Data validation study of the National surveillance of nosocomial infections in intensive care units (SIZ-IPH)

Study protocol

October 2000
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2 SUMMARY

- The objective of this data validity study is to measure the sensitivity, specificity, predictive values and correctness of the data reported to the ICU component of the National Surveillance of Hospital Infections (NSIH).

- The study will be performed in 45 hospitals selected from a list of participation-quarters from 1-1-1997 to 31-12-1999 through random systematic sampling.

- The retrospective chart review methodology will be used; the gold-standard will be the surveyor results.

- For pneumonia, all NSIH reported infections in the quarter will be reviewed, as well as a 20% random sample of NSIH reported non-infected patients.

- For bloodstream infections, all laboratory-reported positive cultures will be investigated from a laboratory listing, and chart-reviewed whenever the microbiological criteria for lab-confirmed bloodstream infection are met.

- The expected total number of charts to be reviewed is approximately 1300, which means 70 days of fieldwork dedicated to data collection. The study will be conducted from November 2000 to August 2001 using 5 surveyors.

- In January 2001, a pre-test will be carried out in 4 hospitals in order to evaluate the data collection methods and to train the surveyors. These hospitals will be revisited in order to measure the reproducibility of the investigator team.

- Specific studies will be undertaken taking the opportunity of field hospital visits (feasibility will be evaluated during the pre-test phase).
  - factors influencing sensitivity and specificity
  - workload associated with data collection & entering
  - validity of the AB resistance data
  - antibiotic use (empiric, therapeutic)
  - co-morbidity in ICU-acquired infections
  - outcome of positive cultures
3 **GENERAL REMARKS**

1. Before the study, informed consent will be obtained from the selected hospitals. The randomly selected hospitals will be invited to participate by a letter addressed to the Head Medical Officer and to the person in charge of the surveillance of nosocomial infections in intensive care. In case of refusal to participate in the study, available indicators of data validity (see secondary research questions) will be examined in order to estimate potential bias of the national results.

2. Of course, the proviso of confidentiality and anonymity should be stressed and is guaranteed.

3. Validation of national results will not ensure the validity at participant level. However, during the study, the results of the validation will be communicated at the end of the validation process and possible problems with regard to case definitions and data collection will be discussed with the hospital staff involved in the surveillance (training opportunity).

4. Data validation studies of surveillance networks are essential to ensure credibility and validity of the data\(^1,2,3\). However, they are **time-consuming and require a fastidious methodology**\(^4\). The experience of the US NNIS system\(^5\), which performed a pilot validation study presenting severe methodological limitations after more than 20 years of data collection should inspire us as a difficult but necessary experience (the NNIS system started in 1970, and the ICU component in 1986; a pilot validation study was initiated in 1993 and published in 1998).

5. Within a multi-center surveillance network, data validity (incl. sensitivity) should be monitored on a **continuous basis**, despite these difficulties.

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Feedback on the internal consistency and quality of the data recorded by the participants is given since end 1998 and showed to be efficacious in improving the quality of the data sent to the IPH. More importantly, before their participation to a surveillance period, surveillance participants should agree upon the principle of an external evaluation of their own results (incl. charts reviews). This could e.g. be achieved by the evaluation of all files of a randomly selected surveillance quarter every two years.

4 INTRODUCTION

4.1 Background

In January 1996 the Scientific Institute of Public Health (IPH) in collaboration with the Belgian Society of Intensive Care Medicine and Emergency Medicine (SIZ), started the Intensive Care Unit (ICU) component of the Belgian National Program for the Surveillance of Infections in Hospitals (NSIH). The surveillance protocol is based on the HELICS (Hospitals in Europe Link for Infection Control through Surveillance) protocol developed in 1995. Two ICU-acquired infections are being recorded: nosocomial bacteremia, with a reported overall incidence of 2.4% patients, and nosocomial pneumonia, with a reported incidence of 4.7%.

In 1997, a financial incentive was established for participating hospitals (fixed amount provided by the federal Ministry of Health), and the number of participants increased. Since this might have changed the hospitals participation policy and hence the data quality, this study will focus on the participation from 1997 onwards. Furthermore, the initial version of the protocol (January 1996) was updated in January 1997, bringing slight changes to the previous version. The changes to the infection definitions however were minor.

Figure 1. Participation to the ICU component of the NSIH surveillance, 1996-1999. Percentage hospitals participating by surveillance quarter and cumulative percentage having participated at least once (n=137 hospitals).
Study Objectives
The general objective is to validate the reported data against a reference gold standard (surveyors results).

4.2 Main research questions
1. Exhaustively (completeness) of the denominator: are all patients that stay longer than 24 hours in the ICU included in the surveillance
2. Sensitivity (SE) : what proportion of all ICU-acquired PN and BSI is reported to the national surveillance of nosocomial PN and BSI (or inversely 1-SE, i.e. the proportion of PN/BSI missed by the surveillance system)
3. Specificity: what proportion of reported infections are true infections according to the definitions of the protocol (or 1-specificity=false positives)
4. Positive and negative predictive value (the probability to be NI+ when Surveillance+ or NI- when Surveillance-)

4.3 Secondary research questions
The feasibility of collecting data to address secondary research questions during the validation study will be assessed during the pretest phase. The following list is thus still subject to discussion and changes.

1. validation of other data/definitions included in the protocol : SAPS II score, day-by-day procedures, AB resistance data
2. workload associated with data collection & entering
3. factors influencing sensitivity and specificity of the surveillance
4. collection of additional data to interpret results of studies of antimicrobial resistance (AMR) in ICU-acquired infections (trends, attributable mortality)
   4.1. assessment of bias in the epidemiological estimates of AMR figures due to missing data
   4.2. therapeutic and empiric antibiotic use in ICU
   4.3. co-morbidity in ICU-acquired infections not included in surveillance
   4.4. cause of death
5. outcome of positive cultures
5 METHODS

5.1 Gold Standards and case definitions

5.1.1 General remarks

5.1.1.1 Gold standard
A real gold standard, i.e. a test that is 100% sensitive and 100% specific in detecting the outcome or disease of interest, is seldom, if ever, available in validity studies of surveillance systems. A gold standard for ICU-acquired pneumonia would even be more subject to discussion since there is a lack of agreement upon the definition of pneumonia in scientific literature.

5.1.1.2 Definition of “ICU-acquired”
The term “ICU-acquired infection” refers to an infection that was “not present or not in incubation at admission to the ICU”, and that may occur after discharge from the ICU. Usually, the period cut-off points for ICU-acquired are arbitrarily set at 48 hours after admission until 48 hours after discharge from the ICU. Before 48 hours of admission there is indeed a higher variability in reporting infections, due to the fact that these infections are not considered as related to the ICU-stay. An exception to the 48h criterion is made whenever the relationship with the origin can be clearly established, which may be the case for e.g. catheter-related bacteremia.

5.1.1.3 Validation of post (ICU)-discharge infections
The case definition of ICU-acquired infections in the WIV/SIZ protocol includes infections occurring within 48 hours after discharge from the ICU. In order to validate these “post (ICU)-discharge infections”, the patient files should include data on the total hospital stay of the patient (at least up to 48h after discharge from the ICU).
Under the latter condition, the validation of post-discharge pneumonia will be possible. For the validation of bacteremia however, this moreover supposes that microbiological data (positive blood cultures) from ICU-patients can be linked to bacteriological results obtained during their post-ICU hospital stay (see below). The feasibility of this method will be assessed during the pre-test phase in 4 hospitals.

5.1.1.4 First and subsequent episodes of infections.
All infections are included (reported as well as detected), so that the sensitivity calculation will include the first and further infections reported / the first and further infections detected. This will be called the sensitivity of detecting infections. The main indicator however is the sensitivity of detecting infected patients, i.e. the number of patients reported with at least an infection / number of patients detected with at least an infection.

This indicator is actually closer to the incidence figure, which does not take into account infections after the first one. It could be that missed infections are those occurring after a first episode, which are, for incidence figures rather less important.

5.1.2 Pneumonia (PN)
The reference used for pneumonia is the retrospective chart review. Selected patient files from randomly selected hospitals are systematically reviewed by a trained team of investigators of the IPH and verified for evidence of criteria of pneumonia as defined in the study protocol.
As a reminder, a pneumonia episode should have been included if one of the three inclusion criteria is positive:
1. Decision to treat for pneumonia: a treatment for pneumonia is installed
2. X-ray signs of pneumonia: recent or persistent infiltrate, opacity or cavity on X-ray examination of the thorax
3. Purulent sputum or change in the character of sputum

Furthermore, the presence of secondary criteria will be verified to assess the validity of applying HELICS (definite/possible) and/or CDC case definitions for PN in the analysis process. These criteria include:
1. Isolation of an etiologic agent from specimen obtained using standardized methods,
2. Clinical signs suggestive of pneumonia,
3. Microorganisms cultured from blood, etc (see surveillance protocol).

5.1.3 Bloodstream infections (BSI)
The reference used for laboratory-confirmed bacteremia is the list of positive hemocultures obtained from the microbiological laboratory. Furthermore, the list of catheter tip cultures should be obtained to verify if the bacteremia is catheter-associated. The patient files will further be examined to determine the origin if not catheter-related.
Case definition of bacteremia: positive hemoculture if recognized pathogen, or 2 separate positive hemocultures (within 72 h) of common skin contaminant.
Remark: The frequency of detecting lab-confirmed bacteremia depends on the strategy of performing blood cultures in the hospital. In a hospital where blood cultures are systematically performed if the patient has fever e.g., one will expect to find more false negatives than in a hospital that takes blood samples only in presence of more severe clinical signs. Therefore, the blood culturing strategy must be described in each hospital intensive care unit to interpret the data of the validity study.

5.1.4 Denominator data
The exhaustivity of the denominator, i.e. the total number of patients that were admitted to the ICU and stayed longer than 24 hours, will be collected from the administrative hospital database. The list will include admission date and hour to the ICU as well as date and hour of discharge. Subsequently, the total

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number and the total number of patient-days will be compared with the respective figures in the national surveillance database. This parameter is of major importance for a correct estimate of the NI incidence rate. The exhaustivity has been reported to be only 78% in the French (Réa Sud-Est network)\textsuperscript{8} experience.

\textit{Note: this will allow an estimation of the number of patients excluded because they stay only one day in the ICU.}

### 5.1.5 Training of surveyors

In order to apply the gold standard in a uniform manner, training of investigators (surveyors) is essential. The investigator(s) will be IPH employed. They should be familiar with the protocol, the definitions and the surveillance system.

The investigator(s) should not look at the reported NSIH data before the field survey visit. This will ensure a impartiality, and checking files without ‘a priori’ feelings.

The training of the surveyors will be organized by one person of the NSIH team, and will consist in:
1. Training sessions on nosocomial pneumonia and bacteremia, group discussions on case definitions and standardized application of diagnostic criteria
2. Development and discussion of an algorithm for file examination, detection of infections and determining the origin of bloodstream infections
3. Case studies
4. Field visits: during the pre-test of the data collection process, four hospitals will be visited by the training responsible with each of the other investigators, in order to obtain a uniform method for file examination.

In order to assess the reproducibility of the investigator team (“validation of the reference”) these four hospitals will be re-visited shortly afterwards by another investigator who will re-examine the same files (see 5.2.4).

### 5.2 Study design

#### 5.2.1 General remarks

The sampling method differs for pneumonia and bacteremia.

For pneumonia, a sample from the surveillance- charts will be taken to estimate the proportion of false negatives. The sample size is determined by the a priori estimation of this proportion (number of PN+ charts/ total number of surveillance PN- charts=1-negative predictive value) and by the desired precision of this estimate. The precision of 1-NPV will eventually determine the width of the confidence interval around the sensitivity of detecting PN in the surveillance (which is the main outcome of the study).

\textit{Since this sampling process also requires the highest sample size, the sampling design for pneumonia determines the total sampling population of the study.}

In order to determine sensitivity and specificity for bacteremia, an exhaustive laboratory list of positive hemocultures for all patients admitted to the ICUs in the hospitals selected for pneumonia will be used. The true negatives for BSI are patients without positive hemoculture and reported as negative in the surveillance system.

5.2.2 Pneumonia

5.2.2.1 Sample size formulas

The sampling method can be derived from the validation study described by Broderick et al, originating from Fleiss JI (a simplification of the classic large sample standard error of a function of multinomial proportions. Am Stat 1982; 36:377-8). They calculate the 95% confidence interval (CI) on the basis of the following formula:

Formula 1

$$95\% \ CI = P \pm 1.96 \sqrt{\frac{P(1-P)}{n}}$$

Where :
P = estimated sensitivity, specificity or positive predictive value
n = number of observations used to compute P.
$$\alpha$$ risk is 0.05

This formula is derived from the estimation of a sample size for single proportions:

Formula 2

$$n = \frac{N \ z^2 \ P \ (1-P)}{d^2 \ (N-1) + z^2 \ P \ (1-P)}$$

Where:
n = sample size
N = total population,
z = Z value (confidence interval)
P = prevalence
d = absolute precision

5.2.2.2 Sample size calculation
The sample size calculation is developed from a simulation of the true situation (based on surveillance database, from Jan 1997 to March 1998 with 31600 reported patients).

Table 1. Simulation of the sensitivity and specificity of the surveillance of ICU-acquired pneumonia

<table>
<thead>
<tr>
<th>Surveillance PN</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>a (TP)</td>
<td>1433</td>
<td>147</td>
</tr>
<tr>
<td>b (FP)</td>
<td>1580</td>
<td></td>
</tr>
<tr>
<td>c (FN)</td>
<td>779</td>
<td>29241</td>
</tr>
<tr>
<td>d (TN)</td>
<td>30020</td>
<td></td>
</tr>
<tr>
<td>a+c</td>
<td>2212</td>
<td>29388</td>
</tr>
<tr>
<td>b+d</td>
<td></td>
<td>31600</td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TP : true positive  
FP : false positive  
FN : false negative  
TN : true negative

**Known parameters:**
- the total number of surveillance positives : a+b (5%)  
- the total number of surveillance negatives : c+d (95%)

**Unknown parameters:**
1. the true prevalence of ICU-acquired pneumonia (a+c): here, the true prevalence rate is estimated at 7% (2212/31600), yielding an anticipated sensitivity for the national surveillance of 65% (a/a+c).
2. the proportion of false positives among the reported pneumonias (1-PPV): this % is expected to be low (from literature) and estimated at 9.3% of the reported PN+ from an anticipated specificity of 99.5% (d/b+d)

To estimate the total of PN positives, a sample must be drawn from all surveillance PN− files to estimate the number of false negatives (c).  
To estimate the number of false positive PN, a sample must be drawn from all surveillance PN+ to estimate the number of false positives (b).

With this anticipated estimation of 65% sensitivity and 99.5% specificity, the proportion (of false negatives) to be estimated among all surveillance negatives is 2.6% (c/c+d).

**Definition of other parameters in the formula:**
- we wish to obtain 95% confidence around our estimates : \( z = 0.05 \) (formula 2)  
- we choose a relative precision of 50% for both c and b, yielding an absolute precision (\( d \) in formula 2) of 1.3% for c and 4.7% for b
- given the clustering (in hospitals) of the chart finding, a design effect of 2 should be included to obtain a reliable national estimate, so that \( n \) is \( 2 \times n \).

**Results of the sample size calculation (design effect=2):**
- estimation of \( c \) (false negatives) : sample of 904 surveillance negative files
- estimation of \( b \) (false positives) : sample of 268 surveillance positive files

**5.2.2.3 Expected results for PN**
The “anticipated” results of the validation study for the above mentioned scenario are (design effect of 2):
- estimated proportion of false negatives among surveillance negatives \( \frac{c}{c+d} \) : 2.6% (95%CI 1.3%-3.9%)
- hence, anticipated sensitivity : 65% (95% CI 55%-79%), and
- negative predictive value \( \frac{d}{c+d} \) : 97.4%
- estimated proportion of false positives among surveillance negatives \( \frac{a}{a+b} \) : 9.3% (95%CI 4.7%-14.0%)
- anticipated specificity (fixed) : 99.5% (95% CI 99.3% - 99.8%), and
- positive predictive value : 90.7%

**5.2.2.4 Hospital sampling**
Since the national database consists of surveillance quarters, a list of hospital-quarters is used as sampling basis for hospital selection. Thus the composition of the national database with regard to hospital size and frequency of participation is respected in the study sample. The limiting factor in the number of hospitals to be selected is the number of PN reported, which is at average 6 PN by quarter. Hence the number of hospital-quarters to be selected is 268/6 = 45.
The sample is drawn using systematic random sampling from a list of all hospital-quarters from 1 January 1997 to 31 December 1999.

**5.2.2.5 Selection of patient files**
Files for examination by the investigator team are selected as follows:
- PN+ : all PN+ files reported to the surveillance during the selected surveillance quarter
- PN- : a 20% random sample of the PN negative files reported to the surveillance (20% from the total number of PN- in 45 hospital quarters to obtain at least 904 files from an estimated total of 5130 PN- files)
Since data are anonymously transmitted to the IPH, a list of characteristics allowing the identification of the patient at the level of the person in charge of the surveillance will be sent to the selected hospitals.

**5.2.3 Bloodstream Infections**

**5.2.3.1 Sample size calculation**
The sample size for blood stream infection is determined by the total population from the pneumonia sample. A different methodology will be used
for the assessment of the occurrence of blood stream infections. Here the gold standard will be based on laboratory data completed by patient file examination, as by definition blood stream infections have to be laboratory confirmed.

It is expected that in the same sample of hospitals selected for pneumonia, approximately 123 nosocomial blood stream infections will be reported (on the basis of the overall incidence). From this figure, the following estimation of the true situation is made (table 2).

Table 2. Simulation of the sensitivity and specificity of the surveillance of ICU-acquired bacteremia

<table>
<thead>
<tr>
<th>Laboratory/ Patient files</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance BSI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>98</td>
<td>25</td>
</tr>
<tr>
<td>a (TP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b (FP)</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>(a+b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>40</td>
<td>4967</td>
</tr>
<tr>
<td>c (FN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d (TN)</td>
<td>5007</td>
<td></td>
</tr>
<tr>
<td>(c+d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>138</td>
<td>4992</td>
<td>5130</td>
</tr>
</tbody>
</table>

**Known parameters**
- Total number of surveillance BSI+
- Total number of surveillance BSI-

**Unknown parameters**
- False negatives : can be detected (theoretically with 100% certainty) by reviewing the laboratory result.
- False positives : BSI reported to the surveillance that do not figure on the laboratory list; reported BSI that do not match the definitions of the surveillance protocol.

**5.2.3.2 Expected results for Blood Stream Infections**
- Sensitivity : $\frac{98}{138} = 70.8\%$
- Specificity : $\frac{4867}{4992} = 99.5\%$
- Negative predictive value (d/c+d) : 99.2%
- Positive predictive value (a/a+b) : 79.8%

Since we are 100% exhaustive in the selected hospitals with regard to positive blood cultures, confidence limits will be calculated considering that the surveillance-quarter under study is a sample of all surveillance-quarters, and thus to take into account variability over time.

Other indicators that will be verified during BSI validation are:
- Proportion of cases with origin of BSI not discrepant
- Proportion of cases with degree of certainty (definite/possible) not discrepant
- Proportion of cases with Coagulase Negative Staphylococci reported infections / total N of reported BSI

5.2.3.3 Steps for BSI validation

a) Solicit laboratory data (all positive blood cultures + positive catheters samples) from all ICU patients (>1 day) during the same participation period (3 months), up to 48 hours after ICU-discharge (as in 5.1.1.3)
b) Exclusion of non-eligible (contaminated) positive blood culture results based on the criteria of the study protocol; check with NSIH reported infections for possible false positives, which should be included for chart review
c) Send to the selected hospitals a list with identification data of eligible charts (<48 hours included, since the definition of ICU-acquired catheter-associated bacteremia includes early infections):
In example at table 2, the total number of charts to be examined is 98 + 40 + 25 = 163, with a mean of 3.6 charts per hospital-quarter (n hospital-quarters=45, see pneumonia)
d) Field study: review all selected charts and determine origin, false negatives and false positives

5.2.4 Pre-test

The study protocol will be pre-tested in 4 hospitals selected from the same list as those included in the study sample. The person responsible for the training of the surveyors will visit the 4 hospitals with each one of the other surveyors (IM, EL, HC, CS).
During the pre-test, following actions will be undertaken:
- Apply the questionnaire to the person in charge of the surveillance, determine the amount of time necessary to obtain answers for each question, evaluate the relevance and appropriateness of each question to obtain the requested data.
- Examination of a maximum number of files within the time limit of one day. Determination of necessary time for data collection. Test the algorithm for the examination of patient files.
Those hospitals will be revisited (by another surveyor) as first hospitals of the national sample.
The same hospitals will be revisited as first hospitals of the national sample, by another surveyor. This will allow the assessment of the reproducibility of the surveyors.
Agreement between surveyors will be expressed by the kappa statistic.

<table>
<thead>
<tr>
<th>Surveyor 1</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveyor 2</td>
<td>+</td>
<td>a</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>c</td>
</tr>
<tr>
<td></td>
<td>a+c</td>
<td>b+d</td>
</tr>
</tbody>
</table>
Agreement (%) = a+d/a+b+c+d

Disagreement (%) = b+c/a+b+c+d

5.2.5 Secondary research questions
The number of secondary research questions addressed during the study depends on the result of the pre-test. Methods used for data collection are briefly reviewed below.

5.2.5.1 Validation of other data/definitions included in the surveillance
1. SAPS II score, other risk factors at admission: chart review on 10% of the total sample
2. Day-by-day procedures: questionnaire to the person in charge of the surveillance
3. Microbiological results and AB resistance data: review of infection files

5.2.5.2 Workload associated with data collection & entering
By questionnaire administered to the person in charge of the surveillance, determine: number of persons involved in data collection and verification, data entering + time spent to each of these activities

5.2.5.3 Factors influencing sensitivity and specificity of the surveillance
By questionnaire administered to the person in charge of the surveillance, determine:
- Person in charge of collecting data for each of the components of the surveillance,
- Who decides whether an infection is reported as ICU-acquired or not,
- Criteria for blood culturing,
- Micro-organisms reported (e.g. for BSI, % of CNS)
- Degree of adherence to the protocol definitions,
- Staff to patient ratio (ICU, infection control staff),
- Hospital size
- Active surveillance of post-discharge infections Y/N (from national database and questionnaire)
- Quality of surveillance data sent to the IPH (from national database)

Following data should be obtained in order to interpret correctly the results from studies based on the antibiotic resistance data collected by the surveillance (trend analysis, studies of attributable mortality and excess length of stay).

5.2.5.4 Therapeutic and empiric antibiotic use in ICU
By chart review, identify antibiotics used for prophylaxis, empiric treatment (before the microbiological results are available) and for therapeutic use. These data can be used to validate the results of the ESAP study (European Study of Antibiotic Prophylaxis) and will allow to study the associations between previous antibiotic use and antimicrobial resistance. By questionnaire, assess the existence of local guidelines for AB use.
5.2.5.5 Co-morbidity in ICU-acquired infections
By chart review, identify endogenous risk factors (co-morbidity, e.g. diabetes, renal failure) for nosocomial infections that are not included in the surveillance protocol. This might be done for all infections and a matched sample of the non-infected.

5.2.5.6 Outcome of positive cultures
Furthermore, after linking the laboratory list with the patient files in the national database, a study of the outcome of all positive blood cultures will be done in order to assess the clinical significance of a positive blood culture.

6 Time schedule
The time schedule of the study is described in the table below. Before starting the study in the 45 randomly selected hospitals, the hospital medical director, the head of the ICU and the laboratory should accept to participate in the study. Potential biases of the national findings resulting from refusal to participate should be assessed by available indicators of data validity (as in 5.2.4.3).

<table>
<thead>
<tr>
<th>Period</th>
<th>Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 2000</td>
<td>Send letter of acceptance (agreement from medical director, laboratory and ICU staff) for the selected hospitals</td>
</tr>
<tr>
<td>November 2000</td>
<td>Ask laboratory list of positive blood cultures in selected period</td>
</tr>
<tr>
<td>December 2000</td>
<td>Send list of charts to be reviewed to 4 pre-test hospitals</td>
</tr>
<tr>
<td></td>
<td>Training of surveyors</td>
</tr>
<tr>
<td></td>
<td>Fix an appointment for the pre-test</td>
</tr>
<tr>
<td>January 2001</td>
<td>Pre-test</td>
</tr>
<tr>
<td>February – June 2001</td>
<td>Send complete list of patient charts to be reviewed (total = 904 PN- + 268 PN+ + 151 BSI+ = 1335)</td>
</tr>
<tr>
<td></td>
<td>Fix an appointment with the person in charge of the surveillance ; adapt questionnaires from pre-test</td>
</tr>
<tr>
<td></td>
<td>Field visits : chart reviews and other data collection (questionnaire)</td>
</tr>
<tr>
<td>July - August 2001</td>
<td>Data analysis and reporting</td>
</tr>
</tbody>
</table>
7 GLOSSARY OF TERMS AND ABBREVIATIONS

AB = antibiotic
AMR = antimicrobial resistance
BSI = blood stream infection
FN = false negative
FP = false positive
HELICS = Hospitals in Europe Link for Infection Control trough Surveillance
ICU = Intensive Care Unit
IPH = Institute of Public Health
NNIS = National Nosocomial Infections Surveillance system
NSIH = Nosocomial Surveillance for Infections in Hospitals
NPV = Negative predictive value
PN = pneumonia
PPV = Positive predictive value
SAPS II = Simplified Acute Physiology Score II
SE = sensitivity
TN = true negatives
TP = true positives

<table>
<thead>
<tr>
<th>Test (Surveillance)</th>
<th>Reference (chart review)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>a (TP) b (FP) a+b</td>
</tr>
<tr>
<td>-</td>
<td>c (FN) d (TN) c+d</td>
</tr>
<tr>
<td></td>
<td>a+c b+d a+b+c+d</td>
</tr>
</tbody>
</table>

- TP (a): true positives: both the test (here: the surveillance system) and the reference (here: chart review by the surveyors) detect illness
- TN (d): true negatives: neither test or reference detect illness
- FP (b): false positives: detected as ill by test but not confirmed by reference (case definition not met)
- FN (c): false negatives: not detected as ill by test but diagnosed as ill (case definition positive) by reference

- Sensitivity (SE) = a/a+c: the probability of being test positive when ill
- Specificity (Sp) = d/b+d: the probability of being test negative when not ill
- Positive predictive value (PPV) = a/a+b: the probability of being ill when test positive
- Negative predictive value (NPV) = d/c+d: the probability of not having the disease when test negative

Remark: NPV and PPV in the population depend on the prevalence (here in fact: incidence) of the disease. Since the entire surveillance population is considered in the protocol, the PPV and NPV are also directly applicable.
8 REFERENCES


