Material and methods

Analyses of ISIS-AR data

Since 2008, the Infectious Disease Surveillance Information System for Antibiotic Resistance (ISIS-AR) has collected antimicrobial susceptibility data from Dutch medical laboratories. ISIS-AR is coordinated by the Centre for Infectious Disease Control, at the National Institute for Public Health and the Environment (RIVM) in Bilthoven, the Netherlands, and is a combined initiative of the Ministry of Health, Welfare and Sport and the Dutch Society of Medical Microbiology (NVMM). Between 2008 and 2011, 23 laboratories continuously reported data to ISIS-AR and could be included in the analyses.

The overall proportion of antibiotic resistance in hospitals and the community was estimated, based on routinely collected antimicrobial susceptibility data obtained from medical microbiology laboratories in the Netherlands. In 2011, 27 laboratories reported results to ISIS-AR; two laboratories serving university hospitals, 24 laboratories serving non-university hospitals and public health institutions and 1 laboratory only serving public health institutions. Between 2008 and 2011, 23 laboratories continuously reported data to ISIS-AR and could be included in the analyses.

The susceptibility of the isolates reported to ISIS-AR is determined by the participating laboratories and is mostly based on results from automated testing systems. For the analyses, compound-pathogen combinations were only included if at least 50% of the isolates was tested for that specific compound in at least 6 different laboratories. EUCAST breakpoints were applied to the reported MICs to calculate the proportion of resistant isolates (R) if at least 80% of the reported MICs could be interpreted. This was true for all included gram-negative species (*E. coli, P. mirabilis, K. pneumoniae, E. cloacae, P. aeruginosa, Acinetobacter spp*.) and *S. aureus* and coagulase-negative staphylococci including *S. epidermidis*. For *H. influenzae, S. pneumoniae, E. faecium* and *E. faecalis* less than 80% of the MICs could be interpreted according to the EUCAST recommendations and therefore the “S-I-R” interpretations as reported by the local laboratories were used for calculating the proportion of non-susceptible isolates (I+R). To enable comparisons over time, the proportion of I+R isolates is reported, because before 2010, S-I-R interpretations were

mainly based on CLSI breakpoints, and the I breakpoint of CLSI is identical to the R breakpoint of EUCAST for most antibiotics. From 2010 onwards a growing number of laboratories has applied EUCAST breakpoints. All reported exceptional phenotypes were confirmed by the specific laboratories.

For analyses, the first isolate per species per patient was included, and isolates for screening and inventory purposes were excluded. Data are presented separately for each compound-pathogen combination and for isolates from general practice (GP), outpatient departments (OPD), ICU departments and non-ICU hospital departments. Antimicrobial susceptibility results for GP and OPD are based on urinary isolates only. For the hospital departments, the antimicrobial susceptibility results are from isolates of blood, liquor, wound and urinary combined, except for *H. influenza* and *M. catarrhalis* for which only isolates from higher and lower respiratory tract were included.
Trends in resistance proportions over time were tested by the Cochran-armitage test. A $p<0.05$ was considered significant.

Differences in resistance rates between NethMap 2011 and 2012 may appear because of:

1. an increasing number of participating laboratories (providing retrospective data as well);
2. separate analyses for ICU and non-ICU hospital departments in NethMap 2012;
3. application of EUCAST breakpoints for most compound-pathogen combinations, and subsequent reporting of the number of resistant isolates (R) in NethMap 2011, instead of reporting of the proportion of nonsusceptible (I+R) isolates as reported by laboratories (mostly based on CLSI breakpoints before 2011);
4. ignoring expert rules in NethMap 2011