Resistance of Gram-Negative Organisms: Studying Intervention Strategies

WORK PACKAGE 5

Patient isolation strategies for ESBL carriers in medical and surgical hospital wards

PROTOCOL

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LIST OF ABBREVIATIONS USED IN THIS PROTOCOL

AHC	Alcohol-based handrub consumption
ABHR	Alcohol-based handrub
CI	Contact isolation
cRCT	Cluster-randomized controlled study
ESBL	Extended-spectrum beta-lactamase
ESBL-E	Extended-spectrum beta-lactamase producing *Enterobacteriaceae*
FTE	Full-time-equivalent
GEE	Generalized Estimating Equation
HCW	Health care worker
HH	Hand hygiene
HICPAC	Healthcare Infection Control Practices Advisory Committee
IC	Infection control
LOS	Length of stay
MDR-GNB	Multi-drug resistant Gram-negative bacteria
MDRO	Multi-drug resistant organism
SP	Standard precautions
WP	Work Package

1. SYNOPSIS

Title of the Protocol	Patient isolation strategies for extended-spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL-E)-carriers in medical and surgical hospital wards
Protocol chair	Petra Gastmeier
Intervention	The study will compare 2 Non-ICU-level infection control strategies designed to reduce transmission of ESBL-E among patients in adult medical and surgical wards with universal admission and discharge screening**.**
The 2 strategies are as follows:	
Standard Precautions (SP)	• Hand hygiene (HH) • Use of gloves and other barriers as needed for interactions involving contact with mucous membranes, wounds, and body fluids by healthcare workers (HCWs) during the care of all patients
Contact Isolation (CI)	• HH and standard precautions for all patients AND • Use of gloves and gowns during the care of all patients known to be colonized/infected with ESBL-E prior to admission or who are identified as such during their stay on the ward. These patients should be cared for preferably in a single room or in a shared room with patients colonized or infected with the same organism.
Objectives	
Primary Objective	To determine the additional effects of CI compared to a SP strategy on the incidence density of ESBL-E-acquisition among hospitalized patients in adult Non-ICU wards in hospitals with universal ESBL-E admission and discharge screening.
Secondary Objectives	• To determine the prevalence of ESBL-E carriage on admission • To determine the incidence of nosocomial ESBL-E infections in the study periods • To evaluate compliance with hand hygiene in the study intervention periods • To evaluate compliance with contact precautions in the study intervention periods • To compare ESBL-E-incidence detected with and without universal surveillance screening (study intervention periods vs. baseline period and post intervention period

Hypotheses/Outcome	
Primary Hypothesis and Outcome	If all ESBL-E-carriers are identified through universal surveillance screening, Contact Isolation (CI) will not reduce incidence densities of ESBL-E-acquisition among patients in medical and surgical wards when compared to SP. The primary outcome is the ESBL-E acquisition rate per 1,000 patient days. Acquisition of ESBL-E-carriage is defined as recovery of ESBL-E isolates from clinical and/or rectal/perianal/stool screening specimens >3 days after admission (admission day = day 1) from patients with negative admission screening results. If a patient is discharged from the ward and re-admitted to the ward on the same or the following day, then the discharge will be ignored in the primary analysis. If the readmission occurs later, the patient will be treated as a new case.
Secondary Hypotheses	1. Healthcare workers (HCWs) will not practice HH more frequently during contact with known ESBL-E-carriers in CI than in SP 2. HCWs will practice HH more frequently during contact with known ESBL-E-carriers than with patients not known to be ESBL-E-carriers
Secondary Outcomes	The trial will assess the efficacy of the CI strategy in reducing the incidence density of colonization with ESBL-E by the methods described above. In addition, the trial will evaluate the efficacy of the CI strategy in reducing the cumulative incidence of ESBL-E infections as determined by laboratory-based surveillance of clinical culture results. The trial will evaluate the frequency of hand hygiene and the use of gloves and gowns by HCWs, as assessed by bedside observations of a trained monitor. The antibiotic use will be analysed for all patients in defined daily doses (DDD) preferably weekly/at least monthly. In a subset of ESBL-E-patients antibiotic use will also be analysed at patient level in days of therapy (DOT). The trial will evaluate the consumption of alcohol-based handrub (ABHR) per patient days to evaluate differences between ESBL-E-carriers and Non-ESBL-E-patients as well as differences between the two IC strategies. Because the interventions involve minimal risk, no specific safety measures will be made.
Study Design	The study is a two-arm, cluster-(Non-ICU) randomized, controlled study (cRCT) of two IC strategies with cross-over design, which will be performed in different European countries. Randomization will be performed at the ward level. Primary analyses will be performed at the ward level.

Study population	
Inclusion criteria	• Adult medical and surgical Non-ICUs with approval from the medical director and head nurses, approximately 1000 admissions/year and an expected non-varying average length of stay for the 2 intervention periods • Ability to implement a universal ESBL-E admission and discharge screening • Written approval of the study from the local Institutional Review Board (IRB)
Exclusion criteria	• Transplant and paediatric wards, ICUs • Wards planning to enrol subjects in a study of an investigational agent administered for the purpose of eradicating or preventing colonization with ESBL-E or to reduce the likelihood of transmission of these bacteria
Sample Size	Assuming an average new acquisition of ESBL-producers in hospital of 0.8/100 patients on non-ICUs, a design effect (DE) of 2.9 and a corresponding intracluster correlation coefficient (ICC) of 0.003, 20 wards with 36.788 included patients (18.394 per study arm) will have the a power of at least 80% to detect at least a 50% reduction in risk in wards during CI vs. SP period with a Type I error rate of 0.05 for a 2-sided test.
Randomization	Randomization will occur at the ward level with a block size of 2. Groups of two consecutive wards will be randomized to one of the two arms.
Data Analyses	For the primary efficacy analysis, incidence density of nosocomial ESBL-E acquisition will be computed at hospital level and ward level. A one degree of freedom test from an analysis of multivariance model will be used to test for differences in mean incidence density ratios of ESBL-E acquisition between the two strategies. This will be calculated by Poisson or negative-binomial regression analysis with monthly aggregated data using Generalized Estimating Equation (GEE) models with adjustment by several confounding parameters besides cluster effects by ward and hospital.

2. PERSONS / INSTITUTIONS INVOLVED IN THE STUDY

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R-GNOSIS is an EU-funded research project funded by the Seventh Framework Programme (FP7) under the grant agreement number 282512.

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3. BACKGROUND

Approximately 30 % of all healthcare-associated infections are caused by *Enterobacteriaceae*. The rapidly increasing prevalence of extended-spectrum beta-lactamase producers among common *Enterobacteriaceae* species (ESBL-E) in Europe is a cause for concern[1, 2].

"To isolate or not to isolate" patients with ESBL-E is currently one of the most controversial questions in the field of infection control (IC). Most national guidelines recommend CI (CI) of patients with MRSA (methicillin-resistant *Staphylococcus aureus*) or VRE (vancomycin-resistant enterococci). For ESBL-E, the evidence is less conclusive [3], [4] and is not investigated in wards with endemic ESBL-E levels but instead is often only derived from outbreak investigations. A recently published systematic review to examine the efficacy of IC interventions for the control of ESBL-E in hospital in non-outbreak settings identified only four uncontrolled retrospective studies[5].

Consequently, only few national guidelines recommend isolating patients with ESBL-E on general hospital wards. The German guidelines for management of patients with multidrug resistant Gram-negative organisms[6] do not recommend isolation of ESBL-E-patients in non-high risk wards. The 2006 US HICPAC guideline for "Management of multi-drug resistant organisms in healthcare settings" recommends CI, which includes physical separation of colonized patients in single rooms and wearing gloves and gowns by the HCWs[7]. If this is impossible, HCWs should, at least, wear gloves and gowns, but again, there is no convincing scientific evidence supporting this recommendation.

Moreover, isolation measures may be associated with increased costs and side effects for the individual patient such as depression and reduced contact with attending physicians [8, 9, 10, 11]. The importance of the environment as an intermediary in the transmission of multidrug resistant organisms (MDRO) is also poorly understood [12]. As *Enterobacteriaceae* generally lose viability quickly and are recovered less frequently from hospital environments than Gram-positive organisms, isolation in single rooms may not be required [13]. However, a recent study found substantial contamination of gloves and gowns with multidrug-resistant bacteria, thus supporting the use of gloves and gowns for treating these patients [14, 15, 16].
Standard precautions (SP) may be as effective for limiting the spread of ESBL-E, especially when hand hygiene compliance is high [17], and one study even found lower hand hygiene compliance under isolation conditions [18].

Currently, many hospitals in Europe are unable to isolate patients with MDRO due to shortage of single rooms, while, the prevalence of intestinal ESBL-E-carriage among healthy people [19, 20, 21] and people admitted to the hospital [22, 23] has risen sharply to 3-7 % depending on the setting and the population studied. Moreover, if ESBL-E-carriers are identified solely by cultures

obtained for clinical purposes, many asymptomatic patients colonized with ESBL-E will remain undetected and thus will not be cared for with contact precautions.
Hence, a combined approach of active surveillance screening at admission and CI of detected ESBL-E-carriers would be the logical consequence. However, this would increase the management costs for ESBL-E-patients even further.

Implementing HICPAC guideline recommendations would have considerable cost implications and impact on the quality of patient care[24]. Therefore, adding contact precautions for the rapidly increasing number of patients colonized with ESBL-E should be based on solid evidence.
Last but not least, transmission prevention should not be considered an end in itself but rather one particular strategy to achieve the higher goal of reducing clinical infections and associated morbidity and mortality[12]. This should also be investigated before final conclusions about isolation strategies for ESBL-E-patients are made.

4. OBJECTIVES AND HYPOTHESES

4.1. OBJECTIVES

4.1.1. PRIMARY OBJECTIVE

- To determine the additional effects of CI compared to a SP strategy on the incidence density of nosocomial ESBL-E-acquisition among hospitalized patients in adult Non-ICU wards in hospitals with universal ESBL-E admission and discharge screening

4.1.2. SECONDARY OBJECTIVES

- To determine the prevalence of ESBL-E-carriage on admission
- To determine the incidence of nosocomial ESBL-E infections in the study periods
- To evaluate the compliance with hand hygiene in the study intervention periods
- To evaluate the compliance with contact precautions in the study intervention periods
- To compare ESBL-E-incidence detected with and without universal surveillance screening (study intervention periods vs. baseline period and post intervention period)

4.2. HYPOTHESES AND PARAMETER ESTIMATES

4.2.1. PRIMARY HYPOTHESIS

- If all ESBL-E-carriers are identified, CI will not reduce ESBL-E incidence densities of ESBL-E-acquisition among patients in medical and surgical wards when compared to SP

4.2.2. SECONDARY HYPOTHESES

- HCWs will not practice hand hygiene (HH) more frequently during contact with known ESBL-E-carriers in CI than in SP
- HCWs will practice HH more frequently during contact with known ESBL-E-carriers than with patients not known to be ESBL-E-carriers

5. METHODS

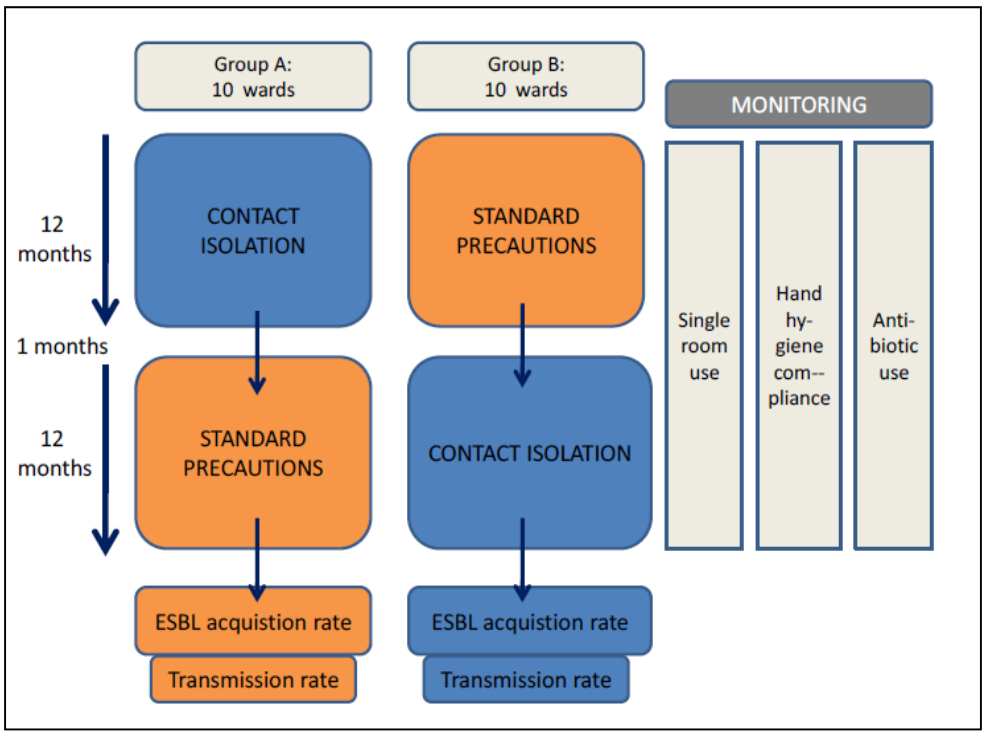
5.1. STUDY DESIGN

The study is a two-arm, cluster-randomized, controlled study (cRCT) of two IC strategies with cross-over design, which will be performed in 4 European countries to achieve high external validity of study results.

An attempt will be made to identify all intestinal ESBL-E-carriers by active surveillance testing and cultures obtained for clinical indications.

Two IC strategies (CI and SP) will be compared for ESBL-E-positive patients in different units for 12 months each. Because these IC strategies will be implemented as a unit-wide measure, all patients hospitalized in a specific unit will be subjected to the allocated IC strategy of the unit (figure 1). Wards will be assigned to the IC strategy in a random order and will then switch strategies after a wash-out period of one month in the following year.

Figure 1: Study design WP5



The two strategies are as follows:

5.2. STANDARD PRECAUTIONS (SP) (= CONTROL ARM)

For all patients – including known ESBL-E-carriers – SP will be performed. The indications and technique for HH will be consistent with those recommended by the WHO's "Five Moments" [25]. Clean gloves and gowns/aprons will be used for all interactions that involve potentially infectious procedures[7]. Non-sterile gloves are considered adequate; non-latex-gloves are used for medical staff and/or patients with latex allergy. Gloves should be changed after contact with

infectious material, such as blood, stool, urine or wound drainage. Gloves should be removed immediately after use and HH should be practiced before touching non-contaminated surfaces or going to another patient. Accordingly, clean gowns/aprons should be donned if contact with patient's blood or body fluids is expected. Gowns should be removed promptly after use and HH should be practiced before touching non-contaminated surfaces or going to another patient. This strategy represents the current standard of care and all patients will be subjected to this IC strategy on wards in the SP phase of the trial.

5.3. CONTACT ISOLATION (CI) (= INTERVENTION ARM)

All patients who are known to be colonized/infected with ESBL-E prior to admission or as a consequence of the surveillance cultures and/or of cultures obtained for clinical indications will be cared for using contact precautions, preferably in a single room or in a shared room with patients who are colonized with the same organism. If isolation in a single room or a shared room with patients colonized with the same organism is impossible, gloves and gowns/aprons will be used for all interactions with the patient or the patient's environment in a shared room. Clean gloves and gowns/aprons will be used for all interactions that involve direct contact with ,the patient or the patient's environment[7]. Non-sterile gloves are considered adequate; non-latex-gloves are used for medical staff and/or patients with latex allergy. Gloves should be changed after contact with infectious material, such as blood, stool, urine or wound drainage. Gloves should be removed immediately after use and hand hygiene should be practiced before touching non-contaminated surfaces or going to another patient. Clean gowns/aprons should be donned if contact with the patient or with environmental surfaces in the patient's room is expected. Gowns should be removed promptly after use and HH should be practiced before touching non-contaminated surfaces or going to another patient. HH will be performed according to WHO's "Five Moments"[25]. As the intervention strategy will be implemented as a unit-wide IC measure, all patients known to be colonized/infected with ESBL-E-producing bacteria will be subjected to this IC strategy on wards in the CI phase of the trial.

Both strategies (SP and CI) will be applied in all units for a period of 12 months each with a washout period of one month between the 2 study periods.

5.4. ISOLATION FOR OTHER MULTIDRUG-RESISTANT BACTERIA

In the event that CI is indicated in patients positive for other pathogens (e.g. MRSA, multi drug resistant *Acinetobacter baumannii*, *Clostridium difficile* etc.), it will be implemented according to the hospitals' IC and isolation policies. However, in both periods, patients with known carriage/infection with Carbapenem-resistant *Enterobacteriaceae* will be assigned to strict CI, following widely accepted European guidelines[26].

5.5. SURVEILLANCE CULTURES

In both arms of the trial, wards will collect surveillance cultures to identify patients who are colonized with ESBL-E using the same procedures. The results of the surveillance cultures will be reported back to the wards immediately in both arms of the trial.

All patients will be screened at admission (admission day = day 1) to the ward or as soon as possible within 3 days. Repeated surveillance cultures will be obtained for patients staying longer than 7 days on a specific day each week (i.e., every Wednesday, Friday etc.). Patients discharged from the ward will have samples obtained on the day of discharge, if possible, or the day before. Patients readmitted to the ward will be treated as new cases.

The procedures for obtaining and processing swabs are outlined in Section 6.4. (SURVEILLANCE CULTURES).

Surveillance cultures will be obtained by the ward nurses and/or research personnel.

All specimens will be processed by the institutional microbiology laboratories. In all wards, clinicians may order microbiological cultures at any time for clinical indications. All results will be reported as soon as possible to the wards. ESBL-E-isolates will be sent to the microbiologic laboratory of the Hospital Ramon y Cajal in Madrid (SERMAS) for further molecular epidemiologic analysis.

5.6. TRAINING

All IC measures (including SP and HH policies) will be introduced to HCWs by local study personnel at the beginning of each intervention period. An introductory course for local study personnel will include the training of all methods and the monitoring process.

The introductory course will take place at the study sites and will be organized by Charité Berlin.

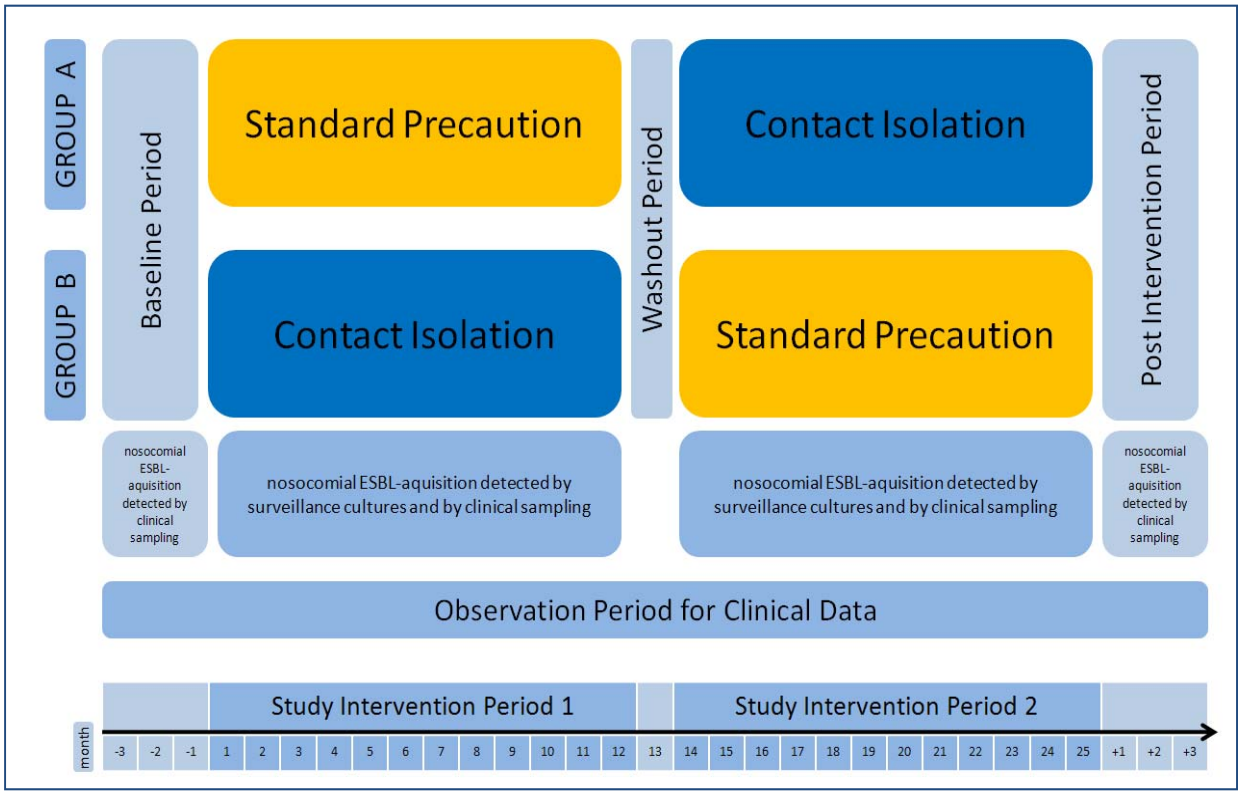
5.7. STUDY PERIODS AND TIMELINE

The study will be divided into a three-month baseline period, a first 12-month intervention phase, a one-month washout period, a second 12-month intervention phase and a three-month post intervention period.

During the baseline and the post-intervention period, only data on nosocomial ESBL-E-acquisition detected by clinical sampling will be collected on the participating wards. In the intervention phases, data on ESBL-E-acquisition detected by active surveillance testing as well as clinical sampling will be collected.

During the one-month washout period, the protocol of the following intervention period will be applied. Only data on nosocomial ESBL-E-acquisition detected by clinical sampling will be collected except for the Follow-up of patients admitted during the preceding period.

Figure 2: Timeline WP5 for Participating Wards



5.8. SELECTION AND WITHDRAWAL OF SITES

The study will be realized in 20 wards in 5 hospitals in 4 European countries (Netherlands, Switzerland, Spain and Germany) during a 31-month period from 08/2013 to 02/2016.
Hospitals with adult medical and surgical wards will be selected for the study.
Because IC strategies will be applied at the ward level, the participation of each unit requires the signed approval of the physician and nursing directors of the ward instead of each patient's approval.

Minimum patient turnover should reach approximately 1000 admissions per year. To have equal conditions in both intervention periods average length of stay should be expected to be non-varying.

Wards that meet any of the following criteria are excluded from the study:

- transplant wards
- paediatric wards

Table 1: Number of hospitals and wards per country

Country	Total number of hospitals	Total number of wards
Netherlands	1	4
Switzerland	1	4
Spain	1	4
Germany	2	8

The medical or nursing directors or the site investigator may withdraw his or her site from the study for any reason at any time.

The study investigators may discontinue the participation of a study site for the following reasons:

- The site does not follow the trial protocol with regard to obtaining the surveillance cultures
- The site does not implement the assigned IC strategy to satisfaction.
- During the trial, the ward enrols subjects in a study administering an investigational agent for the purpose of controlling, eradicating or preventing colonization with ESBL-E.
- The site's IRB does not provide a waiver for informed consent

In case the protocol is not sufficiently implemented this issue should be discussed with the WP5 partners. They will decide whether replacement of the ward is necessary.

In the event of an unexpected change in antimicrobial resistance epidemiology in a certain ward (e.g. an outbreak), creating a situation in which adherence to protocol can no longer be recommended, the site will temporarily be withdrawn. If withdrawal exceeds three months, the site will be excluded. In the event of the withdrawal or discontinuation of a ward, the R-GNOSIS WP5 partners will decide whether replacement of the ward is necessary.

However, an ITT (intention to treat) analysis will be performed.

5.9. RANDOMIZATION

Randomization will occur at the ward level. Groups of two consecutive wards will be randomized to one of the two arms.

The investigators will be aware of the assigned IC strategy in order to monitor implementation of each strategy. Data analysts will be unaware of the IC strategy assignment.

5.10. ENDPOINTS AND OUTCOMES

5.10.1. PRIMARY ENDPOINT

Incidence density of colonization with ESBL-E across the study periods.

- The primary outcome is the nosocomial ESBL-E-acquisition rate per 1,000 patient days. Acquisition of ESBL-E-carriage is defined as recovery of ESBL-E isolates from clinical and/or rectal screening specimens >3 days after hospital admission (admission day = day 1) from patients with negative admission screening results. If a patient is discharged from the ward and re-admitted to the ward on the same or the following day, then the discharge will be ignored in the primary analysis. If the readmission occurs later, the patient will be treated as a new case.

5.10.2. SECONDARY ENDPOINTS

- New events of nosocomial ESBL-E infections expressed as incidence density of nosocomial ESBL-E-infections per 1000 patient days.
  - Definitions for urinary tract infections (UTI), hospital-acquired pneumonia (HAP), blood stream infections (BSI), and surgical site infections (SSI) will be in accordance with modified CDC definitions[27].
- Compliance with hand hygiene and contact precautions of healthcare workers during patient care, assessed by direct observation performed by a trained monitor using a standardized observation procedure.
  - The frequency of hand hygiene and use of gloves and gowns/aprons by healthcare workers per patient contact during the intervention periods per indicated opportunities
- Aggregate data on antibiotic use at the ward level will be collected monthly, preferably in DDD per 1000 patient-days.
- Individual-level systemic antibiotic use (according to the Anatomical Therapeutic Chemical Classification System [ATC- J01]) expressed as days of therapy for known ESBL-E-carriers in a subset of patients.
- Alcohol-based handrub (AHC) consumption for known ESBL-E-carriers as well as for non-ESBL-E-patients in both intervention periods.
  - AHC for patients known to be colonized/infected with ESBL-E in ml per day (use in ESBL-E-positive patient days as known on the ward, i.e. the days the ESBL-positive result is known on the ward and after).
  - AHC for non-ESBL-E patients and unknown carriers in ml/day (median use in ESBL-E-negative patient days as known on the ward, i.e. all patient days of non-ESBL-E-patients plus all patient days of an ESBL-E-patient before the first positive result is known on the ward).
  - Total AHC on the ward in liters/month, including belt pockets and disinfection dispensers other than automated counting devices.

6. DATA COLLECTION

6.1. HOSPITAL DATA (ANNEX I WP5 DF1 HOSPITAL DATA)

In order to make descriptive comparisons of the groups of wards randomized to the two strategies, hospital and ward characteristics will be collected.

Data	Collected by	
	Local study personnel	Ward personnel
Hospital and ward characteristics[1]	X	
x^1 once x^a annually x^m monthly x^d daily		

6.2. WARD DATA (ANNEX II WP5 DF2 WARD DATA)

Data	Collected by	
	Local study personnel	Ward personnel
General characteristics [1]	X	
Total AHC[m]	X	
Pharmacy report[m]	X	
Number of admissions[d]	X	X
Patients on ward[d]	X	X
Patients isolated[d] (only Study Intervention Periods)	X	X
Patients isolated for ESBL-E[d]	X	X
AHC assessed by disinfection dispensers with monitoring system (patient rooms only) [d]	X	
x^1 once x^a annually x^m monthly x^d daily		

Occupancy rates will be collected daily at the same time (preferably midnight patient census).

6.3. PATIENT DATA (ANNEX III WP5 DF3 ESBL-E PATIENT)

The following data will be only obtained from patients who are ESBL-E-positive ("Cases")

Data	Collected by	
	Local study personnel	Ward personnel
Known ESBL-E patient at admission (Yes / No) [1]	X	
Day of admission (Day of study) [1]	X	
Day of discharge (Day of study) [1]	X	
Day of finding (Day of study) [1]	X	
Reason for sampling (Screening/ Clinical/ No sample) [d]	X	
Sample: ESBL-E (Positive: E. coli; Klebsiella; other/ Negative / No data) [d]	X	
Pos. Result known (documented in patient file on the ward) (Yes / No / Known ESBL-E) [d]	X	
Contact Precautions (CI 1-4 / SP 1-4 / No data) [d]	X	
ESBL-E Infection (No / Yes ___) [d]	X	
Handrub Consumption (ml / day) [d]	X	
Antibiotic Use (Yes / No ___, if yes, type of antimicrobial substance ___) [d,e]	X	

x^1 once x^a annually x^m monthly x^d daily x^e in a subset of patients

If a patient is ESBL-E-positive for the first time during the study these data should be filled in retrospectively preferably from the day of admission onwards, but at least for the 6 days prior to the first ESBL-E result.

6.4. SURVEILLANCE CULTURES

Surveillance cultures of the rectal skin will be obtained as soon as possible after admission to the ward, at the latest within three days and once a week thereafter for patients staying longer than 7 days. Patient care nurses and/or research personnel will obtain the surveillance cultures from the patients.

Swabs of the rectal area will be obtained following a standardized procedure. Swabs will be processed in the institutional microbiology laboratory.

Rectal swabs will be plated on chromogenic media. If no characteristic colonies are present, the culture will be recorded as negative. Characteristic colonies will be confirmed with ESBL-E-disk tests and E-tests, if possible. The laboratory will report surveillance culture results back to the wards as soon as possible after final confirmation and identification. Efforts will be implemented to speed up the notification process, including weekends.

All confirmed ESBL-E isolates will be frozen in appropriate storage at -70°C. At three months intervals, the isolates will be shipped in batches to Madrid (SERMAS) for further molecular analysis.

7. MONITORING

7.1. CONTINUOUS MONITORING OF CI

The implementation of CI will be monitored once a week by local research personnel. The monitor will observe whether gloves and gowns are available for known ESBL-E-carriers, whether correct signage is placed on the patient bed and material, and if the patient is placed in a single or a shared room.
The implementation of CI will be listed on the patients' data forms (Annex III DATA FORM 3 «ESBL-E Patient»).

7.1.1. OBSERVATION OF HAND HYGIENE AND USE OF PROTECTIVE CLOTHING

Research personnel at each site will conduct direct human observations of compliance with HH and use of protective clothing. A minimum of 200 HH opportunities for each ward and intervention arm will be observed semiannually according to WHO methods [28]. At least 20 opportunities will be monitored for patients known to be colonized/ infected with ESBL-E-producing organisms. The use of protective clothing for CI as well as SP will also be recorded. All health care workers in the ward at the time of the observations will be eligible for monitoring. Observations will be recorded anonymously for both the patient and the HCW.
Monitoring personnel will be trained by Charité Berlin during the introductory course at the study site (see point 5.6.Training).
The results of the observations will be reported back to the wards.
In order to assess AHC from belt/pocket bottles and other disinfection dispensers beside the electronic counting devices, total AHC of the ward per year will be recorded.

7.1.2. AUTOMATIC HAND HYGIENE COUNT DEVICES

HH compliance will also be monitored by the use of ABHR dispensers with automatic hand hygiene count devices for every patient. Each hand hygiene event and the amount of disinfectant dispensed per stroke will be documented.
If the automatic count devices cannot be installed for all patient beds, if other disinfectant sources in the study sites cannot be replaced, or if a clear allocation to a specific patient bed is impossible, weekly point prevalence observations of compliance with HH are required.

7.2. MONITORING OF ANTIBIOTIC USE

The systemic antibiotic use at the ward-level will be collected monthly, in DDD per 1000 patient-days in ATC J01 classes.

8. DATA MANAGEMENT

Research Online's internet-based remote data entry system will be used to capture data for this study, including hospital, ward and patient level data.
Clinical and study personnel will collect data on paper forms, which will be stored securely at the study site. After the data have been recorded, on-site study personnel will use an internet browser to enter data into electronic case report forms (eCRFs). For completing both paper and electronic forms, guidelines will be provided to each site. All data on paper forms must be legibly recorded. Data are submitted to Research Online's secure web server and stored in the study's operational database. Authorized site personnel may log in to the system at any time, review and correct previously entered data, or put in additional data. Personnel will only be able to access information for subjects at their site.

Data will only be stored in the central database.

No study participants or HCWs will be identified by name on any study documents or electronic data submissions.

The Julius Center located at UMC Utrecht will provide data management support for this project. UMCU's programming team will create and validate datasets for statistical analysis.

9. STATISTICAL ANALYSIS

9.1. SAMPLE SIZE

20 wards in Europe will participate in this cluster-randomized, multi-center, crossover-design study.

Calculations are based upon the following assumptions:

- For this study, the average incidence of nosocomial acquisition of ESBL-E-producing *Enterobacteriaceae* determined using regular surveillance cultures is assumed to be at least 0.8 per 100 patients in Non-ICUs, a ratio of 1:1 for exposed (CI) and unexposed (SP) patients, alpha=0.05, and beta = 0.80. This assumption is considered to be reasonable because the incidence of MDRO colonization determined by regular surveillance cultures is substantially higher than MDRO incidence determined by cultures obtained for clinical indications only[29, 30].
- Because CI does have side effects for the patients and is both resource- and time-intensive and all ESBL-E-patients are identified by routine surveillance cultures, the study is powered to detect a 50% reduction in the incidence of ESBL-E-acquisition compared to the SP strategy.
- Based on these preconditions, 12,686 patients will be observed in the trial, 6,343 in each intervention phase.
- In order to determine the number of cases for a cluster-randomized study that correlates to the power of the number of cases determined by randomization at the individual level, this has to be multiplied with a design-effect factor: DE=1 + (n-1)*p. N is the number of individuals per cluster, and p is the intracluster correlation coefficient (ICC). The ICC is a measure for the similarity of the data of the cluster. It describes the similarity of cluster data by comparing the variance within clusters with the variance between clusters. According to the authors' knowledge, there is no study which describes inter- and intra-cluster variance in this setting. In various studies with dichotomous outcome, the design effect (DE) varies between 1.0 and 3.0[31-34].
- We assume a conservative design effect (DE) of 2.9. This results in a necessary number of cases of 36,788 patients, or 18,394 per study arm. With a DE of 2.9 in an individual randomization, 20 clusters and 635 patients pro cluster, the corresponding ICC is 0.003. This assumed ICC is justified because we assume only a small variance between clusters.
- Assuming an average number of 30 beds per ward, an average length of stay of 10 days per patient and 90% bed occupancy, a single ward will treat 988 patients per year, 20 wards will treat 19,764 patients each year and 39,528 patients in total. Thus, 20 wards will be enrolled.

9.2. STATISTICAL PLAN

9.2.1. DESCRIPTIVE STATISTICS

Description of parameters will be done as figures and percentages for categorical parameters, as mean and standard deviation for normal-distributed continuous parameters and as median and interquartile range (25% percentile, 75% percentile) for nonnormal-distributed continuous parameters.
Depending on the distribution of the parameters, differences will be tested using Fisher's Exact test, Chi-square test, T-test or Wilcoxon rank-sum test. Differences in incidence densities will be tested by Chi-square test for incidence densities..

9.2.2. COMPARISON OF HOSPITAL AND WARD CHARACTERISTICS

Ward-level data will be compared between the two study arms.

9.2.3. ANALYSES OF PRIMARY OUTCOMES

The incidence density of ESBL-E-acquisitions in the SP strategy and the CI strategy will be compared in total and at study arm, hospital level and ward level.
In the univariate and multivariable analysis, crude and adjusted incidence-density ratios of ESBL-E-acquisition between the two strategies will be calculated by Poisson or negative-binomial regression analysis with, at best, weekly (if this is impossible at least monthly) aggregated data using Generalized Estimating Equation (GEE) models. Additionally, a Generalized Linear Mixed Model (GLMM) will be used to consider temporary trends in the periods. In total, 480 observation months will be analysed for the 20 wards with 12 observation months each per IC strategy. To analyse 1 degree of freedom in the regression model (e.g. a dichotomous parameter or a continuous parameter), 20 observations are required. The log number of patient days will be treated as offset parameter.

The models will take into account for the clustering effects "hospital" and "ward" and will consider the following parameters: strategy, type and size of ward, type and size of hospital, antibiotic use of different antibiotic groups (DDD/1000 patient days or PDD/100 patients), staff equipment and the burden of ESBL-E at admission (ESBL-E patients on admission per 100 admitted patients), after grouping wards into "higher" or "lower" ESBL-E burden based on median proportion of ESBL-E carriers on admission.

A GLMM model with parameters not on the causal pathway between exposure and outcome and based on expert knowledge and will be considered (i.e. strategy, antibiotic use, staff equipment, burden of ESBL-E on admission, time trend). Parameters with a causal connection

to nosocomial ESBL-E-acquisitions such as AHC and single room use will not be considered in this model.

9.2.4. ANALYSES OF SECONDARY OUTCOMES

The incidence density of hospital-acquired infections caused by ESBL-E in the CI period with the SP period will be compared in total and ward levels. Additionally, a regression model will be performed to adjust by confounders.

The incidence density of clinical isolates with ESBL-E will be analysed by segmented regression using 31 observation months (3 month baseline, 12 month first intervention, 1 month washing out, 12 month second intervention, 3 month post intervention). Incidences of the different study phases will also be compared and tested.

To analyse the difference in HH practice for known ESBL-E patients in the two intervention periods, AHC will be calculated for ESBL-E-positive patient days (per ESBL-E-positive patient day) in both intervention periods at total and ward levels and differences will be tested.

To analyse the differences in the HH practice between known ESBL-E-carriers (use in ESBL-E-positive patient days) and patients not known to be ESBL-E-carriers (use in ESBL-E-negative patient days), AHC consumption in ESBL-E-positive and -negative patient days will be calculated separately at total and ward levels and by intervention period and differences will be tested.

10. ETHICS

This study is conducted in agreement with the declaration of Helsinki and with the guidelines of Good Clinical Practice (ICH-GCP-Guidelines, CPMP/ICH/135/95) issued by the EMEA (European Medicines Agency).

10.1. INFORMED CONSENT

To adequately determine the efficacy of both IC strategies, they must be applied uniformly to all the patients in a unit, as though the strategy had become standard practice in that unit. As ESBL-E-producing bacteria are transmissible agents, colonization/infection events in separate patients cannot be regarded as independent events. Ward level rates of colonization/infection will appropriately reflect non-independence of these events.

Thus, the trial will request a waiver of written informed consent of individual patients in the participating wards. This waiver has been granted at Charité University Hospital in Berlin (decision EA17323/12, 25.04.2013).

The study will involve no more than minimal risk of harm to patients. Several trials have suggested a low transmissibility of ESBL-E in the hospital setting [35], in particular of ESBL-producing *Escherichia coli* [21, 36]. In addition adverse effects of CI have also been repeatedly demonstrated.[8-11]. A waiver will not adversely affect the rights and welfare of patients and the trial cannot practicably be carried out without a waiver.

Given these considerations, a waiver of informed consent from patients in the participating wards is both important and appropriate for the proper conduct and analysis of this trial.

10.2. CONFIDENTIALITY

Information linking patient's medical data to study materials, including the CRF, will be maintained in a secure location at the site. This information will not be transmitted to the UMCU data management center. Individual subject data, ward and hospital data will be held in strict confidence by the investigator and R-GNOSIS-partners as permitted by law. Information contained in this protocol and data and results from the trial may not be disclosed without the written permission of the principal investigator. If results from this study are published, the ward's and the individual's identity will remain confidential.

11. PUBLICATION OF RESEARCH FINDINGS

Manuscripts and abstracts prepared from the data collected during this trial will be prepared through the study investigators. Site investigators will not publish or present interim results without written consent of the principal investigator. Investigators will provide the principal investigator with publication or presentation materials in advance of publication/presentation to allow for review and comment as means of ensuring confidentiality, accuracy, and objectivity.

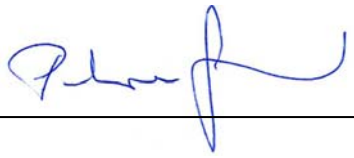
12. PROTOCOL SIGNATURE PAGE

12.1. PRINCIPAL INVESTIGATOR

I, Prof. Petra Gastmeier , MD agree to conduct: "R-GNOSIS WP5 Patient isolation strategies for ESBL-E carriers in medical and surgical hospital wards".

I understand that no deviations from this protocol, dated July 09th, 2013 may be made without the written permission of the R-GNOSIS WP5 protocol chair, except where necessary to eliminate immediate hazards to trial subjects, or when the change(s) involve only logistical or administrative aspects of the trial.

Date: 09.07.2013

Signature: 

12.2. UNIT DIRECTOR OR UNIT PHYSICIAN

I have read the protocol entitled: "R-GNOSIS WP5 Patient isolation strategies for ESBL-E carriers in medical and surgical hospital wards".

I agree to allow my ward to participate in this study and will make my staff available for training.

Name, printed _____

Date:

Signature: _____

12.3. UNIT NURSE DIRECTOR

I have read the protocol entitled: "R-GNOSIS WP5 Patient isolation strategies for ESBL-E carriers in medical and surgical hospital wards".

I agree to allow my ward to participate in this study and will make my staff available for training.

Name, printed _____

Date:

Signature: _____

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R-GNOSIS

Resistance of **G**ram-**N**egative **O**rganisms:

Studying **I**ntervention **S**trategies

WORK PACKAGE 5

Patient isolation strategies for ESBL carriers in medical and surgical hospital wards

MICROBIOLOGICAL PROTOCOL

Principal investigator:	
Version:	01
Funding source:	European Commission, DG Research
EU Project ID:	FP7-HEALTH-2011-SINGLE STAGE - N°282512

INDEX

1. SCOPE

This document describes the standard microbiological procedures used for R-GNOSIS Work Package 5 (WP5) for ESBL producing *Enterobacteriaceae* (ESBL-E) carrier detection.

2. CULTURE MEDIA AND REAGENTS

-Chromo ID ESBL (BioMerieux, France) agar

-Mueller-Hinton agar

-Antibiotic disks: amoxicillin/clavulanate (AMC; 20/10 µg), ceftazidime (CAZ; 30 µg), cefotaxime (CTX; 30 µg) and cefepime (CEP; 30 µg)

3. EQUIPEMENT

-Incubator (35±2ºC)

-Fridge (2-8ºC)

-Freezer (at least -20ºC)

4. SAMPLES: TYPE AND COLLECTING TIME

-In both arms of the trial, rectal swabs will collect for surveillance cultures in order to identify patients who are colonized with ESBL-E.

-All patients will be screened:

a) At admission (day 1) to the ward or as soon as possible within 3 days.

b) Repeated surveillance cultures will be obtained for patients staying longer than 7 days on a specific day each week (i.e., every Wednesday, Friday etc.).

c) At patient discharge from the ward: on the same day of discharge, if possible, or the day before.

-Patients readmitted to the ward will be treated as new cases.

-All specimens will be processed in the institutional microbiology laboratory and results will be reported as soon as possible to the wards

5. CULTURE PROCESSING AT LOCAL MICROBIOLOGY LABORATORY

a) Inoculation of rectal swabs and plates incubation

-The swabs will be processed immediately after delivery to the Microbiology lab, or at least the same day. If the swab could not be processed during the same working day, it will be kept at fridge temperature.

-Swabs will be platted on chromo ID ESBL (BioMerieux) chromogenic plates.

-Plates will be incubated at 35±2**º**C under normal atmosphere

b) Culture assessment and reporting:

Plates will be assessed at 24 and 48 h

-If after 48 h of incubation there is no growth in the chromogenic plates, the culture of the rectal swab will be informed as negative for ESBL detection.

-If after 24h or 48 h of incubation there are colonies in the chromogenic plates, then ESBL production must be confirmed.

c) Presumptive bacterial identification

-In chromo ID ESBL (BioMerieux) plates the presumptive bacterial identification will be performed as follows:

Pink colouration: *Escherichia coli*

Green, brownish-green or blue colouration: *Klebsiella* spp., *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp.

Dark to light brown colouration: *Proteus* spp., *Providencia* spp. and *Morganella* spp.

-Final identification will be performed at central microbiology laboratory using MALDI TOF MS.

d) Phenotypic confirmation of ESBL-production

-Growing colonies in chromogenic plates will be confirmed for ESBL-production, since bacterial expressing other resistance mechanisms (i.e chromosomal AmpC hyperproduction or plasmid AMPc) can also growth in these plates.

-ESBL-production will be confirmed by double-disk synergy (DDS) test using the following disks:

a) Pink colonies: AMC, CAZ and CTX

b) Other colouration: AMC, CAZ and CEP

-For inoculum preparation, pick colonies from a 18 to 24 h agar plate to 0.9% saline and adjust turbidity to 0.5McFarland scale. Dip a sterile cotton swab into the inoculum

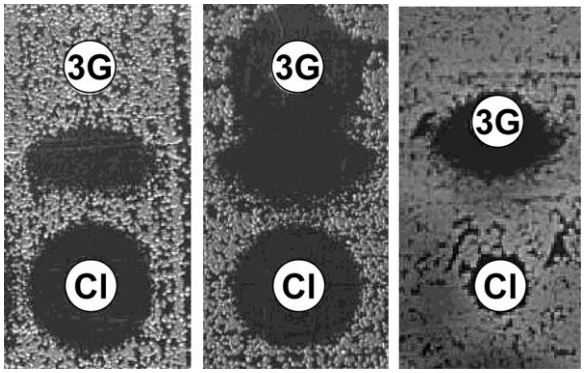
suspension streaked over the entire surface for three times rotating the plate approximately 60º each time.

-After moisture is totally absorbed, CAZ, CTX, or CEP disks will be placed at a distance of 20-30 mm (center to center) from AMC disk.

-Plates will be incubated at 35±2ºC for 16 to 18 hours.

-The presence of ESBL will be inferred when the inhibition zone around any of the cephalosporin disks will be enhanced on the side of the AMC disk, resulting in a characteristically shaped zone (Fig. 1).

Figure 1. Examples of positive double-disk synergy tests between a disk containing clavulanic acid (Cl) and a disk containing an extended-spectrum cephalosporin (3G).



Garrec H et al. J. Clin. Microbiol. 2011;49:1048-1057

-Alternatively, semiautomatic or automatic microdilution systems can be used to confirm ESBL production according to the standard microbiological procedures of each hospital.

6. STORAGE AND SHIPMENT OF STRAINS:

-ESBL-E isolates will be stored on cryogenic vials with 20% of glycerol at least at -20ºC.

-ESBL-E-isolates will be sent to the microbiology laboratory of the Hospital Ramón y Cajal in Madrid (SERMAS) for further microbiology and molecular epidemiologic analysis. Details concerning transports, specifically time points, are to be determined.

7. QUALITY CONTROL STRAINS:

K. pneumoniae ATCC 700603 (SHV-18 ESBL)

E. coli ATCC 25922 ESBL (ESBL-negative)

CharitéCentrum für diagnostische und präventive Labormedizin

Institut für Hygiene und Umweltmedizin
Hindenburgdamm 27, 12203 Berlin
Direktorin: Prof. Dr. med. P. Gastmeier

R-GNOSIS

Resistance of Gram-Negative Organisms:
Studying Intervention Strategies

WORK PACKAGE 5
Patient isolation strategies for ESBL carriers in medical and surgical hospital wards

SOP-Module:	II Processes 5. Observation Compliance
SOP-short name:	II_5_VS1.3_27/05/2014

Content

Responsible: Friederike Maechler Date: 27.05.2014

Review by: _____ Date:

Approved by (Project coordinator): _____ Date:

Content

SOP II_5_Observation compliances aims to describe the process of observation of CI and SP.

First version

Aimed at

Authorized persons in participating study teams in the following cities/countries:

Berlin/Germany
Utrecht/Netherlands
Geneva/Switzerland
Madrid/Spain

Distribution

Project office

5. Observation Compliance

Observations should be performed once per study month:

- 10 opportunities of CI / SP will be observed for ESBL-E-patients according to the current intervention phase.
- During **CI-period**, contact precautions for ESBL-E-patients will be observed. If no ESBL-E-patients are present on the study ward at the time of observation, other MDRO-patients treated with contact precautions will be observed in the CI-phase.
- During **SP-period**, standard precautions for ESBL-E-patients will be observed. If no ESBL-E-patients are present on the study ward at the time of observation, other patients treated with standard precautions will be observed.

5.1. General characteristics

New opportunities to put on gloves and/or gowns (aprons)	= ON
New opportunities to take off gloves and/or gowns (aprons)	= OFF

- New opportunities for gloves or gowns are monitored.

5.2. Observation of Compliance with Contact Precautions for ESBL-E-patients in CI

We will focus only on opportunities which are relevant for cross-transmissions **between** patients.
Other opportunities which may require a new set of gloves or a new gown while caring for one patient and which may have an impact on infection prevention (e.g. before aseptic procedures) but have no influence on cross-transmission between patients will not be monitored.

If a patient is treated with contact precautions, a set of gloves and gown is required before contact with the patient and/or the patient's surroundings. This will be monitored as follows:

bef-pat	**ON**

Subsequent contacts with the patient within the direct patients' surrounding which require a new set of gloves and/or gown will not be monitored, because they are not relevant for cross-transmissions between patients.

Taking off the equipment will be monitored accordingly. Taking off gloves in CI will be monitored as "After leaving the patient and/or the patients' surroundings":

aft-pat	**OFF**

While caring for one patient, a change of gloves will only be documented if the health care worker leaves the direct patients' surroundings (e.g. to get some equipment from the shelves).

5.3. Observation Compliance with Standard Precautions

In the SP-period, only the use of gloves will be documented. Relevant opportunities for the use of gloves in SP are before and after contacts with body fluids.

	Gloves
bef-b.f **ON**	Care of body sites with potentially infectious material (even dry wounds)
aft-b.f. **OFF**	After contact with potentially infectious material

R-GNOSIS

WP5: Patient isolation strategies for MDR-GNB carriers

CONTACT-ISOLATION - ESBL-Patient

Date: ______________ **Observer:** ________ **Session No:** ____

Ward ID: **RGNO** └┘.└┘└┘

OBSERVATION FORM

GLOVES

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

GOWNS

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-pat (= on) ☐ yes ☐ no
	☐	aft-pat (= off) ☐ yes ☐ no

R-GNOSIS

WP5: Patient isolation strategies for MDR-GNB carriers

CONTACT-ISOLATION - ESBL-Patient

Date: ______________ Observer: ________ Session No: ____

Ward ID: RGNO __ . __ __

GLOVES

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

GOWNS

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-pat	(= on)	☐ yes	☐ no
	☐	aft-pat	(= off)	☐ yes	☐ no

OBSERVATION FORM

GLOVES

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.
	☐	bef-b.f. (= on) ☐ yes ☐ no
	☐	aft-b.f. (= off) ☐ yes ☐ no

R-GNOSIS

WP5: Patient isolation strategies for MDR-GNB carriers

STANDARD PRECAUTIONS - ESBL-Patient

Date: _______________ Observer: _________ Session No: ____

Ward ID: RGNO └┘.└┘└┘

GLOVES

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

Nurse ☐ Physician ☐ Student ☐ Other ☐

Pat.No	monitored	opp.			
	☐	bef-b.f. (= on)	☐ yes	☐ no	
	☐	aft-b.f. (= off)	☐ yes	☐ no	

R-GNOSIS

Resistance of Gram-Negative Organisms:
Studying Intervention Strategies
WORK PACKAGE 5
Patient isolation strategies for ESBL carriers in medical and surgical hospital wards

Observation Form – Hand Hygiene

Ward ID: _____ Date: _____ Observer: _____ Session No.: ____

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
1	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
6	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
2	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
7	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
3	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
8	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
4	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
9	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
5	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No

Nurse ☐ Physician ☐ Student ☐ Other ☐

Opp.	Indication	Action
10	☐ bef-pat. ☐ bef-asept. ☐ aft-b.f. ☐ aft-pat. ☐ aft.p.surr.	☐ Yes ☐ No