THE LANCET
Infectious Diseases

Supplementary appendix 3

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Catho G, Sauser J, Coray V, et al. Impact of interactive computerised decision support for hospital antibiotic use (COMPASS): an open-label, cluster-randomised trial in three Swiss hospitals. *Lancet Infect Dis* 2022; published online July 20. https://doi.org/10.1016/S1473-3099(22)00308-5.

Supplementary materials

Table S1. Deviation in outcomes from the published protocol

Category of outcome	Outcome component planned	Outcomes component analysed
Primary outcome	• Days of therapy (DOT) of antibiotics[a] per admission	Performed for Geneva and Ticino
Secondary outcomes		
Quantitative antimicrobial use[b]	• DOT per 100 patient-days (PD) • Defined Daily Doses (DDD) per 100 PD and per admission • Antimicrobial days (AD)[c] per 100 PD and per admission • Days per treatment period overall and for specific indications[d]	Performed for Geneva and Ticino
Clinical outcomes	• In hospital mortality • 30 days mortality • Unplanned hospital readmissions within 30 days after discharge • Hospital length of stay • Intensive or intermediate care unit admission from COMPASS wards • Number of infectious diseases consultation	• 30 days in-hospital mortality: performed for Geneva and Ticino (in hospital 30 days mortality) • 30 days mortality: not performed because data not available for death outside the hospital • Unplanned hospital readmissions within 30 days after discharge: performed for Geneva and Ticino: 30 days readmission was changed for 18 days readmission because the data was routinely collected in the billing system in Geneva • Hospital length of stay • Intensive or intermediate care unit admission from COMPASS wards • Number of infectious diseases consultation
Qualitative antimicrobial use	• Concordance of empirical antibiotic therapy with local guidelines (taking into account justified exceptions) with regard to the choice of molecules and duration of treatment • Switch to oral therapy when appropriate • De-escalation of antimicrobial therapy by calendar day 4 of treatment • Treatment adapted to microbiological results	Performed for Geneva and Ticino
Microbiologic outcomes and healthcare associated infections	• Incidence of healthcare facility onset *Clostridium difficile* denominated per 10 000 PD and admission (attributed to unit) • Incident clinical cultures with multi-drug resistant organisms (MRSA, ESBL-E, CPE, VRE, multidrug resistant *P. aeruginosa*) denominated per 1000 PD and admission	• Incidence of healthcare facility onset *Clostridium difficile* denominated per 10 000 PD and admission (attributed to unit) : Performed for Geneva only; data not available in Ticino • Incident clinical cultures changed for incidental bloodstream infection with multi-drug resistant organisms (MRSA, ESBL-E, CPE, VRE, multidrug resistant *P. aeruginosa*) attributed to the unit: performed for Geneva only; data not available in Ticino (numbers very low)
Process outcomes	• CDSS use during the stay in the ward • Delay of use from the first antimicrobial prescribed • Empiric or targeted therapy • Reevaluation process performed	• CDSS use during the stay in the ward • Delay of use from the first antimicrobial prescribed • Empiric or targeted therapy and reevaluation process not collected
Physician satisfaction	• User satisfaction with the system	Performed for Geneva and Ticino
Economic	• Costs of administered antimicrobials (overall and by class) per admission and per admission receiving antibiotics	Not performed, data not available

	• Costs of the intervention • Total costs of hospitalisation	

a

Table S2: CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Page No *
Title and abstract				
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	4/5
Introduction				6
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	6
	2b	Specific objectives or hypotheses	Whether objectives pertain to the the cluster level, the individual participant level or both	
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		6 and supplementary materials
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	9
	4b	Settings and locations where the data were collected		7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	8
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	9, table 2, table S1
	6b	Any changes to trial outcomes after the trial commenced, with reasons		Table 2 and supplementary table S1
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	Supplementary
	7b	When applicable, explanation of any interim analyses and stopping guidelines		Not applicable
Randomisation:				

Sequence generation	8a	Method used to generate the random allocation sequence		8
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	8
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c	Published protocol
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	Published protocol
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	9
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	Supplementary materials "Ethic section" and published protocol
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		Supplementary text S5
	11b	If relevant, description of the similarity of interventions		
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	10, 11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		11
Results				
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	For each group, the numbers of clusters that were randomly assigned, received intended treatment, and were analysed for the primary outcome	Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up		8
	14b	Why the trial ended or was stopped		
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	Table 3

Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	Figure 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	Tables 4, 5, 6
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		Supplementary tables
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		
Discussion				
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	18
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		16, 17
Other information				
Registration	23	Registration number and name of trial registry		2
Protocol	24	Where the full trial protocol can be accessed, if available		6
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		21

Text S1. Details of the participating hospitals

Geneva University Hospitals (HUG) is a tertiary care center with 1 100 patient beds and 26 000 admissions per year in acute-care wards. The 16 participating wards in Geneva (8 internal medicine, 8 geriatric) were included from the internal medicine department located in the main hospital and the 300-bed geriatric hospital in a separate location but with rotation of physicians in training across the two sites and common consultants, and both hospitals were therefore considered as single study site.

The 8 participating wards in EOC (2 surgery and 2 internal medicine wards per site) were recruited from the internal medicine and surgical departments. Antimicrobial stewardship programs are implemented in the three participating hospitals (table 1). All study sites (HUG, Bellinzona, Lugano) have an electronic health record (EHR) and electronic prescribing system with CPOE. The EHR are in-house software, originally developed based on the system from Geneva starting in 2007 but with separate development since then.

The study period was extended in Geneva because of an initial low uptake of the CDSS, which required additional informatics development during the study. The extension was planned until 31 March 2020 but due to COVID-19 the study ended on February 29 2020, after 14 months. The additional informatics feature was launched in September 2019, after 9 months of intervention, and made mandatory the use of the CDSS for a patient transferred into a COMPASS intervention unit and already receiving antimicrobials (previously it was possible to just confirm the prescription started elsewhere).

Table S3. List of secondary outcomes and sources of the data

Category of outcomes	Indicators	Data sources and methodology
Quantitative indicators of antibiotic consumption	Antimicrobial days (AD) by admission	Automatic extraction from the electronic prescribing system
Qualitative indicators of antibiotic prescription (details in appendix Text S4)	• Appropriateness of therapy defined by appropriate choice of the molecule in concordance with local guidelines and taking into account justified deviations • Appropriate duration • De-escalation performed whenever possible • Oral switch performed by day 7 • Treatment adapted to microbiological results	Random selection of 50 patients per ward Manual chart review using a standardised CRF (REDCap) (appendix text S3)
Clinical outcomes	• In-hospital 30-day mortality • Transfer to intensive or intermediate care unit • Hospital readmission within 18 days after discharge from the hospital • ID consultation • Ward length of stay (LOS)	Automatic extraction from the financial hospital database and from the electronic health record
Microbiological outcomes	• Incidence of healthcare associated CDI • Incidence of bloodstream infection with multidrug resistant organisms (carbapenemase-producing Enterobacterales; extended spectrum beta-lactamase producing Enterobacterales; methicillin-resistant *Staphylococcus aureus* (MRSA); vancomycin-resistant enterococci (VRE))	Routine surveillance data
Process outcomes	Uptake of the CDSS	Automatic extraction from the EHR database
User-satisfaction with the system	Online survey (appendix S10)	Distributed by email

CDSS: computerised decision support system, EHR: electronic health record, CRF: case report form, CDI: *Clostridoides difficile* infection

Table S4. Characteristics of the participants at the cluster level (ITT population), including only patients who received antimicrobials during their stay in the participating wards.

	Control (N= 4142)	COMPASS (N= 4578)	Total (N= 8720)
Age (in years), median (IQR)	77 (65 85)	76 (63- 85)	77 (64- 85)
Gender (Female), n (%)	1 992 (48.1)	2 091 (45.7)	4 083
Comorbidities			
Chronic cardiac disease, n (%)	1 274 (30.8)	1 428 (31.2)	2 702
Chronic lung disease, n (%)	1 264 (30.5)	1 322 (28.9)	2 586
Diabetes, n (%)	936 (22.6)	927 (20.2)	1 863
Chronic kidney disease, n (%)	925 (22.3)	899 (19.6)	1 824
Neoplasia, n (%)	205 (4.9)	254 (5.5)	459
Chronic liver disease, n (%)	116 (2.8)	146 (3.2)	262
Immunosuppression, n (%)	106 (2.6)	102 (2.2)	208
HIV/AIDS, n (%)	2 (0.0)	18 (0.4)	20

Table S5. Characteristics of the participants at the cluster level (PP population), including only patients who received antimicrobials during their stay in the participating wards.

	Control (N= 3253)	COMPASS (N=3404)	Total (N= 6657)
Age (in years), median (IQR)	77 (65 85)	76 (63- 85)	77 (64- 85)
Gender (Female), n (%)	1 550 (47.7)	1 568 (46.1)	3 118
Comorbidities			
Chronic cardiac disease, n (%)	1069 (32.9)	1100 (32.3)	2169
Chronic lung disease, n (%)	1034 (31.8)	1020 (30.0)	2054
Diabetes, n (%)	808 (24.8)	702 (20.6)	1510
Chronic kidney disease, n (%)	790 (24.3)	704 (20.7)	1494
Neoplasia, n (%)	169 (5.2)	213 (6.3)	382
Chronic liver disease, n (%)	101 (3.1)	119 (3.5)	220
Immunosuppression, n (%)	82 (2.5)	68 (2.0)	150
HIV/AIDS, n (%)	2 (0.1)	16 (0.5)	18

Text S2. Four components of the intervention

(1) Decision support for the choice of antimicrobial treatment based on indication entry (from a list with the possibility to enter free text) and current, local guidelines with request for an accountable justification in case of guideline deviation (from a list (appendix S8) with the possibility to enter free text);

(2) Alert for self-guided re-evaluation of antimicrobial therapy on calendar day 2 to 4 of therapy with clinical criteria for oral switch displayed;

(3) Decision support for the duration of antimicrobial treatment;

(4) Quarterly feedback delivered by e-mail to physicians working in intervention wards of unit-wide antimicrobial prescribing indicators (details in appendix).

Figure S2. Screen shots of the two CDSS

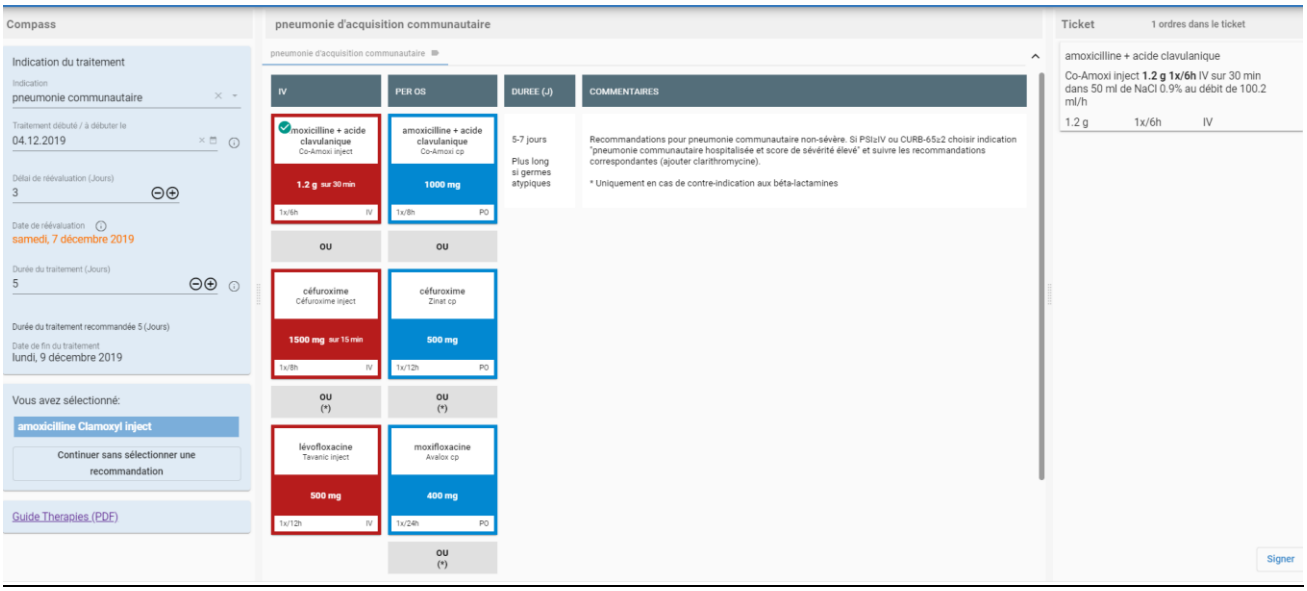

***Figure S2.A. Screen-shot of the CDSS of Geneva**. Example for the indication "community-acquired pneumonia". From left to right (1) selection of the indication of the date for reevaluation and total duration, (2) recommended therapy accorded to local guidelines (in red intravenous / in blue oral), (3) final prescription.*

***Figure S2.B. Screen-shot of the CDSS of Geneva**. Example of a prescription to be re-evaluated.*

At HUG use of the CDSS was initially not mandatory in case of patient's transfer from a non-intervention ward to an intervention ward and already receiving antimicrobials in the previous ward. The electronic prescribing system allowed a simple revalidation of on-going prescriptions without going through the CDSS.

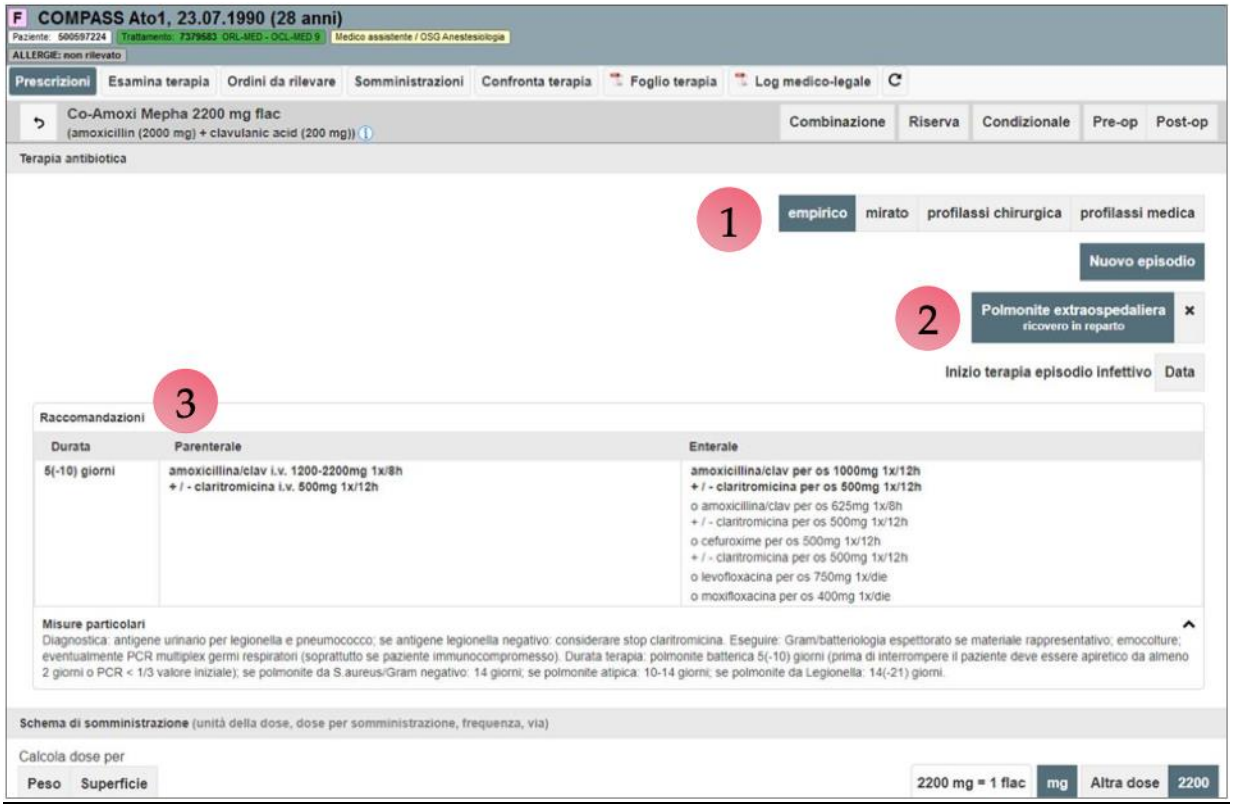

Figure S2.C. Screen-shot of the CDSS of Ticino*. (1) Selection of the type of treatment (empiric/targeted/surgical prophylaxis/medical prophylaxis), (2) selection of the indication, (3) recommended treatment and duration according to local guidelines.*

Figure S3. Examples of feedback reports

Feedback reports were initially planned to be delivered every month, but provided only every four months for two reasons 1) the amount of time needed to extract and analyse the data was longer than expected 2) we realized that the small number of prescriptions per unit per made data aggregated data over four months more meaningful.

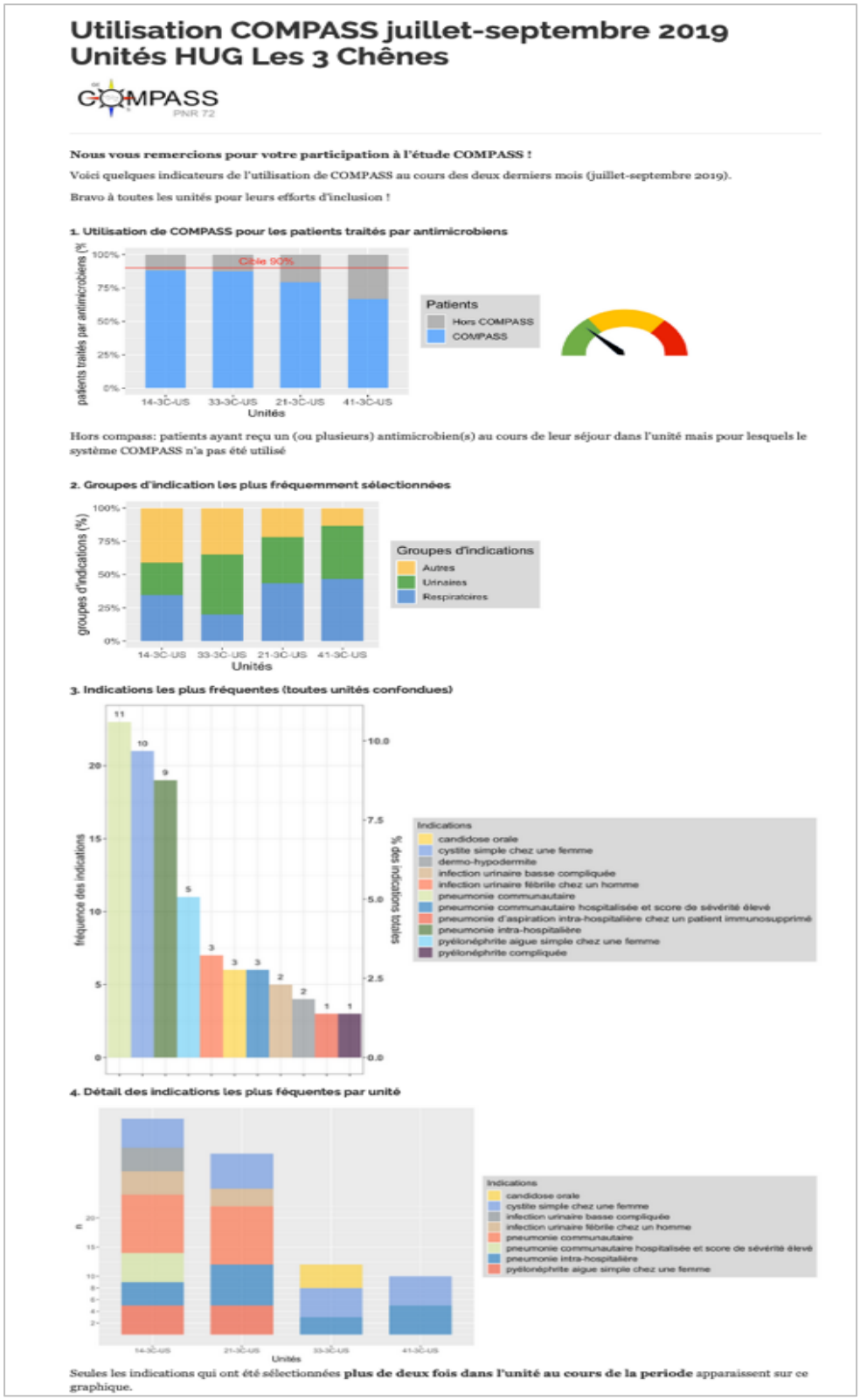

Figure S3.A. Example of feedback report from Geneva*. From top to bottom the report provides (1) the overall use of the CDSS, (2) the most frequently selected group of indications, (3) the most frequently selected indications, (4) the most frequently selected indications by units*

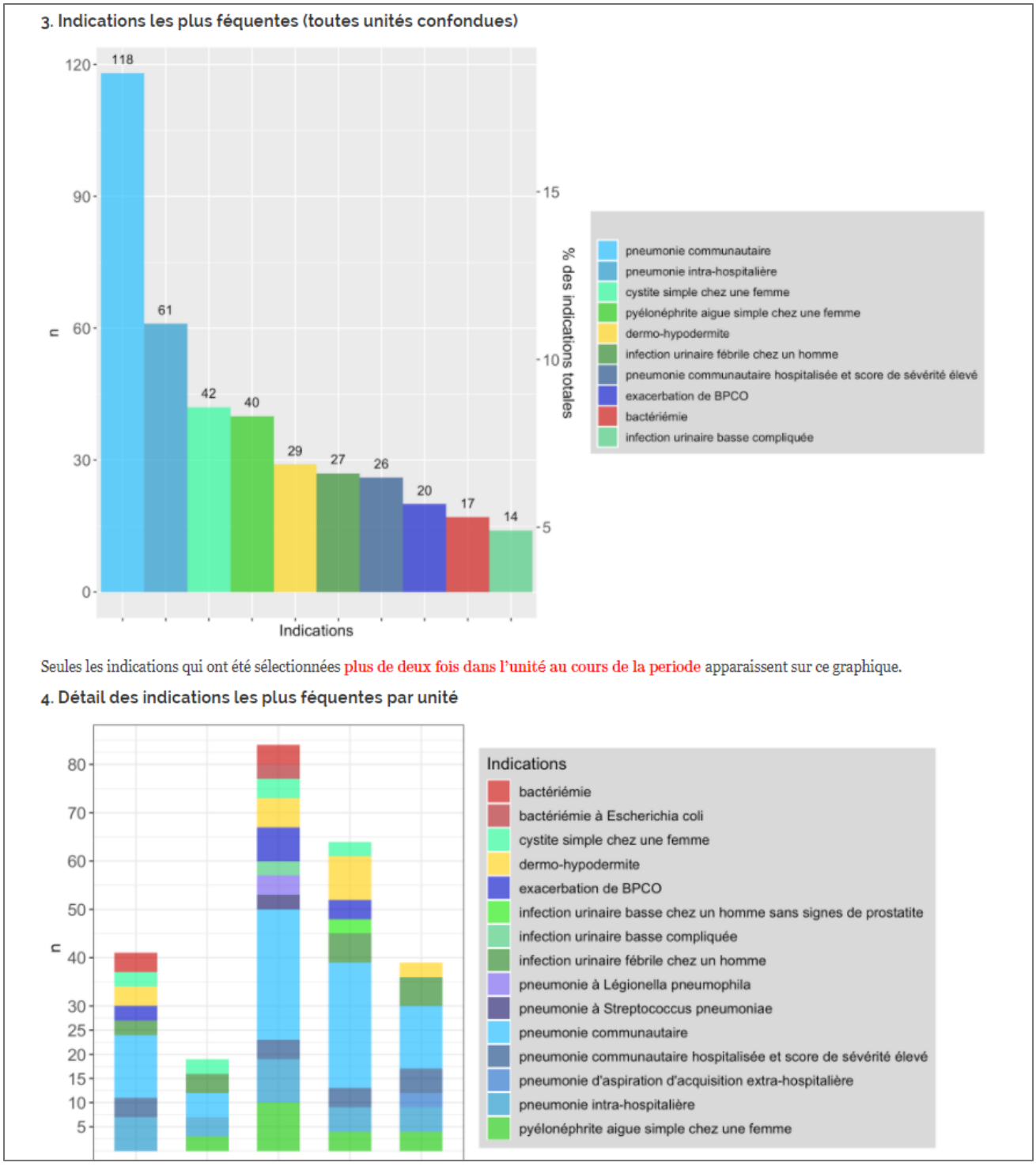

Figure S3.B. Details of feed-back reports from Geneva*. From top to bottom the report provides (1) the most frequently selected indications, (2) the most frequently selected indications by units*

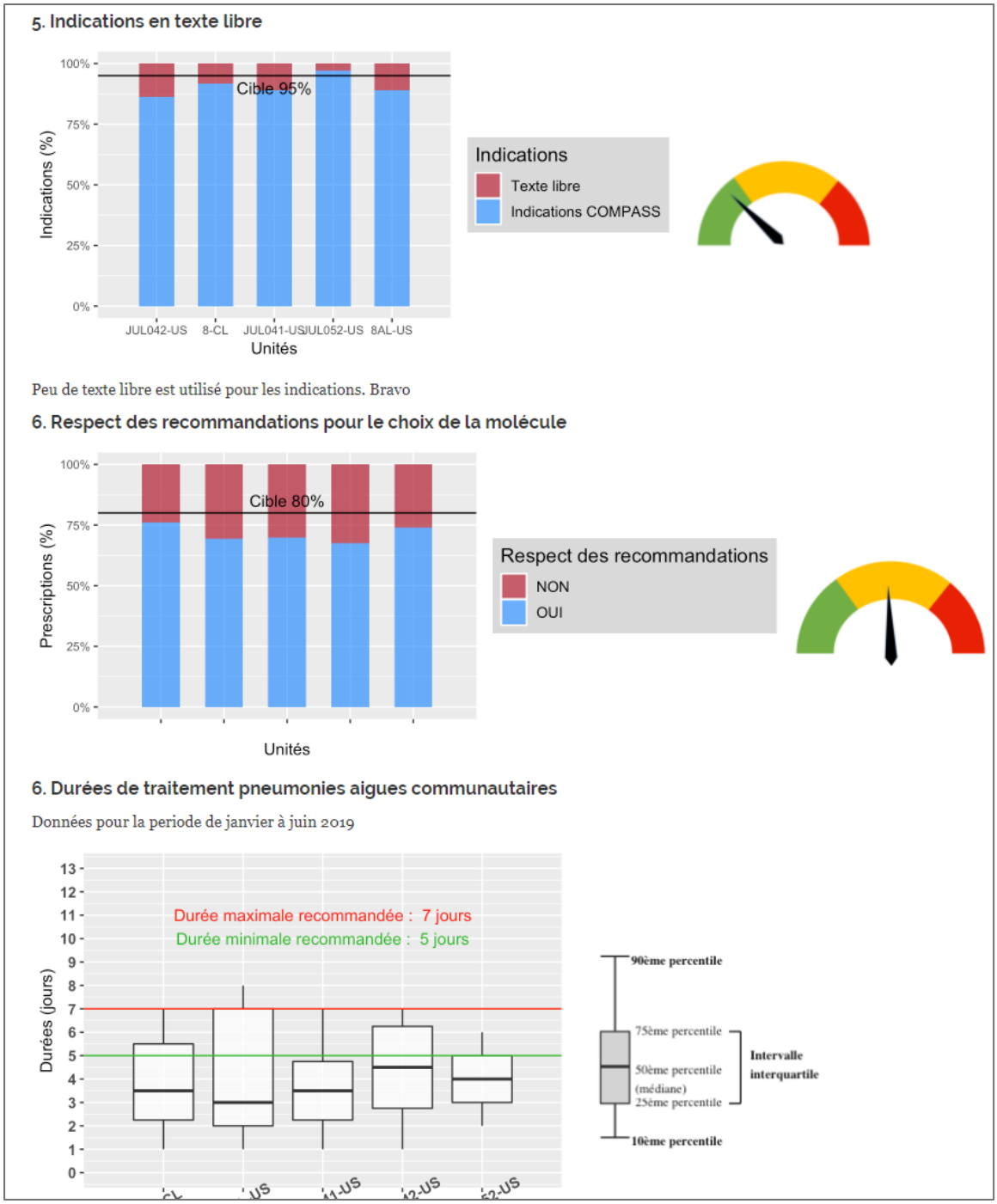

***Figure S3.C. Example of feedback report from Geneva**. From top to bottom the report provides (1) the percentage of indications entered as structured indications (in blue) versus free-text (in red), (2) the percentage of prescriptions who follow the guidelines (blue), (3) the duration of therapy for community-acquired pneumonia by unit (presented as box plot with maximal recommended duration in red and minimal recommended duration in green).*

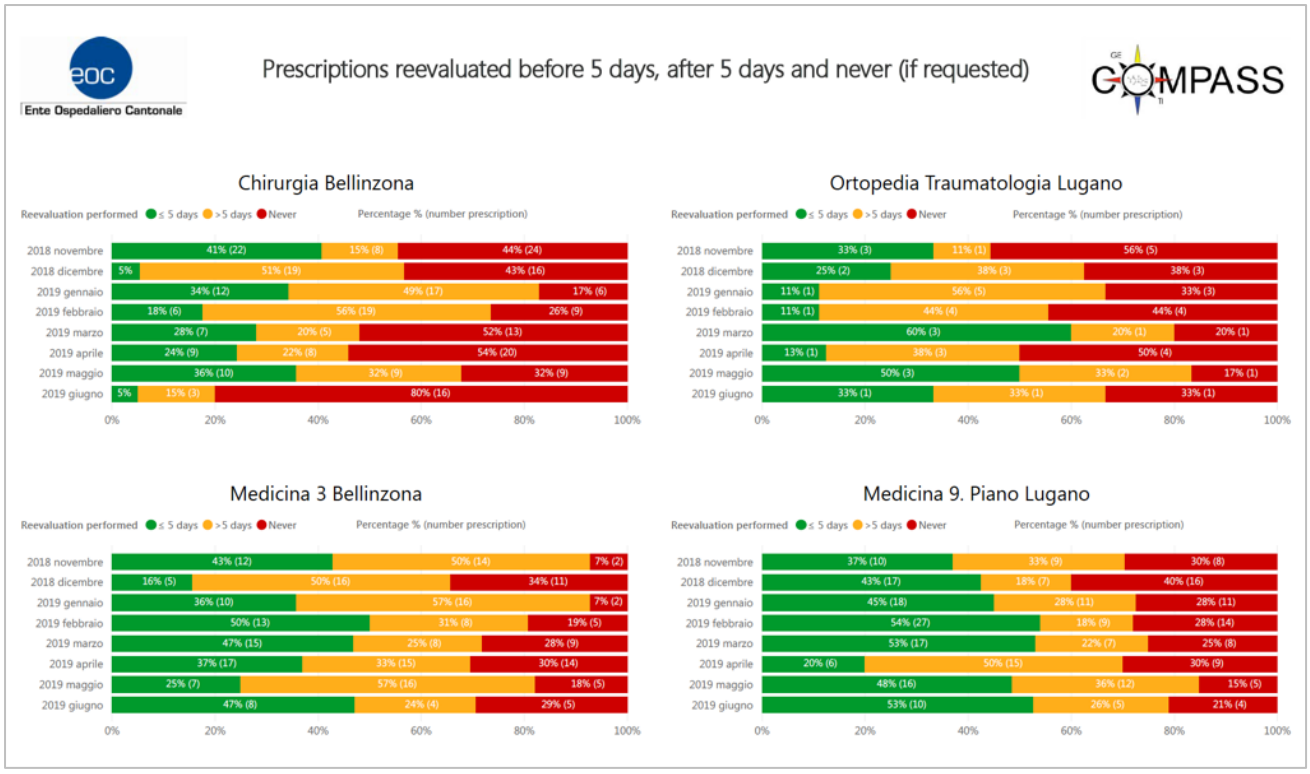

Figure S3.D Example of feedback reports from Ticino. *The report provides the percentage of re-evaluation performed by unit (green: performed within 5 days, orange: performed after day 5, red: never performed)*

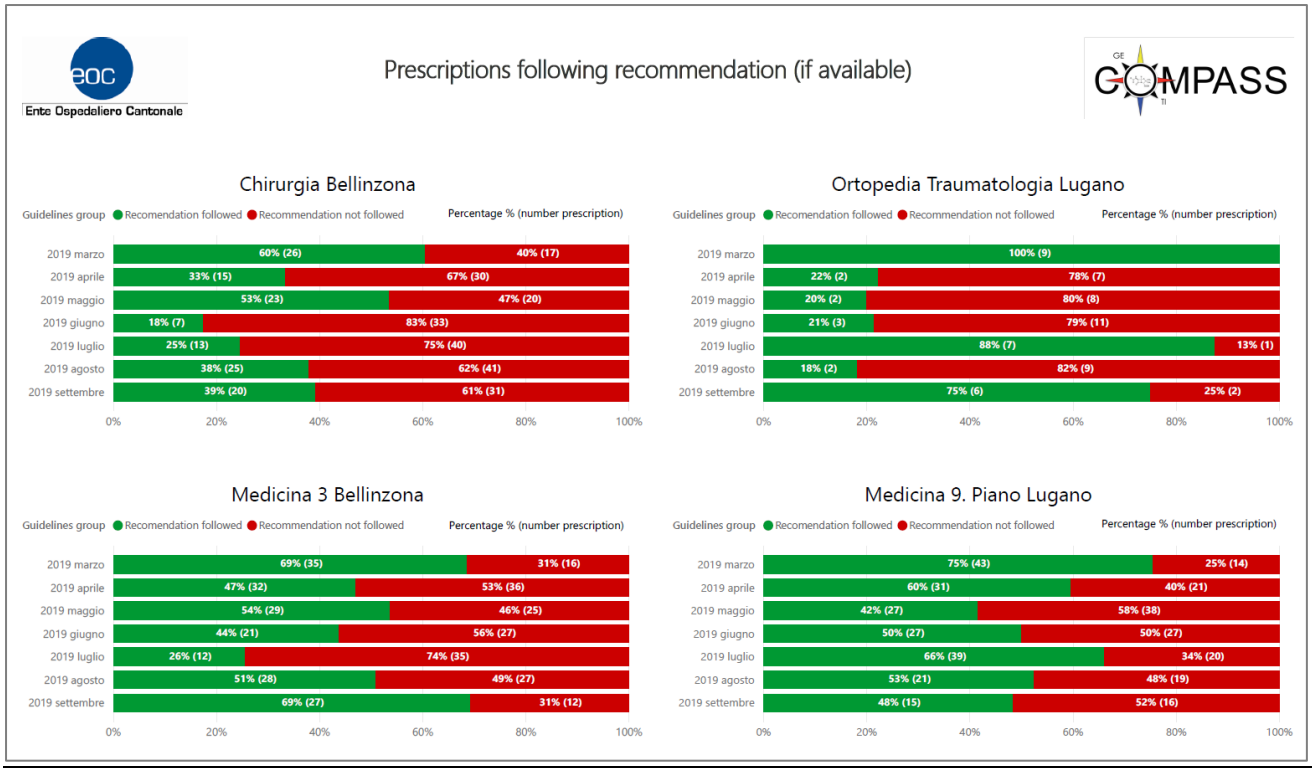

Figure S3.E ***Example of feedback reports from Ticino****. The report provides the percentage of prescriptions who followed the local guidelines (green) by unit*

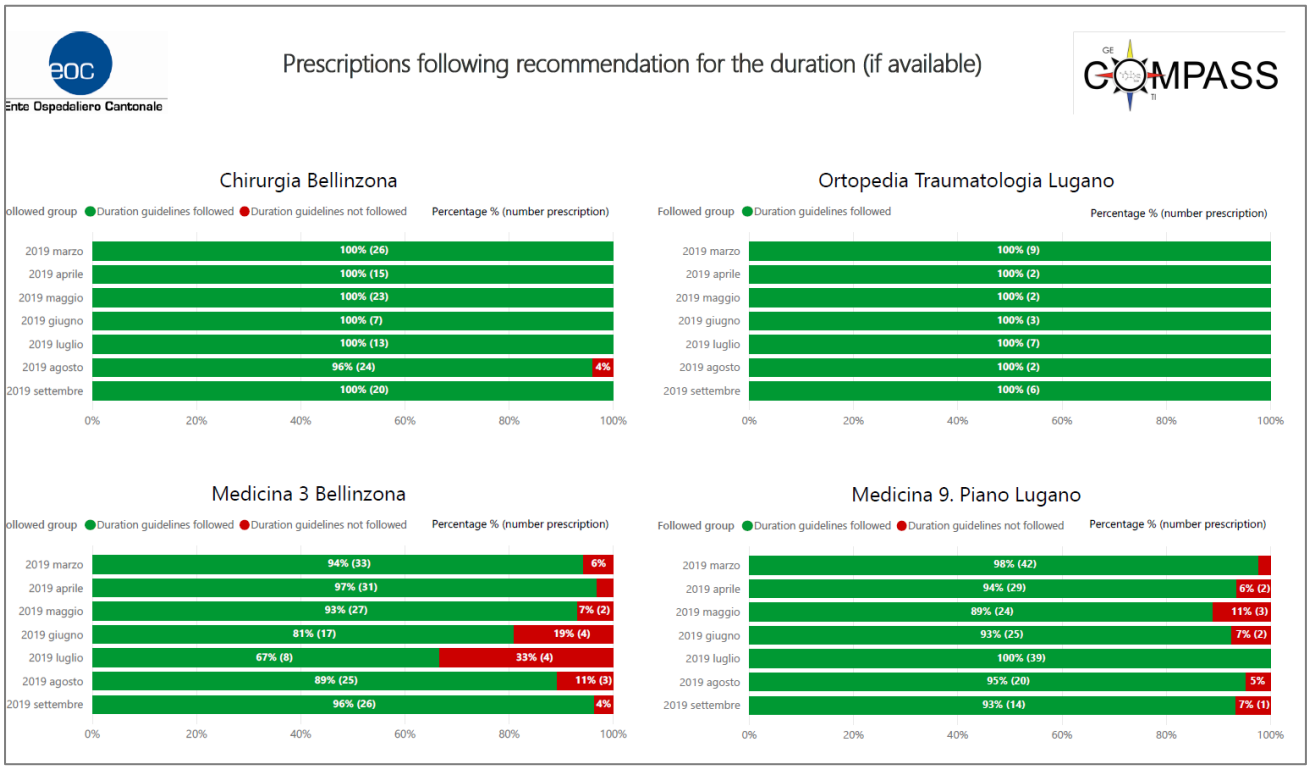

Figure S3.F Example of feedback reports from Ticino. *The report provides the percentage of prescriptions who followed the local guidelines for the duration of therapy (green) by unit*

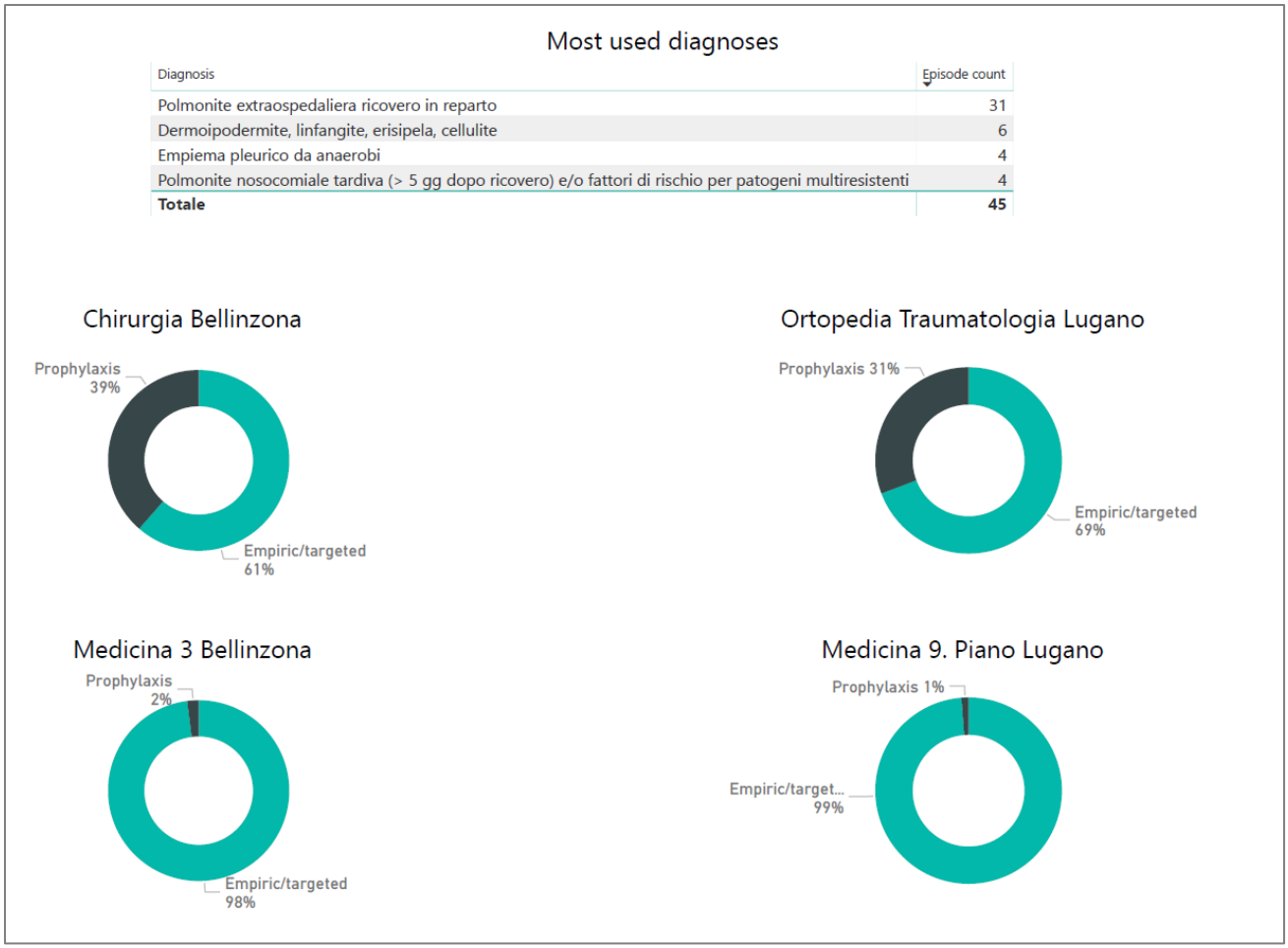

Figure S3.G Example of feedback reports from Ticino. The report provides the most frequent indications and the proportion of type of prescriptions (empiric/targeted/medical prophylaxis/surgical prophylaxis).

Text S3. Methodological details

Methodological details for assessment of clinical outcomes

Clinical outcomes extracted from the electronic health record database include in hospital 30-day mortality, 18-day hospital readmission (surveillance criteria part of the regular monitoring at Geneva), intensive care (ICU) or intermediate care unit (IMC) transfer and unit length of stay (LOS).

Clinical outcomes were assessed as follows:

- ICU or IMC transfer: only a direct transfer from an intervention or a control ward to the ICU or intermediate care unit was taken into account.
- In-hospital 30 day mortality: the death was attributed to the last study ward the patients stayed in (within a limit of 30 days from his/her transfer from the ward).
- Hospital readmission: attributed to the last study ward the patients stayed in and was taken into account only if the last ward the patient stayed in before being discharged was a study ward.

Methodological details for assessment of qualitative antimicrobial use indicators

Qualitative antimicrobial indicators include the following indicators: appropriateness of antimicrobial therapy for the choice of the molecule and the duration, re-evaluation of the prescription, antibiotic plan documented in the progress notes, de-escalation whenever feasible, oral switch whenever feasible and adaptation to microbiological results. These indicators, except the last one, were assessed by selecting randomly 50 patients by ward among patients who received at least one antimicrobial dose during their stay in the ward. These charts were manually reviewed and data were entered in a standardised CRF (REDCAP, Vanderbilt, supplementary). For a random subsets of charts (10%), two assessors reviewed the charts separately until reaching 90% concordance for guidelines concordance assessment.

Methodological details for sample size calculation, blinding, data collection and management and ethics

Sample size

The sample size calculation was based on the primary outcome (DOT per admission) and was performed taking into account the pair-matched and clustered design of the study according to the approach proposed by Hayes and Bennett (14). Assuming 12 wards per arm, with an average of 500 admissions per year, antibiotic use of 4.0

DOT/admission in the control group with a standard deviation of 1.0 (based on preliminary antibiotic use data) and a two-sided type I error of 0.05 would have a power of 80% to detect a relative difference in average DOT/admission between the intervention and control arm of at least 7.7%. No interim analysis was planned nor realised.

Blinding

Neither the study staff implementing the intervention, nor the physicians targeted by the intervention, nor patients were blinded to an individual ward's assignment group since the nature of the intervention made this impossible. Extraction of the primary and secondary outcome measures was performed primarily by administrative staff not involved in the study. Assessors of qualitative antibiotic indicators and data analysts were blind to the study arm.

Data collection and management

Data were retrieved from the hospitals' data warehouses. De-identified data were stored in password protected Microscoft Excel (Microsoft Corporation, Redmond, USA) files on secured hospital servers. For assessment of qualitative antimicrobial use indicators an electronic Case Report Form was created in an electronic data capture system such as REDCap (REDCap Consortium, Location, USA). For analysis, data were imported into the statistical program, "R" version 4.0.2 (R Foundation for Statistical Computing).

Ethics

The requirement for informed consent by patient was waived because the intervention was deemed to be of minimal risk. Printed flyers distributed to each patient at admission in a participating ward described how to opt-out of data collection. No informed consent was obtained from physicians practising in participating wards, but an agreement was signed by the head of each participating unit and physicians were informed about the study.

Table S6: Effect of the intervention for the per-protocol population

One DOT represents a specific antibiotic administered to an individual patient on a calendar day independent of dose and route. Admissions rather than patient days as denominator were selected to take into account the possibility that the intervention impacts length of stay.

	OR / IRR	Lower and Upper 95% CI
Any antibiotic	1.12	0.79 - 1.58
DOT for those who received antibiotics	1.05	0.97 - 1.13

DOT: days of therapy

Table S7. Subgroups and sensitivity analysis for the effect of the intervention (primary outcome) for the ITT population by study site and by type of wards

	OR / IRR	Lower and Upper 95% CI
Geneva (ITT)		
Any antibiotic	1.19	0.92 - 1.53
DOT for those who received antibiotics	0.99	0.95 - 1.03
Geneva (PP)		
Any antibiotic	0.90	0.44 - 1.84
DOT for those who received antibiotics	1.00	0.94 - 1.06
Ticino (ITT)		
Any antibiotic	0.97	0.86 - 1.09
DOT for those who received antibiotics	1.00	0.80 - 1.25
Ticino (PP)		
Any antibiotic	1.30	1.08 - 1.56
DOT for those who received antibiotics	1.13	0.92 - 1.39
Geriatrics wards (ITT)		
Any antibiotic	1.09	0.78 - 1.53
DOT for those who received antibiotics	1.01	0.94 - 1.09
Geriatrics wards (PP)		
Any antibiotic	1.14	0.84 - 1.53
DOT for those who received antibiotics	1.02	0.93 - 1.12
Medical wards (ITT)		
Any antibiotic	1.20	0.96 - 1.50
DOT for those who received antibiotics	0.96	0.88-1.05
Medical wards (PP)		
Any antibiotic	0.80	0.28 - 2.32
DOT for those who received antibiotics	1.03	0.94 - 1.12
Surgical wards (ITT)		
Any antibiotic	0.86	0.73 - 1.00
DOT for those who received antibiotics	1.00	0.66 - 1.52
Surgical wards (PP)		
Any antibiotic	1.26	0.88 - 1.80
DOT for those who received antibiotics	1.18	0.80 - 1.73
Period 2 Geneva (1.09.2019-28.02.2020) (ITT)		

Any antibiotics	1.27	0.89 - 1.82
DOT for those who received antibiotics	0.94	0.78 - 1.13
Period 2 Geneva (1.09.2019-28.02.2020) (PP)		
Any antibiotic	1.12	0.79 – 1.60
DOT for those who received antibiotics	0.97	0.79 – 1.19

Calculation based on non-missing values. DOT present the summary based on strictly positive values.
DOT: days of therapy,
Odds ratio (OR) are displayed for the binary part (zi), incidence rate ratio (IRR) for the positive part (cond). Both cases compare COMPASS with respect to control. 95% CI are shown. Geriatrics analysis did not adjust for liver, AIDS and immunosupression (almost complete separation). Medical analysis did not adjust for study site (only Geneva) and AIDS (almost complete separation). Surgical analysis did not adjust for study site (only Ticino), liver, neoplasia, AIDS and immunosupression (almost complete separation). ITT population with an o set for unit length of stay

Table S8. Effect of the intervention on antimicrobial days by admission

	OR / IRR	Lower and Upper 95% CI
Any antibiotic	1.12	0.94 - 1.32
DOT for those who received antibiotics	0.98	0.91 - 1.05

Table S9. Effect of the intervention using different models for the ITT and PP population

	OR / IRR	Lower and Upper 95% CI
Model 2 (LOS as an offset)		
ITT population		
Any antibiotic	1.12	0.94 – 1.33
DOT for those who received antibiotics	1.00	0.91 – 1.11
PP population		
Any antibiotic	1.07	0.71 1.62
DOT for those who received antibiotics	1.02	0.92 – 1.12
Model 3 (LOS as a covariate)		
ITT population		
Any antibiotic	1.12	0.88 1.43
DOT for those who received antibiotics	1.00	0.91 1.09
PP population		
Any antibiotic	1.06	0.65-1.72
DOT for those who received antibiotics	1.02	0.92-1.12

DOT: days of therapy, LOS: Length of stay;

Table S10. Effect of the intervention considering only the first admission by patient

ITT: There are 14 392 unique patients for 21 057 unique admissions.
PP: There are 13 345 unique patients for 18 994 unique admissions.

	OR / IRR	Lower and Upper 95% CI
ITT population		
Any antibiotic	1.10	0.94 – 1.29
DOT for those who received antibiotics	1.02	0.94 – 1.10
PP population		
Any antibiotic	1.10	0.78 – 1.56
DOT for those who received antibiotics	1.08	0.10 – 1.18

Figure S3. DOT before and after the launch of the intervention by pairs of units in Geneva

The figure S3 represents the unadjusted DOT by paired wards in Geneva over the year before the intervention, and during the study period.

Table S11. Most frequent reasons for deviation from guidelines selected from the list in the COMPASS CDSS (from manual chart review)

Reason for deviation from local guidelines (ranked by frequency)	N (133)	(%)
Recent pre-treatment with antimicrobials	32	24.1
Recommended by infectious diseases	31	23.3
Allergy, other contraindication	26	19.5
Colonization with multidrug resistant organism	19	14.3
Immunosuppression	14	10.5
Isolated pathogen not susceptible to recommended treatment	9	6.8
Oral treatment not possible	2	1.5

Table S12. Proportion of prescriptions by AWARE WHO categories (2019 version)

	Control	Intervention	Total
All			
Access	16 347 (44.8)	19 270 (44.9)	35 617 (44.8%)
Watch	19 630 (53.7)	22 966 (53.5)	42 596 (53.6%)
Reserve	548 (1.5)	655 (1.5)	1 203 (1.5%)
Geneva			
Access	10 503 (47.8)	11 699 (46.7)	22 202 (47.2%)
Watch	11 079 (50.5)	12 947 (51.7	24 026 (51.1%)
Reserve	372 (1.7)	409 (1.6)	781 (1.7%)
Ticino			
Access	5 844 (40.1)	7 571 (42.4)	13 415 (41.4%)
Watch	8 551 (58.7)	10 019 (56.2)	18 570 (57.3%)
Reserve	176 (1.2)	246 (1.4)	422 (1.3%)

Table S13. Number of healthcare associated bloodstream infection due to multidrug resistant organisms (Geneva only) attributed to the wards of each arm.

	control	intervention
Escherichia coli ESBL	3	**3**
Klebsiella pneumoniae ESBL	1	1
Pseudomonas aeruginosa MR	3	0
*Staphylococcus aureu*s methicillin-resistant	2	0
Total	7	4

ESBL: extended spectrum beta-lactamase; MR: multiresistant (resistant to at least three class of antimicrobials)

Only bloodstream infections attributed to the wards from each arm are presented here

Hospital length of stay

We computed the hospital length of stay, excluding patients who switched arm over the same hospital stay (n=513) and excluding patients with missing data on hospital admission date or hospital discharge date (n=891) and considering all hospital admissions for each patient (a patient could have several admissions). The LOS was calculated by passage of midnight (e.g., if patient admitted on 1st and discharged on 2nd, 1 day is counted). When using this approach, the overall median hospital length of stay was 8 days (IQR 4-15) and was similar overall, in the intervention and in control arm (8 days (IQR 4-15)).

When considering only patients who received antibiotics during their stay in the participating wards, after excluding patients who switched arm (n=160) and excluding patients with missing hospital admission date or discharge date (283), the median overall hospital LOS was 10 days (IQR 6-18) with similar values in both arms: 10 days (IQR 5-17) in the intervention arm and 10 days (IQR 6-18) in the control arm.

End user survey satisfaction

Methodology of the survey on user satisfaction

An invitation to fill a satisfaction survey was send to institutional emails to all physicians working in the participating wards during the study period, regardless of the level of seniority (resident, senior physicians). The first invitation was sent four months after the launch of the intervention and three reminders were send iteratively every 4 months.

Table S13. Results of the survey on user satisfaction (n=90) by study center

	Ticino (n=26)	**Geneva (n=64)**
Easiness to enter the indication (mean score, 0 worst, 100 best)	64	54
Usefulness of entering indication (mean score, 0 worst, 100 best)	73	55
Usefulness of guidelines suggestion (mean score, 0 worst, 100 best)	76	67
Easiness of reassessment of antibiotic prescriptions on day 3 (mean score, 0 worst, 100 best)	56	53
Usefulness of reassessment of antibiotic prescriptions on day 3 (mean score, 0 worst, 100 best)	62	56
Usefulness of suggestion of treatment duration (mean score, 0 worst, 100 best)	62	74
Overall evaluation of the COMPASS system (mean score, 0 worst, 5 best)	3.4	3.0

We collected 90 answers from physicians from the on-line satisfaction survey (64 from Geneva and 26 from Ticino). The median rating of the system was 3.0/5 in Geneva and 3.4/5 in Ticino on 5-point Likert scale with 1 indicating the worst and 5 the best satisfaction. The best-rated feature was the usefulness of guidance for treatment choice and treatment duration.

Supplementary figures legend

Figure S4. Overall framework for the COMPASS intervention

Figure S4.A. Framework of the initial prescription process. The part on the top represents the user interface and the part on the bottom (grey) represents the system algorithm.

Figure S4.B. Framework of the re-evaluation process. The part on the top represents the user interface and the part on the bottom (grey) represents the system algorithm.