**Healthcare-associated infections in neonates and children in the first European point prevalence survey - THELANCETID-D-16-01041-R3**

# Supplementary material

**Supplementary table 1.** Definitions of healthcare-associated infections for neonates, bloodstream infections and clinical sepsis – Paediatric data, standard protocol, ECDC point prevalence survey 2011-2012

| BSI: BLOODSTREAM INFECTION | |
|---|---|
| **BSI: Laboratory-confirmed bloodstream infection** | |
| One positive blood culture for a recognised pathogen<br>**or**<br>patient has at least one of the following signs or symptoms: fever (> 38 °C), chills, or hypotension<br>**and**<br>two positive blood cultures for a common skin contaminant (from two separate blood samples, usually within 48 hours) | Skin contaminants: coagulase-negative staphylococci (including S. epidermidis), *Micrococcus* spp., *Propionibacterium acnes*, *Bacillus* spp., *Corynebacterium* spp.<br><br>- Primary bloodstream infections include catheter-related BSI and BSI of unknown origin.<br>- A CVC-associated bloodstream infection according to CDC/NHSN definitions (different from CVC-related BSI) is a primary BSI with central vascular catheter use (even intermittent) in the 48 hours preceding the onset of the infection: therefore the presence of 'the relevant device' (central/peripheral vascular catheter) in the 48 hours before onset of infection is collected even in the absence of microbiological confirmation |
| **CRI: CATHETER-RELATED INFECTION** | |
| **CRI1-CVC: local CVC-related infection (no positive blood culture)** | |
| Quantitative CVC culture ≥ 103 CFU/ml (1) or semi-quantitative CVC culture > 15 CFU<br>**and**<br>pus/inflammation at the insertion site or tunnel | |
| **CRI1-PVC: local PVC-related infection (no positive blood culture)** | |
| Quantitative PVC culture ≥ 103 CFU/ml or semi-quantitative PVC culture > 15 CFU<br>**and**<br>pus/inflammation at the insertion site or tunnel | |

**CRI2-CVC: General CVC-related infection (no positive blood culture)**

Quantitative CVC culture ≥ 103 CFU/ml or semi-quantitative CVC culture > 15 CFU
**and**
clinical signs improve within 48 hours after catheter removal

**CRI2-PVC: General PVC-related infection (no positive blood culture)**

Quantitative PVC culture ≥ 103 CFU/ml or semi-quantitative PVC culture > 15 CFU
**and**
clinical signs improve within 48 hours after catheter removal

**CRI3-CVC: microbiologically confirmed CVC-related bloodstream infection**

BSI occurring 48 hours before or after catheter removal
**and**
positive culture with the same microorganism of either:

- quantitative CVC culture ≥ 103 CFU/ml or semi-quantitative CVC culture > 15 CFU
- quantitative blood culture ratio CVC blood sample/peripheral blood sample > 5 (3)
- differential delay of positivity of blood cultures (4): CVC blood sample culture positive two hours or more before peripheral blood culture (blood samples drawn at the same time)
- positive culture with the same microorganism from pus from insertion site

**CRI3-PVC: microbiologically confirmed PVC-related bloodstream infection**

BSI occurring 48 hours before or after catheter removal
**and**
positive culture with the same microorganism of either:

- quantitative PVC culture ≥ 103 CFU/ml or semi-quantitative PVC culture > 15 CFU
- positive culture with the same microorganism from pus from insertion site

- CVC=central vascular catheter; PVC=peripheral vascular catheter
- Central vascular catheter colonisation should not be reported
- A CRI3 (-CVC or -PVC) is also a bloodstream infection with source C-CVC or C-PVC respectively; however: when a CRI3 is reported, the BSI should not be reported in the point prevalence survey; microbiologically confirmed catheter-related BSI should be reported as CRI3

## SYS: SYSTEMIC INFECTIONS

### SYS-CSEP: clinical sepsis in adults and children

Patient has at least one of the following criteria:
- clinical signs or symptoms with no other recognised cause
- fever (38 °C)
- hypotension (systolic pressure < 90 mm)
- or oliguria (20 cm3(ml)/hr)

**and**
- blood culture not done or no organisms or antigen detected in blood

**and**
- no apparent infection at another site

**and**
- physician institutes treatment for sepsis

- Do not use this code unless absolutely needed (last-resort definition)
- For CSEP in neonates, use NEO-CSEP case definition (see below)

## NEO: SPECIFIC NEONATAL CASE DEFINITIONS

### NEO-CSEP: clinical sepsis in neonates

All of the three following criteria:
- supervising physician started appropriate antimicrobial therapy for sepsis for at least five days
- no detection of pathogens in blood culture or not tested
- no obvious infection at another site

**and**

two of the following criteria (without other apparent cause):
- fever (> 38 °C) or temperature instability (frequent post-set of the incubator) or hypothermia (< 36.5°C)
- tachycardia (> 200/min) or new /increased bradycardia (< 80/min)
- capillary refilling time (CRT) > 2s
- new or increased apnoea(s) (> 20s)
- unexplained metabolic acidosis
- new-onset hyperglycemia (> 140mg/dl)
- another sign of sepsis (skin colour (only if the CRT is not used), laboratory signs (CRP, interleukin), increased oxygen requirement (intubation), unstable general condition of the patient, apathy)

A one-time detection of coagulase-negative staphylococci (CNS) in blood cultures should not exclude the diagnosis of clinical sepsis. A clinical sepsis can also be diagnosed with a single positive blood culture with CNS, which is considered as a blood culture contamination, while other criteria of CNS bloodstream infection are not met and criteria of clinical sepsis have been met.

## NEO-LCBI: laboratory-confirmed BSI

At least two of:

- temperature > 38 °C or < 36.5 °C  or temperature instability
- tachycardia or bradycardia,
- apnoea
- extended capillary refilling time (CRT)
- metabolic acidosis
- hyperglycaemia
- other sign of BSI such as apathy;

**and**

- a recognised pathogen other than coagulase-negative staphylococci (CNS) cultured from blood or cerebrospinal fluid (CSF; this is included because meningitis in this age group is usually haematogenous, so positive CSF can be regarded as evidence of BSI even if blood cultures are negative or were not taken)

- In order to be consistent with BSI reporting in adults (including secondary BSI), the criterion 'the organism is not related to an infection at another site' was removed from the Neo-KISS definition for the purposes of the ECDC PPS
- Report the origin of the neonatal BSI in the field BSI origin
- If both the case definitions for NEO-LCBI and NEO-CNSB are matched, report NEO-LCBI

## NEO-CNSB: laboratory-confirmed BSI with coagulase-negative staphylococci (CNS)

At least two of:

- temperature > 38 °C or < 36.5 °C  or temperature instability
- tachycardia or bradycardia,
- apnoea
- extended capillary refilling time (CRT)
- metabolic acidosis
- hyperglycaemia
- other sign of BSI such as apathy;

**and**

- CNS is cultured from blood or catheter tip;

**and**

patient has one of:

- C-reactive protein > 2.0 mg/dL
- immature/total neutrophil ratio (I/T ratio) > 0.2
- leukocytes < 5/nL
- platelets <100/nL

- Report the origin of the neonatal BSI in the field BSI origin
- If both the case definitions for NEO-LCBI and NEO-CNSB are matched, report NEO-LCBI

## NEO-PNEU: pneumonia

Respiratory compromise
**and**
new infiltrate, consolidation or pleural effusion on chest x-ray;
**and**
at least four of:

- temperature > 38 °C or < 36.5 °C or temperature instability
- tachycardia or bradycardia
- tachypnoea or apnoea
- dyspnoea
- increased respiratory secretions
- new onset of purulent sputum
- isolation of a pathogen from respiratory secretions
- C-reactive protein > 2.0 mg/dL
- I/T ratio >0.2
-

## NEO-NEC: necrotising enterocolitis

Histopathological evidence of necrotising enterocolitis
**or**
at least one characteristic radiographic abnormality (pneumoperitoneum, pneumatosis intestinalis, unchanging ‘rigid’ loops of small bowel)
**and**
at least two of the following without other explanation:

- vomiting
- abdominal distention
- prefeeding residuals
- persistent microscopic or gross blood in stools

**Supplementary table 2.** Prevalence of children with one or more healthcare-associated infections – Paediatric data, ECDC point prevalence survey 2011-2012

| Country | HAI (N) | Children (N) | HAI prevalence |
|---|---|---|---|
| Poland | 97 | 934 | 10.4% |
| Finland | 33 | 413 | 8.0% |
| Cyprus | 9 | 116 | 7.8% |
| Iceland | 3 | 39 | 7.7% |
| Croatia | 28 | 432 | 6.5% |
| Netherlands | 33 | 529 | 6.2% |
| Estonia | 6 | 100 | 6.0% |
| Greece | 44 | 744 | 5.9% |
| Spain | 47 | 882 | 5.3% |
| Luxemburg | 3 | 63 | 4.8% |
| Portugal | 31 | 670 | 4.6% |
| Belgium | 42 | 936 | 4.5% |
| United Kingdom | 121 | 2857 | 4.2% |
| Malta | 3 | 71 | 4.2% |
| Hungary | 35 | 878 | 4.0% |
| Norway | 4 | 115 | 3.5% |
| Denmark | 1 | 30 | 3.3% |
| Austria | 7 | 210 | 3.3% |
| Latvia | 11 | 336 | 3.3% |
| Bulgaria | 37 | 1193 | 3.1% |
| Slovenia | 17 | 617 | 2.8% |
| France | 10 | 367 | 2.7% |
| Ireland | 21 | 801 | 2.6% |
| Slovakia | 28 | 1073 | 2.6% |
| Lithuania | 14 | 619 | 2.3% |
| Italy | 25 | 1166 | 2.1% |
| Romania | 8 | 471 | 1.7% |
| Germany | 4 | 280 | 1.4% |
| Czech Republic | 4 | 331 | 1.2% |

HAI: Healthcare-associated infection

**Supplementary table 3.** Predicted HAI prevalence among clinical settings and according to the number of children a hospital included in the survey – Paediatric data, standard protocol, ECDC point prevalence survey 2011-2012

| | Prevalence (%) | 95%CI |
|---|---|---|
| **Clinical setting** | | |
| Paediatric intensive care | 18.6 | 13.0-25.9 |
| Neonatal intensive care | 12.6 | 10.6-14.9 |
| Neonatology | 3.8 | 3.7-5.3 |
| Paediatric surgery | 3.8 | 2.3-6.1 |
| General paediatrics | 2.2 | 1.4-3.4 |

95%CI: 95% confidence interval; ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection

**Supplementary table 4.** Distribution of case-mix indicators compared to the number of children enrolled by the hospitals – Paediatric data, standard protocol, ECDC point prevalence survey 2011-2012

| | Number of children enrolled in the survey | | | | *P*-value |
|---|---|---|---|---|---|
| | ≤25 | 26-40 | 41-70 | >70 | |
| **McCabe classification** | | | | | |
| Nonfatal | 3846 (90.2%) | 3287 (87.5%) | 3586 (83.6%) | 3159 (80.4%) | <0.001 |
| Ultimately fatal | 13 (0.3%) | 22 (0.6%) | 54 (1.3%) | 24 (0.6%) | |
| Rapidly fatal | 59 (1.4%) | 70 (1.9%) | 100 (2.3%) | 158 (4.0%) | |
| **Clinical setting** | | | | | |
| Neonatal intensive care | 258 (6.1%) | 518 (13.8%) | 704 (16.4%) | 658 (16.8%) | <0.001 |
| Paediatric intensive care | 102 (2.5%) | 148 (4.0%) | 246 (5.7%) | 268 (6.9%) | |
| General paediatrics | 2760 (64.8%) | 1915 (51.0%) | 1632 (38.0%) | 1549 (39.4%) | |
| Neonatology | 1040 (24.4%) | 1011 (26.9%) | 1277 (29.8%) | 853 (21.7%) | |
| Paediatric surgery | 102 (2.4%) | 166 (4.4%) | 431 (10.1%) | 599 (15.3%) | |
| **Presence of an invasive medical device** | | | | | |
| None | 2548 (59.8%) | 2247 (59.8%) | 2323 (54.1%) | 1976 (50.3%) | <0.001 |
| 1 device | 1664 (39.0%) | 1362 (36.2%) | 1653 (38.5%) | 1654 (42.1%) | |
| 2 devices | 39 (0.9%) | 101 (27%) | 215 (5.0%) | 190 (4.8%) | |
| ≥devices | 11 (0.3%) | 48 (1.3%) | 99 (2.3%) | 107 (2.7%) | |
| **Length of stay (days)*** | | | | | |
| <4 | 2135 (49.5%) | 1703 45.3(%) | 1869 (43.6%) | 1430 (36.4%) | <0.001 |
| 4-7 | 1247 (28.9%) | 1033 (27.5%) | 1069 (24.9%) | 1061 (27.0%) | |
| 8-14 | 467 (10.8%) | 471 (12.5%) | 575 (13.4%) | 604 (15.4%) | |
| >14 | 465 (10.8%) | 551 (14.7%) | 777 (18.1%) | 832 (21.2%) | |

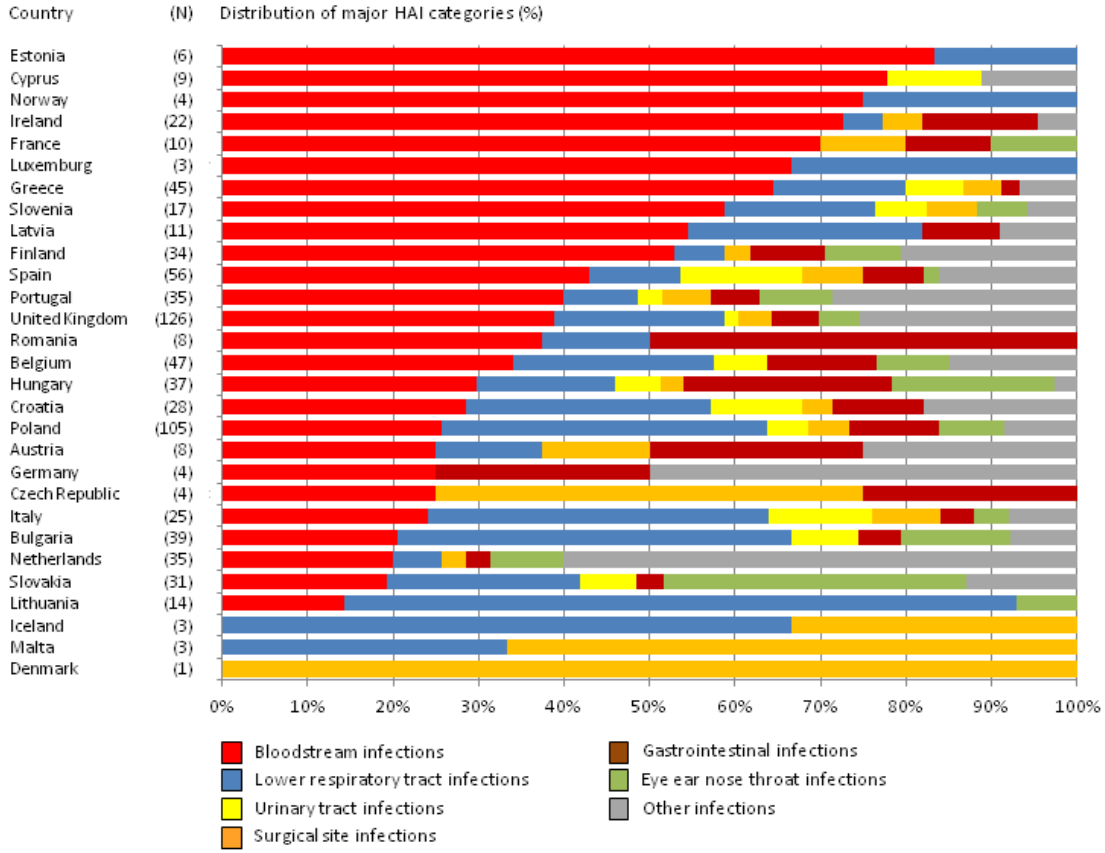
*Before and including the day of the point prevalence survey

**Supplementary table 5.** Distribution of the major types of healthcare-associated infection, by country – Paediatric data, ECDC point prevalence survey 2011-2012

| Country | HAI<br>N | BSI<br>N (%) | LCBI<br>N (%) | UTI<br>N (%) | SSI<br>N (%) | GI<br>N (%) | EENT<br>N (%) | OTH<br>N (%) |
|---|---|---|---|---|---|---|---|---|
| Estonia | 6 | 5 (83.3) | 1 (16.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Cyprus | 9 | 7 (77.8) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (11.1) |
| Norway | 4 | 3 (75.0) | 1 (25.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Ireland | 22 | 16 (72.7) | 1 (4.5) | 0 (0.0) | 1 (4.5) | 3 (13.6) | 0 (0.0) | 1 (4.5) |
| France | 10 | 7 (70.0) | 0 (0.0) | 0 (0.0) | 1 (10.0) | 1 (10.0) | 1 (10.0) | 0 (0.0) |
| Luxembourg | 3 | 2 (66.7) | 1 (33.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Greece | 45 | 29 (64.4) | 7 (15.6) | 3 (6.7) | 2 (4.4) | 1 (2.2) | 0 (0.0) | 3 (6.7) |
| Slovenia | 17 | 10 (58.8) | 3 (17.6) | 1 (5.9) | 1 (5.9) | 0 (0.0) | 1 (5.9) | 1 (5.9) |
| Latvia | 11 | 6 (54.5) | 3 (27.3) | 0 (0.0) | 0 (0.0) | 1 (9.1) | 0 (0.0) | 1 (9.1) |
| Finland | 34 | 18 (52.9) | 2 (5.9) | 0 (0.0) | 1 (2.9) | 3 (8.8) | 3 (8.8) | 7 (20.6) |
| Spain | 56 | 24 (42.9) | 6 (10.7) | 8 (14.3) | 4 (7.1) | 4 (7.1) | 1 (1.8) | 9 (16.1) |
| Portugal | 35 | 14 (40.0) | 3 (8.6) | 1 (2.9) | 2 (5.7) | 2 (5.7) | 3 (8.6) | 10 (28.6) |
| United Kingdom | 126 | 49 (38.9) | 25 (19.8) | 2 (1.6) | 5 (4.0) | 7 (5.6) | 6 (4.8) | 32 (25.4) |
| Romania | 8 | 3 (37.5) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 4 (50.0) | 0 (0.0) | 0 (0.0) |
| Belgium | 47 | 16 (34.0) | 11 (23.4) | 3 (6.4) | 0 (0.0) | 6 (12.8) | 4 (8.5) | 7 (14.9) |
| Hungary | 37 | 11 (29.7) | 6 (16.2) | 2 (5.4) | 1 (2.7) | 9 (24.3) | 7 (18.9) | 1 (2.7) |
| Croatia | 28 | 8 (28.6) | 8 (28.6) | 3 (10.7) | 1 (3.6) | 3 (10.7) | 0 (0.0) | 5 (17.9) |
| Poland | 105 | 27 (25.7) | 40 (38.1) | 5 (4.8) | 5 (4.8) | 11 (10.5) | 8 (7.6) | 9 (8.6) |
| Austria | 8 | 2 (25.0) | 1 (12.5) | 0 (0.0) | 1 (12.5) | 2 (25.0) | 0 (0.0) | 2 (25.0) |
| Germany | 4 | 1 (25.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (25.0) | 0 (0.0) | 2 (50.0) |
| Czech Republic | 4 | 1 (25.0) | 0 (0.0) | 0 (0.0) | 2 (50.0) | 1 (25.0) | 0 (0.0) | 0 (0.0) |
| Italy | 25 | 6 (24.0) | 10 (40.0) | 3 (12.0) | 2 (8.0) | 1 (4.0) | 1 (4.0) | 2 (8.0) |
| Bulgaria | 39 | 8 (20.5) | 18 (46.2) | 3 (7.7) | 0 (0.0) | 2 (5.1) | 5 (12.8) | 3 (7.7) |
| Netherlands | 35 | 7 (20.0) | 2 (5.7) | 0 (0.0) | 1 (2.9) | 1 (2.9) | 3 (8.6) | 21 (60.0) |
| Slovakia | 31 | 6 (19.4) | 7 (22.6) | 2 (6.5) | 0 (0.0) | 1 (3.2) | 11 (35.5) | 4 (12.9) |
| Lithuania | 14 | 2 (14.3) | 11 (78.6) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (7.1) | 0 (0.0) |
| Iceland | 3 | 0 (0.0) | 2 (66.7) | 0 (0.0) | 1 (33.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Malta | 3 | 0 (0.0) | 1 (33.3) | 0 (0.0) | 2 (66.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Denmark | 1 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

BSI: Bloodstream infection; EENT: Eye, ear, nose, throat infection; HAI: Healthcare-associated infection; GI: Gastrointestinal infection; LCBI: Lower respiratory tract infection; OTH: Other infection; SSI: Surgical site infection; UTI: Urinary tract infection

**Supplementary figure 1.** Distribution of the major types of healthcare-associated infection, by country – Paediatric data, ECDC point prevalence survey 2011-2012




HAI: Healthcare-associated infection; N: Number of healthcare-associated infections

**Supplementary figure 2.** Proportion of antimicrobial-resistant isolates for the major microorganisms documented in the survey (n=136) – Paediatric data, ECDC point prevalence survey 2011-2012. The antimicrobial-microorganism combinations were chosen as markers for multidrug resistance.