator) decreased by 35.6 % in the period 2012–20 (Figure 2). Of the indicators evaluated, the standard indicator (A1) showed the smallest reduction in use (14.5 %). Indicators that adjusted for admissions (B1, B2) or for patients (C1, C2) showed highly similar reductions (23.5–24.7 %), independent of whether inpatient admissions alone were considered, or all admissions. Additional adjustment for case mix (A1 p, B1 p, B2 p, C1 p, C2 p) resulted in a 4.1 % greater reduction on average than adjusting solely for activity. Adjusting for both the total number of patients admitted and the case mix (C2 p) resulted in the largest reduction in use (29.3 %) and accorded best with the consumption rate.

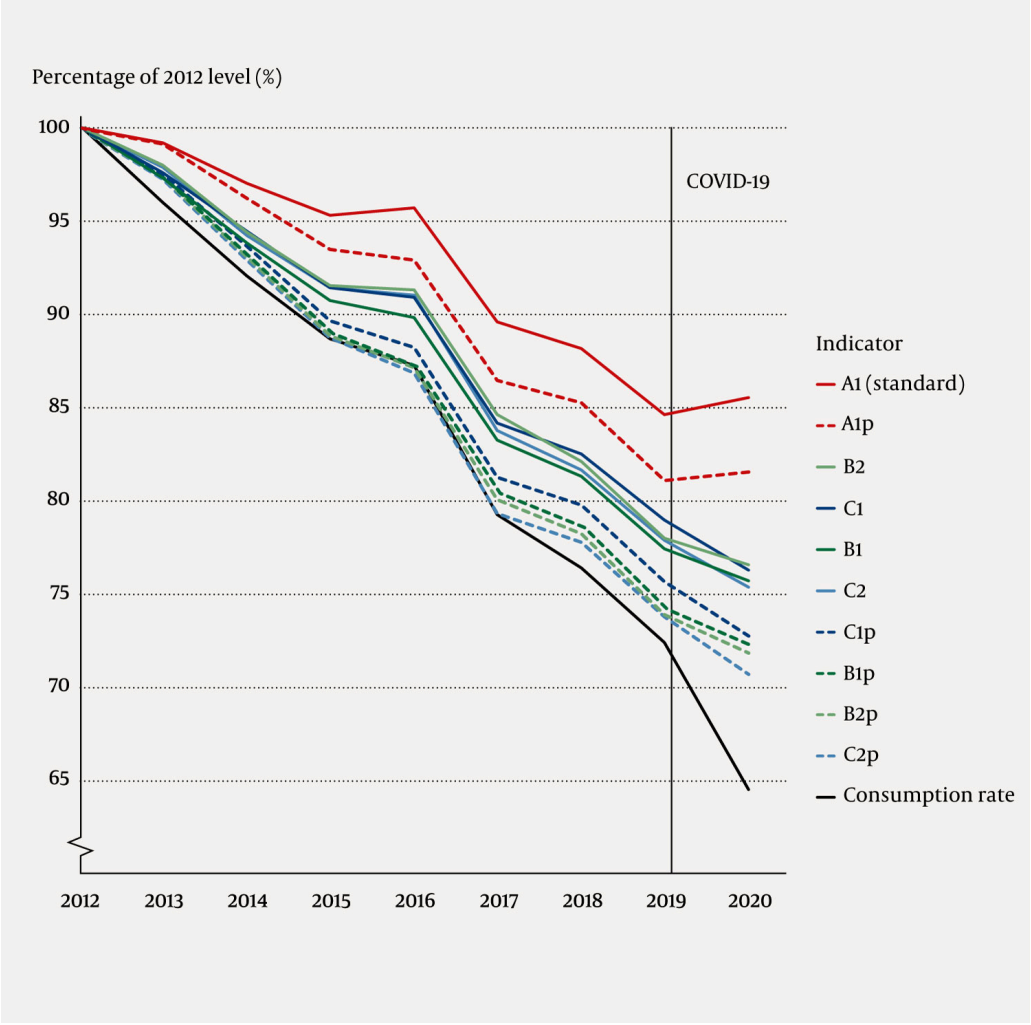

Figure 2 Percentage change in use of broad-spectrum antibiotics in hospitals in the period 2012–20 with valid indicators (Table 1). Solid lines = adjustment for activity (A = bed days, B = admissions, C = patients), dashed lines = additional adjustment for case mix (p). Numbers in the indicator names reflect admission category (1 = inpatient admissions, 2 = all admissions).

The overall pattern was the same at the regional level (data not shown), but the difference between the standard indicator and indicators adjusting for admissions or for patients varied between health regions (smallest difference in Northern Norway, largest difference in Western Norway). Indicators that adjusted for all admissions (B2 and C2) showed reductions in antibiotic use up to 3.0 % lower in Northern Norway and up to 2.9 % higher in Western Norway, compared to indicators that adjusted for inpatient activity alone (B1 and C1). Additional adjustment for case mix resulted in greater reduction in use in all regions, but the reduction varied from an average of 1.1 % in Central Norway to 5.1 % in South-Eastern Norway.

Rankings of regional health authorities and acute hospitals according to their use of broad-spectrum antibiotics varied greatly depending on which indicator was used (Table 2). All regional health authorities achieved at least a 30 % reduction in consumption rate, but only Western Norway achieved a 30 % reduction with at least one of the evaluated indicators (Table 3). The number of hospitals that achieved a 30 % reduction varied from 1 (out of 22) with the standard indicator A1, to 13 with indicator C2 p.

Table 2

Ranking of regional health authorities and acute hospitals according to their use of broad-spectrum antibiotics in 2020 (calculated with valid indicators, Table 1). Order reflects ranking according to use as calculated with the standard indicator DDD per 100 bed days (A1). R = regional health authority, U = university hospital, unmarked = other acute hospital, CR = consumption rate (not calculated for individual hospitals).

Regional health authority and hospital	Ranking by use (from low to high) of broad-spectrum antibiotics[1]										
	A1	A1 p	B1	B1 p	B2	B2 p	C1	C1 p	C2	C2 p	CR
Northern Norway (R)	1	1	4	4	4	4	4	4	4	4	4
Central Norway (R)	2	2	1	2	2	2	2	2	2	2	3
Western Norway (R)	3	4	2	3	1	3	1	3	1	3	2
South-Eastern Norway (R)	4	3	3	1	3	1	3	1	3	1	1
1	1	6	4	8	3	8	1	7	1	5	
2	2	4	1	4	1	1	2	4	2	2	
3 (U)	3	2	14	6	16	7	16	8	17	8	
4	4	5	3	3	6	4	3	3	6	4	
5	5	8	2	5	4	5	4	6	5	7	
6	6	18	5	14	7	16	6	14	8	15	
7	7	9	8	11	10	12	8	10	7	10	
8 (U)	8	3	9	1	11	2	9	2	11	3	
9	9	17	12	19	12	18	12	19	12	19	
10	10	10	7	9	8	9	7	9	9	9	
11	11	12	11	13	2	10	10	12	3	11	
12 (U)	12	1	20	2	18	3	15	1	16	1	
13	13	13	6	7	5	6	5	5	4	6	
14	14	11	10	10	9	11	11	11	10	12	
15	15	19	13	20	13	21	13	20	14	21	
16	16	14	17	18	19	17	18	18	19	18	
17 (U)	17	7	22	12	21	13	21	13	22	13	

Regional health authority and hospital	Ranking by use (from low to high) of broad-spectrum antibiotics[1]										
	A1	A1 p	B1	B1 p	B2	B2 p	C1	C1 p	C2	C2 p	CR
18 (U)	18	16	15	15	14	14	14	16	13	14	
19 (U)	19	15	19	17	22	19	17	15	20	17	
20	20	22	18	22	20	22	20	22	21	22	
21	21	20	16	16	15	15	19	17	15	16	
22	22	21	21	21	17	20	22	21	18	20	

[1]Broad-spectrum antibiotics as defined in the Action Plan against Antibiotic Resistance in the Norwegian Health Service (2). Includes the ATC groups J01CR (penicillins with an enzyme inhibitor), J01DC (second-generation cephalosporins), J01DD (third-generation cephalosporins), J01DH (carbapenems), and J01M (quinolones).

Table 3

Reduction in the use of broad-spectrum antibiotics by regional health authorities and acute hospitals from 2012 to 2020 (calculated with valid indicators, Table 1). Order reflects ranking according to use as calculated with the standard indicator DDD per 100 bed days (A1) in 2020 (Table 2). R = regional health authority, U = university hospital, unmarked = other acute hospital, CR = consumption rate (not calculated for individual hospitals), – indicates <30 % reduction, + indicates 30–39.9 % reduction, ++ indicates ≥ 40 % reduction.

Regional health authority and hospital	Reduction in use of broad-spectrum antibiotics[1]										
	A1	A1 p	B1	B1 p	B2	B2 p	C1	C1 p	C2	C2 p	CR
Northern Norway (R)	–	–	–	–	–	–	–	–	–	–	30.1 %
Central Norway (R)	–	–	–	–	–	–	–	–	–	–	35.3 %
Western Norway (R)	–	–	–	+	+	+	–	+	+	+	39.8 %
South-Eastern Norway (R)	–	–	–	–	–	–	–	–	–	–	34.8 %
1	+	++	++	++	++	++	++	++	++	++	
2	–	–	–	+	–	+	–	+	+	+	

Regional health authority and hospital	Reduction in use of broad-spectrum antibiotics[1]										
	A1	A1 p	B1	B1 p	B2	B2 p	C1	C1 p	C2	C2 p	CR
3 (U)	–	–	–	–	–	–	–	–	–	–	
4	–	–	++	+	++	+	++	+	++	+	
5	–	–	+	+	+	+	+	+	+	+	
6	–	–	–	–	–	–	–	–	–	–	
7	–	–	–	+	–	+	+	+	+	+	
8 (U)	–	–	+	+	+	+	+	+	+	++	
9	–	–	–	–	–	–	–	–	–	–	
10	–	–	–	–	–	–	–	–	–	–	
11	–	–	–	–	–	–	–	–	–	+	
12 (U)	–	–	–	–	–	–	–	–	–	–	
13	–	–	–	–	–	–	–	–	–	–	
14	–	–	+	+	+	+	+	+	+	+	
15	–	–	–	–	–	–	–	–	–	–	
16	–	–	–	–	–	–	–	–	–	+	
17 (U)	–	–	–	–	–	–	–	–	–	–	
18 (U)	–	–	+	+	+	+	–	–	+	+	
19 (U)	–	–	–	+	–	+	–	+	–	+	
20	–	–	–	–	–	–	–	–	–	–	
21	–	+	+	++	+	++	+	+	+	+	
22	–	–	+	+	–	+	+	+	+	+	

[1]Broad-spectrum antibiotics as defined in the Action Plan against Antibiotic Resistance in the Norwegian Health Service (2). Includes the ATC groups J01CR (penicillins with an enzyme inhibitor), J01DC (second-generation cephalosporins), J01DD (third-generation cephalosporins), J01DH (carbapenems), and J01M (quinolones).

Discussion

The absence of a gold standard for measuring antibiotic use in hospitals is reflected in a diversity of indicators and recommendations (6, 7, 17). A literature review in 2015 identified 74 unique indicators, of which 12 were judged suitable by an expert panel through a consensus process (7). Among

those twelve were three of the indicators evaluated in the current study (the standard indicator A1 as well as A1 p and B1). Two further indicators included in our study were considered but rejected by the expert panel (B1 p and C1).

To the best of our knowledge, our study is the first to evaluate indicators for antibiotic use in hospitals according to objective criteria. As a basis for comparison, we used a highly significant reference correlation between regional consumption rates for TZP/3GC in hospitals and the incidence of bacteraemia with ESBL-*E. coli*. Findings from previous studies suggest that the reference correlation reflects a causal relationship (16, 18).

We chose DDD-based consumption rate as an activity-neutral reference indicator, as it is suitable for surveillance of antibiotic use in hospitals across national borders (6). Introduction of the consumption rate as standard indicator for nationwide antibiotic use in hospitals in Norway would be consistent with European practice and facilitate cross-sectoral surveillance, including of antibiotic use in municipal health facilities (6, 8, 13). The demonstration of a strong correlation (the reference correlation) between regional consumption rates for TZP/3GC and the incidence of resistance to the same agents supports the idea that the consumption rate can also be used for surveillance and benchmarking of antibiotic use at a regional level. Ideally, the same indicator should be used at all hospital levels, but the consumption rate is not suitable for use in individual hospitals (6). This issue can be resolved through parallel use of an alternative indicator that correlates well with the consumption rate. We found that all alternative indicators met the validation criterion of a correlation between antibiotic use and resistance that was at least as strong as that observed with the standard indicator. Of the five indicators that showed a significant correlation in our evaluation, the new indicator C2 p (combined adjustment for number of patients admitted and case mix) was notable for showing the greatest accordance with the consumption rate. In contrast to the standard indicator DDD per 100 bed days, the indicator C2 p was also largely unaffected by changes in hospital activity in 2020 as a result of the pandemic.

All indicators that are constructed as fractions will be influenced by factors that affect the size of the denominator, and if such factors (for example population density and the size of the catchment area) vary between hospitals, the usefulness of the indicator for benchmarking will be reduced. This is illustrated by the fact that Northern Norway has the longest hospital stays of the regional health authorities, and the lowest use of broad-spectrum antibiotics measured with the standard indicator (3, 10). Indicators that adjust for number of bed days or inpatient admissions are also vulnerable to confounding by low efficiency and/or poor quality of care. For example, a high number of readmissions can mask high antibiotic use through the increase in size of the denominator. Conversely, improvement measures that result in fewer bed days or inpatient admissions (such as more day case admissions) will increase calculated use. The impact of such factors can be reduced by using the total number of unique admitted patients as an adjustment factor instead.

The case mix index is calculated based on hospital diagnosis coding and is part of the activity-based funding system for hospitals in Norway (11). The positive correlation between the case mix index and the use of broad-spectrum antibiotics indicates that the index reflects differences in patient complexity that affect prescribing of antibiotics. As such factors are often non-modifiable (such as the proportion of patients with infection as their primary diagnosis), use of a smoothing factor would provide a stronger basis for benchmarking (9, 19, 20). However, this principle is rarely applied in practice (7, 17). Our findings are consistent with a Swiss study that found a significant correlation between the case mix index and total antibiotic use in hospitals (9). Although the quality of DRG coding can vary between hospitals, and the case mix index does not compensate for all variation in antibiotic use related to differences in patient complexity, the findings support the use of the index as an adjustment factor.

Our findings illustrate that the current standard indicator should be replaced by other indicators that are better suited for surveillance and benchmarking of antibiotic use in hospitals. Based on the overall performance of the evaluated alternative indicators – taking into account the correlation between antibiotic use and resistance, the accordance with consumption rates, and robustness to variation in activity, quality, and efficiency between hospitals and over time – we consider the most suitable indicator to be one that combines adjustment for the total number of admitted patients and for case mix.

This study has several limitations. In the absence of prescribing data, we had to use sales figures for antibiotics. Our evaluation also relied on a single correlation between antibiotic use and resistance, and the results should be verified by follow-up studies with other reference correlations. Another limitation is that we only evaluated indicators that use DDD as a measure of total antibiotic use, despite the fact that defined daily doses do not always correspond to the doses administered (17, 19).

We conclude that the standard indicator DDD per 100 bed days underestimated the reduction in the use of broad-spectrum antibiotics in hospitals in Norway, and that the actual reduction in the period 2012–20 was close to 30 %. The novel indicator that combines adjustment for the total number of admitted patients and for case mix is reliable, robust, and suitable for hospitals at all levels. The indicator can be used in parallel with the consumption rate, and consideration should be given to introducing the latter as the new standard indicator for antibiotic use in hospitals at national and regional levels.

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